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Maternal, not paternal PTSD, is related to increased risk for PTSD in offspring of Holocaust survivors

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Abstract

Background—A significant association between parental PTSD and the occurrence of PTSD in offspring has been noted, consistent with the idea that risk for PTSD is transmitted from parent to child. Two recent reports linking maternal PTSD and low cortisol in offspring prompted us to examine the relative contributions of maternal vs. paternal PTSD in the prediction of PTSD and other psychiatric diagnoses.

Methods—117 men and 167 women, recruited from the community, were evaluated using a comprehensive psychiatric battery designed to identify traumatic life experiences and lifetime psychiatric diagnoses. 211 of the subjects were the adult offspring of Holocaust survivors and 73 were demographically comparable Jewish controls. Participants were further subdivided based on whether their mother, father, neither, or both parents met the diagnostic criteria for lifetime PTSD.

Results—A higher prevalence of lifetime PTSD, mood, anxiety disorders, and to a lesser extent, substance abuse disorders, was observed in offspring of Holocaust than controls. The presence of maternal PTSD was specifically associated with PTSD in adult offspring. However, the other diagnoses did not show specific effects associated with maternal PTSD.

Conclusion—The tendency for maternal PTSD to make a greater contribution to PTSD risk suggests that classic genetic mechanisms are not the sole model of transmission, and pave way for the speculation that epigenetic factors may be involved. In contrast, PTSD in any parent contributes to risk for depression, and parental traumatization is associated with increased anxiety disorders in offspring.

Keywords

parental PTSD; intergenerational transmission of trauma; Holocaust survivors; depressive disorder; prevalence

Introduction

Trauma survivors who develop posttraumatic stress disorder (PTSD) have greater rates of familial psychopathology compared to similarly-exposed persons who do not develop this disorder (Davidson et al., 1985; Davidson et al., 1989; Davidson et al., 1998; Dijanic et al.,

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2007; Reich et al., 1996; Dierker & Merikangas, 2001). Parental PTSD, in particular, has been demonstrated to be associated with PTSD and related psychopathology in offspring (Rosenheck, 1986; Solomon et al., 1988; Yehuda et al., 1998b; Yehuda et al., 1998c). We previously reported that there was a specific association between parental PTSD and the occurrence of PTSD in offspring when the relative contributions of parental exposure, parental PTSD, and the offspring's own history of trauma to the development of PTSD, depressive, and anxiety disorders in the offspring were evaluated (Yehuda et al., 2001a). Additionally, parental trauma exposure, more than parental PTSD, was found to be significantly associated with lifetime depressive disorder (Yehuda et al., 2001b).

The potential utility of identifying parental PTSD as a risk factor for PTSD in offspring of Holocaust survivors is that they represent a sample in which the biological and psychological correlates of risk for PTSD can be further examined. In pursuing this goal, we demonstrated that, though not having their own lifetime PTSD, Holocaust offspring with parental PTSD, compared to those without, displayed low urinary (Yehuda et al., 2000; Yehuda et al., 2001b) and plasma (Yehuda et al., 2007b) cortisol levels; and increased glucocorticoid responsiveness as measured by plasma cortisol levels in response to low dose dexamethasone administration (Yehuda et al., 2007a); the former has been linked with increased risk for PTSD in other populations (Anisman et al., 2001; Delahanty et al., 2003; Resnick et al., 1995; Yehuda et al., 1998a).

The possibility that low cortisol in offspring was a transmitted risk factor was further supported by observations of lower salivary cortisol levels in year old infants born to mothers with PTSD compared to infants born to mothers without PTSD, following their direct exposure to the collapse of the World Trade Center on 9/11 during pregnancy (Yehuda et al., 2005). Although the contribution of paternal PTSD to cortisol levels in infant offspring was not examined, there was a significant effect of trimester (i.e., the effect was most present in the third trimester), consistent with *in utero* contributions to low cortisol in offspring. Alternatively, the trimester effect might reflect the proximity of the birth to the trauma exposure, affecting maternal behavior. Both possibilities are consistent with epigenetic mechanisms for low cortisol in offspring, which may depend on the gender of the traumatized parent.

In view of these findings, a subsequent study examining plasma cortisol release at 30 minute intervals over the diurnal cycle in Holocaust offspring with no lifetime PTSD and examining effects of maternal vs. paternal PTSD found low plasma cortisol to be associated with maternal PTSD, even after controlling for the contribution of paternal PTSD (Yehuda et al., 2007b). Thus, it was of interest to extend our previous observations about the impact of parental PTSD on offspring PTSD, depression, and anxiety, distinguishing among maternal PTSD, paternal PTSD, or both parents having PTSD. This was accomplished by doubling the original sample size of Holocaust offspring and comparable controls. The increased sample size also afforded the opportunity to report findings on less prevalent conditions: eating disorders, substance abuse, and adjustment disorders. We hypothesized that the previously observed association between parental PTSD and PTSD in offspring would reflect the effect of maternal PTSD. In the prediction of depression (Yehuda et al., 2001a), anxiety and other disorders, we hypothesized that we would not observe a relationship with parental PTSD because an epigenetic model for the transmission of PTSD risk would not generalize to transmission from PTSD to other psychiatric disorders. In that we previously observed an association between parental trauma exposure and depression, we hypothesized that parental trauma might be associated with other psychiatric disorders. Since children are potentially affected by both parents, it was necessary to adjust for the possible impact of PTSD in the other parent when evaluating the effect of either maternal or paternal PTSD and their interaction. Finally, we examined the interaction of the gender of the offspring with parental PTSD gender, since such an interaction would distinguish between a purely genetic model and one involving epigenetics.

Accordingly, we hypothesized that such interactions would only be present for PTSD, but not for the other diagnoses.

Methods

Participants

117 men and 167 women participated in the study (mean age: 43.16 ± 9.08; range: 23 to 66). Participants were recruited through advertisements requesting Jewish volunteers for research examining effects of the Holocaust on second generation offspring. The procedures were approved by the institutional review boards of Mount Sinai School of Medicine and the James J. Peters Veterans Affairs Medical Center. Written informed consent was obtained from all participants. Data regarding psychiatric diagnoses from 115 of these subjects were previously reported in Yehuda et al., 1998c, with a reanalysis by parental PTSD reported in a subset plus 24 new participants (Yehuda et al., 2001a). The remaining subjects (n = 145) represent new observations from data collected since 2001.

Offspring were either born after World War II or after their parents had escaped to safety during the War, and were raised through adolescence by at least one parent who had been interned in a Nazi concentration camp during World War II or had faced comparably severe threats in hiding. In the current sample, 70.5% of offspring were born to and raised by two Holocaust survivors. These participants were further subdivided based on whether their mother, father, neither, or both parents met the diagnostic criteria for lifetime PTSD. PTSD diagnosis was made primarily on the basis of the self-report of offspring, using the Parental PTSD Questionnaire (PPQ) (Yehuda et al., 2006). This scale was recently validated against 58 clinical interviews of the parents using the Clinician-Administered PTSD Scale (CAPS) and was found to have good convergent validity for PTSD diagnosis (Blake et al., 1995). PTSD diagnosis was determined on the basis of a positive endorsement of at least 6 symptoms distributed in the 3 required categories according to DSM-IV criteria.

Comparison subjects were Jewish, of comparable age to offspring (born from 1938 to 1979) and from the same communities, but with parents who were not exposed to the Holocaust or other events such as war, rape or torture. Comparison subjects were not chosen to be without psychiatric diagnoses, but were recruited and selected on the basis of being demographically similar to Holocaust offspring, with the exception of parental exposure or parental PTSD to a different trauma. All the participants were born to parents of European or American descent with 68.0% of offspring and 88.1% of comparison subjects born in the U.S. or Canada.

Participants were not included in the study if they or a parent had evidence of a psychotic illness. Also excluded were offspring with a serious medical condition that might interfere with their ability to consent to research. Subjects were not withdrawn from medication and 33 subjects (31 offspring, 2 controls) were using psychiatric medication at the time of evaluation.

Clinical Assessment—All subjects were evaluated for current and lifetime Axis I diagnoses by clinical psychologists or psychiatrist raters using the Structured Clinical Interview for DSM-IV (Spitzer et al., 1995). Diagnoses were confirmed by consensus conference using the Best Estimate Diagnosis (BED) to ensure accurate group placement (Leckman et al., 1982). PTSD symptom severity was determined by psychologist or psychiatrist raters using the CAPS (Blake et al., 1995).

Statistical Analyses—Preliminary analyses considered five groups of subjects according to parental PTSD status: comparison subjects, and four Holocaust offspring groups, that is, neither parent with PTSD, father only with PTSD, mother only with PTSD, or both parents

with PTSD. Since there were significant differences in age (F= 7.54; df=4,281; p<.0005) and in gender, (χ^2=11.75, df=4, p=.019), both variables were used as covariates in all analyses.

Logistic regression analyses were performed comparing the five groups controlling for age and gender, examining whether there were differences in the extent of psychiatric diagnoses according to PTSD status of the parents of Holocaust offspring or comparison status. This produced an overall test of significance (chi-square on four degrees of freedom) comparing the five groups. These analyses were repeated with an additional step to control for the presence of comorbid conditions.

To more closely examine parental effects, we compared all subjects with neither parent having PTSD to those in the other three groups, respectively, and report results as odds ratios and their significance levels from a logistic regression analysis comparing the four groups. These associations were interpreted as simple assessments of the effects of paternal PTSD, maternal PTSD, and both parents having PTSD. In order to insure that all the subjects were comparable in so far as they were Holocaust offspring, we replicated these analyses limiting subjects with neither parent having PTSD to Holocaust offspring. For a clearer comparison between the results of these parallel analyses, we also performed an analysis limiting subjects with neither parent having PTSD to the controls. Since the differences among these three analyses were not substantial, only the first analyses -- including all subjects -- are presented.

To determine the impact of paternal and maternal PTSD status, a two-way design was employed using paternal and maternal PTSD status as independent variables. This was important because of the strong correlation between maternal and paternal PTSD (r=.714, n=284, p <.0005). Stepwise logistic regression analyses provided tests of significance for effects of paternal PTSD and maternal PTSD (controlling for the presence of the other), and the interaction of paternal and maternal PTSD (i.e. what was the effect of both parents having PTSD beyond the sum of effects for each parent separately).

Finally, we investigated the interaction of offspring gender with parental PTSD status to see whether similarity to or difference in gender with respect to a parent with PTSD made a difference in the occurrence of offspring psychiatric diagnoses. Specifically, the two-way analysis described above was expanded to a three-way analysis with offspring gender added as an independent variable, rather than as a covariate, to examine its interactions with the other independent variables, namely paternal and maternal PTSD and their interaction.

Results

In the entire sample, 60.2% met criteria for at least one psychiatric disorder. The average number of disorders was 1.19 (1.33), and among those with at least one disorder, the mean was 2.04 (1.13). Table 1 presents data on the prevalence rates of psychiatric diagnoses in the total sample, highlighting effects of gender and group (comparison vs. all offspring). The tests of significance do not control for age and gender. In the sample overall, there was a 17.6% prevalence rate of PTSD, but differences in gender were not significant. Moreover, when all Holocaust offspring were compared to controls, there was no significant difference in lifetime PTSD prevalence. For other disorders, there were also no gender differences, with the exception of a non-significant trend for men to have more lifetime substance abuse or dependence than women. Here, however, comparing the Holocaust offspring sample to controls demonstrated significantly more mood, anxiety, and substance abuse disorders, but not significantly more eating disorders or adjustment disorder. Among the Holocaust offspring, there were also no significant gender differences in prevalence of disorders.

Table 2 presents prevalence rates of psychiatric diagnoses in the five groups. The test of significance of the differences among them controlled for age and gender. There were

significant differences in rates of PTSD, depression, and anxiety disorders, but each showed a distinct pattern of findings. There was a greater prevalence of PTSD among offspring with maternal PTSD, whether this occurred with or without paternal PTSD. In contrast, depressive disorder was significantly associated with paternal and/or maternal PTSD. Presence of anxiety disorders was higher among all Holocaust offspring than comparison subjects, regardless of parental PTSD status. Presence of any diagnosis was also higher for all offspring than comparison subjects. There were no differences in prevalence in relation to either parental Holocaust exposure or PTSD in eating disorders, substance abuse disorders, or adjustment disorder. When the analyses were repeated controlling for the presence of other disorders, significances were maintained but levels were slightly reduced.

In Table 3, all offspring and comparison subjects with no parental PTSD are compared to those with only paternal, only maternal, or both parents with PTSD. With regard to PTSD, there were significant differences for both groups with maternal PTSD (maternal only and both). In contrast, for depressive disorder all three Holocaust offspring groups with parental PTSD differed from the subjects without parental PTSD. This was also the case for having any psychiatric diagnosis. For anxiety disorders, there were trend significances for the two groups with paternal PTSD (paternal only and both).

Next we performed two-way analyses to determine the contributions of maternal and paternal PTSD (each correcting for the possible presence of the other) and the interaction of maternal and paternal PTSD. These analyses, summarized in Table 4, provide interpretations for the results presented in Table 3. For lifetime PTSD, there was a maternal effect controlling for the effect of paternal PTSD, but no significant paternal PTSD effect controlling for maternal PTSD. There was a significant interaction demonstrating a relatively greater effect of paternal PTSD when maternal PTSD was present than when it was absent, reflected in the relatively higher rate for both parents having PTSD than only mothers. With respect to depression, there were significant paternal and trend level maternal effects, but no interaction. The effect for both parents having PTSD was stronger than for either parent alone having PTSD, reflecting the accumulation of the separate paternal and maternal effects. For anxiety disorder, there was a paternal effect but no maternal effect or interaction, reflected in the highest rates for the two groups with parental PTSD, father only and both. For any diagnosis, there was a paternal effect, reflected in the highest rates for the two groups with paternal PTSD.

When offspring gender was included as an additional independent variable to examine its interaction with maternal and paternal PTSD in the prediction of offspring diagnosis, there was only one significant interaction, in the prediction of offspring PTSD. Here the significant interaction reflected that among females, if the father had PTSD, they were more likely to develop PTSD; among males, if the father had PTSD, they were slightly less likely to develop PTSD (χ^2=3.94, df=1, p=.047). The absence of a corresponding gender by maternal PTSD effect indicated that a corresponding preferential vulnerability to the development of PTSD in response to the mother's PTSD was not observed.

Discussion

The findings demonstrate that there are substantial differences between offspring of Holocaust survivors and demographically-comparable subjects in the prevalence of lifetime mood and anxiety disorders, and to a lesser extent, substance abuse disorders. Although being an offspring of Holocaust survivors did not increase the risk for lifetime PTSD per se, the presence of maternal PTSD was specifically associated with PTSD in adult offspring. In contrast, the other diagnoses did not show specific effects associated with maternal PTSD. Rather, depressive disorder was associated with PTSD in either parent, whereas the other disorders were relatively similar for all Holocaust offspring regardless of parental PTSD. In the case of anxiety disorders,

all four subgroups of Holocaust offspring were substantially higher in prevalence than comparison subjects.

Upon examination of parental PTSD status by gender in analyses that also accounted for presence or absence of PTSD in the other parent, it became clear that only for offspring PTSD did the effect of one parent's PTSD depend on whether the other parent had PTSD. Paternal PTSD had an effect only if the mother also had PTSD; the effect of the mother's PTSD was greater in the presence of paternal PTSD, but still present in its absence. With depressive disorder, however, the effects accumulated; having both parents with PTSD increased the risk compared to having only one. In anxiety disorders, analyses of parental gender only revealed an effect of paternal gender.

The current observations are consistent with findings from a recent study demonstrating different psychiatric outcomes in male war veterans based on maternal and paternal psychiatric illness. Combat veterans with maternal psychiatric illness were more likely to exhibit diagnoses of partial PTSD, whereas paternal psychiatric illness was associated with the development of other conditions (e.g., substance abuse, psychosis, personality disorder) (Dijanic Plasc et al., 2007). However, children of EMT workers did show a higher prevalence of probable PTSD after 9/11. These were children drawn from a large public school survey and their rate was 18.9%, far higher than that observed in the general sample from which they were drawn (Duarte et al., 2006).

The analysis of the interaction of gender of the offspring with the parental characteristics indicated that for maternal PTSD, there was no discrepancy in the effect of PTSD in male or female offspring. However, paternal PTSD increased the risk for PTSD preferentially in female compared to male offspring. These findings suggest that with respect to PTSD risk, girls may be particularly responsive to paternal PTSD effects; as noted above, paternal effects appear to be potentiated by maternal PTSD. Such interactions were not observed for other diagnoses.

Studies examining paternal PTSD as it occurs in war veterans have also documented behavioral and psychological problems in offspring of combat veterans with this disorder, but have not demonstrated the presence of PTSD per se (Rosenheck, 1986; Harkness, 1993). In fact, the offspring of combat veterans with PTSD did not differ in measures of posttraumatic stress symptomatology, but did demonstrate problems in affective responsiveness and problem solving (Davidson & Mellor, 2001). Offspring with paternal PTSD also rated their families as more dysfunctional (Davidson & Mellor, 2001). Although these studies are consistent with our failure to find a link between paternal PTSD and PTSD in Holocaust offspring, these studies differ because the other parent was not specifically exposed to trauma. Although PTSD in combat veterans has been known to affect spouses as well as offspring (Dekel & Solomon, 2006; Franciskovic et al., 2007), it has also been proposed that the effect of paternal combat PTSD on offspring may be partially buffered by non-affected wives of these veterans (Westerink & Giarratano, 1999). Yet, the contribution of maternal trauma or PTSD in such studies has not been examined. Holocaust offspring may be particularly vulnerable to symptoms of their parents because of the absence of such buffers. In the current study, almost all offspring had two Holocaust survivor parents.

This study does not provide conclusive evidence regarding the mechanism of transmission of effects from parent to offspring. To the extent that the effects of parental PTSD are uniform, this would be more consistent with a genetic interpretation since genetic antecedents might be more likely to occur based on presence or absence of illness in either parent, or perhaps a greater effect of both parents having the disease than one. This speculation may be relevant to mood disorder in offspring for which there were both paternal and maternal effects. With anxiety disorder, the effect was particularly associated with parental trauma exposure, so it is less likely

to be related to genetic differences per se. With PTSD, however, the tendency for maternal PTSD to make a greater contribution to risk suggests that classic genetic mechanisms are not the sole model of transmission. Yet, since paternal PTSD was also a predictor of PTSD (particularly in female offspring), mechanisms of transmission may be manifestations of developmental programming by environmental effects occurring after birth as distinguished from purely maternal effects which might occur before birth (e.g., in utero effects).

We have previously suggested that parental PTSD may confer risk of PTSD in the offspring by affecting the predisposition to a modification that may later affect the response to a traumatic event (Yehuda et al., 2005; Yehuda et al., 2007a). This hypothesis is raised by the demonstration that low plasma cortisol levels in offspring are also associated particularly with maternal PTSD (Yehuda et al., 2007b). Thus, a possible mechanism for this association is transmission via early glucocorticoid programming (Matthews, 2002; Seckl & Meaney, 2006). In such “programmed” offspring, trauma exposure may increase the probability of PTSD as a result of the pre-existing biological vulnerability, which in turn may result from epigenetic changes in the glucocorticoid receptor genes similar to those induced postnatally by maternal behavior (Liu et al., 1997; McCormick et al., 2000; Weaver et al., 2004).

The animal literature which focuses on the biological outcomes in the adult offspring of early maternal behaviors (e.g., Lyons et al., 2000; Ladd et al., 2005; Champagne & Meaney, 2001; Schmidt et al., 2002); does not preclude a role for paternal behavior in the modulation of subsequent offspring behavior or risk for psychopathology. Animal studies do not tend to examine effects of paternal behavior. However, paternal effects are certainly plausible to the extent that the changes that result in epigenetic modification in offspring are a function of an environmental change to the offspring induced by the behavior or a parent. In this regard, it has been hypothesized that the strongest effect of combat PTSD on offspring occurs from the emotional inaccessibility of the father (Harkness, 1993; Reich et al., 1996; Rosenheck, 1986). Similarly, faulty attachment behavior might explain increased vulnerability to psychopathology from mothers (Madigan et al., 2007).

The distinction between genetic and familial effects of offspring is important and may help explain some of the difficulties in the literature regarding the lack of consistency of effects that might be anticipated from purely genetic models. For example, examination of the psychological complaints in postwar children of Dutch WWII victims failed to reveal a consistent pattern of psychological disturbance in all family members, leading the authors to question the generality of interfamilial transmission routes due to its selectivity of members of the same family (Mook et al., 1997). However, certainly parental behavior towards offspring may depend on a variety of circumstances that might result in precisely these types of different outcomes.

One of the limitations of this study is that it represents a convenience sample from a subpopulation with extraordinarily high rates of parental PTSD. Thus, its prevalence rates of psychiatric disorders do not reflect the general population to which we wish to make inferences. Furthermore, the comparison sample was selected to be demographically similar to Holocaust offspring (i.e., Jewish, and with other similar sociodemographic characteristics such as education, marital status, ethnicity and income). Accordingly, differences between the comparison subjects in this sample and others might reflect this selection bias. A major difference between this and other published reports of the prevalence of psychiatric disorders in the community is the absence of significant gender differences in mood and anxiety disorders (Breslau et al., 1997; Kessler et al., 1996), though the rates of psychiatric disorders in the current comparison group are comparable to those reported in the recent replication of the National Comorbidity Study. That study reported a population prevalence of depressive disorder of 16.4% compared to the current sample’s prevalence of 17.6% in comparison subjects (Kessler

et al., 2003). Similarly, rates for eating disorder at 3.5% in the current study accord with estimates for lifetime prevalence of bulimia (3.5% women, 2% men) and anorexia (0.9% women 0.3% men) (Hudson et al., 2007). In the current study, if prevalence rates of PTSD and anxiety disorders are combined, they are roughly equal to the prevalence rate of 28.8% reported for anxiety disorders (Kessler et al., 2005). There was a lower prevalence of substance abuse in the current sample than the 14.6% reported (Kessler et al., 2005), but conditional risk for PTSD was about twice as high at 14.1% than other estimates ranging from 6–9% (Kessler et al., 1995; Breslau et al., 1998). Our comparison sample also included a smaller percentage of subjects meeting criteria for "any" psychiatric disorder, and endorsed fewer lifetime comorbid conditions than reported in other epidemiologic reports (Kessler et al., 1994).

While the comparison sample is not representative of the general population, certainly the offspring sample is even less representative, as they were restricted to Jewish persons of European descent born to parents who defied the odds and survived to safety, which was not the fate of the majority of European Jews. If Jews are different from non-Jews, this study may not even represent a general phenomenon in traumatology.

Another limitation of the study is that offspring provided the information pertaining to parental PTSD symptoms on which group distinctions were based. Although we previously established that there is strong agreement between offspring ratings of parental PTSD and independent clinician ratings of the parent (Yehuda et al., 2006) if offspring diagnoses were associated with their perception of parental PTSD, this could lead to a circularity of inference. Thus, if diagnoses reflect offspring characteristics such as irritability, emotional withdrawal or other symptoms, this might result in a greater projection of analogous parental characteristics so that "parental" PTSD was an expression of offspring characteristics. If PTSD ratings were largely based on the extent of parental contact, having more contact with mothers would be reflected by substantially greater prevalence of maternal than paternal PTSD. However, this attributional bias does not appear to be present in the current sample. Rather, the findings, with all their limitations, highlight the importance of maternal PTSD as a specific risk factor for PTSD in offspring, but demonstrate that PTSD in any parent associates with risk for depression.

References

Anisman H, Griffiths J, Matheson K, Ravindran AV, Merali Z. Posttraumatic stress symptoms and salivary cortisol levels. The American Journal of Psychiatry 2001;158:1509–1511. [PubMed: 11532740]

Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, Keane TM. The development of a clinician-administered PTSD scale. Journal of Traumatic Stress 1995;8:75–90. [PubMed: 7712061]

Breslau N, Davis GC, Andreski P, Peterson EL, Schultz LR. Sex differences in posttraumatic stress disorder. Archives of General Psychiatry 1997;54:1044–1048. [PubMed: 9366662]

Breslau N, Kessler RC, Chilcoat HD, Schultz LR, Davis GC, Andreski P. Trauma and posttraumatic stress disorder in the community: The 1996 Detroit area survey of trauma. Archives of General Psychiatry 1998;55:626–632. [PubMed: 9672053]

Champagne F, Meaney MJ. Like mother, like daughter: evidence for non-genomic transmission of parental behavior and stress responsivity. Progress in Brain Research 2001;133:287–302. [PubMed: 11589138]Review.

Davidson AC, Mellor DJ. The adjustment of children of Australian Vietnam veterans: Is there evidence for the transgenerational transmission of the effects of war-related trauma? The Australian and New Zealand Journal of Psychiatry 2001;35:345–351. [PubMed: 11437808]

Davidson J, Smith R, Kudler H. Familial psychiatric illness in chronic posttraumatic stress disorder. Comprehensive Psychiatry 1989;30:339–345. [PubMed: 2758806]

Davidson J, Swartz M, Storck M, Krishnan RR, Hammett E. A diagnostic and family study of posttraumatic stress disorder. The American Journal of Psychiatry 1985;142:90–93. [PubMed: 3966591]

Davidson JR, Tupler LA, Wilson WH, Connor KM. A family study of chronic post-traumatic stress disorder following rape trauma. Journal of Psychiatric Research 1998;32:301–309. [PubMed: 9789209]

Dekel R, Solomon Z. Secondary traumatization among wives of Israeli POWs: The role of POWs' distress. Social Psychiatry and Psychiatric Epidemiology 2006;41:27–33. [PubMed: 16341620]

Delahanty DL, Raimonde AJ, Spoonster E, Cullado M. Injury severity, prior trauma history, urinary cortisol levels, and acute PTSD in motor vehicle accident victims. Journal of Anxiety Disorders 2003;17:149–164. [PubMed: 12614659]

Dierker LC, Merikangas KR. Familial psychiatric illness and posttraumatic stress disorder: Findings from a family study of substance abuse and anxiety disorders. The Journal of Clinical Psychiatry 2001;62:715–720. [PubMed: 11681768]

Dijanic Plasc I, Peraica T, Grubisic-Ilic M, Rak D, Jambrosic Sakoman A, Kozaric-Kovacic D. Psychiatric heredity and posttraumatic stress disorder: Survey study of war veterans. Croatian Medical Journal 2007;48:146–156. [PubMed: 17436379]

Duarte CS, Hoven CW, Wu P, Bin F, Cotel S, Mandell DJ, Nagasawa M, Balaban V, Wernikoff L, Markenson D. Posttraumatic stress in children with first responders in their families. Journal of Traumatic Stress 2006;19:301–306. [PubMed: 16612825]

Franciskovic T, Stevanovic A, Jelusic I, Roganovic B, Klaric M, Grkovic J. Secondary traumatization of wives of war veterans with posttraumatic stress disorder. Croatian Medical Journal 2007;48:177–184. [PubMed: 17436382]

Harkness, LL. Transgenerational transmission of war-related trauma. In: Wilson, JP.; Raphael, B., editors. International Handbook of Traumatic Stress Studies. New York: Plenum; 1993. p. 635-643.

Hudson JI, Hiripi E, Pope HG Jr, Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. Biological Psychiatry 2007;61:348–358. [PubMed: 16815322]

Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, Rush AJ, Walters EE, Wang PS. The epidemiology of major depressive disorder: Results from the National Comorbidity Survey Replication (NCS-R). JAMA : The Journal of the American Medical Association 2003;289:3095–3105. [PubMed: 12813115]

Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry 2005;62:593–602. [PubMed: 15939837]

Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. Archives of General Psychiatry 1994;51:8–19. [PubMed: 8279933]

Kessler RC, Nelson CB, McGonagle KA, Liu J, Swartz M, Blazer DG. Comorbidity of DSM-III-R major depressive disorder in the general population: Results from the US National Comorbidity Survey. The British Journal of Psychiatry 1996;(30):17–30.

Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. Archives of General Psychiatry 1995;52:1048–1060. [PubMed: 7492257]

Ladd CO, Thrivikraman KV, Huot RL, Plotsky PM. Differential neuroendocrine responses to chronic variable stress in adult Long Evans rats exposed to handling-maternal separation as neonates. Psychoneuroendocrinology 2005;30:520–533. [PubMed: 15808921]

Leckman JF, Sholomskas D, Thompson WD, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis: A methodological study. Archives of General Psychiatry 1982;39:879–883. [PubMed: 7103676]

Liu D, Diorio J, Tannenbaum B, Caldji C, Francis D, Freedman A, Sharma S, Pearson D, Plotsky PM, Meaney MJ. Maternal care, hippocampal glucocorticoid receptors, and hypothalamic-pituitary-adrenal responses to stress. Science 1997;277:1659–1662. [PubMed: 9287218]

Lyons DM, Yang C, Mobley BW, Nickerson JT, Schatzberg AF. Early environmental regulation of glucocorticoid feedback sensitivity in young adult monkeys. Journal of Neuroendocrinolology 2000;12:723–728.

Madigan S, Moran G, Schuengel C, Pederson DR, Otten R. Unresolved maternal attachment representations, disrupted maternal behavior and disorganized attachment in infancy: links to toddler behavior problems. Journal of Child Psychology and Psychiatry 2007;48:1042–1050. [PubMed: 17915005]

Matthews SG. Early programming of the hypothalamo-pituitary-adrenal axis. Trends in Endocrinology and Metabolism: TEM 2002;13:373–380. [PubMed: 12367818]

McCormick JA, Lyons V, Jacobson MD, Noble J, Diorio J, Nyirenda M, Weaver S, Ester W, Yau JL, Meaney MJ, Seckl JR, Chapman KE. 5′-heterogeneity of glucocorticoid receptor messenger RNA is tissue specific: Differential regulation of variant transcripts by early-life events. Molecular Endocrinology 2000;14:506–517. [PubMed: 10770488]

Mook J, Schreuder BJ, van der Ploeg HM, Bramsen I, van Tiel-Kadiks GW, Feenstra W. Psychological complaints and characteristics in postwar children of Dutch World War II victims: Those seeking treatment as compared with their siblings. Psychotherapy and Psychosomatics 1997;66:268–275. [PubMed: 9311032]

Reich J, Lyons M, Cai B. Familial vulnerability factors to post-traumatic stress disorder in male military veterans. Acta Psychiatrica Scandinavica 1996;93:105–112. [PubMed: 8686479]

Resnick HS, Yehuda R, Pitman RK, Foy DW. Effect of previous trauma on acute plasma cortisol level following rape. The American Journal of Psychiatry 1995;152:1675–1677. [PubMed: 7485635]

Rosenheck R. Impact of posttraumatic stress disorder of World War II on the next generation. The Journal of Nervous and Mental Disease 1986;174:319–327. [PubMed: 3711873]

Schmidt M, Okimoto DK, Dent GW, Gordon MK, Levine S. Maternal regulation of the hypothalamic-pituitary-adrenal axis in the 20-day-old rat: consequences of laboratory weaning. Journal of Neuroendocrinolology 2002;14:450–457.

Seckl JR, Meaney MJ. Glucocorticoid "programming" and PTSD risk. Annals of the New York Academy of Sciences 2006;1071:351–378. [PubMed: 16891583]

Solomon Z, Kotler M, Mikulincer M. Combat-related posttraumatic stress disorder among second-generation Holocaust survivors: Preliminary findings. The American Journal of Psychiatry 1988;145:865–868. [PubMed: 3381934]

Spitzer, RL.; Williams, JBW.; Gibbon, M. Structured clinical interview for DSM-IV (SCID). New York: New York State Psychiatric Institute, Biomedical Research; 1995.

Weaver IC, Cervoni N, Champagne FA, D'Alessio AC, Sharma S, Seckl JR, Dymov S, Szyf M, Meaney MJ. Epigenetic programming by maternal behavior. Nature Neuroscience 2004;7:847–854.

Westerink J, Giarratano L. The impact of posttraumatic stress disorder on partners and children of Australian Vietnam veterans. The Australian and New Zealand Journal of Psychiatry 1999;33:841–847. [PubMed: 10619210]

Yehuda R, Bierer LM, Schmeidler J, Aferiat DH, Breslau I, Dolan S. Low cortisol and risk for PTSD in adult offspring of Holocaust survivors. The American Journal of Psychiatry 2000;157:1252–1259. [PubMed: 10910787]

Yehuda R, Blair W, Labinsky E, Bierer LM. Effects of parental PTSD on the cortisol response to dexamethasone administration in their adult offspring. The American Journal of Psychiatry 2007a; 164:163–166. [PubMed: 17202561]

Yehuda R, Engel SM, Brand SR, Seckl J, Marcus SM, Berkowitz GS. Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the World Trade Center attacks during pregnancy. The Journal of Clinical Endocrinology and Metabolism 2005;90:4115–4118. [PubMed: 15870120]

Yehuda R, Halligan SL, Bierer LM. Relationship of parental trauma exposure and PTSD to PTSD, depressive and anxiety disorders in offspring. Journal of Psychiatric Research 2001a;35:261–270. [PubMed: 11591428]

Yehuda R, Halligan SL, Grossman R. Childhood trauma and risk for PTSD: Relationship to intergenerational effects of trauma, parental PTSD, and cortisol excretion. Development and Psychopathology 2001b;13:733–753. [PubMed: 11523857]

Yehuda R, Labinsky E, Tischler L, Brand SR, Lavin Y, Blair W, Bierer LM, Goodman RZ, Grossman RA. Are adult offspring reliable informants about parental PTSD? A validation study. Annals of the New York Academy of Sciences 2006;1071:484–487. [PubMed: 16891603]

Yehuda R, McFarlane AC, Shalev AY. Predicting the development of posttraumatic stress disorder from the acute response to a traumatic event. Biological Psychiatry 1998a;44:1305–1313. [PubMed: 9861473]

Yehuda R, Schmeidler J, Giller EL Jr, Siever LJ, Binder-Brynes K. Relationship between posttraumatic stress disorder characteristics of Holocaust survivors and their adult offspring. The American Journal of Psychiatry 1998b;155:841–843. [PubMed: 9619162]

Yehuda R, Schmeidler J, Wainberg M, Binder-Brynes K, Duvdevani T. Vulnerability to posttraumatic stress disorder in adult offspring of Holocaust survivors. The American Journal of Psychiatry 1998c; 155:1163–1171. [PubMed: 9734537]

Yehuda R, Teicher M, Seckl J, Grossman RA, Morris A, Bierer LM. Parental PTSD is a vulnerability factor for low cortisol trait in offspring of Holocaust survivors. Archives of General Psychiatry. 2007b

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Table 1

Prevalence of lifetime psychiatric disorder by gender and offspring status

	Total Sample Prevalence (n=284)	Prevalence in Women (n=167)		Prevalence in Holocaust Offspring (n=200)		Prevalence in Women Among Offspring (n=130)		Prevalence in Women Among Comparison Subjects (n=37)	
Diagnosis	*%*	*%*	*χ^2, p[4] (df=1)*	*%*	*χ^2, p[5] (df=1)*	*%*	*χ^2, p[6] (df=1)*	*%*	*χ^2, p[7] (df=1)*
PTSD	17.6	20.4	2.17, .14	19.0	.94, .33	22.3	2.78,.10	13.5	.032, .86
Mood Disorder[1]	37.3	40.1	1.36, .24	45.5	20.79,< .001	47.7	.72,.40	13.5	.87, .35
Anxiety Disorder[2]	26.4	28.1	.63, .43	32.5	14.34, <.001	31.5	.16,.69	16.2	1.16, .28
Eating Disorder[3]	4.9	6.0	1.01, .32	6.0	1.89, .17	6.9	.59,.44	2.7	.03, .86
Substance Abuse	8.5	6.0	3.12, .08	10.5	4.26, .039	7.7	3.0,.08	.0	3.57, .06
Adjustment Disorder	9.5	11.4	1.71, .19	10.0	.20, .66	11.5	1.03,.31	10.8	.53, .47
Any Diagnosis	60.2	63.5	1.80, .18	69.5	24.12, <.001	70.8	.28,.60	37.8	.002, .97

[1] Prevalence of MDD (30.3) and Dysthymia (7.0). For all women: MDD (34.7) and Dysthymia (6.0). For all offspring: MDD (36.5) and Dysthymia (9.5). For all female offspring: MDD (40.8) and Dysthymia (7.7).

[2] Prevalence of GAD (6.3), Panic Disorder (5.3), OCD (2.8), Social Anxiety (7.4), and Specific Phobia (8.5). For all women: GAD (8.4), Panic Disorder (6.6), OCD (2.4), Social Anxiety (6.0), and Specific Phobia (9.0). For all offspring: GAD (8.5), Panic Disorder (7.0), OCD (3.5), Social Anxiety (8.5), and Specific Phobia (10.0). For all female offspring: GAD (10.0), Panic Disorder (7.7), OCD (3.1), Social Anxiety (6.9), and Specific Phobia (8.5).

[3] Prevalence of Bulimia (3.2), Anorexia (1.1), and Eating Disorder Not Otherwise Specified (.7). For all women: Bulimia (3.6), Anorexia (1.2), and Eating Disorder Not Otherwise Specified (1.2). For all offspring: Bulimia (3.5), Anorexia (1.5), and Eating Disorder Not Otherwise Specified (1.0). For all female offspring: Bulimia (3.8), Anorexia (1.5), and Eating Disorder Not Otherwise Specified (1.5).

[4] Chi-square compares men and women in the entire sample.

[5] Chi-square compares offspring to comparison subjects.

[6] Chi-square compares women and men in the offspring group.

[7] Chi-square compares women and men in the comparison group.

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Table 2

Lifetime prevalence of psychiatric disorder according to presence or absence of paternal and maternal PTSD

	Comparison (n=73)	Offspring No Parental PTSD (n=37)	Offspring Paternal PTSD (n=49)	Offspring Maternal PTSD (n=40)	Offspring Both PTSD (n=35)	Chi Square	Chi Square Controlling for Other Diagnoses
Diagnosis	***% (n)***	***% (n)***	***% (n)***	***% (n)***	***% (n)***	***χ^2, p (df=4)***	***χ^2, p (df=4)***
PTSD	14.1 (12)	7.5 (3)	9.3 (5)	25.9 (14)	31.4 (16)	13.6, .009	10.6, .031
Mood Disorder	17.6 (15)	27.5 (11)	48.1 (26)	46.3 (25)	56.9 (29)	27.0,<.001	22.0, .001
Anxiety Disorder	11.8 (10)	37.5 (15)	31.5 (17)	25.9 (14)	37.3 (19)	13.9, .007	12.6, .014
Eating Disorder	2.4 (2)	7.5 (3)	1.9 (1)	5.6 (3)	9.8 (5)	5.0, .28	4.2, .38
Substance Abuse[9]	3.5 (3)	12.5 (5)	9.3 (5)	11.1 (6)	9.5 (5)	5.2, .27	3.9, .42
Adjustment Disorder	8.2 (7)	12.5 (5)	14.8 (8)	7.4 (4)	5.9 (3)	3.6, .46	2.4, .66
Any Diagnosis[12]	37.6 (32)	57.5 (23)	74.1 (40)	66.7 (36)	78.4 (40)	27.3,<.001	

Table 3

Comparison of Three Groups of Subjects with Parental PTSD to all Subjects without Parental PTSD

Three groups of subjects with distinct patterns of parental PTSD (paternal only, maternal only, and both) were compared with all subjects without any parental PTSD to assess differences in prevalence of psychiatric diagnoses. The odds ratios were obtained by logistic regression controlling for age and gender.

	Father	Mother	Both
Diagnosis	***Odds ratio, p***	***Odds ratio, p***	***Odds ratio, p***
PTSD	.73, .57	2.40, .039	3.21, .005
Depressive Disorder	3.66, <.0005	3.06, .002	4.63, <.0005
Anxiety Disorder	1.98, .07	1.25, .56	2.07, .052
Eating Disorder	.43, .45	1.29, .74	2.50, .18
Substance Abuse	1.83, .32	1.98, .24	1.52, .50
Adjustment Disorder	1.63, .33	.65, .47	.52, .33
Any Diagnosis	3.78, <.0005	2.33, .015	4.18, <.0005

Table 4

Effects of Paternal and Maternal PTSD and their Interaction

Chi square tests reflect the effects of paternal and maternal PTSD, respectively, controlling for age, gender, and PTSD of the other parents. The interaction tests the impact of having both paternal and maternal PTSD, controlling for age, gender, and the effects of paternal and maternal PTSD occurring separately.

	Father	Mother	Interaction
Diagnosis	***χ^2, p (df = 1)***	***χ^2, p (df = 1)***	***χ^2, p (df = 1)***
PTSD	1.18, .28	6.49, .011	5.51, .019
Depressive Disorder	5.96, .015	2.96, .09	.03, .87
Anxiety Disorder	4.78, .029	.15, .70	.75, .39
Eating Disorder	.005, .94	1.58, .21	.49, .48
Substance Abuse	.28. .60	.75, .39	1.78, .18
Adjustment Disorder	1.65, .20	2.12, .15	1.33, .25
Any Diagnosis	8.28, .004	.85, .36	.006, .94