Psychoneuroendocrinology (2014) 43, 20—29

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Yoga reduces inflammatory signaling in fatigued breast cancer survivors: A randomized controlled trial

Julienne E. Bower [a,b,c,d,*], Gail Greendale [e], Alexandra D. Crosswell [a], Deborah Garet [c], Beth Sternlieb [f], Patricia A. Ganz [d,g], Michael R. Irwin [a,b,c,d], Richard Olmstead [b,c], Jesusa Arevalo [h], Steve W. Cole [c,h]

[a] UCLA Department of Psychology, Los Angeles, CA, United States
[b] UCLA Department of Psychiatry and Biobehavioral Sciences, Los Angeles, CA, United States
[c] Cousins Center for Psychoneuroimmunology, Semel Institute at UCLA, Los Angeles, CA, United States
[d] Jonsson Comprehensive Cancer Center at UCLA, Los Angeles, CA, United States
[e] UCLA Department of Geriatrics, Los Angeles, CA, United States
[f] Pediatric Pain Program, Mattel Children's Hospital at UCLA, Los Angeles, CA, United States
[g] UCLA Schools of Medicine and Public Health, Los Angeles, CA, United States
[h] UCLA Department of Medicine, Los Angeles, CA, United States

Received 11 September 2013; received in revised form 23 January 2014; accepted 23 January 2014

KEYWORDS
Yoga;
Inflammation;
Gene expression;
Fatigue;
Cancer;
Cortisol

Abstract
Background: Yoga is a popular mind—body therapy that has demonstrated beneficial effects on psychological, behavioral, and functional outcomes. However, few studies have investigated effects on inflammatory processes. This study tested the hypothesis that an Iyengar yoga intervention specifically designed for fatigued breast cancer survivors would lead to decreases in inflammation-related gene expression and circulating markers of proinflammatory cytokine activity.
Methods: Breast cancer survivors with persistent cancer-related fatigue were randomized to a 12-week Iyengar yoga intervention ($n = 16$) or a 12-week health education control condition ($n = 15$). Blood samples were collected at baseline, post-intervention, and at a 3-month follow-up for genome-wide transcriptional profiling and bioinformatic analyses. Plasma inflammatory markers and salivary cortisol were also assessed.

* Corresponding author at: UCLA Psychology and Psychiatry and Biobehavioral Sciences, 300 UCLA Medical Plaza, Box 957076, Los Angeles, CA 90095-7076, United States. Tel.: +1 310 825 3004.
E-mail address: jbower@ucla.edu (J.E. Bower).

0306-4530/$ — see front matter
http://dx.doi.org/10.1016/j.psyneuen.2014.01.019

Results: In promoter-based bioinformatics analyses, the yoga group showed reduced activity of the pro-inflammatory transcription factor nuclear factor kappa B (NF-κB), increased activity of the anti-inflammatory glucocorticoid receptor, and reduced activity of cAMP response element-binding protein (CREB) family transcription factors relative to controls (all $ps < .05$). There was also a significant intervention effect on the soluble tumor necrosis factor receptor type II (sTNF-RII), a marker of TNF activity; plasma levels of sTNF-RII remained stable in the yoga group, whereas levels of this marker increased in the health education group ($p = .028$). A similar, non-significant trend was observed for the interleukin 1 receptor antagonist ($p = .16$). No significant changes in C reactive protein (CRP), interleukin 6 (IL-6), or diurnal cortisol measures were observed.
Conclusions: A 12-week restorative Iyengar yoga intervention reduced inflammation-related gene expression in breast cancer survivors with persistent fatigue. These findings suggest that a targeted yoga program may have beneficial effects on inflammatory activity in this patient population, with potential relevance for behavioral and physical health.

1. Introduction

Yoga is an ancient mind—body practice that has become increasingly popular in Western culture. In Western countries, yoga typically refers to postures (asanas), breath control (pranayama), and/or meditation. Yoga is traditionally believed to have beneficial effects on physical and mental health, and research conducted over the past several decades has subjected those beliefs to empirical scrutiny. Indeed, randomized controlled trials of yoga interventions conducted with a wide range of healthy and clinical populations suggest that yoga has beneficial effects on stress, anxiety, depressive symptoms, pain, and aspects of physical function, although conclusions are limited by poor trial quality in many cases (Raub, 2002; Bower et al., 2005; Bussing et al., 2012a,b).

There is growing interest in the effects of yoga on physiological processes that may underlie effects on health. Inflammation plays a key role in the onset and progression of a number of physical conditions, including cancer, cardiovascular disease, and diabetes (Libby and Theroux, 2005; Pierce et al., 2009), and is also linked to depression, pain, fatigue, and other behavioral disturbances (Irwin and Cole, 2011). However, there have been surprisingly few studies examining effects of yoga on inflammatory processes. Two randomized trials conducted with heart failure patients found that an 8-week Hatha yoga program led to significant reductions in serum concentrations of IL-6 and CRP relative to standard medical treatment (Pullen et al., 2008; Pullen et al., 2010). Another study examined the impact of a single session of Iyengar-based restorative yoga on inflammatory markers in experienced and novice yoga practitioners (Kiecolt-Glaser et al., 2010). Although the inflammatory response to a single yoga session was not different from a movement or passive video control condition, experienced yoga practitioners did show evidence of lower inflammatory activity than novices, suggesting an effect of more sustained yoga practice on inflammation. Finally, there is limited evidence that other mind—body interventions that incorporate some component of yoga may have anti-inflammatory effects. In particular, mindfulness-based stress reduction (which includes gentle yoga postures), as well as yogic meditation, have recently been shown to reduce inflammatory signaling through the pro-inflammatory NF-κB control pathway (Creswell et al., 2012; Black et al., 2013). However, the few studies to assess gene expression profiles in experienced yoga practitioners did not report effects on inflammation-related genes (Sharma et al., 2008; Qu et al., 2013).

The current study examined the effects of an Iyengar yoga intervention targeted at fatigue on genomic and circulating markers of inflammation in fatigued breast cancer survivors. The primary outcome of this randomized controlled trial was fatigue, and results showed improvements in fatigue and energy among women assigned to the yoga group relative to women assigned to the health education control condition (Bower et al., 2012). In addition to behavioral outcomes, the trial was designed to examine effects on inflammatory processes, which may underlie symptoms of cancer-related fatigue (Bower et al., 2002; Collado-Hidalgo et al., 2006; Orre et al., 2011; Bower et al., 2011b; Alfano et al., 2012). Based on preliminary work suggesting beneficial effects of yoga on inflammation (Pullen et al., 2008, 2010), we hypothesized that women randomly assigned to the targeted Iyengar yoga intervention would show decreases in markers of inflammatory activity relative to health education controls. We were particularly interested in the NF-κB signaling pathway, given its central role as a regulator of pro-inflammatory gene expression (Aggarwal et al., 2009) and evidence of elevated NF-κB activity in fatigued breast cancer survivors (Bower et al., 2011a). Specifically, we hypothesized that Iyengar yoga would lead to reductions in NF-κB signaling, as has been seen following other mind—body interventions (Creswell et al., 2012; Black et al., 2013). We also hypothesized that this intervention would lead to reductions in circulating markers of inflammation. Further, given the role of the HPA axis and the sympathetic nervous system as key regulators of inflammatory processes (Irwin and Cole, 2011), we evaluated the impact of the yoga intervention on transcription control pathways linked to these systems and on diurnal cortisol production.

2. Methods

2.1. Yoga randomized controlled trial

Data came from a study of 31 stage 0-II breast cancer survivors who had completed local and/or adjuvant therapy (with the exception of endocrine therapy) at least 6 months