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Authors

Corey, Sarah M
Epel, Elissa
Schembri, Michael
et al.

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Effect of restorative yoga vs. stretching on diurnal cortisol dynamics and psychosocial outcomes in individuals with the metabolic syndrome: the PRYSMS randomized controlled trial

Sarah M. Corey, PhD^{1,*}, Elissa Epel, PhD^{1,a}, Michael Schembri, BS¹, Sarah B. Pawlowsky, DPT², Roger J. Cole, PhD³, Maria Rosario G. Araneta, PhD⁴, Elizabeth Barrett-Connor, MD⁴, and Alka M. Kanaya, MD^{1,a}

¹University of California, San Francisco, CA, 94115, USA

²San Francisco State University, San Francisco, CA, 94132, USA

³Synchrony Applied Health Sciences, Del Mar, CA, 92014, USA

⁴University of California, San Diego, CA, 92093, USA

Abstract

Purpose—Chronic stimulation and dysregulation of the neuroendocrine system by stress may cause metabolic abnormalities. We estimated how much cortisol and psychosocial outcomes improved with a restorative yoga (relaxation) versus a low impact stretching intervention for individuals with the metabolic syndrome.

Methods—We conducted a 1-year multi-center randomized controlled trial (6-month intervention and 6-month maintenance phase) of restorative yoga vs. stretching. Participants completed surveys to assess depression, social support, positive affect, and stress at baseline, 6 months and 12 months. For each assessment, we collected saliva at four points daily for three days

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*Corresponding Author, Sarah Corey, UCSF Osher Center for Integrative Medicine, 1545 Divisadero St, San Francisco, CA 94115, sarahmcorey@yahoo.com.

^aco-senior author

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Prisms Contributors

Sarah Corey: literature search, data analysis, data interpretation, wrote first draft of manuscript and revisions.

Elissa Epel: study design, data analysis, data interpretation and critical revision.

Michael Schembri: data analysis, data interpretation, writing, and critical revision.

Sarah Pawlowsky: stretch protocol design, ensured fidelity of stretch intervention, data interpretation, and critical revision.

Roger Cole: literature search, study design, yoga and stretch protocol design, ensuring fidelity of yoga intervention, data interpretation, and critical revision.

Maria RG Araneta: study design, data collection, data analysis, data interpretation, and critical revision.

Elizabeth Barrett-Connor: study design, data collection, data interpretation, and critical revision.

Alka Kanaya: literature search, study design, data collection, data analysis, data interpretation, and writing.

Conflict of Interest

The authors for this manuscript do not have any actual or potential conflicts of interest including any financial, personal or other relationships to disclose.

and collected response to dexamethasone on the fourth day for analysis of diurnal cortisol dynamics. We analyzed our data using multivariate regression models, controlling for study site, medications (antidepressants, hormone therapy), body mass index, and baseline cortisol values.

Results—Psychosocial outcome measures were available for 171 study participants at baseline, 140 at 6 months, and 132 at the 1 year. Complete cortisol data were available for 136 of 171 study participants (72 in restorative yoga and 64 in stretching) and were only available at baseline and 6 months. At 6 months, the stretching group had decreased cortisol at waking and bedtime compared to the restorative yoga group. The pattern of changes in stress mirrored this improvement, with the stretching group showing reductions in chronic stress severity and perseverative thoughts about their stress. Perceived stress decreased by 1.5 points ($-0.4; 3.3, p=0.11$) at 6 months, and by 2.0 points ($0.1; 3.9, p=0.04$) at 1 year in the stretching compared to restorative yoga groups. Post hoc analyses suggest that in the stretching group only, perceived increases in social support (particularly feelings of belonging), but not changes in stress were related to improved cortisol dynamics.

Conclusions—We found significant decreases in salivary cortisol, chronic stress severity, and stress perception in the stretching group compared to the restorative yoga group. Group support during the interactive stretch classes may have contributed to these changes.

Keywords

Stress; Metabolic Syndrome; Waking Cortisol; Diurnal Cortisol; Dexamethasone; Social Support

1. Introduction

Activation of the stress response by cortisol is essential for life. However, chronic stimulation of the autonomic nervous system (ANS) by chronic life stresses can lead to metabolic changes including abdominal obesity, high triglycerides, low HDL-cholesterol, hypertension, and hyperglycemia. The clustering of these factors is called the metabolic syndrome, and may be at least partially due to dysregulation of the neuroendocrine system (Rosmond, 2005; Walker, 2006; Anagnostis et al., 2009). To date, studies investigating the relationship between cortisol and the metabolic syndrome have yielded mixed results, with some studies showing an association with hypercortisolism (Steptoe et al., 2004; Boyle et al., 2007; Vogelzangs and Penninx, 2007; Weigensberg et al., 2008; Stalder et al., 2013), some showing hypocortisolism (Bengtsson et al., 2010; Ljung et al., 2012; Champaneri et al., 2013) and some showing no association (Filipovský et al., 1996; Rosmond, 2005; Walker, 2006; Anagnostis et al., 2009; Abraham et al., 2013).

Due to the complex interplay between stress, cortisol and the development of the metabolic syndrome, reducing stress and cortisol has been identified as a potential treatment target for the metabolic syndrome (Steptoe et al., 2004; Walker, 2006; Boyle et al., 2007; Vogelzangs and Penninx, 2007; Weigensberg et al., 2008; Tamashiro et al., 2011; Stalder et al., 2013). Mind-body therapies may aid in this process (Bengtsson et al., 2010; Woodyard, 2011; Ljung et al., 2012; Champaneri et al., 2013). Yoga interventions have demonstrated improved cortisol and stress outcomes in diverse populations. Plasma serum cortisol was decreased after a yoga intervention in healthy controls (Rocha et al., 2012), patients with

type 2 diabetes (Beena and Sreekumaran, 2013), and a mixed population of overweight/obese individuals with chronic inflammatory disease (Yadav et al., 2012). After a yoga intervention, salivary cortisol was found to decrease in breast cancer patients (Raghavendra et al., 2009) and breast cancer survivors (Banasik et al., 2010). In addition, yoga has been shown to improve self-reported psychosocial outcomes including stress, depression and overall quality of life (Danahauer et al., 2009; Büssing, et al., 2012; D'Silva et al., 2012; Li and Goldsmith, 2012; Rocha et al., 2012).

Yoga practices traditionally involve multiple components including physical postures with stretching, breathing exercises and deep relaxation. We hypothesized that the relaxation response (Benson et al., 1974) would drive improved cortisol, stress, and psychosocial outcomes. To isolate this relaxation response, we focused on the physical components of restorative yoga, an intervention developed by B.K.S. Iyengar to induce relaxation, reduce stress, and minimize muscular strain through the use of props and supported poses that are held for extended periods of time (Iyengar and Razazan, 2001; Lasater, 2011). Supine and inverted body positions stimulate baroreceptor activity, inducing reflexes that produce a wide range of relaxing effects, including shifting sympathetic/parasympathetic balance toward predominant parasympathetic nervous system activity, thus reducing blood pressure, lowering plasma epinephrine and norepinephrine levels (Gharib et al., 1988; Vybiral et al., 1989; Shiraishi et al., 2002), and calming brain activity via ascending inhibitory pathways (Dell and Marillaud, 1966; Cole, 1989). By contrast, upright postures reduce baroreceptor activity, generally producing opposite effects (Cole, 1989; László et al., 2001).

Consistent with this, Blank (2006) showed that several indicators of physiological arousal including heart rate, oxygen uptake (VO_2 max), and brachial arterial blood pressure, are lower in reclining and inverted yoga poses when compared to upright yoga poses (Blank, 2006). Still more relevant to the present study, Khattab et al. (2007) demonstrated that a restorative yoga intervention dramatically increased cardiac vagal tone and reduced heart rate, as compared to two different control conditions (Khattab et al., 2007). We previously performed a pilot study which demonstrated the feasibility and acceptability of a restorative yoga intervention for overweight individuals with the metabolic syndrome (Cohen et al., 2007). For a comparison group we selected a low-impact stretching intervention, with the body in standing and seated upright positions to increase a healthful activity in overweight underactive adults and to allow for the evaluation of stretching, another component of many traditional yoga practices.

In the present study, we evaluated the effects of restorative yoga (relaxation) versus low-impact stretching on the neuroendocrine function of the hypothalamic-pituitary-adrenal axis by measuring salivary cortisol on three consecutive days. At baseline and following the 6-month intervention we conducted a dexamethasone suppression test on the fourth day to evaluate the negative feedback of this system. We also examined the effects of restorative yoga versus stretching on self-reported measures of stress and psychosocial outcomes after 6 and 12 months. Our primary hypothesis was that the restorative yoga intervention, as compared to the stretching intervention, would lead to decreased waking salivary cortisol. Secondary hypotheses were that restorative yoga would lead to decreased salivary cortisol at

night and thus an improved diurnal slope, and better negative feedback as measured by improved dexamethasone suppression and improved psychosocial and stress outcomes.

2. Methods

2.1 Study population

We analyzed data from a 1-year multi-center randomized controlled trial (6 month intervention phase followed by a 6 month maintenance phase) of restorative yoga versus stretching interventions for the metabolic syndrome. Details of the research study design, specific inclusion and exclusion criteria and primary outcomes have been published (Kanaya et al., 2013). Briefly, individuals from 21 to 65 years of age with the metabolic syndrome, as defined by the International Diabetes Federation criteria (Alberti et al., 2005), were recruited for a two-arm randomized control trial comparing restorative yoga vs. stretching interventions at two locations: University of California, San Francisco and University of California, San Diego. Participants were excluded for metabolic criteria (fasting glucose ≥ 126 mg/dl, HbA1c $\geq 7.0\%$, fasting triglycerides ≥ 300 mg/dl, weight ≥ 400 lb), conditions affecting metabolic factors (neurological conditions limiting mobility, hospitalization for coronary heart disease in past 6 months, current pregnancy or lactation, history of bariatric surgery, substance abuse, or use of medications affecting metabolic factors), current physical activity practice (yoga, stretching or similar physical activity), current involvement in a clinical trial or inability to participate in or commit to the length of the study (non-English speaking, uncontrolled psychiatric problems, cognitive impairment, limited life expectancy or anticipated change in living circumstances). Each institution obtained Institutional Review Board approval and all participants provided informed consent.

Recruitment at both sites involved advertising on the web and in newspapers, posting flyers, conducting outreach into the community, and direct mailings. Trained clinical research coordinators and study recruiters performed the telephone screening using a script with each eligibility question listed. During the clinical screening visit, a trained clinical coordinator went through all of the eligibility criteria again. All study coordinators were trained with an in-person training visit conducted by the study PI and the project directors at the UCSF coordinating center before the start of the intervention. They trained in how to administer all of the study questionnaires and were certified on their conduct of the clinical exam measurements (blood pressure, anthropometry). Eligibility was determined after a clinical screening visit and randomization was conducted at the baseline study visit. Randomization was blocked and stratified by sex and race/ethnicity for each site (Kanaya et al., 2013). Study participants and clinic staff were not blinded to the intervention group assignment. For this sub-study, psychosocial outcomes were collected at baseline, 6 months and at the end of the 12-month maintenance period. Cortisol outcomes and the life stress assessment survey were collected at baseline and after the 6-month intervention phase.

2.2 Measures

2.2.1 Salivary Cortisol—Saliva samples for cortisol analysis were collected from participants at baseline before any classes began and at the 6-month time-point. At each time-point, study participants were given labeled saliva collection kits containing 15

salivette tubes (4 tubes for Days 1, 2, and 3 and 3 tubes for Day 4) with fixed cryolabels, insulated freezer bags with icepacks, and a sample collection log to record when samples were taken. Samples were collected at waking, 30 minutes after waking, 60 minutes after waking and at bedtime on 3 consecutive days. After collection of the evening saliva sample on Day 3, participants were instructed to take the dexamethasone suppression test pill. On Day 4, saliva samples were collected at waking, 30 minutes and 60 minutes after waking. For sample collection, participants were instructed to provide the first sample immediately upon waking (no eating, drinking or brushing teeth), the second sample 30 minutes after the first sample (no eating or brushing teeth), the third sample 60 minutes after the first sample (no eating, no brushing teeth 30 minutes before taking the sample and no water 10 minutes before sampling), and the fourth sample at bedtime (before brushing teeth or more than 30 minutes after, no eating, no water 10 minutes prior to sampling). To measure an individual's salivary cortisol during their sleep/wake cycle, we collected evening cortisol measures at the study participants' bedtime rather than a fixed evening time, an approach that has been used in recent large-scale studies involving salivary cortisol measurement (DeSantis et al., 2011; Golden et al., 2014). To account for real outliers, we asked study participants not to collect their bedtime sample after 11:59 pm or their morning sample after 11 am, to restrict the potentially wide range of sampling. To reduce variability in the times that samples were collected, participants were asked to collect their 6-month cortisol on the same consecutive days of the week as they did for their baseline cortisol collection.

Samples were inventoried and stored at -20°C until being shipped in a single batch for processing and analysis to Biochemisches Labor, Universität Trier (Trier, Germany). Only participants with cortisol samples from both study time-points (baseline and 6-month samples) had their samples analyzed. After duplicate participant and control sample preparation, cortisol levels were determined with a competitive solid phase time-resolved fluorescence immunoassay with fluorometric end point detection as previously described (Dressendorfer et al., 1992).

2.2.2 Psychosocial measurements—Study participants completed surveys to assess depression, social support, positive affect, and stress at baseline, 6 months (post-intervention) and at 12 months (following the maintenance period). Depression symptoms over the prior week were measured with the 21-item Beck Depression Index (Radloff, 1977). Overall social support was measured by calculating a summary score from the 40-item Interpersonal Support Evaluation (Cohen and Hoberman, 1983). Positive affect was quantified with the Positive States of Mind Scale (Horowitz et al., 1988), a 6-item questionnaire that evaluates the extent to which a person experiences satisfying states of mind over the previous week. Stress was measured with 2 scales: the Perceived Stress Scale and the Life Stress Assessment. Cohen's Perceived Stress Scale is a 10-item survey that was used to assess the perception of stress over the prior month (Cohen et al., 1983). The Life Stress Assessment Scale is a new survey for chronic stress that was developed to assess emotional well-being by measuring how an individual feels about a chronically stressful situation in their lives (see Appendix for Life Stress Assessment Scale). Participants were instructed to think of the most stressful ongoing situation in their lives that has lasted a minimum of 3 months. The instructions gave a number of examples including: financial

strain, health problems, relationship conflict or stress at work. Participants were asked to briefly describe the situation and how long it has been going on. Next, participants were asked to rate their feelings concerning the situation on a 5-point scale from none to extreme/a lot on two subscales: severity of the stressor and cognitive stress. For severity of the stressor there are two questions: “How emotionally stressed or anxious do you feel about the situation?” and “How much does it interfere with your daily life?” For the cognitive stress induced by the event there are two questions: “How much does this situation make you feel badly about yourself?” and “How frequently do you think about the aspects of this situation that have already occurred by getting caught up in repetitive thoughts?” A mean score from 1 to 5 was calculated for each subscale: severity of stressor (Chronbach’s alpha at baseline = 0.75, at 6 months = 0.77) and cognitive stress (Chronbach’s alpha at baseline = 0.70, at 6 months = 0.69).

2.3 Interventions

At the first group class session, all participants received a 30-minute didactic presentation on healthy lifestyle including nutrition and physical activity information tailored for individuals with the metabolic syndrome. Study participants in both groups participated in twice-weekly, 90-minute classes for the first 12 weeks, once-weekly for weeks 12–24, and once-monthly group classes for an additional 6 months (the maintenance period). For home practice, study staff and intervention instructors encouraged study participants to practice at least 3 times per week for at least 30 minutes per session. To support the individual home practice, all participants received written handouts with photographs and DVDs, as well as a diary to keep track of practice time and frequency. For instructor qualifications, yoga instructors were required to be certified, insured, trained in restorative yoga and have at least two years of experience teaching restorative yoga and group yoga classes. Stretching instructors needed to either be a certified personal trainer or a licensed physical therapist with at least a Bachelor’s degree. In addition, stretching instructors needed to be insured and have experience treating patients/clients with obesity and/or diabetes for at least two years. In order to ensure fidelity of each intervention at both of the study sites and with each of the group instructors (two per site), the primary yoga consultant and the primary stretching consultant conducted training sessions with the instructors before the start of each intervention. They also conducted monthly phone conference calls with all of the instructors to discuss quality control and any other participant issues that may have emerged. The consultants conducted unannounced observations of each of the instructors leading a group session in order to insure that they were following the study protocol.

The restorative yoga intervention used supported poses and props with the goal of inducing the relaxation response (Iyengar and Razazan, 2001; Lasater, 2011). An expert yoga panel developed the intervention with a focus on five main poses including: supported reclining pose, forward bend with head on chair, baby bridge pose, reclining pose with legs on chair, and final relaxation pose with modified pose options. The full yoga intervention protocol that was provided to participants is presented in the supplementary materials. Briefly, participants in the restorative yoga intervention were given props for their home practice including a nonskid mat, bolster, blankets, towels, belt, and eye pillow. Participants were encouraged to select a regular time each day for home practice, and to find an environment

that would be quiet, warm, safe, comfortable and dark. They were instructed to find a comfortable position: stay warm by covering with a blanket, enhance relaxation by covering the eyes, release the muscles throughout the body, and to remain in the pose for at least 10–15 minutes, setting an alarm if necessary. Participants were informed that thoughts and feelings will come and go, which is normal, and to just observe them without judging them. This restorative yoga intervention focused on the effects of physical relaxation and there were no additional instructions for breathing, the repeating of mantras, body scans or other forms of meditation.

The stretching intervention was designed by a physical therapist and yoga instructor to have similar attention, social support, and physical exertion elements as compared to the restorative yoga intervention without the goal of inducing a relaxation response (no reclining stretches or inversions). The full stretching protocol that was provided to participants is included in the supplementary materials. In summary, participants were provided instructions on performing sustained stretching with the goal of mobilizing the soft tissues to improve muscle length and range of motion by holding each stretch for 30 seconds and repeating each stretch 3 times. Photographs and instructions for performing 27 sitting and standing stretches (as well as recommended combinations) were provided in the manual. The stretches covered most areas of the body including neck and arm stretches, back and leg stretches, and whole body stretching.

2.4 Statistical Analyses

Salivary cortisol data was screened for protocol compliance and samples were found to be within an appropriate collection window (waking: 20 minutes after waking, waking + 30 minutes: < 60 minutes after waking, and waking + 60 minutes: < 105 minutes). Salivary cortisol samples were taken over 3 days, and no substantial variance was found across days. For cortisol analysis, sample measurements were screened for biological outliers that were above 100 nmol/l and none were found. With the exception of the dexamethasone suppression test day, cortisol data were averaged over the 3 days of regular saliva collection. Waking dexamethasone suppression was calculated by subtracting the waking cortisol from the waking dexamethasone cortisol levels. Cortisol slope was calculated by subtracting evening cortisol from waking cortisol, and cortisol percent change was calculated as the evening cortisol minus the waking cortisol divided by the waking cortisol. Psychosocial and cortisol outcomes measures were approximately normally distributed with the exception of cortisol slope which was log transformed due to skewness and dexamethasone suppression values, which were winsorized due to extreme values on the negative tail. Graphs of cortisol profiles were generated using mean cortisol values across participants and compared between groups.

Univariate and multivariate GEE/GLM regression models were used to compare change in cortisol and psychosocial outcomes at 6 months with change in scores between intervention groups, controlling for study site, medications (antidepressants and hormone therapy), body mass index (BMI; kg/m²) and baseline cortisol and/or psychosocial values as covariates. Post-hoc exploratory analysis was conducted using partial Spearman rank correlations between improvement in psychosocial measures and change in cortisol to identify outcomes

that may represent potential mechanisms for an improved stress response. All data analyses were conducted with SAS 9.3 (Cary, North Carolina) computing software.

3. Results

Of the 180 study participants randomized to the restorative yoga or stretching interventions, 171 initiated the group classes, 88 in the restorative yoga group and 83 in the stretching group. Overall adherence (>80%) to attending group classes and completing home practice was higher in the restorative yoga group compared to the stretching group (62% vs 46%; $p=0.04$). Out of 30 group classes restorative yoga participants attended a mean of 22.9 (± 9.1) and stretching participants attended 19.8 (± 10.2 ; $p=0.04$). Further details on adherence to classes and home practice are described in Kanaya et al. 2013.

For psychosocial outcomes data were available for 171 participants at baseline, 140 at 6 months and 132 at the 1-year time-point. Complete cortisol data were available for 136 study participants (72 in restorative yoga and 64 in stretching) at baseline and at 6 months. At baseline, the mean age of participants was 55 ± 7 years, 72% were women and 35% were from ethnic minority groups. The two groups were balanced on most demographic factors, cortisol levels, stress, and psychosocial measures. However, individuals in the restorative yoga group had a higher mean BMI and were more likely to be unmarried and taking anti-depressants, as compared to the stretching group (Table 1). Statistical analysis of outcomes at 6 months and 1 year were controlled for site, BMI, and anti-depressant and hormone therapy medication usage. Statistical adjustment for marriage as a control variable did not meaningfully change the results and therefore was not included in final analyses. Overall there was a higher than anticipated rate of attrition. The reason for this is unclear, as individual's reasons for leaving the study were not systematically collected and most individuals did not respond to requests for further contact. Additional details on study retention at various time-points is described in Kanaya et al. (2013).

After the 6-month intervention, significant changes in cortisol were observed within and between the restorative yoga and stretching groups. For between group differences, there were significant decreases in cortisol measurements in the stretching group compared to the restorative yoga group (Table 2). The daily change in cortisol profile from baseline to 6 months in the restorative yoga and stretching groups is shown in Figure 1. Waking cortisol and waking dexamethasone cortisol levels at baseline and 6-months in the yoga and stretching groups is visually depicted in Figure 2. While a statistically significant difference in dexamethasone suppression was found between the restorative yoga and stretching groups at 6 months, this could be predominantly due to the decreased waking cortisol levels in the stretching group rather than a change in cortisol specifically after dexamethasone (Figure 2).

For psychosocial outcomes, there was little evidence of change between intervention groups for the depression and interpersonal support scales, yet, there was a trend toward increased positive states of mind in the stretching group at 1 year (Table 3). Compared to the restorative yoga group, perceived stress in the stretching group decreased by 1.5 points at 6 months in the stretching group, and by 2.0 points at 1 year. The Life Stress Assessment – Severity of Stressor subscale decreased by 0.4 points and the Life Stress Assessment –

Cognitive Stress subscale decreased by 0.4 points in the stretching group compared to the restorative yoga group.

In considering why the stretching group improved in both cortisol and psychosocial measures, we observed that a main difference in the conduct of the groups was the opportunity to interact socially. The stretching group talked during each session whereas the restorative group was mostly silent with eyes covered by pillows in relaxation poses. Therefore we examined whether changes in stress and/or social support, might help explain improvements in diurnal cortisol regulation among the stretching group. Using the entire sample, there was little evidence of correlation between changes in stress and cortisol measures (data not shown), but there was a correlation between changes in overall social support and cortisol measures. There was a consistent pattern of correlation between overall support and cortisol in the stretching group and a less consistent pattern in the restorative yoga group. As shown in Table 4, these correlations may be due to increases in feelings of belonging.

4.0 Discussion

This study evaluated the effects of restorative yoga and stretching on cortisol and psychosocial outcomes in individuals with the metabolic syndrome. We found statistically significant improvement in cortisol diurnal dynamics in the stretching group compared to the restorative yoga group. Concordantly, we also found that perceived stress and life stress assessment measures improved more in the stretching group. In the stretching group, the improvements in cortisol measures correlated with the interpersonal support evaluation subscale of “belonging.” Improved quality or frequency of social interactions may have promoted feelings of safety and stress reduction, which might have also improved diurnal cortisol dynamics. Social support is a powerful buffer of stress, and it can reduce threat reactivity, neurally, and reduce peripheral reactivity of neuroendocrine and inflammatory pathways (Coan et al., 2006; Kiecolt-Glaser et al., 2010).

More recent reviews of the literature have concluded that the overall evidence for an association between obesity and cortisol levels is not strong (Abraham et al., 2013). Positive correlations were found between anthropometric measures and cortisol in hair (Stalder et al., 2013) and between BMI and urinary cortisol excretion (Rask et al., 2001). Further, cortisol levels in tissue were higher in obese compared to non-obese men (Sandeep et al., 2005). However, decreased serum cortisol (Travison et al., 2007; Ljung et al., 2012) and decreased plasma cortisol have been found in individuals with obesity (Walker et al., 2000) as well as other components of the metabolic syndrome (Tyrka et al., 2012). In addition, other studies have not found an association between metabolic syndrome components and cortisol measurements (Abraham et al., 2002; DeSantis et al., 2011) or have found a blunted response to dexamethasone testing of negative feedback (Rosmond et al., 1998).

Few large-scale (>100 participants) studies to date have focused on hypothalamic-pituitary-adrenal (HPA) axis function in overweight individuals diagnosed with metabolic syndrome. In the current study, we measured activity of the HPA axis with daily salivary cortisol measures and a dexamethasone test to evaluate sensitivity to negative feedback in a larger

sample of overweight/obese individuals with the metabolic syndrome. Interestingly, we found that waking cortisol levels at baseline in individuals with the metabolic syndrome (8.4nmol/l) were on average lower than reported for other adult populations without the metabolic syndrome (12–15nmol/l) (Fries et al., 2009). These results are in agreement with a small, population-based study of the cortisol awakening response, where individuals with metabolic syndrome had waking salivary cortisol levels with a mean of 8.92nmol/l as compared to a mean of 12.33 nmol/l in people without metabolic syndrome (12.33 nmol/l) (Bengtsson et al., 2010).

We had hypothesized that cortisol outcomes would improve more after the restorative yoga intervention, but our results demonstrated that waking, evening and mean cortisol values decreased more in the stretching group. Increased cortisol clearance may be a reason why we observed decreased overall waking cortisol in the stretching group. In addition, baseline BMI was higher in the restorative yoga group, which may have contributed physiologically to a lack of improvement in this group. Further study of both circulating salivary cortisol and urinary cortisol excretion is needed to better understand this relationship.

The dexamethasone suppression test measures the sensitivity of the negative feedback system of the hypothalamic-pituitary-adrenal axis. In prior studies of obese (Ljung et al., 2002) or stressed populations (Powell et al., 2002), waking dexamethasone was less inhibited. In all of our participants, waking dexamethasone suppression levels were similar to those observed in non-stressed populations (Powell et al., 2002), demonstrating appropriate negative feedback. Interestingly, at 6 months, dexamethasone suppression was greater in the restorative yoga group compared to the stretching group at 6 months. However, Figure 2 demonstrates that post-intervention waking cortisol was lower in the stretching group, and thus there was less room for dexamethasone suppression, perhaps accounting for this difference between groups.

Even though restorative yoga is often carried out in a group setting, the focus is on relaxation of the individual, with the body fully supported by yoga props such as blankets and bolsters. Poses are held for extended periods of time (10 to 15 minutes) and communication between participants is minimal. In the stretching intervention, the group conversed with weekly discussion topics and stretching poses changed approximately every 30 seconds. It is possible that the increased social interaction or the physical movement associated with the stretching intervention led to our observed outcomes. To better understand whether social support could explain the decreased cortisol levels we observed in the stretching group, we conducted exploratory analyses. Analyses included correlations between cortisol outcomes and ISEL summary scores, in particular the ISEL “Belonging” subscale that measures the availability of having people one can do things with. We found statistically significant correlations with feelings of support in both the stretching and the yoga groups. Statistically significant correlations were not found with perceived stress, depression, positive affect or life stress. More recently, social evaluation and support has been found to associate with stress and cardiovascular outcomes that may be important for health (Smith et al., 2012). In a breast cancer study, a similar pattern was observed; social support was found to negatively correlate with mean cortisol (Turner-Cobb et al., 2000). Physical activity was also a component of the stretching intervention that was different from

the restorative yoga group. For physical activity, we did not measure the difference in physical exertion between the restorative yoga and stretching interventions, but both groups had improved their overall physical activity as measured by survey (Kanaya et al., 2013).

For psychosocial outcomes the perceived stress scores were similar to levels others have found in individuals with metabolic syndrome (Abraham et al., 2013). These values are higher in individuals with the metabolic syndrome and lower in individuals without. In addition, the sample overall had lower perceived social support compared to non-clinical samples (Brookings and Bolton, 1988; Rogers et al., 2004). Overall this study sample showed above average levels of depression at baseline compared to the US mean score of 6.75 (Van Hemert and Van De Vijver, 2002). Post-intervention, depression levels had decreased significantly within the stretching group. Compared to the restorative yoga group post-intervention, individuals in the stretching group demonstrated a trend in decreased perceived stress that further decreased and became significant at 1 year. In addition, a second new stress measurement tool, the Life Stress Assessment, demonstrated decreased severity of their major life stressor and decreased cognitive stress post-intervention in the stretching group only.

For this specific restorative yoga intervention, the focus was on the effects of the poses on the physical body and allowing relaxation to happen on its own. Few instructions were given to study participants for how they should respond to thoughts that arise other than to observe the thought without judgment. There were no additional instructions for breathing, the repeating of mantras, body scans or other forms of meditation. For neuroendocrine function in individuals with metabolic syndrome, further study is needed to determine whether there may be additive benefits of combining stretching with relaxation and/or breathing, mindfulness, the repeating of mantras and instruction to increase body awareness. Stretching and relaxation (via restorative yoga poses) are often combined in yoga practices and it is possible that the combination of these components may lead to improved outcomes. One limitation of the current study is that it did not include a combined restorative yoga and stretching intervention group, nor a usual care comparison group. A recent pilot study with overweight and obese subjects found decreased plasma cortisol after a yoga intervention that incorporated physical postures as well as breathing and relaxation exercises (Yadav et al., 2012). A second limitation of this study is that the induction of relaxation was not directly measured in the restorative yoga or stretching interventions. Similarly designed studies have demonstrated that compared to the upright poses utilized in the stretching intervention, supine and gentle inversions of the body used in the yoga intervention led to physiological changes including decreases in heart rate and blood pressure (Blank 2006). However, we did not directly confirm these findings, an important addition to future studies on this topic. A third limitation of this study that could have biased results is that even though study participants were randomized, there were baseline imbalances. Individuals randomized to the restorative yoga group were more likely than those in the stretching group to be unmarried, with a higher BMI and to be taking anti-depressants. While statistical analysis methods were used to control for BMI and medication use at 6-month and 1-year time-points, it is important to note that marital status, BMI, and depression may individually or collectively contribute to increased levels of stress, potentially impacting cortisol levels in the body. It is possible that the randomly generated group composition of the stretching

group led to a more cohesive environment for social support (in addition to the more social atmosphere of the stretching group versus the silent yoga group). Further, our sample consisted of more than 50% white females, potentially limiting the generalizability of our outcomes.

An additional limitation of this study is that cortisol and Life Stress Assessment outcomes were only available at 6 months, and metabolic changes can take time to manifest. Possible effects of restorative yoga or stretching on cortisol outcomes at 1 year or beyond were not captured in this study. Overall, the field of psychoneuroendocrinology is plagued by not having an accessible measure of physiological chronic stress. Repeated days of cortisol sampling across the diurnal rhythm is both commonly used and often altered in clinical states of chronic stress. The assessment of cortisol as a biomarker of stress is further complicated since it can be regulated during stress to have decreased output, not just increased output. Future studies that aim to measure chronic output of cortisol might consider hair cortisol. Although hair cortisol does not index changes in diurnal rhythmicity, it uniquely measures accumulated output over several months, offering a second and different measure of HPA function (total output) (D'Anna-Hernandez et al., 2011; Stalder et al., 2013).

Furthermore, the time of day when the restorative yoga or the stretching intervention was carried out may have also influenced study outcomes. While the majority of group classes for the study were carried out in the afternoon or evening, participants did not record the time of day when they completed the home practice. Due to this limitation, further investigation is needed to determine the potential impact of intervention time of day on neuroendocrine outcomes.

In conclusion, waking cortisol measures were low in this population of individuals with the metabolic syndrome, and greater decreases in waking cortisol concentrations were found after a 6-month stretching intervention as compared with a 6-month restorative yoga intervention. In addition, the stretching group had greater decreases in stress that persisted at 1 year. Perceptions of social support, in particular belonging, may be responsible for the effects we observed in this study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

Neuroendocrine system dysregulation by stress may cause metabolic abnormalities

We evaluated the impact of restorative yoga versus stretching interventions on stress

Stress was measured with salivary cortisol and self-report

We report that stretching decreases salivary cortisol and self-reported stress

Social support correlated with beneficial changes in cortisol in the stretching group.

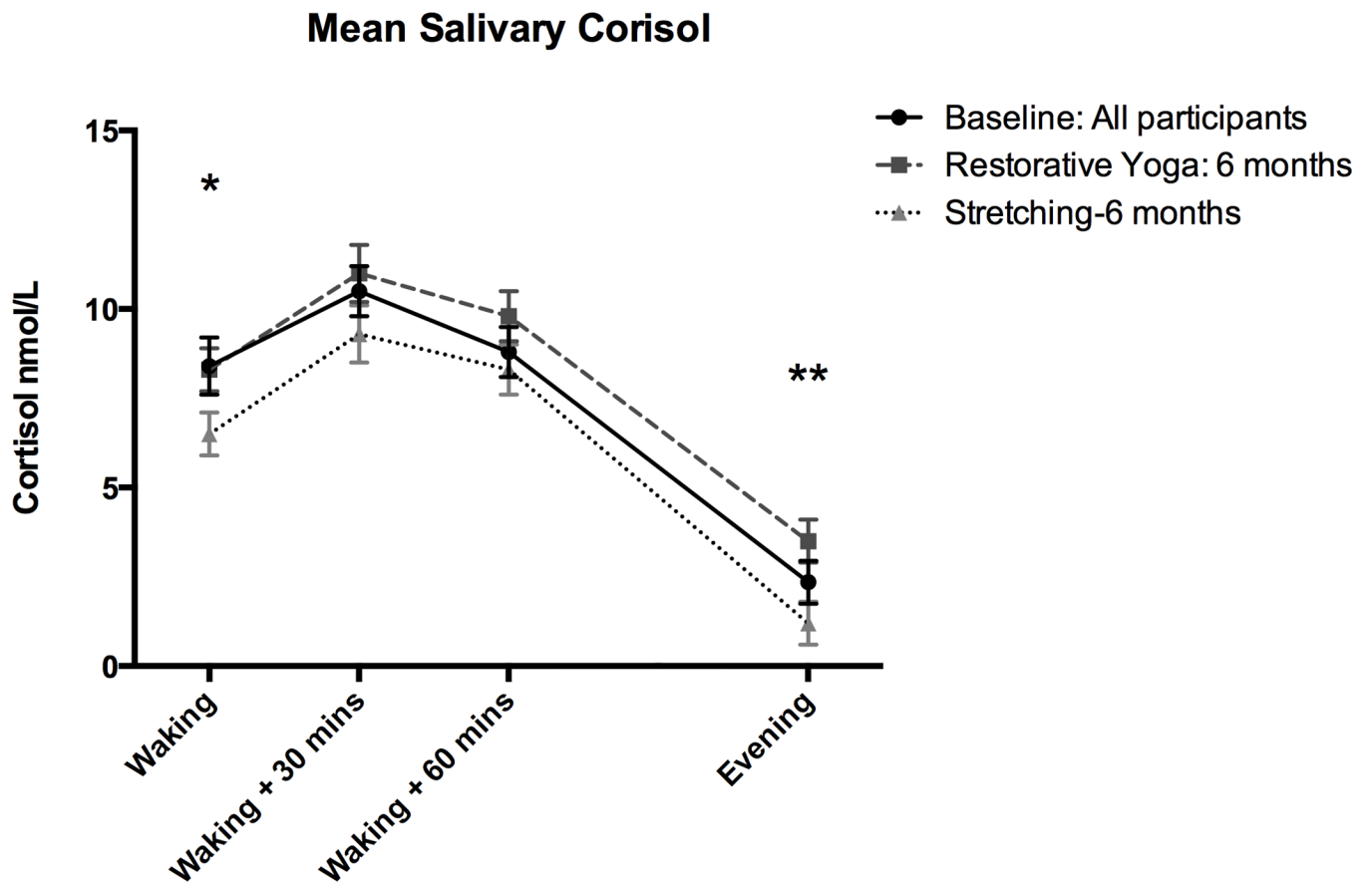


Figure 1.

Mean baseline salivary cortisol for all participants (solid line) at waking, waking +30 minutes, waking + 60 minutes, and evening collection times. Mean 6-month post-intervention salivary cortisol for restorative yoga (dashed line) and stretching (dotted line) at the four collection times. Error bars represent standard error and 6-month post-intervention outcomes are adjusted for medication use, BMI and baseline values. * $p < 0.05$, ** $p < 0.01$ for group differences at 6 months.

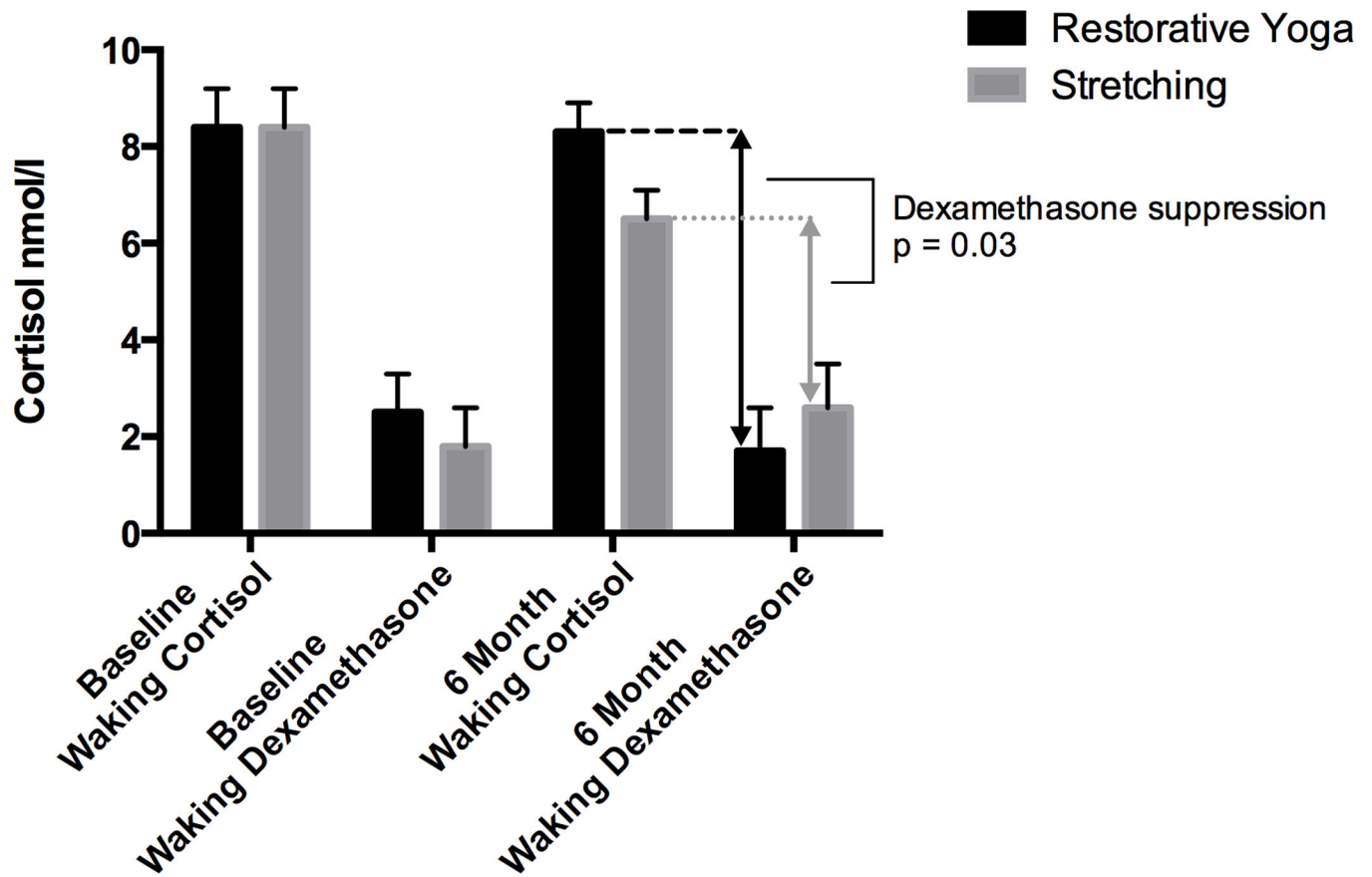


Figure 2.

Mean waking salivary cortisol and mean waking dexamethasone salivary cortisol levels (error bars represent the standard error) at baseline and 6 months. Dotted lines and arrows show the difference in relative dexamethasone suppression between the restorative yoga (black bars) and stretching (grey bars) groups. Error bars represent standard error and 6-month post-intervention outcomes are adjusted for medication use, BMI and baseline values.

Table 1

Population Demographics and baseline measurements of all randomized study participants.

	Restorative Yoga Mean (Standard Deviation) or N (%)	Stretching Mean (Standard Deviation) or N (%)	p value
Demographic Measures:	N=88	N=83	
Age (years)	55 (7)	54 (7)	0.42
Female Gender	65 (74%)	59 (71%)	0.68
White Race	56 (64%)	56 (67%)	0.60
Married	42 (48%)	56 (67%)	0.030
College graduate	57 (65%)	58 (70%)	0.26
Body Mass Index (kg/m ²)	36.0 (7.3)	32.5 (5.9)	<0.001
Antidepressants	13 (15%)	5 (6%)	0.060
Hormone Therapy	3 (4%)	1 (1%)	0.34
Psychosocial Questionnaire measures:	N=88	N=83	
Cohen Perceived Stress Scale	16.4 (6.3)	16.5 (6.6)	0.91
Beck Depression Inventory	8.4 (6.7)	7.8 (5.8)	0.56
Positive States of Mind	3.4 (0.55)	3.3 (0.60)	0.66
Interpersonal Support Evaluation	0.72 (0.49)	0.72 (0.42)	0.94
Life Stress Assessment			
Severity of Stressor	2.9 (0.69)	2.9 (0.78)	0.94
Cognitive Stress	2.6 (1.1)	2.7 (1.1)	0.77
Cortisol measures:	N=72	N=64	
Waking Cortisol	8.4 (6.6)	8.4 (6.7)	0.96
Waking + 30 minutes	11.1 (6.8)	10.4 (4.1)	0.46
Waking + 60 minutes	8.8 (6.7)	8.9 (4.9)	0.93
Evening Cortisol	2.3 (4.8)	2.4 (4.6)	0.86
Mean Cortisol ^a	7.6 (5.4)	7.5 (3.7)	0.86
Peak Cortisol ^b	47.2 (53.6)	56.8 (82.2)	0.41
Cortisol Slope	-6.2 (5.0)	-6.0 (7.5)	0.86
Log Cortisol Slope	-1.7 (0.68)	-1.7 (0.90)	0.93
Cortisol % change	-0.76 (0.20)	-0.67 (0.55)	0.21
Dexamethasone Waking	2.5 (8.6)	1.8 (3.3)	0.52
Waking Cortisol Dexamethasone Suppression	6.3 (8.0)	6.6 (6.4)	0.85

^a Mean Cortisol: cortisol averaged over all 4 time points^b Peak Cortisol: 30 minutes after waking cortisol – waking cortisol

Table 2

Mean salivary cortisol outcomes at baseline and 6 months.

Outcomes	Baseline Mean (SE)		6 Month Mean (SE)		Change at 6 Months (95% CI) ^a		p value	
	Restorative Yoga	Stretching	Restorative Yoga	Stretching	Restorative Yoga	Stretching		Difference b/w groups
Waking Cortisol (nmol/l)	8.4 (0.8)	8.4 (0.8)	8.3 (0.6)	6.5 (0.6)	-0.08 (-1.2-1.1)	-1.9 (-3.2-0.7)**	1.9 (0.2-3.6)*	0.032
Waking + 30 mins (nmol/l)	11.0 (0.7)	10.0 (0.7)	11.0 (0.8)	9.3 (0.8)	0.5 (-1.0-1.9)	-1.5 (-3.0-0.1)	1.9 (-0.3-4.2)	0.090
Waking + 60 mins (nmol/l)	8.8 (0.7)	8.8 (0.7)	9.8 (0.7)	8.3 (0.7)	1.0 (-0.4-2.3)	-0.5 (-1.9-1.0)	1.4 (-0.6-3.5)	0.16
Evening Cortisol (nmol/l)	2.3 (0.6)	2.4 (0.6)	3.5 (0.6)	1.2 (0.6)	1.2 (0.1-2.3)*	-1.2 (-2.3-0.0)	2.3 (0.7-4.0)**	0.005
Mean Cortisol (nmol/l)	7.7 (0.6)	7.5 (0.6)	8.2 (0.5)	6.3 (0.6)	0.6 (-0.4-1.7)	-1.3 (-2.4-0.2)**	1.9 (0.3-3.5)*	0.017
Peak Cortisol	47.0 (8.1)	56.0 (8.6)	54.0 (7.0)	54.0 (7.4)	2.5 (-11.3-16.3)	2.3 (-12.4-17.0)	0.2 (-20.5-20.9)	0.98
Cortisol Slope	-6.2 (0.7)	-6.0 (0.8)	-5.0 (0.5)	-5.2 (0.6)	1.1 (0.1-2.1)*	0.9 (-0.2-2.0)	0.2 (-1.3-1.7)	0.80
Log Cortisol Slope	-1.7 (0.09)	-1.7 (0.1)	-1.4 (0.1)	-1.7 (0.1)	0.2 (0.06-0.4)**	0.01 (-0.2-0.2)	0.2 (-0.04-0.5)	0.095
Cortisol % change	-0.8 (0.05)	-0.7 (0.05)	-0.6 (0.04)	-0.8 (0.04)	0.08 (0.001-0.2)*	-0.032 (-0.1-0.05)	0.1 (-0.01-0.2)	0.064
Dexamethasone Waking	2.5 (0.8)	1.8 (0.8)	1.7 (0.9)	2.6 (0.9)	-0.5 (-2.2-1.3)	0.4 (-1.4-2.3)	-0.9 (-3.5-1.7)	0.50
Waking Cortisol Dexamethasone Suppression	6.3 (0.9)	6.5 (0.9)	6.8 (0.7)	4.4 (0.7)	0.4 (-1.1-1.8)	-2.0 (-3.4-0.5)**	2.3 (0.2-4.4)*	0.029

^a Statistical analysis models have been adjusted for site, BMI, medication use and baseline values.

SE: Standard Error.

* p<0.05,

** p<0.01 for changes within groups.

Table 3

Mean psychosocial outcome measures at 6 months and 1 year.

Outcomes	Baseline mean (SE)			Change at 6 Months (95% CI) ^a			Change at 1 year (95% CI) ^a			
	Restorative Yoga	Stretching	Restorative Yoga	Stretching	Difference b/w groups	p value	Restorative Yoga	Stretching	Difference b/w groups	p value
PSS	16 (0.7)	16 (0.7)	0.7 (-0.6-1.9)	-0.8 (-2.1-0.5)	1.5 (-0.4-3.3)	0.11	0.05 (-1.2-1.3)	-1.9 (-3.3-0.6)*	2.0 (0.1-3.9)*	0.042
BDI	8.3 (0.7)	7.8 (0.7)	-0.98 (-2.1-0.2)*	-1.4 (-2.7--0.2)	0.4 (-1.3-2.2)	0.61	-1.0 (-2.2-0.3)	-1.9 (-3.2-0.6)*	1.0 (-0.9-2.8)	0.31
PSOM	3.4 (0.06)	3.3 (0.06)	0.008 (-0.08-0.1)	0.07 (-0.03-0.2)	-0.06 (-0.2-0.08)	0.39	0.04 (-0.05-0.1)	0.2 (0.07-0.3)*	-0.1 (-0.3-0.01)	0.069
ISEL Summary Score	0.72 (0.05)	0.72 (0.05)	-0.01 (-0.07-0.04)	-0.02 (-0.08-0.04)	0.009 (-0.07-0.09)	0.82	-0.002 (-0.07-0.07)	-0.04 (-0.1-0.04)	0.04 (-0.07-0.1)	0.50
LSA Severity of Stressor	3.0 (0.1)	3.0 (0.1)	-0.2 (-0.4-0.04)	-0.6 (-0.8--0.4)**	0.4 (0.1-0.7)	0.007				
LSA Cognitive Stress	2.6 (0.1)	2.7 (0.1)	-0.1 (-0.32-0.08)	-0.5 (-0.7-0.3)**	0.4 (0.06-0.7)	0.019				

PSS: Perceived Stress Scale, BDI: Beck Depression Index, PSOM: Positive States of Mind Scale, ISEL: Interpersonal Support Evaluation, LSA: Life Stress Assessment, and SE: Standard Error.

^a Statistical analysis models have been adjusted for site, BMI, medication use and baseline values.

* p<0.05,

** p<0.01 for changes within groups.

Table 4

Spearman partial correlations of the difference from baseline to 6 months in: cortisol, the ISEL Summary Score and the ISEL Belonging subscale.

	Restorative Yoga		Stretching	
	ISEL-Belonging	ISEL-Summary Score	ISEL-Belonging	ISEL-Summary Score
Waking Cortisol (nmol/l)	-0.26	-0.22	-0.44**	-0.28
Waking + 30 mins (nmol/l)	-0.01	0.005	-0.08	0.09
Waking + 60 mins (nmol/l)	0.06	0.04	-0.06	0.004
Evening Cortisol (nmol/l)	-0.008	-0.07	-0.07	0.02
Mean Cortisol	-0.09	-0.07	-0.23	-0.10
Peak Cortisol (30 mins -waking)	0.17	0.16	0.41**	0.37*
Cortisol Slope	0.36*	0.37**	0.43**	0.23
Log Cortisol Slope	0.23	0.16	0.41**	0.31*
Cortisol % change	0.24	0.20	0.39**	0.34*
Dexamethasone Waking	-0.15	-0.07	0.05	0.23
Waking Cortisol Dexamethasone Suppression	-0.23	-0.22	-0.40**	-0.34*

ISEL: Interpersonal Support Evaluation,

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p<0.05,

**
p 0.01.