

## Alterations in morning cortisol associated with PTSD in women with breast cancer

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### Abstract

**Objective:** Diagnosis and treatment of breast cancer can be a stressful experience, putting women at risk of posttraumatic stress disorder (PTSD). The current study investigated morning cortisol levels in newly diagnosed (i.e., within 6 months) breast cancer patients. **Methods:** Structured DSM-IV interviews determined current and past incidence of PTSD and major depressive disorder (MDD) in 71 women with Stage 0–3 breast cancer. **Results:**

Significantly decreased plasma cortisol was found in women meeting current or lifetime criteria for PTSD or past diagnosis of MDD. **Conclusions:** These results reinforce the importance for both psychological and physiological outcomes of a clinical evaluation of both current and past psychiatric status in newly diagnosed cancer patients.

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*Keywords:* Breast cancer; Cortisol; PTSD; MDD

### Introduction

Although a diagnosis of posttraumatic stress disorder (PTSD) requires exposure to an extreme traumatic stressor, surprisingly large percentages of the population have been exposed to traumatic events. Resnick et al. [1] found that approximately two thirds of women in the United States had experienced a significant traumatic event, with PTSD prevalence rates of 12.3% lifetime diagnosis and 4.6% current diagnosis. Recent research has found symptoms of PTSD in women with breast cancer, and estimates of the prevalence of PTSD in newly diagnosed patients range from 3% to 10% [2,3]. Elevated symptoms of anxiety and depression near the time of diagnosis are also common and have been reported in 30% to 40% of patients [4]. Although few studies of the prevalence of clinically diagnosed major depressive disorder (MDD) have been reported, Dausch et al. [5] found prevalence rates of 6.7%

for a current diagnosis and 23% for a lifetime diagnosis in women newly diagnosed with breast cancer.

The level of emotional distress of breast cancer patients may have physiological consequences relevant to cancer [6]. Numerous investigations have shown cortisol and immune alterations associated with distress. Neuroendocrine function can be influenced by a variety of genetic or environmental factors, including trauma exposure. In noncancer populations, lower cortisol has been associated with PTSD [7]. In contrast, increased cortisol has been associated with MDD, although decreased cortisol has been reported in “atypical depression” [8]. Variations in cortisol levels can directly impact neoplastic growth and immune parameters (e.g., T-cell proliferation) relevant to the progression of breast cancer, suggesting that psychological factors that influence immune function may also influence cancer outcomes [6].

This study evaluated cortisol levels associated with PTSD and MDD in women newly diagnosed with breast cancer. Women with MDD were expected to show elevated cortisol relative to those with no diagnosis. In contrast, women with PTSD were expected to show lower cortisol. High rates of comorbid PTSD and MDD have been found [9]; thus, it was anticipated that women with PTSD would show high rates of comorbid MDD.

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## Methods

### Participants

Participants included 71 women (age 34–82, mean 53; 98% Caucasian) newly diagnosed (i.e., within the last 6 months) with breast cancer. The sample included women participating in a larger study of psychosocial intervention. Data reported represent preintervention measures. Cancer stage at diagnosis included 14% Stage 0 (in situ), 38% Stage 1, 42% Stage 2, and 6% Stage 3.

### Measures and procedure

PTSD and MDD prevalence were determined with structured DSM-IV diagnostic interviews developed as an adaptation of the DSM-IV checklist ([10]; interrater reliability  $\kappa=.96$ ). Current symptoms of anxiety and depression were measured using the Beck Anxiety Inventory [11] and the Beck Depression Inventory-II [12]. Blood samples for cortisol analyses were drawn between 8 a.m. and noon and were analyzed at the University of Vermont Hospital by Bayer chemiluminescence. Patients undergoing chemotherapy had blood drawn at least 2 weeks after their most recent treatment.

### Statistical analyses

Analyses of covariance were conducted predicting cortisol from PTSD or MDD status, with time of day of the blood draw and the use of antianxiety or antidepressant medication as covariates. Age, cancer stage, chemotherapy, radiation therapy, hormonal therapy, menopausal status, body mass index, food or alcohol intake, caffeine, and smoking were not significantly associated with DSM-IV diagnoses or cortisol levels. Partial correlations (controlling for time of day and medication) evaluated associations between cortisol and the number of symptoms of PTSD or MDD.

## Results

### Rates of PTSD and MDD in the sample

Current or past PTSD was diagnosed in 18.3% of the women (5.6% current, 12.7% past). Diagnoses were attributable to abuse or assault (57%), the diagnosis and treatment of breast cancer (15%), witnessing a death (14%), or other causes (13%). Comparable to previous studies, 3% of women in the entire sample met criteria for current PTSD due to breast cancer. No women met criteria for a current diagnosis of MDD, although a past diagnosis was found in 25%. A high level of comorbidity was found; 39% of women with past MDD had past or current PTSD and 54% of women with past or current PTSD had past MDD.

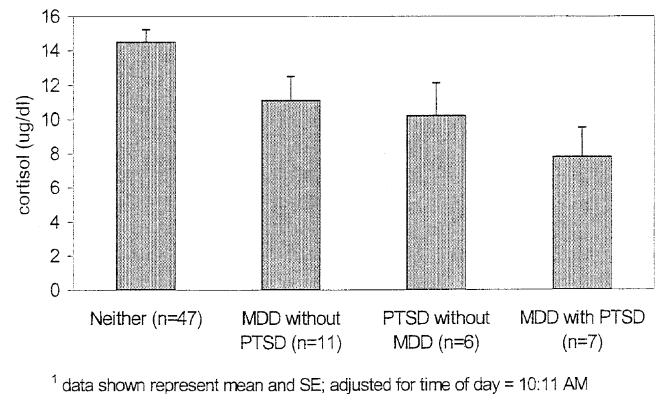


Fig. 1. Plasma cortisol by psychiatric diagnosis<sup>1</sup>.

### Analysis of cortisol

Significantly lower cortisol was found in women with either a current or past diagnosis of PTSD relative to women with no diagnosis,  $F(1,67) = 10.2$ ,  $P < .01$ . Comparison of three groups (none, current, or past) found significant differences,  $F(2,66) = 5.4$ ,  $P < .01$ , including lower cortisol in those with current ( $M = 7.5$   $\mu\text{g/dl}$ ,  $S.E. = 2.3$ ) and past ( $M = 9.8$   $\mu\text{g/dl}$ ,  $S.E. = 1.5$ ) PTSD relative to no diagnosis ( $M = 13.7$   $\mu\text{g/dl}$ ,  $S.E. = 0.60$ ), and no difference between current and past diagnoses. The number of PTSD symptoms endorsed was significantly correlated with cortisol,  $r = -.34$ ,  $P < .01$ .

Women with a past diagnosis of MDD had significantly lower cortisol ( $M = 9.8$   $\mu\text{g/dl}$ ,  $S.D. = 1.1$ ) than those with no diagnosis ( $M = 13.8$   $\mu\text{g/dl}$ ,  $S.E. = 0.70$ ),  $F(1,67) = 8.3$ ,  $P < .01$ . However, the number of MDD symptoms endorsed was not associated with cortisol,  $r = -.11$ ,  $P = .39$ . Post hoc analyses evaluated the hypothesis that comorbidity of PTSD in women with past MDD accounted for observed lower cortisol. Women were categorized as having neither MDD nor PTSD ( $n = 47$ ), past MDD without PTSD ( $n = 11$ ), past or current PTSD without MDD ( $n = 6$ ), or both MDD and PTSD ( $n = 7$ ). Significant differences between the groups,  $F(3,65) = 5.4$ ,  $P < .01$ , included lower cortisol in women with MDD only ( $P = .04$ ), PTSD only ( $P = .04$ ), and both MDD and PTSD ( $P < .001$ ) relative to women with neither diagnosis (see Fig. 1).

To investigate if the associations of MDD and PTSD with lower cortisol were attributable to current negative affectivity, analyses were repeated controlling for current symptoms of anxiety and depression. Anxiety or depressive symptoms were not significantly associated with cortisol, and both PTSD ( $P = .01$ ) and MDD ( $P < .01$ ) remained significant predictors.

## Discussion

A diagnosis of PTSD (current or past) was found in 18% of women in this sample of newly diagnosed breast cancer

patients. Psychobiological correlates were evident, including lower cortisol in women with current or past PTSD. The number of PTSD symptoms endorsed was negatively correlated with cortisol, suggesting that the amount of HPA disruption varies with the severity of the PTSD symptoms experienced. Surprisingly, cortisol levels did not differ between women with a current or a past diagnosis of PTSD. Participants were currently experiencing a significant stressor, raising the possibility of reactivation of past PTSD symptoms and associated HPA dysregulation [13]. The previous experience of a traumatic stressor may also increase vulnerability to subsequent traumatic stressors [7]. The current results support previous findings of long-lasting neuroendocrine changes associated with PTSD.

Previous research has associated major depression with elevated cortisol; however, none of the women in the sample met criteria for a current diagnosis of MDD. Interestingly, women with a past diagnosis of MDD had significantly lower cortisol than women with no diagnosis, even after controlling for current or past PTSD and current symptoms of anxiety or depression. However, the lowest cortisol levels were found in those with past MDD along with current or past PTSD. These results support findings by Oquendo et al. [14] of lower cortisol associated with major depressive episodes, with the lowest cortisol levels in those with comorbid PTSD.

The effects of decreased secretion of cortisol on breast cancer progression are unclear. In theory, lower cortisol levels may be associated with enhancement of some aspects of immune function. Recent studies have found elevated [15] or lowered [16] natural killer cell activity in patients with PTSD, suggesting the need for further research into the implications for cancer progression. The current results likely represent dysregulation of HPA axis functioning that may have complex effects on immune parameters relevant to cancer.

The current study has several limitations. Typical of the region of the country from which the sample was drawn, the sample was almost entirely Caucasian. Although age was not statistically associated with cortisol, the large age range may have introduced heterogeneity in results. Cortisol levels were determined through the use of a single blood draw within a 4-h timeframe in order to minimize the burden on participants. Statistical analyses controlled for the time of the blood draw. Nonetheless, the collection of multiple blood samples during a 24-h period may provide important information concerning the full extent of cortisol alterations. It was not feasible to exclude women receiving chemotherapy, radiation, or hormonal therapy. However, no significant effects of adjuvant treatments on cortisol levels or DSM-IV diagnosis were found.

The current results suggest neuroendocrine alterations associated with PTSD and MDD in women newly diagnosed with breast cancer. Consistent with studies in other populations, women with PTSD showed significantly lower morning cortisol levels and greater disruption associated with more severe PTSD. Women with a past diagnosis of MDD also had lower cortisol. These results underscore the

importance of evaluating psychiatric status in women with breast cancer as it may impact physiological functioning relevant to progression of the cancer. In addition, evaluation should go beyond symptoms specific to the cancer diagnosis, as past psychiatric disorder or current unrelated distress may also affect neuroendocrine function.

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