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Stress, Inflammation, and Yoga Practice

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Abstract

Objective—To address the mechanisms underlying hatha yoga's potential stress-reduction benefits, we compared inflammatory and endocrine responses of novice and expert yoga practitioners before, during, and after a restorative hatha yoga session, as well as in two control conditions. Stressors before each of the three conditions provided data on the extent to which yoga speeded an individual's physiological recovery.

Methods—50 healthy women (mean age=41.32, range=30–65), 25 novices and 25 experts, were exposed to each of the conditions (yoga, movement control, and passive-video control) during three separate visits.

Results—The yoga session boosted participants' positive affect compared to the control conditions, but no overall differences in inflammatory or endocrine responses were unique to the yoga session. Importantly, even though novices and experts did not differ on key dimensions including age, abdominal adiposity, and cardiorespiratory fitness, novices' serum IL-6 levels were 41% higher than those of experts across sessions, and the odds of a novice having detectable CRP were 4.75 times as high as that of an expert. Differences in stress responses between experts and novices provided one plausible mechanism for their divergent serum IL-6 data; experts produced less LPS-stimulated IL-6 in response to the stressor than novices, and IL-6 promotes CRP production.

Conclusion—The ability to minimize inflammatory responses to stressful encounters influences the burden that stressors place on an individual. If yoga dampens or limits stress-related changes, then regular practice could have substantial health benefits.

Keywords

yoga; inflammation; psychoneuroimmunology; complementary medicine; IL-6; CRP

Inflammation is a robust and reliable predictor of all-cause mortality in older adults (1). Proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) play a role in cardiovascular disease, type II diabetes, arthritis, osteoporosis, Alzheimer's disease, periodontal disease, and frailty and functional decline (2–3). In addition, inflammation is now regarded as a risk factor for most cancers because of the

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evidence that inflammation influences tumor promotion, survival, proliferation, invasion, angiogenesis, and metastases (4).

Behavioral lifestyle factors can substantially influence inflammation. Obesity has been characterized as a state of chronic inflammation because of the elevated plasma levels of IL-6, TNF-α, and CRP (5). One obvious mechanism is provided by the fact that adipocytes (fat cells) are capable of producing and secreting IL-6 and TNF-α; in fact, up to 30% of IL-6 may be derived from adipose tissue (6).

Physical activity is also an important behavioral cofactor; people who describe themselves as active have lower levels of inflammatory biomarkers than their sedentary counterparts (7). Indeed, when physical or cardiorespiratory fitness is assessed rigorously and objectively by maximal exercise testing, fitness is inversely associated with inflammation, even after adjusting for confounds including age, smoking, medications, and visceral fat (8–11).

Although regular physical activity is associated with lower levels of IL-6 and other proinflammatory cytokines, acute exercise transiently boosts production and release of IL-6 from skeletal muscles; the IL-6 that is released during physical activity inhibits TNF-α production and can induce IL-10 production, one mechanism underlying exercise's anti-inflammatory function (1). Lower levels of circulating IL-6 at rest as well as following exercise appear to be the normal adaptation to training (12)

In addition to exercise and obesity, behavior affects inflammation through other pathways; even relatively modest levels of anxiety and depressive symptoms can raise proinflammatory cytokine production (13). Additionally, psychological stressors can directly provoke transient increases in proinflammatory cytokines (14–15), and chronic stressors have been linked to sustained overproduction of IL-6 (16–17).

Yoga's reputation for stress reduction and mental health benefits has bolstered its popularity in recent years, and data from randomized trials suggest that yoga reduces symptoms of anxiety and depression (18–19). Hatha yoga, the most common form practiced in the western world, combines body postures or *asanas*, breath control or *pranayama*, and meditation (20). Mechanistic explanations for yoga's potential mental and physical health benefits have highlighted reductions in sympathetic nervous system tone (21–22), and increases in vagal activity (22), both of which could have favorable endocrine and immune consequences, including lower inflammation.

In fact, one recent randomized trial suggested that yoga might have positive benefits for inflammation; 9 heart failure patients randomized to a two-month hatha yoga intervention showed a 22% reduction in IL-6 and a 20% reduction in CRP compared to minimal change in the 10 patients who received standard medical care (23). In contrast, CRP did not change following a 6-week nonrandomized trial in 33 individuals both with and without established coronary artery disease, but the group did show significant reductions in blood pressure, heart rate, and body mass index (BMI) (24). Surprisingly few studies have attempted to relate endocrine or immune function to yoga practice, even though some hatha yoga postures are characterized as immune enhancing or restorative (25).

We assessed cardiovascular, inflammatory, and endocrine responses in novice and expert yoga practitioners before, during, and after a hatha yoga session, as well as in two control conditions. To test yoga's restorative potential, stressors preceded each of the three conditions, providing data on the extent to which yoga speeded an individual's physiological recovery. In addition, tape stripping a small area of forearm skin before each of the conditions provided data on the course of skin barrier repair, a stress-sensitive process modulated by both cortisol and cytokine production (26–27).

The ability to minimize autonomic and inflammatory responses in stressful situations undoubtedly influences the burden that stressors place on an individual. Thus, we designed this study to assess yoga's ability to promote recovery from a stressor. We elected to conduct the yoga session after the stressor, rather than prior to the stressor, for several reasons. First, anticipation of a stressor following the yoga session could reduce participants' ability to fully relax and concentrate during the yoga session, particularly among novices; completing the stressor prior to the yoga session could allow for a more relaxing yoga experience, providing greater power to detect effects of yoga. In addition, our ability to track changes in physiological markers of interest *during* the yoga session was improved by eliciting a physiological response prior to the session. Finally, using a stressor prior to the yoga session allowed us to examine whether regular yoga practice resulted in differential magnitude of reactivity to the stressor, independent of the effects of a recent yoga session.

We hypothesized that: (1) experienced yoga practitioners would have lower levels of inflammation, and smaller autonomic, endocrine, and inflammatory responses to the stressors than novices. (2) During and following the yoga session, subjects would demonstrate more rapid declines (recovery) in stress hormones and proinflammatory cytokine production, and better skin barrier repair than evidenced following either of the control conditions. Mood measures would reflect greater positive change following yoga compared to the control conditions.

METHOD

Participants

Women were recruited through online ads and notices posted in yoga studios. All women participated in some form of hatha yoga. We excluded women who were taking medications with obvious immunological or endocrinological consequences, as well as individuals who had chronic health problems with implications for these systems (e.g., cancer, recent surgeries, diabetes, etc.). Additional exclusion criteria included smoking, use of statins, beta blockers, psychoactive drugs, excessive alcohol use, convulsive disorders, or a BMI ≥ 30.

The average age of the final sample of 50 women who completed all 3 visits was 41.32 (SD=10.33, range=30–65); 44 were white, 3 were African American, 2 were Native American, 1 was Asian, and all had at least some college education. One expert and one novice dropped out after one session because of time constraints. Data were collected between August, 2005 and October, 2008.

Screening Session

Participants were screened and classified as novices versus experts using a two-step process. First, participants completed an online screening questionnaire assessing the type, frequency, and duration of yoga practice over the past year and over their lifetimes. Women were classified as novices if they had participated in yoga classes or home practice with yoga videos for 6 – 12 sessions. Experts had practiced yoga regularly 1–2 times per week (75–90 min sessions) for at least 2 years, and at least 2 times per week for the past year. Others were rated as intermediate and deemed not eligible for further participation. Each participant was classified by two raters. Raters conferred when classifications were discrepant, obtaining additional information as needed to reach consensus.

The screening session was used to assess yoga skills, flexibility, and cardiovascular fitness. Participants performed 8 selected poses under the guidance of an experienced instructor, blind to their reported experience, who evaluated their form to assure that novices and experts had skills commensurate with their self-reports. Each pose was rated on a 1–5 scale, focusing on

5–7 indicators of form specific to the pose, with higher ratings indicating better form. Four women were excluded because their self-report indicated expert practice, but they showed lack of familiarity and/or limited ability to perform poses during the screening session. To further objectively characterize hamstring and low back elasticity, participants completed the sit-and-reach test, a common flexibility test (28).

Sagittal abdominal diameter (SAD) measurements provided data on the total amount of abdominal fat. Validational studies using computerized axial tomography and dual-energy X-ray absorptiometry have demonstrated its utility as a noninvasive central adiposity measure (29).

Cardiopulmonary endurance was evaluated during a maximal graded cycle ergometry exercise test, starting at 25 watts and increasing by 25 watts every two minutes, with continuous monitoring via 12-lead EKG (MedGraphics Cardio2, Cardio Perfect). Maximum oxygen consumption (VO_2max) was calculated from 10-second averages of breath-by-breath expired air (MedGraphics Cardio2, Breeze Suite).

Three Clinical Research Center (CRC) Visits

Each participant completed three CRC sessions (yoga and two control conditions), scheduled at least 2 weeks apart. The order of the three conditions was randomly assigned. Each visit followed the timeline, illustrated in Figure 1, differing only in the condition randomized for that visit; participants returned for a 30 minute follow-up the morning after each session. On arrival, participants completed questionnaires and ate a standardized breakfast after fasting since midnight. A heparin well was placed in one arm for subsequent serial blood draws, and remained in place until the end of each 6-hour session. Next they rested in a hospital bed for a 20-minute relaxation period, and then provided baseline blood and saliva samples.

A tape-stripping session followed the baseline blood samples (26,30). Skin barrier disruption was evaluated by measuring transepidermal water loss (TEWL), as described under skin barrier studies.

During the next 12–14 minutes subjects participated in a Stroop task which served both as a mild stressor and an unobtrusive mood measure. Two additional stressors (a cold pressor test and mental arithmetic), described below, preceded each of the three conditions. Catecholamine samples were drawn from the catheter twice during each of the conditions and again at the end, as shown in Figure 1; we had successfully piloted catheter placement so that we could obtain blood samples during the conditions without disturbing the subjects or the condition routine. To control for the known positional effects in stimulating catecholamine release, subjects spent the same amount of time lying down in the movement and video conditions before each of these blood draws as they did in the yoga session (in the hospital bed for the former, on the yoga mat for the latter).

Following the hour and 15-minute intervention and blood draws, participants completed another Stroop task. Subjects remained in the CRC until approximately 1:30 PM, with additional TEWL measurements of the tape-stripped sites, as well as regular salivary cortisol sampling and a standardized lunch. Participants returned at 7:30 AM the following morning for a final blood draw.

Hatha yoga condition—Iyengar yoga, the form of hatha yoga used in this study, emphasizes the use of props to help students achieve precise postures safely and comfortably according to their particular body types and needs. The screening sessions and the yoga condition sessions were directed by four experienced yoga teachers following a script. The poses were chosen based on their purported relationship to immune function and/or restorative effects (25). A

restorative session was selected rather than a vigorous sequence in order to best promote recovery from the stressor. In addition, we wanted poses that could be performed without undue strain by both novice and experienced practitioners so we could compare endocrine and inflammatory changes in the two groups.

The poses used were (in order) Supta Baddha Konasana (Reclining Bound Angle Pose), Adho Mukha Svanasana (Downward Facing Dog), Supported Uttanasana (Intense Forward Stretch), Parsvotanasana (Intense Side Stretch Pose), Prasarita Padottanansana (Wide-Legged Forward Bend), Janu Sirsasana (Head to Knee Pose), Bharadvajasana (Simple Seated Twist Pose), Viparita Karani (Restful Inversion), Supported Setu Bandha Sarvanagasana (Bridge Pose), and Savasana (Corpse Pose). Blood draws occurred during the last two minutes of Supta Baddha Konasana (pose held 10 minutes), Viparita Karani (10 minutes), and Savasana (15 minutes).

Control conditions—Walking on a treadmill at .5 miles per hour was used to control for general physical movement/cardiovascular expenditure because it best approximated the heart rates during the restorative yoga session. To match the lower heart rate, women also rested supine on a bed for several minutes after walking, before and after getting their blood drawn.

The second control condition, a neutral video that did not include any music, allowed us to contrast the effects of yoga with no activity. It included a sequence on how to design physics experiments for a high school classroom, as well as segments from two lectures on polymers and quantum mechanics.

Self-Report Measures

During the screening session participants completed the version of the Food Frequency Questionnaire (FFQ) validated for the Women's Health Initiative (31). Participants reported the type, frequency, and quantity of foods and beverages consumed in the past 90 days.

The Pittsburgh Sleep Quality Index assessed sleep quality and disturbances over a one-month interval; it has good diagnostic sensitivity and specificity in distinguishing good and poor sleepers (32). Completed during the screening session, we also assessed sleep prior to and following each visit.

Evidence suggests that the scales of the Mood and Anxiety Symptom Questionnaire (MASQ) measure anxiety and depression well, with limited overlap, compared with other self-report measures (33–34). The MASQ was administered during the screening session and at the beginning of each of the three admissions.

The Positive and Negative Affect Schedule (PANAS) includes two 10-item mood scales (35). The positive and negative scales are largely uncorrelated, and show good convergent and discriminant validity when related to state mood scales and other variables (35). Several additional words were added to better capture low positive affect: happy, satisfied, disappointed, discouraged, low, sad (36). The PANAS was administered during the screening session, as well as three times during each CRC visit (at baseline, after the intervention, and at the session's end).

Stressors

For the emotional Stroop, participants name the color in which negative or threatening words are printed. Following work by Mogg et al. (37), we used 60 words (divided into three sets) from their lists in each of the following categories: anxiety- and depression-relevant negative words, positive words, and neutral household words. Interference scores were calculated as previously described (30).

Widely used in behavioral and psychophysiological research, the cold pressor provides a reliable and safe way to induce mild acute pain and provoke endocrine and inflammatory changes (15,30). After sitting for a 15-minute adaptation period, participants immersed their right foot for 2 minutes in warm (37° C) water, and then immersed their foot in a pan of 4° C water for 1 minute (38).

After the cold pressor, the participant performed mental arithmetic serial subtraction tasks for 5 minutes. To maintain a high level of task difficulty and involvement, the subtrahend was reset each minute based on performance in the preceding minute, such that better performance led to more demanding subtraction (39). When participants made a mistake, the experimenter administering the task said “error,” and gave them the correct number.

Endocrine Data

All cortisol and catecholamine samples for a subject were frozen after collection and analyzed within the same assay run after the participant had completed the study. Assay methods are described in prior publications (30,39).

Skin Barrier Assessment

Cellophane tape stripping, a common dermatological paradigm for studying restoration of the skin barrier, was used to examine whether the time necessary for recovery from minor physical insults varied by condition or yoga expertise. Measurement of the rate of transepidermal water loss (TEWL) through human skin provides a noninvasive method to monitor changes in the skin’s barrier function as previously described (30). TEWL was measured twice during the session using a computerized evaporimetry instrument, the DermaLab® (CyberDERM, Media, PA), and barrier recovery was calculated (26).

Cardiovascular Data

Participants wore a Polar™ heart rate monitor which sampled beat by beat intervals. Heart rate was monitored throughout the yoga and activity control exercise sessions.

Immunological Data

We assayed IL-6, the soluble IL-6 receptor (sIL-6r), TNF-α, CRP, as well as LPS-stimulated production of IL-6 and TNF-α. Elevated levels of these cytokines, including the sIL-6r, are associated with an activated inflammatory response. Serum levels of TNF-α, IL-6, and the sIL-6r were assayed using Quantikine High Sensitivity Immunoassay kits (R&D), per kit instructions (16,40).

In addition, supernatants from PBLs stimulated with 5μg/ml lipopolysaccharide (LPS) for 72 h were assayed for IL-6 and TNF-α using ELISA kits (B–D Pharmingen). Unstimulated cells incubated in media were used as a control. The assay was run according to kit instructions. Blood samples were obtained prior to each condition in the morning, immediately following the two stressors, after the condition, and at the end of the day for stimulated cytokine production. Because the time course for stress-induced changes in serum cytokine levels is slower than for stimulated cytokine production (15), we omitted the immediate post-stressor sample for serum cytokines.

The high sensitivity C-reactive protein (hsCRP) assay was performed using chemiluminescence methodology with the Immulite 1000 (Siemens Medical Solutions, Los Angeles, Ca.) The lowest level of detection is .3 mg/dL. Intra-assay coefficient of variation is 5.1% and inter-assay coefficient variation is 7.3%.

Statistical Analyses

Mixed models from SAS 9.1 (SAS Institute Inc, Cary, NC) were used to analyze differences between novices and experts in the repeated measures across the three visits, and differences between time points within visits. The three-way interaction of expertise by condition by time, as well as all lower order interactions and main effects were considered; visit order number was included as a possible confounding variable. For all cytokine analyses, the MASQ depression score from each visit and the participant's age, $V0_2$max, and SAD were included as additional possible confounding variables. A heterogeneous Toeplitz covariance structure was used to account for the unequal distance between time points and allow for some flexibility in the estimation of variances/covariances parameters without reducing power by allowing for unnecessary complexity. Application of the Kenward-Roger correction (41) to the degrees of freedom brought Type I errors rates back to the nominal level (42), sometimes resulting in noninteger values for degrees of freedom. Log (base 10) transformations were used for serum IL-6 and TNF-α, LPS-stimulated TNF-α production, epinephrine, and norepinephrine to correct for nonnormality. The hsCRP values and the PANAS negative mood scale could not be normalized and thus were dichotomized and analyzed with logistic regression. All tests used a 2-sided, α = .0.5 significance level; when necessary, p-values for unplanned multiple comparisons were adjusted using the Tukey-Kramer procedure (43). For planned comparisons with multiple tests, the family-wise Type I error rate was set at α = .15 and a Bonferroni adjustment was used to determine critical p-values for individual tests.

Results

As shown in Table 1, novice and expert practitioners did not differ on key variables that have been associated with inflammation. Seven women in each of the groups were postmenopausal. As a consequence of our stringent exclusion criteria, overall medication use was low; novices and experts did not differ in the proportion reporting use of aspirin, ibuprofen, or other over-the-counter analgesics, *p*s > .39, birth control pills, hormone replacement therapy, omega-3 supplements, or a daily multivitamin, *p*s > .23.

Mean ratings of novices' (21.92, *SD*=4.93) and experts' (31.86, *SD*=4.83) ability to perform common yoga poses, assessed during the screening session, were clearly different, $F(1,48) = 51.82$, $P < .000$. Similarly, novices (*M*=31.88, *SD*=7.77) had substantially less hamstring and low back flexibility than experts (*M*=41.81, *SD*=5.19), producing the expected differences on the sit-and-reach test, $F(1,49) = 27.91$, $P < .001$.

Self-Report and Behavioral Data

There was a significant time by condition interaction for PANAS positive affect, $F(4, 198) = 14.49$, $P < .001$ (Figure 2). Participants' positive mood scores increased following yoga, decreased following the video, and were unchanged following movement.

Due to a lack of variability in PANAS negative affect scores, values were dichotomized as "at the minimum" (*n* = 280, 62.36%) and "above the minimum" (*n* = 169, 37.64%). Logistic regression on the transformed values was conducted with Generalized Estimating Equations (GEEs) using an unstructured covariance matrix to account for the repeated visits. Results revealed a significant time main effect, $X^2(1) = 14.35$, $P < .001$, and a significant time by yoga expertise interaction, $X^2(2) = 5.45$, $P < .02$. Experts were more apt to report negative affect above the minimum at the end of the conditions than novices.

Stroop interference scores showed no differences for either the positive or negative emotion words as a function of time, expertise, condition, or their interactions, all *P*s > .24. However, as illustrated by the heart rate increase (Figure 3), the Stroop did function as a mild stressor.

Sleep

Novices and experts did not differ in hours of sleep the night before the CRC visits, $F(1,47.8) = 0.63$, p = .43. However, after controlling for the previous night's sleep, novices ($M = 6.75$, $SD = .93$) reported significantly fewer hours of sleep than experts ($M = 7.24$, $SD = 1.00$) following the 6-hour days in the CRC, $F(1,46) = 5.94$, $P = .02$

Skin Barrier Repair

The speed of skin barrier repair following tape stripping did not differ as a function of expertise, condition, time, or their interactions, all *P*s > .08.

Heart Rate

Analysis of participants' heart rates revealed significant main effects for time and condition, as well as significant interactions between time and yoga expertise, $F(7, 247) = 3.97$, $P < .001$, and time and condition, $F(14, 359) = 15.47$, $P < .001$. Comparisons were planned between novices and experts for heart rate during the stressor, as well as three values collected well into the condition. Using a critical p-value of .038, experts had lower heart rates than novices during the stressor, $t = 2.30$, $P = .025$ (Figure 3); no other tested time points reached even an uncorrected level of significance, all *P*'s > .08. Additionally, the degree of change from the Stroop to the stressors differed between the expertise levels, $t=2.16$, $P = .035$, with novices exhibiting larger responses to the stressors than experts. For the time by condition interaction, a critical *P*-value of .025 was used to compare yoga to the other two activities at time points during and after the condition. Participants' heart rate during the yoga condition was higher than when in the video condition 10 minutes into the intervention, $t=9.61$, $P < .001$, and lower than the video condition at the end of the intervention, $t=3.05$, $P = .004$; similarly, yoga was higher than movement 10 minutes into the condition, $t=2.41$, $P = .02$, and lower post-condition, $t=4.96$, $P < .001$. However, as planned in the experimental design, the overall mean heart rate during the yoga condition did not differ from that in the movement condition, $P = .17$.

Cortisol and Catecholamines

The significant time effect for cortisol reflected the normal diurnal fall across the morning as well as the usual post-lunch increase, $F(6, 371) = 80.21$, $P < .001$. There were no significant group or condition effects or interactions.

There was a significant condition by time interaction for norepinephrine, $F(10, 318) = 8.08$, $P < .001$. Similar to the heart rate data, participants' norepinephrine response after 10 minutes of the yoga was significantly higher than the same interval in either the video, $F(1,121) = 27.42$, $P < .001$, or the movement condition, $F(1,121) = 12.77$, $P < .001$. Novices and experts did not differ in norepinephrine production, $F(1, 46.1) = .34$, $P = .56$. The significant time effect for epinephrine reflected a post-stressor peak value for the session, followed by a decrease through the conditions, $F(5,341) = 12.62$, $P < .001$. In addition, experts had higher overall levels of epinephrine than novices, $F(1,48.5) = 8.26$, $P = .006$, a surprising finding in view of the norepinephrine and heart rate data. Examination of raw data showed that 4 experts and 1 novice were outliers across time; comparisons between these individuals and the remainder of the sample showed significantly fewer hours of sleep prior to the three visits, $F(1,49)=9.52$, $P=.003$, but no differences in affect, other health behaviors, or inflammation.

Serum Cytokines and hsCRP

Experts had lower overall IL-6 serum levels than novices, $F(1,45.7) = 4.98$, $P = .03$. Indeed, novices' average IL-6 values were 41% higher than those of experts (Figure 4). Additionally, although the group effect did not reach traditional significance levels for either sIL-6r, *F*

(1,43.5)=3.55, P =.07, or TNF-α, F(1,45.3)=2.25, P =.14, both were in the expected direction, with lower levels of inflammation in yoga experts compared to novices.

Significant time effects were observed for all serum cytokines, all Fs > 16, all Ps < .001. Specifically, we observed elevations in IL-6 at the sessions' end compared to the following morning, t=12.40, adj. P < .001 (Figure 4). For sIL-6r, levels were higher at the sessions' end, t=4.90, adj. P < .001, and the next morning, t=6.11, adj. P < .001, compared to baseline. Although TNF-α did not increase at the sessions' end, it did rise the following morning, t=4.76, adj. P < .001.

We assessed hsCRP once at baseline at each of the three visits; 43% of the values (n = 65) were below the assay's detectable lower bound of .3 mg/dL, and thus hsCRP was dichotomized as undetectable/detectable. The logistic regression with GEEs analysis showed that the odds of a novice having a detectable hsCRP level were 4.75 times that of experts (β = −1.55, P = .009).

LPS-Stimulated Cytokine Production

The expertise by time interaction for stimulated IL-6 production, F(4,275) = 2.57, P < .04, is shown in Figure 5. A planned comparison showed that experts produced less IL-6 in response to the stressors than novices (M_{diff} = 26076, SE_{diff} = 13104), F(1,53.1) = 3.96, P = .05. No other time points approached significance (all P's > .14). Stress-induced LPS-reactivity was significantly correlated with total serum IL-6, r=.33, P=.02.

In the condition by time interaction for TNF-α, F(8,268) = 2.03, P = .04, values obtained immediately following the stressor were lower in the yoga condition, compared to the video and movement conditions combined (M_{diff} = .09, SE_{diff} = .04), F(1,133) = 2.29, P = .02. Values obtained immediately following the stressor were lower in the yoga condition, compared to the video and movement conditions combined (M_{diff} = .09, SD_{diff} = .36), F(1,137) = 4.90, P = .03.

To identify individuals producing high vs. low levels of inflammatory markers across the assay battery, median splits were applied to the average baseline values of our six markers: serum IL-6, TNF-α, sIL-6r, and hsCRP, and LPS-stimulated IL-6 and TNF-α production. Individuals falling into the low or high category on each marker were given a score of 0 or 1, respectively, and the summed values were grouped into low (0 or 1), medium (2 or 3) or high (4–6). Novices and experts showed very different patterns, $\chi^2(2)=13.91$, P < .001 (Figure 6); 60% of the novices were high producers compared to only 24% of experts, while 40% of experts were low producers and 0% of the novices.

Discussion

Emotional and physical stressors activate immune and endocrine pathways that can enhance proinflammatory cytokine production. This study, designed as an initial investigation to address the mechanisms underlying yoga's potential stress-reduction benefits, revealed substantial differences between novices and experts. Novices' average serum IL-6 levels were 41% higher than those of experts, and the odds of a novice having detectable hsCRP were 4.75 times as high as that of an expert.

The differences in stress responses between experts and novices provided one plausible mechanism for their divergent serum IL-6 data. Experts produced less LPS-stimulated IL-6 in response to the stressor than novices. Monocytes/macrophages are a major source for serum IL-6, and thus greater stress-related IL-6 production by these cells would contribute to the larger downstream IL-6 pool; moreover, IL-6 has a central role in promoting CRP production

(9). Furthermore, across the battery of inflammatory assays, 60% of novices were high producers compared to only 24% of experts, and 40% of experts were low producers compared to 0% of novices. These data suggest that regular yoga practice may reduce inflammation below levels predicted by such key risk factors as age, abdominal adiposity, cardiorespiratory fitness, and depressive symptoms.

In spite of these notable baseline group differences in inflammation, there were no significant differences between expert and novice practitioners in stress-induced LPS-stimulated production of TNF-α, and the groups did not differ in their stress-induced or baseline levels of cortisol and catecholamines, or in serum cytokine responses to the sessions. There are several explanations for these discrepancies. For example, a meta-analysis of cytokine responses to laboratory stressors suggested that while IL-6 is responsive to acute psychological stressors, TNF-α is not (15), and we are unaware of any data demonstrating reliable acute stress-related changes in sIL-6r. Similarly, although exercise reliably induces increases in IL-6, TNF-α does not increase with exercise; furthermore, IL-6 can inhibit LPS-induced TNF-α production (1), consistent with the declines observed in LPS-induced TNF-α production following the interventions.

Our sessions began early, when cortisol is falling from its diurnal peak, and an intervention would have had to substantially accelerate the rate of decline to show efficacy; indeed, given its half-life, change within an hour or two would require that our intervention had substantially accelerated cortisol's metabolic breakdown. Furthermore, cortisol adversely affects skin barrier homeostasis (27), and thus our morning session's timing was problematic for both of these secondary measures.

Despite the fact that novices' serum IL-6 levels were 41% higher than those of experts, the magnitude of the serum IL-6 change from baseline to post-intervention did not differ between experts and novices. Exercise-related IL-6 increases are strongly predicted by mode, intensity, and duration of exercise; in addition, more fit individuals have lower basal IL-6 and smaller responses to exercise (12). The fact that novices and experts did not differ in terms of their VO_2max and both were subjected to exactly the same intensity and duration in exercise in the yoga and movement conditions meant that any differential change would be very difficult to detect, particularly against the background of the typical morning rise from IL-6's diurnal nadir (44).

The yoga session boosted participants' positive affect compared to decreases in the movement and video control conditions, but we did not find differences in inflammatory or endocrine responses that were unique to the yoga session. The modest changes produced by our low intensity stressor may not have provided an optimal test of yoga's potential restorative benefits, a limitation of the study. In addition, by designing the yoga portion of the study to be appropriate for novices and experts, we were unable to include some more advanced and purportedly more powerful poses such as full inversions (25).

A central tenet of yoga, meditation, and related practices is the idea that training can reduce stress responses, and several studies have provided supportive data. For example, participants in a compassion meditation randomized trial who practiced more frequently had a smaller rise in IL-6 in response to a laboratory stressor than those who practiced less (45). Performance of 20 minutes of Tai Chi Chih, described as "meditation through movement," acutely diminished preejection period, an index of sympathetic activity, compared to a passive rest control (46). Individuals who had long-term training in elicitation of the relaxation response differed from novices in patterns of gene expression, and pre-post comparisons following 8 weeks of training produced some of the same differences in novices, including the NF-κB cascade, a key pathway for proinflammatory cytokine production (47). Our selection criteria required that our expert

practitioners had practiced yoga for at least two years; it is possible that some of the benefits of yoga may only become evident after years of regular practice.

The ability to minimize autonomic and inflammatory responses to stressful encounters influences the total burden that stressors place on an individual. Larger, more frequent, or more persistent stress-related changes in inflammation would have negative consequences for health. Accordingly, our data provide a window on the pathways through which yoga or related practices may affect physiological functioning and health. If yoga dampens or limits stress-related immunological, endocrinological, and cardiovascular changes, then regular practice could have substantial health benefits.

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Acronyms

BMI	body mass index
CRC	Clinical Research Center
CRP	C-reactive protein
FFQ	Food Frequency Questionnaire
GEEs	Generalized Estimating Equations
HR	heart rate
hsCRP	high sensitivity C-reactive protein
IL-6	interleukin 6
LPS	lipopolysaccharide
MASQ	Mood and Anxiety Symptom Questionnaire
PANAS	Positive and Negative Affect Scale
PBLs	peripheral blood leukocytes
SAD	sagittal abdominal diameter
sIL-6r	soluble IL-6 receptor
TEWL	transepidermal water loss
TNF-α	tumor necrosis factor-alpha
VO_2max	maximum oxygen consumption

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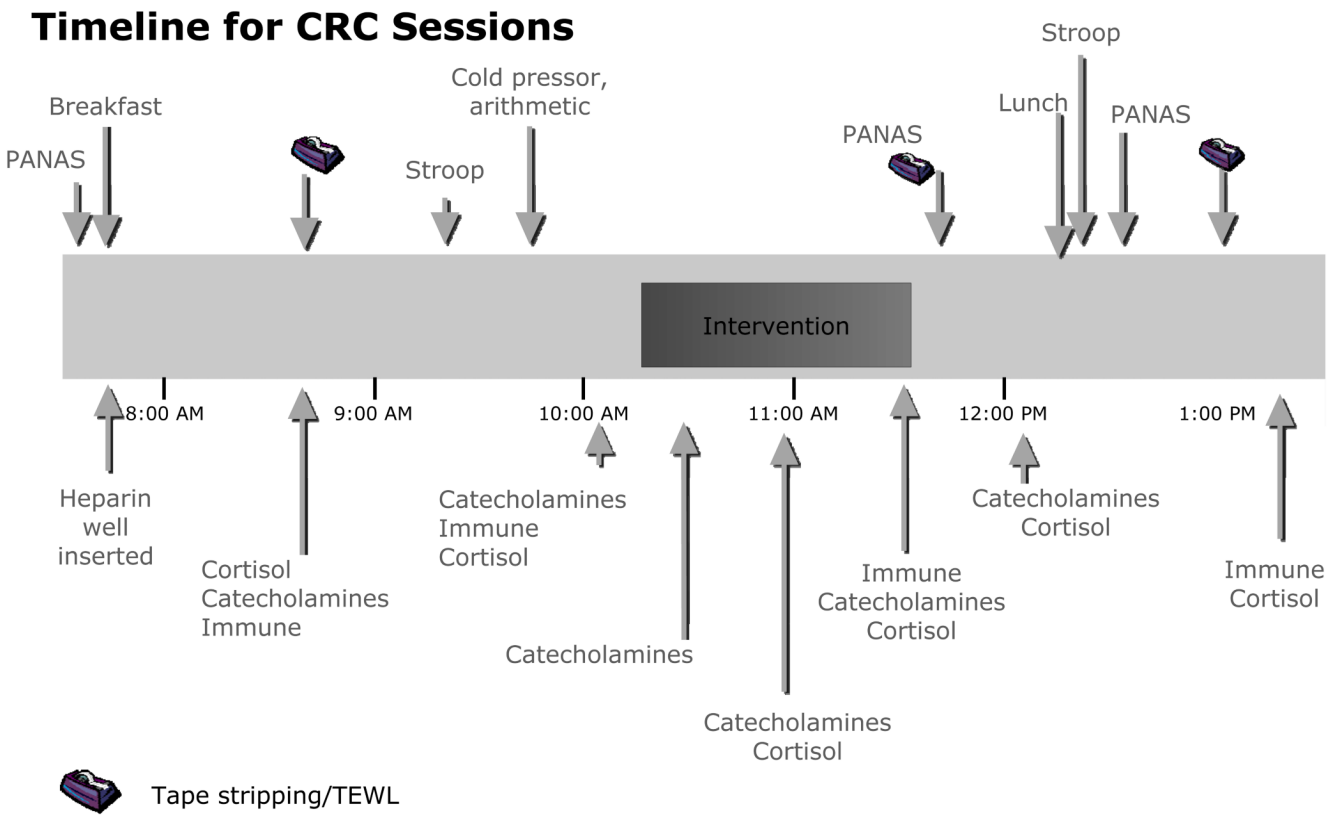

Figure 1.
Timeline for experimental participation during each of the three CRC sessions.

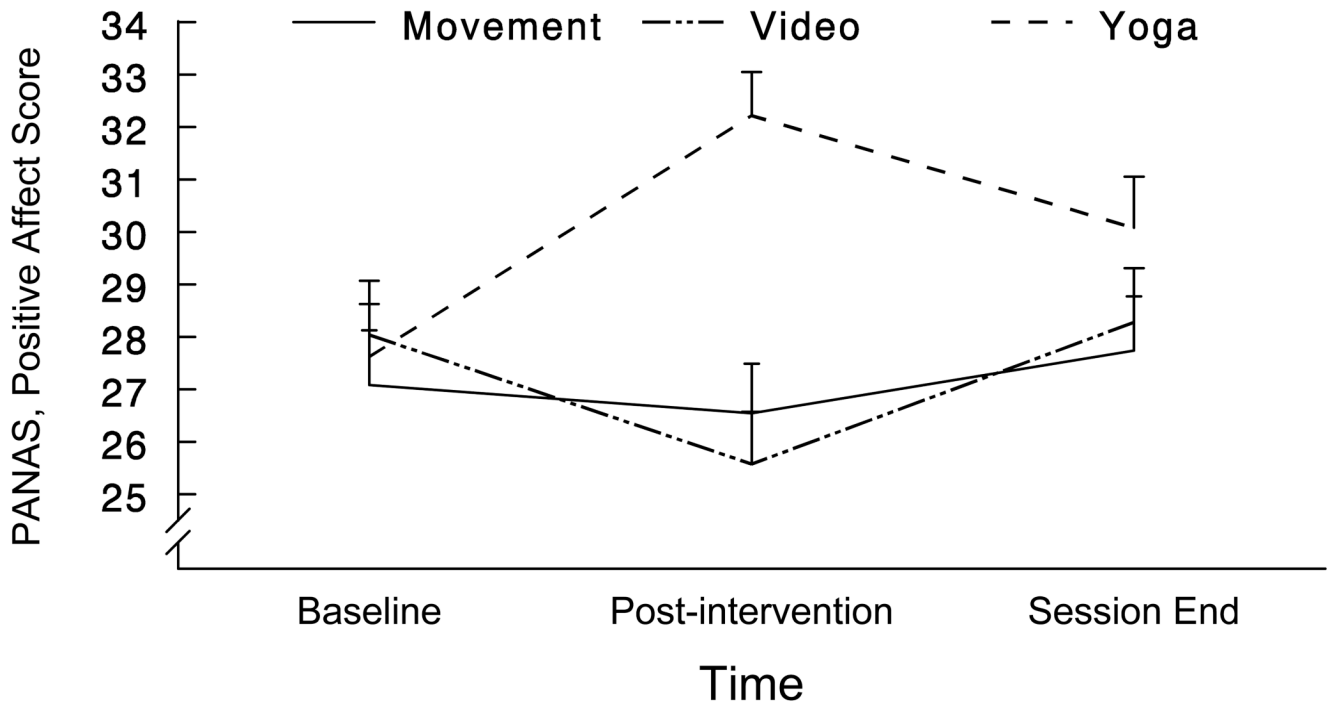

Figure 2.
Mean (± SEM) changes in self-reported positive affect on the PANAS as a function of time and condition. Experts and novices did not differ.

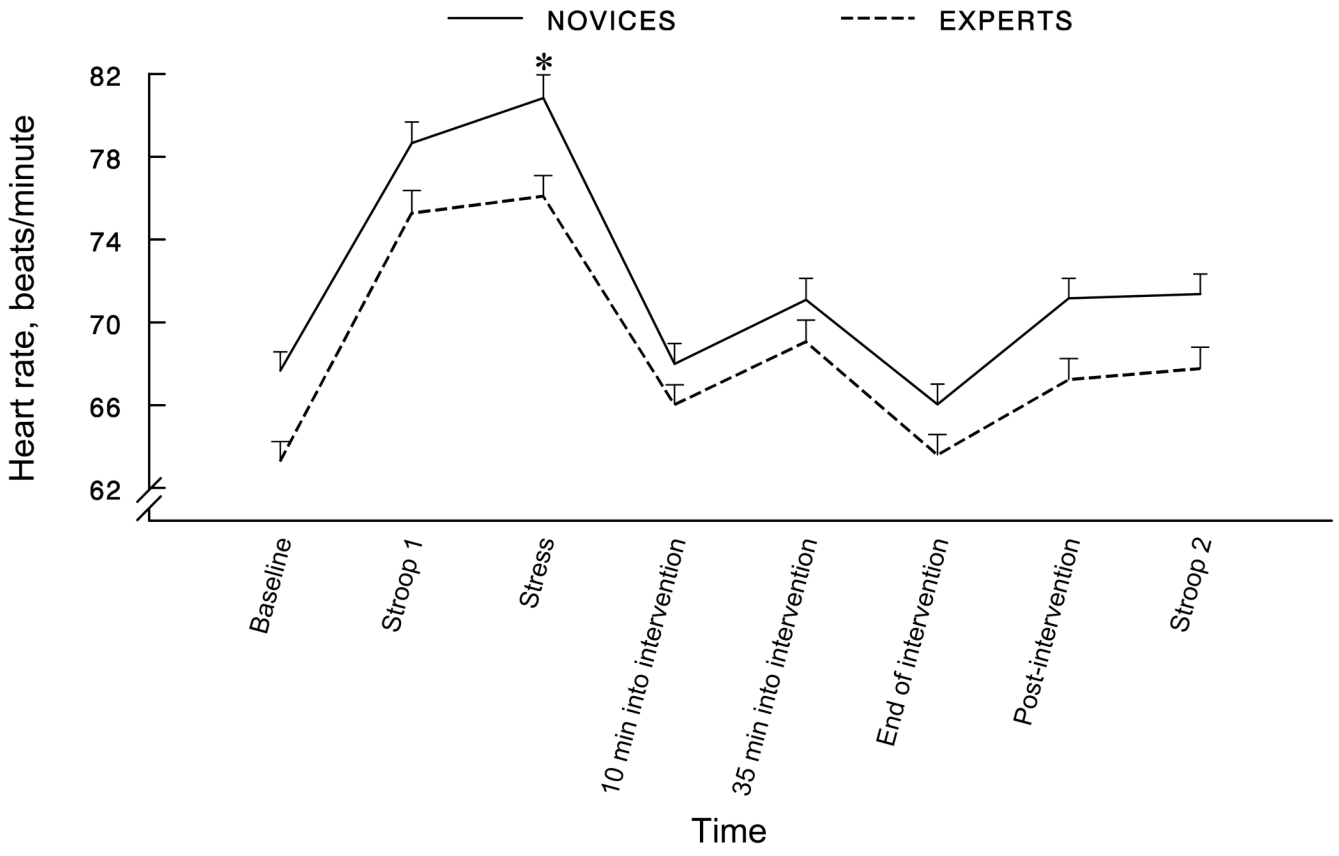

Figure 3.
Mean (± SEM) heart rate throughout the admissions as a function of novice vs. expert yoga practitioner status. * denotes $P = .03$.

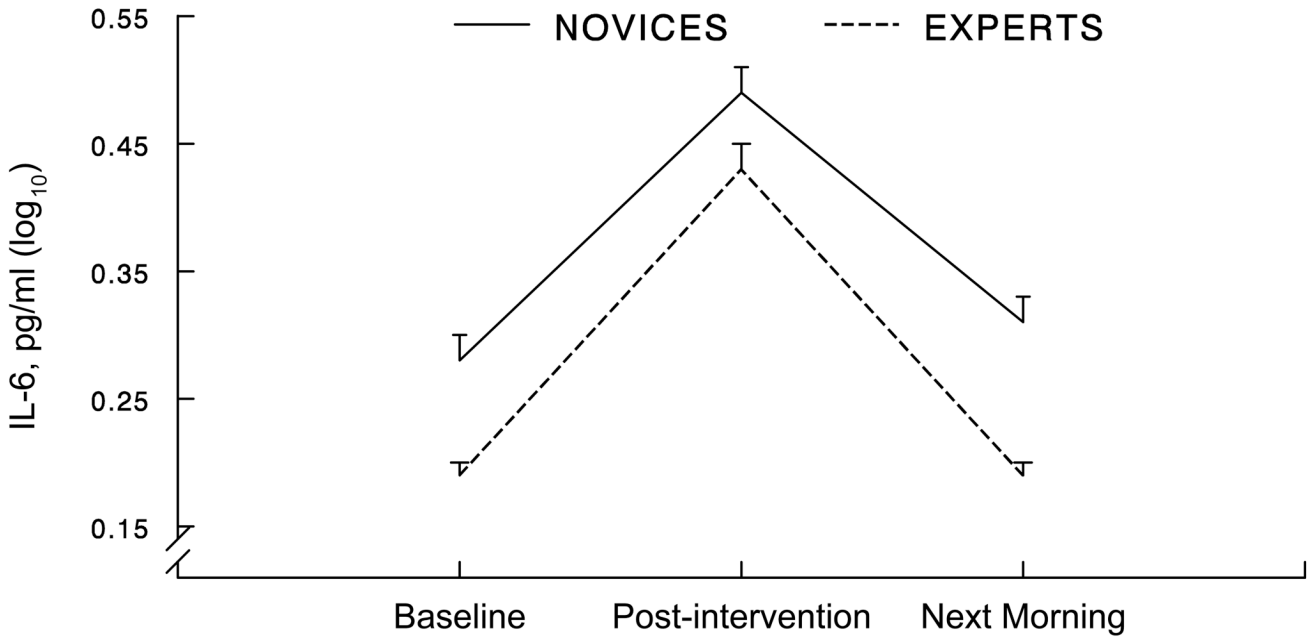

Figure 4.
Mean (± SEM) serum IL-6 as a function of novice vs. expert yoga practitioner status also reflect significantly elevated levels of IL-6 post-intervention.

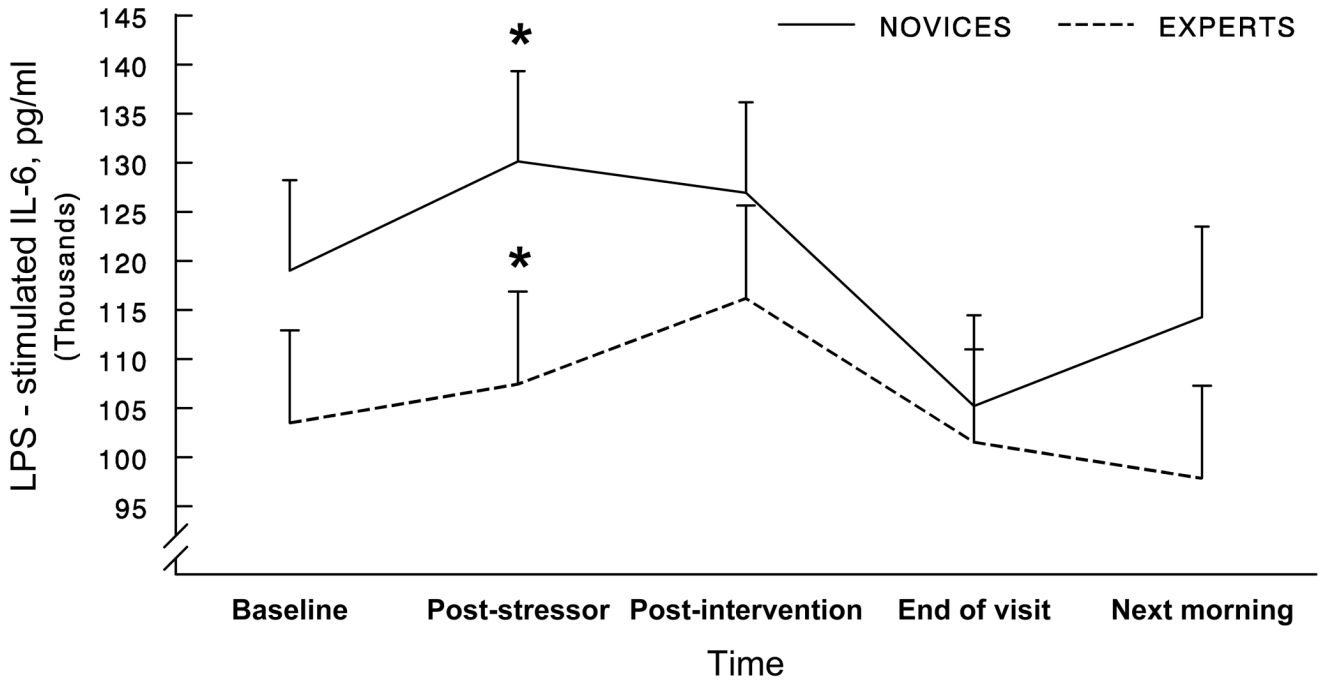

Figure 5.
Mean (± SEM) LPS-stimulated IL-6 production throughout the admissions as a function of novice vs. expert yoga practitioner status. * denotes $P = .05$.

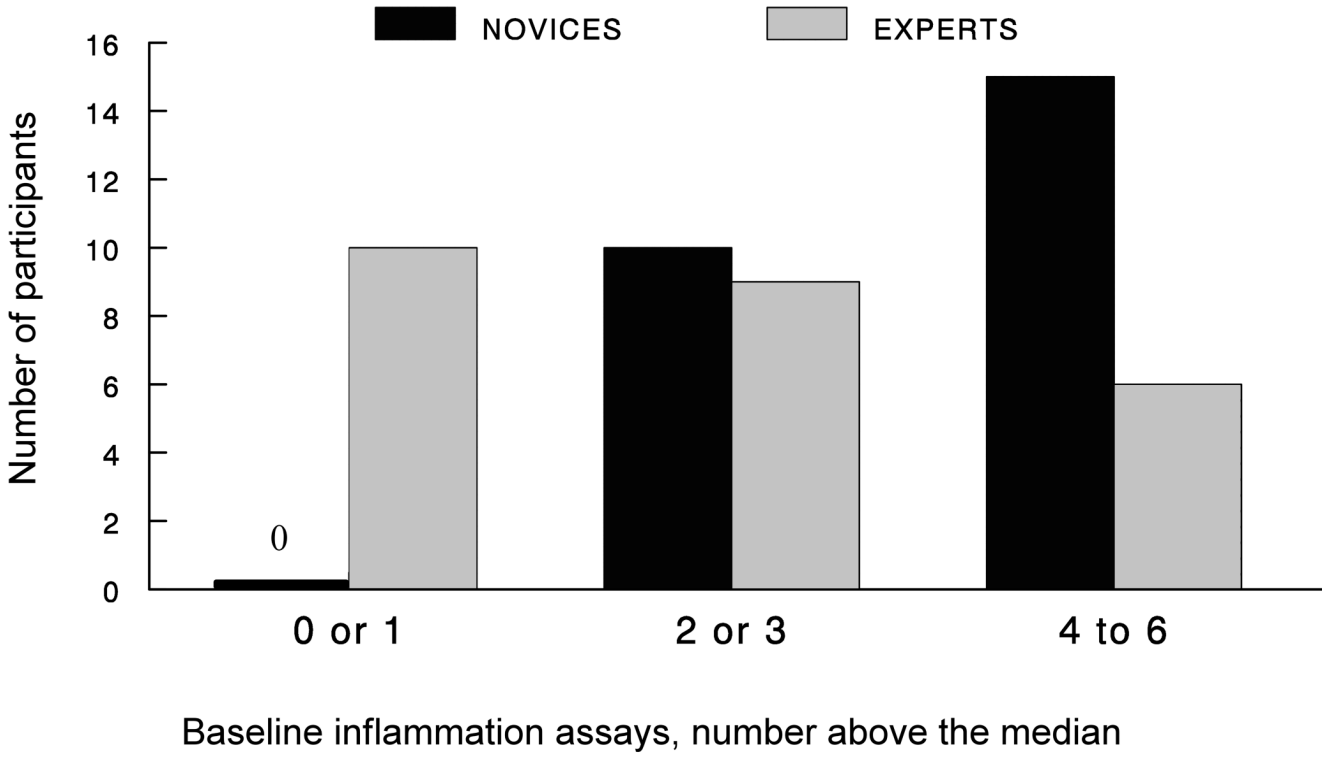

Figure 6.
The numbers of novices and experts falling into low, medium, or high inflammatory groups based on the number of assays on which they were above the baseline median values for serum Il-6, TNF-α, sIL-6r, and hsCRP, and LPS-stimulated IL-6 and TNF-α production.

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Table 1

Mean (SD) demographic, physiological, dietary, and behavioral data for novice and expert yoga practitioners

	Novice (*n*=25)		Expert (*n*=25)		Univariate *p*-value	MANOVA *p*-value
Age	39.96	(10.51)	42.68	(10.18)	0.36	
Education (Hollingshead categories)	5.36	(0.64)	5.36	(0.76)	1.00	
Adiposity measurements						0.75
Body mass index (BMI)	23.56	(2.83)	22.85	(2.71)		
Sagittal abdominal diameter (SAD)	17.91	(2.29)	17.69	(2.52)		
Cholesterol, mg/dL	179.28	(29.13)	176.60	(33.74)	0.12	
Fasting glucose, mg/dL	88.92	(8.13)	86.80	(8.02)	0.44	
Cardiorespiratory fitness						0.13
VO_2 peak	27.43	(5.54)	28.36	(6.62)		
Maximal workload	139.56	(25.25)	148.24	(30.12)		
Maximum heart rate	173.88	(13.12)	166.04	(15.88)		
Baseline heart rate/blood pressure						0.28
Heart rate	69.88	(9.23)	67.04	(9.07)		
Systolic blood pressure, mmHg	111.44	(15.73)	108.12	(12.02)		
Diastolic blood pressure, mmHg	68.08	(12.66)	68.20	(11.52)		
FFQ, Nutrients and Energy						0.11
Energy, kcal	1981.60	(853.64)	1696.25	(412.92)		
Carbohydrate, g	250.70	(113.81)	219.29	(53.42)		
Fat, g (log_{10})	1.81	(0.21)	1.78	(0.16)		
Protein, g (log_{10})	1.88	(0.23)	1.80	(0.15)		
FFQ, Vitamins						0.24
Vitamin E, IU	1.21	(0.23)	1.26	(0.16)		
Vitamin C, mg (log_{10})	2.02	(0.25)	2.11	(0.21)		
Vitamin D, mcg (log_{10})	0.76	(0.26)	0.66	(0.25)		
FFQ, Fruits and Vegetables						0.42
Fruit servings/day	1.81	(1.48)	2.50	(2.05)		
Vegetable servings/day	2.70	(1.64)	3.20	(1.83)		
Alcohol, drinks/week	2.32	(2.85)	1.92	(1.91)	0.56	

	Novice (*n*=25)		Expert (*n*=25)		Univariate *p*-value	MANOVA *p*-value
Pittsburgh Sleep Questionnaire	4.28	(2.32)	4.20	(2.08)	0.90	
Mood/Affect						0.17
PANAS (positive mood)	26.73	(6.88)	28.43	(6.23)		
MASQ-depressive symptoms	19.08	(5.66)	21.08	(8.94)		
MASQ-anxiety symptoms	16.93	(2.98)	18.79	(5.55)		