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ALLOSTATIC LOAD IN WOMEN WITH AND WITHOUT PTSD SYMPTOMS

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Abstract

Allostatic load (AL) is the term used to describe cumulative physiological wear and tear that results from repeated efforts to adapt to stressors over time. Operationalized as a composite index of biological risk factors (e.g., blood pressure, cholesterol, glycosylated hemoglobin, and cortisol, norepinephrine and epinephrine), AL has been shown to increase with age, predict long-term morbidity and mortality among the elderly, and be associated with low parent education in a large adolescent sample. However, AL has not yet been studied in samples with putative “high stress” or posttraumatic stress disorder (PTSD). Accordingly, AL was measured in women with high acute and chronic stress: mothers of pediatric cancer survivors with and without PTSD and control mothers of health children. AL emerged in a “dose-dependent” ranking from high to low: cancer mothers meeting all criteria for PTSD, cancer mothers with no or low symptoms, and control mothers, respectively ($p < .001$). Effects were not altered by self-reported sleep quality or substance use (tobacco, caffeine, alcohol or drugs) and remained significant when analyzing AL without cortisol or catecholamines. Results indicate elevated AL can be detected in relatively young women with high stress histories, and particularly those with PTSD. Future prospective studies must evaluate whether this pattern represents an accelerated aging process and increased risk of disease.

Keywords

Allostatic Load; Stress; Posttraumatic Stress Disorder

Introduction

Allostatic load (AL) is a term used to describe the cumulative physiological wear and tear that results from repeated efforts to adapt to stressors over time (McEwen and Seeman 1999). Unlike other psychobiological models of stress that focus on a single outcome variable (e.g., cortisol) or physiological system (e.g., the hypothalamic-pituitary-adrenal –HPA– axis), the AL model emphasizes multi-system dysregulation (McEwen and Wingfield 2003; Korte, Koolhaas, Wingfield, and McEwen 2005). By combining multiple biological risk factors into a composite score, risk for a variety of stress-exacerbated diseases can be assessed in healthy individuals prior to signs and symptoms of clinical disease. Also, use of a composite AL may allow for quantification of stress burden across multiple (co morbid) mental health diagnoses,

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thereby reducing the problems associated with overlapping diagnostic classifications, particularly among mood and anxiety disorders (see Kaufman and Charney 2000 for a discussion). A composite AL score reflecting cardiovascular activity, atherosclerosis development, HPA axis functioning, glucose metabolism and sympathetic nervous system (SNS) activation has been shown to increase with age (Crimmins, Johnston, Hayward and Seeman 2003) and to predict long-term morbidity and mortality among large elderly samples (Karlman, Singer, McEwen, Rowe and Seeman 2002; Seeman, McEwen, Singer, Albert, and Rowe 1997; Seeman, McEwen, Rose and Singer 2001). In addition, lower AL scores have been associated with positive social experiences in late middle-age (58+) and older adults (Seeman, Singer, Ryff, Love, and Levy-Storms 2002).

The predictive value of a composite AL score in these early and late geriatric samples provides evidence that cumulative risk for cognitive and physical decline can be quantified later in life. Recently, AL was examined in relation to socioeconomic status in a young sample consisting of 758 non-Hispanic black and white high school students (Goodman, McEwen, Bin, Dolan and Adler 2005). The composite AL consisted of risk factors reflective of cardiovascular disease (cortisol, plasma insulin, glucose, glycosylated hemoglobin, fibrogen, blood lipids, body mass index and waist circumference). There was a strong relationship between AL and lower parent education, indicating that known social inequalities in cardiovascular disease can be detected in biological systems of the young prior to development of disease. Future longitudinal research will be needed to examine the predictive value of AL for specific disease states and to explore mechanisms of the risk process.

Individual risk factors used to form the AL composite score vary somewhat across studies. For example, the largest study (N=18,000) (Crimmins, Johnston, Hayward and Seeman 2003) used 13 risk indicators, including inflammation markers that were not included in the first AL study (Seeman et al 1997) which used 10 risk indicators: systolic and diastolic blood pressure, total and HDL cholesterol, cortisol, DHEA; glycosylated hemoglobin, catecholamines (epinephrine and norepinephrine), and waist-to-hip ratio (a measure of central fat storage). The selection of risk indicators is typically guided by the most common disease states found in the sample being studied. For example, Goodman et al (2005) focused on cardiovascular disease, which is known to be influenced by ethnicity and socioeconomic status.

One methodological issue in using AL is specification of the direction of risk for a given indicator. Recent evidence suggests that the direction of risk for cortisol (top or bottom quartile of the sample) requires further clarification. Although a large literature on stress induction studies in animals and humans links stress to increases in cortisol, numerous studies have now shown PTSD symptoms to sometimes be associated with lower cortisol (for recent discussions of these findings see Raison and Miller, 2003; Rasmusson, Vythilingam and Morgan, 2003; Yehuda, 2002, 2004). Variation in cortisol findings have been attributed to the timing of sample collection relative to circadian rhythm (Yehuda et al 1996), timing of the assessment relative to the PTSD precipitating event (acute aftermath vs. months later: Aardal-Eriksson, 2001); "baseline" context (anticipatory vs. tonic/chronic levels: Bremner et al 2003; Elzinga, Schmahl, Vermetten, van Dyck and Bremner, 2003), presence of co morbid depression (Glover and Poland, 2002), past abuse history (Heim, Newport, Bonsall, Miller and Nemeroff, 2001; Resnick, Yehuda, Pitman and Foy, 1995) and other factors too numerous to review here (but see Rasmusson et al, 2001 for more). Most recently, Hellhammer et al (2004) found that hypocortisolism in participants aged 60 and older was associated with higher scores on measures of depression, perceived stress and physical complaints despite a lower total composite AL score relative to a comparison group without hypocortisolism. In light of the ongoing uncertainty surrounding this issue, it seems important to examine the predictive value of AL with and without cortisol in the composite and/or by including extreme cortisol scores on either end (high or low) of the continuum.

Despite promising data suggesting AL reflects cumulative stress on biological systems, the validity of a composite AL has not yet been examined in putative “high stress” samples (McEwen 2003). Individuals experiencing chronic stress due to life events (e.g., caretaking of a sick family member) or those with an affective disorder such as depression or posttraumatic stress disorder (PTSD) are known to show perturbations in some physiological systems represented in the composite AL score (for reviews see Kiecolt-Glaser, McGuire, Robles and Glaser, 2002; Yehuda 1999; Raison and Miller, 2003). The “stress hormones” of cortisol and norepinephrine are often found to differ as a function of stress history in otherwise healthy adults. However, it is unclear whether high stress samples will also show risk in cardiovascular, glucose metabolism or atherosclerosis AL indicators at an earlier age. Recent research among caregiving mothers of chronically ill children provides evidence that psychological stress accelerates cellular aging (Epel et al 2004). Ratings of perceived stress and chronicity of stress (number of years since the child's diagnosis of illness) were negatively correlated with the length and activity of telomeres. Telomeres are DNA-protein complexes associated with cell “chronological” age and potential for further division, or “biological” age (Epel et al 2004, p 17312). Whether an AL composite consisting of biomarkers routinely assessed in medical settings will reflect an accelerated aging process among psychologically stressed individuals is not known.

The purpose of this study was to assess AL in a younger (ages 29-55) high stress sample consisting of mothers of childhood cancer survivors. Because the typical length of treatment for childhood cancers is two to three years, such parents endure the uncertainty of a cancer diagnosis, the distress associated with treatment, and fear of relapse for an extended period of time. Parents also experience multiple discrete traumatic events common to cancer treatment, beginning with their child's diagnosis, and followed by bone marrow aspirations, spinal taps, transplants, surgery and other fear-provoking procedures associated with treatment (Stuber, Kazak, Meeske and Barakat 1998). Some parents will develop clinically significant PTSD symptoms following their child's diagnosis and treatment including hallmark PTSD symptoms of re-experiencing (e.g., flashbacks of worst moments), emotional numbing and avoidance, and hyperarousal (Brown, Madan-Swain and Lambert 2003; Glover and Stuber 2005b; Kazak et al 1997; Manne, Du, Gallelli, Sorgen and Redd 1998; Pelcovitz et al 1996).

Whether a life-threatening illness should qualify as a PTSD-precipitating traumatic event remains controversial more than a decade after diagnostic criteria for what constitutes a trauma was broadened (American Psychiatric Association, 1994). The current Criterion A1 of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, American Psychiatric Association 2000) specifies “an event that involves actual or threatened death or serious injury, or other threat to one's personal integrity” and allows for “learning about the unexpected or violent death, serious harm, or threat of death or injury experienced by a family member or other close associate”. Nonetheless, some criticize the broadening of criteria (e.g., McNalley 2003), and suggest that even extremely stressful events may not be the same as truly extraordinary traumas or what Shalev (2004) calls “the unthinkable”. Another related critical debate is whether the response to a stressful event among those who develop PTSD relative to those who do not is an issue of response severity or a qualitatively different process (see Yehuda 2004). As to cancer-related PTSD specifically, Kangas, Henry and Bryant (2002) propose changes to the diagnostic criteria may be necessary to reflect the illness context. For example, somatic (e.g., nausea, fatigue, hair loss, etc.) and externally imposed reminders (e.g., medication use, medical procedures, doctor visits) associated with cancer and its treatment cannot be avoided. As a result, the predictive value of Criterion C which assesses avoidance symptoms may be diminished in illness-related PTSD. In support, Glover and Stuber (2005b) found that while re-experiencing and arousal symptoms differentiated asymptomatic women from those meeting all symptom criteria for cancer-related PTSD, the avoidance/numbing symptom cluster was of no significant predictive value in the sample (n=57).

Although a full discussion of the PTSD diagnostic controversy is beyond the scope of this article, data show that a proportion of mothers of children diagnosed with cancer meet all current diagnostic criteria for PTSD, as assessed by research instrument (Brown, Madan-Swain, and Lambert 2003; Glover and Stuber 2005b; Kazak et al 1997) and by full clinical interviews (Manne, Du, Gallelli, Sorgen and Redd 1998; Pelcovitz et al 1996). Furthermore, these mothers show physiological dysregulation similar to that seen in other PTSD samples, including differences in cortisol and norepinephrine (Glover and Poland 2002), dopamine (Glover et al 2003) and immune system parameters at rest and under psychological challenge (Glover, Steele, Stuber and Fahey 2005). Examination of AL in those who do and do not meet current diagnostic criteria for illness-related PTSD may help to inform the dialogue about diagnostic issues.

AL and PTSD symptoms were assessed in acutely and chronically stressed cancer mothers and in control mothers of healthy children. Participants were part of a larger study of neuroendocrine and immune functioning at rest and under psychological challenge (Glover and Poland 2002; Glover et al 2003; Glover, Steele, Stuber and Fahey 2005). We hypothesized that AL would be elevated in all cancer mothers relative to controls as a result of the acute and chronic stress associated with their child's cancer. We further hypothesized that AL would be highest among cancer mothers meeting all criteria for PTSD, as flashbacks, emotional numbing, and hyperarousal symptoms intensify the cumulative stress burden. Resting (overnight urinary) cortisol was previously found to be lower and norepinephrine higher among this sample of cancer mothers with PTSD symptoms compared to controls (Glover and Poland 2002). To determine if cortisol and/or catecholamines are necessary indicators for AL to discriminate those with and without PTSD, groups were compared on three composite AL scores: 1) Base AL (cardiovascular, glucose metabolism and atherosclerosis indicators only); 2) Base + Cat AL (with catecholamines epinephrine and norepinephrine); and 3) Total AL (with catecholamines and cortisol).

Method

Participants

Cancer mothers were recruited by mail via tumor registry information on children diagnosed with any type of cancer at 18 years or younger. Only mothers of cancer survivors were included (off active cancer treatment for at least one year, and with no evidence of cancer relapse at the time of study enrollment). Control mothers (recruited from public-posted flyers) were required to have at least one child under the age of 18 with no chronic medical condition. A mailed recruitment letter resulted in 63 cancer mother respondents. Of these, 57 (89%) consented to an initial telephone interview which assessed health and medication status, demographic information and PTSD.

The study was approved by the UCLA Institutional Review Board.

Assessing PTSD and Chronic Stress

PTSD was assessed with the Posttraumatic Stress Diagnostic (PDS) Scale (Foa 1995). In a recent review of PTSD assessment instruments (Brewin 2005), the PDS showed good psychometric properties: sensitivity (.89), specificity (.75), positive predictive power (.79), and negative predictive power (.86). Based on the PDS, those who met all criterion for PTSD (Criterion A-F of DSM-IVR) were categorized as a PTSD group and those who did not meet all criteria were classified as "No PTSD." Although not excluded on the basis of PDS scores, all control mothers showed no or low PTSD symptoms on the PDS and none met all criteria for PTSD. Cancer mothers in the No PTSD group had no or low PTSD symptoms (details described below).

Following exclusion of participants who reported a chronic health problem or medication use known to influence neuroendocrine function, 23 (40.4%) of the cancer mothers provided biological samples. Urine or blood samples for several participants were lost during laboratory assay. The final AL sample consisted of cancer mothers meeting all criteria for PTSD (n=10), those with no or low PTSD symptoms -- No PTSD (n=10), and control mothers (n=8).

Chronic stress associated with non-cancer related events was assessed with the widely used Life Experiences Survey (Sarason, Johnson and Siegel 1978). The LES is a 57-item self-report scale used to characterize the frequency and impact of commonly occurring events during the past year (marriage, births, deaths, change in jobs, etc.). Responders note whether an event has occurred and rate the impact of the event on a scale from -3 (very negative impact) to +3 (very positive impact). Ratings for all items are summed for a total score.

Allostatic Load

Ten indicators of the composite AL score used in previous research were measured: body mass index (weight/height²), resting systolic and diastolic blood pressure, serum dehydroepiandrosterone sulfate (DHEA-S), serum high-density lipoprotein (HDL) cholesterol, total cholesterol, glycosylated hemoglobin, and urinary cortisol, norepinephrine and epinephrine. A composite for the sum of risk indicators was calculated as the number of indicators on which each participant scored in the top quartile of risk for the total sample (except for HDL, and DHEA, where inclusion into the lowest quartile constitutes risk). Also, because of discrepancies in past research on the direction of risk for cortisol, risk for cortisol was calculated as any value in the highest or lowest 12.5% of the total sample.

Participants were instructed to refrain from medication, coffee, or substance use for 24 hours prior to biological sample collection and completed logs of all consumption activities and sleep (amount and quality) for that period. All biological samples were collected at rest. Urinary indicators were collected at home by participants during a 12-hour overnight (7 p.m. – 7 a.m.) collection period. Remaining indicators were recorded (i.e., blood pressure) or collected (i.e., blood samples for DHEA-S, HDL and total cholesterol and glycosylated hemoglobin) following at least one hour of habituation in a laboratory session conducted within 1-2 days of the urine collection. All laboratory sessions occurred in the early evening hours (1700).

Results

Participant Characteristics

Groups did not differ on education, ethnicity, socio-economic status or marital status, but No PTSD cancer mothers were older than controls (for details see Glover and Poland, 2002). Age was used as a covariate in all analyses. All participants reported at least one traumatic event on the PDS, and groups did not differ in the number of traumas reported.

Potential Covariates

Examination and descriptive analyses of participant's logs recording medication, coffee, substance use, exercise and sleep (amount and quality) for 24 hours prior to biological sample collection indicated groups did not differ on any of these variables. Unhealthy lifestyle behaviors were largely absent in the sample. Only five subjects (representing all three groups) reported any use of tobacco, alcohol or drugs and of those who did, the usage was low (e.g., four cigarettes, one alcoholic drink). Caffeine consumption was similarly low. Also, most subjects had engaged in some exercise within the past few days.

Individual Indicators of Allostatic Load

Quartiles for individual indicators and frequency of risk for each indicator as a function of group are shown in Table 1. Analysis of Covariance (ANCOVA) was used to compare raw values of each AL indicator across groups after controlling for age. As reported earlier (Glover and Poland 2002), the PTSD group had the highest mean norepinephrine and lowest mean cortisol levels relative to controls and cancer mothers without PTSD. Groups were significantly different on age-covaried mean body mass index (BMI), with the PTSD group highest ($27.07 \pm SE 1.12$), No PTSD next ($24.24 \pm SE 1.6$) and controls lowest ($23.54 \pm SE 1.5$). Groups were not significantly different on any other AL indicator.

Data for cortisol, the only indicator with risk at high and low ends of the cortisol range, are of special interest. In the PTSD group, 3 of 4 at risk for dysregulated cortisol were in the highest quartile whereas 2 of 2 at risk in the No PTSD cancer group were in the lowest quartile. There were no controls at risk for dysregulated cortisol.

Composite AL

Levine tests indicated violations in homogeneity of variance and thus composites were transformed by rank method before conducting ANCOVA. Groups were significantly different for Total AL (with catecholamines and cortisol) [$F(2,28)=7.39$, $p = .003$], Base + Cat (with catecholamines only) [$F(2,28)=5.10$, $p = .01$] and Base AL [$F(2,28)=3.94$, $p = .03$]. As shown in Figure 1, Total AL appeared “dose-dependent”, with the lowest AL among controls, the highest AL among PTSD and a middle AL score among No PTSD cancer mothers. Mean (and standard deviation) composite AL scores are shown in Table 2. Planned comparisons indicate effects were primarily due to significant elevations in PTSD versus controls and between PTSD versus No PTSD cancer mothers. Post-hoc comparison of No PTSD to controls showed a trend for a significant elevation in Base AL ($p=.07$ for 2-way comparison), but no other significant comparisons. None of these effects were altered when analyses were repeated with self-reported sleep quality or substance use (tobacco, caffeine, alcohol or drugs) as potential covariates.

Linear regression was used to quantify the predictive value of age and group in estimating composite AL scores. As shown in Table 2, models were significant for all of the composites. The proportion of variance in AL accounted for by group status and age was large, as reflected in adjusted R^2 ranges of .38 - .45, depending upon the AL composite.

A cut-off of three and above established in previous research (Seeman et al., 1997) was used to categorize AL scores as high risk. More than half (7 of 10) of the PTSD group, 3 of 10 in the No PTSD group and none of the Controls were high risk AL scorers. These rates were the same for Total AL and Base + Cat AL: cortisol was not a necessary factor for membership in a high risk score of 3 and above.

Subthreshold Symptoms

Among the No PTSD cancer mothers, 50% ($n=5$) showed subthreshold symptoms, meeting at least one DSM-IV symptom cluster (Criterion B, C or D: re-experiencing, avoidance/numbing, and hyperarousal, respectively). This subthreshold group had an elevated mean PDS symptom severity score ($11.60 + 6.8$) relative to the no/low symptoms cancer mothers ($4.40 + 3.8$), but still below the severity score of cancer mothers meeting all criterion (A-F) for PTSD ($22.50 + 10.9$). AL composite scores were not significantly elevated among subthreshold mothers relative to the no/low cancer mothers, for Total AL (1.8 vs. 2.0), Base + Cat AL (1.6 vs. 1.6) or Base AL (1.6 vs. 1.4).

Relationship to PTSD Symptoms

Using all mothers, Total AL correlated with the number of PTSD symptoms reported on the PDS (Pearson $r = .47$, $p = .01$) and with the severity of symptoms ($r = .43$, $p = .02$), but not with the number of traumatic events previously experienced ($r = .05$, $p = .90$). Correlations for Base AL and Base + Cat AL were similar.

Contribution of Other Life Stressors

LES scores were used to assess the contribution of chronic stress other than the cancer trauma to AL composites. Analysis of the total impact score (negative or positive) indicated a significant effect of group [$F(2,27) = 5.50$, $p = .01$] and planned contrasts showed this was due to the mean negative total score for PTSD mothers (-9.70 ± 10.2) relative to controls ($+4.25 \pm 7.6$) ($p = .006$), who did not differ from No PTSD cancer mothers (2.0 ± 10.9). The same pattern was found for total number of life events reported for the past year; the PTSD group reported the greatest number (8.10 ± 5.6), and No PTSD and control mothers did not differ (4.80 ± 5.1 , 4.38 ± 5.0 , respectively). LES scores did not correlate with any AL composite. Furthermore, adding LES (total impact or number of events) to the linear regression models shown in Table 2 did not alter outcomes; LES scores were never a significant predictor of any AL composite with or without age and PTSD status in the model (examined with backward, stepwise and enter regression methods).

Discussion

This study is the first to demonstrate elevated AL in a high stress sample of adult women and further suggests a possible “dose-response” relationship, with controls lowest, cancer mothers with no or low PTSD symptoms in the mid-range and cancer mothers meeting all criteria for PTSD having the highest AL. The data may also be the first to link elevations in body mass index (BMI) to PTSD. BMI, along with norepinephrine and cortisol were significantly different in PTSD mothers, but other individual cardiovascular, glucose metabolism and atherosclerosis indicators were not. Yet when combined into a cumulative risk index, these biological indicators differentiated groups and confirmed the hypothesis that AL would be elevated in all cancer mothers relative to controls, but highest among cancer mothers meeting criteria for PTSD.

These findings extend use of the composite AL score used in previous geriatric (McEwen and Seeman, 1999; Seeman et al, 1997, 2001, 2002; Karlamangla et al 2002) and adolescent (Goodman et al 2005) research to an adult sample of women. In addition, results provide the first validation of elevated AL among individuals with PTSD. Moreover, stress history (group status) was a stronger predictor of AL than age, extending the findings of Crimmins et al (2003). This pattern may be an artifact of the age range of the sample (25-55) rather than a reflection of the relatively greater power of psychological history to impact AL. On the other hand, these data are in keeping with telomere findings (Epel et al 2004) among similarly aged (20-50) caregiving mothers. Women with the greatest perceived stress in that study had shorter telomeres equivalent to a decade of additional “chronological” aging, indicating psychological stress can hasten the “biological” age of cells.

The predictive value of AL in differentiating groups was not dependent on the inclusion of cortisol or catecholamines in the indexed score. These well known “stress” hormones are widely studied, but reflect multiple complex neuromechanisms that may not be “co-regulated” by a common pathophysiological mechanism (Charney, 2004; Liberzon Abelson, Fligel, Raz and Young, 1999). Expression of AL risk in one “stress” indicator did not ensure risk in another and none were a necessary prerequisite for high AL scores. This is in keeping with the concept of evolutionary benefit for individual variation in coping with stress; organisms adopt different

behavioral coping strategies, each with different associated underlying physiology (Korte, Koolhaas, Wingfield and McEwen 2005).

Data provide further evidence for the need to analyze extreme scores on both ends of the cortisol continuum (high and low) in addition to mean levels. Whereas the mean cortisol level was lower for PTSD mothers, ranking cortisol levels showed three of these PTSD mothers had extreme high cortisol and only one had an extreme low cortisol value. PTSD symptoms appear to result in cortisol dysregulation in both directions of extreme values. This may help to explain previous equivocal findings of both low and high cortisol in PTSD samples. The proximal conditions which dictate the direction of dysregulation are numerous and may include timing of the trauma in relation to development (i.e., child, adult or geriatric), frequency or chronicity of previous trauma, or transient state-dependent factors related to the assessment context. Similarly, there have been many potential mechanisms of bi-directional dysregulation put forth, including negative feedback regulation; genetic variations in cortisol sensitivity to corticotrophin releasing factor, ACTH or hippocampal sensitivity to heightened glucocorticoid production; and antiglucocorticoid activity related to endogenous steroids like DHEA, progesterone, estrogen and testosterone. The conditions and mechanisms of bi-directional dysregulation in PTSD will require much more research (see recent discussions: Charney, 2004; McEwen, 2002, 2004; Raison and Miller 2003; Rasmusson, Vythilingam, and Morgan 2003; Yehuda 2002).

AL findings for No PTSD mothers are less clear. Linear regression analyses suggested the cancer stress history may incrementally increase AL even with no or low (subthreshold) PTSD symptoms. However, direct comparisons between No PTSD cancer mothers and controls in the present study were statistically weak for Base AL ($p=.07$) and absent for other AL composites, and for all individual AL indicators. This could be due to the small sample and limited statistical power, but it may also suggest AL elevations will be specific to PTSD. Despite the vast literature on negative effects of chronic stress, most studies do not assess past history of trauma or PTSD directly. For example, PTSD status was not reported in the Epel et al (2004) study of telomere differences in caregivers and thus it is unclear whether accelerated aging effects can be attributed to stress history generally, or to unassessed PTSD symptoms. Indeed, recent stress history as indexed by the life events scale (LES) here showed no relation to AL, while PTSD symptoms were strongly correlated with AL composites.

On the other hand, the No PTSD group here reported fewer recent life events on the LES than PTSD mothers and rated those that did occur as having a positive impact. Is this an unusual "high stress" group? Did No PTSD mothers actually experience fewer negative events? Or, are they particularly resilient, with personality traits like optimism that filter their perceptions? And, does resilience prevent physiological damage associated with stress, or simply reduce it? Previous analyses of this sample (Glover et al 2003) indicated No PTSD mothers did not have elevated dopamine like PTSD mothers, but shared a pattern of reduced left-turn bias relative to controls. Turn bias is an indicator of differential vulnerability to stressors and asymmetry in subcortical dopamine metabolism in rodent studies (Carlson, Fitzgerald, Keller and Glick 1993; Carlson, Visser, Keller and Glick 1996) and has been associated with dopamine levels among humans (e.g., Mohr, Landis, Bracha, and Brugger 2003, Mohr, Landis, Bracha, Fathi, Brugger 2005). Measurement of AL in samples explicitly assessed for past trauma and PTSD will be needed to confirm the impact of chronic stress relative to acute trauma history alone and in conjunction with PTSD.

The present study has several limitations. In addition to modest size, the sample mostly consisted of Caucasian women of middle to upper-class socioeconomic status with healthy lifestyles (i.e., most recorded regular exercise, and limited or no use of tobacco, alcohol or drugs). Results must be replicated across larger and more diverse samples that vary by race/

ethnicity, socioeconomic status, gender and lifestyle behaviors. This would allow more detailed examination of the contribution of sleep quality, diet, and other potential mediators of stress-AL effects. Based on AL scores alone, it is not possible to determine the relative contribution of these more proximal “causes” of health risk. Combat-related PTSD in particular has long been associated with sleep disturbances and substance abuse (for reviews see Harvey, Jones and Schmidt 2003; Jacobsen, Southwick and Kosten 2001, respectively). The extent of these problems is unknown among PTSD-symptomatic parents of children with cancer. Similarly, the role of obesity as measured by BMI needs further close study in relation to trauma. There is growing interest in the “metabolic syndrome” (Love and Oldford 2005) and its relationship to psychological factors (Bjorntorp 2001; Raikonen, Mathews and Kuller, 2002). Whether the elevation in BMI found in women with cancer-related PTSD here will hold for men or for PTSD associated with other types of traumatic events is not known.

Also, prospective, longitudinal studies will be required to confirm the utility of AL in predicting disease among younger samples and assess the direction of causality in the association between chronic stress, PTSD and AL. For example, perhaps individuals with compromised physical health as reflected in elevated AL are at greater risk for PTSD. Indeed, control mothers here reported as many trauma exposures as cancer mothers. Thus, it is not trauma exposure per se that dictates the PTSD-AL association. Finally, studies with larger samples may begin to allow for investigation of psychological factors that mediate or moderate trauma impact, including those outlined by Charney (2004) that are related to mechanisms of reward and motivation (hedonia, optimism and learned helpfulness), fear responsiveness (effective behaviors despite fear) and adaptive social behavior (altruism, bonding and teamwork).

Despite limitations, this is the first evidence for the potential usefulness of a composite AL score to quantify cumulative stress effects in a non-geriatric sample with PTSD symptoms and putative high stress. Identification of the mechanisms of this mind-body connection awaits future research.

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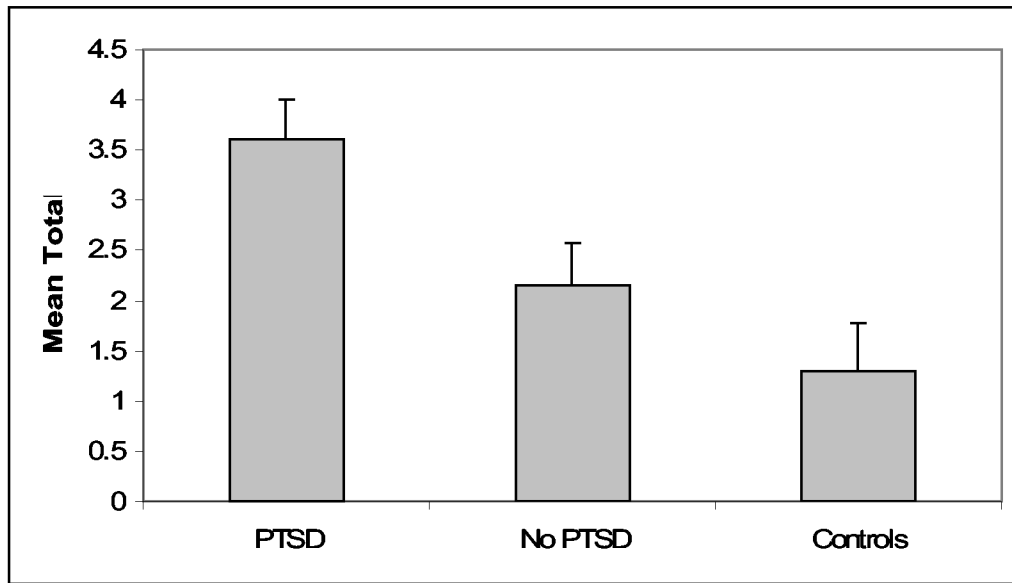


Figure 1. Mean (\pm standard error) of Total AL across groups after controlling for age.

Table 1

AL quartiles and number of participants at high risk as a function of group.

	High Risk Quartile	PTSS (n=10)	No PTSS (n=10)	Controls (n=8)
BMI (weight/height ²)	>=28.4	4	3	0
DBP (mm Hg)	>=79	5	2	0
SBP (mm Hg)	>=136	5	3	0
Glycosylated hemoglobin (%)	>=5.6	1	3	1
HDL cholesterol (mg/dL)	<=46	3	3	1
Total cholesterol (mg/dL)	>=204	4	1	1
DHEA (ng/mL)	<=1226	3	3	0
NE (ug/12 hr)	>=12.4	5	0	2
Epinephrine (ug/12 hr)	>2.0	2	1	2
Cortisol (ug/12 hr) Lowest or Highest 12.5% = Risk	<6.7 OR >23.7	4	2	0

Table 2

AL composite means (\pm standard deviation) and linear regression models predicting AL as a function of group and age.

	Group Mean (SD)			Planned Comparisons		F(2,27)	Linear Regression		
	1 PTSD (n=10)	2 No PTSD (N=10)	3 Controls (n=8)	1 vs. 3	1 vs. 2		Adjusted R ²	Unstandardized Beta	
								Group	Age
Total AL	3.70 (1.5)	2.20 (1.1)	1.00 (1.1)	***	**	11.99***	.45	-1.19***	.05
Base + Cat	3.30 (1.6)	1.90 (1.0)	0.88 (1.0)	**	*	10.23***	.41	-1.04**	.05
Base AL	2.60 (1.7)	1.80 (1.1)	0.38 (0.7)	**	--	9.23***	.38	-.87**	.07

Total AL: with catecholamines and cortisol; Base + Cat: with catecholamines

* p < .05

** p < .01

*** p < .001