

# Toward Identifying the Effects of the Specific Components of Mindfulness-Based Stress Reduction on Biologic and Emotional Outcomes Among Older Adults

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## Abstract

**Objectives:** The objectives of this study were to examine the effects of specific Mindfulness-Based Stress Reduction (MBSR) activities (yoga, sitting and informal meditation, body scan) on immune function, circulating insulin-like growth factor (IGF)-1 concentrations, and positive affect among older adults.

**Design:** The study design comprised longitudinal analyses of data from subjects in an 8-week MBSR program.

**Setting:** The study was conducted at a University-affiliated health center.

**Subjects:** This study involved 100 community-dwelling older adults. Inclusion criteria were as follows:  $\geq 65$  years of age and English-speaking.

**Intervention:** This was an 8-week MBSR program.

**Outcome measures:** Interleukin (IL)-6 and IGF-1 levels were assayed from blood collected at postintervention assessments. Participants were immunized postintervention with keyhole limpet hemocyanin (KLH), and immunoglobulin (Ig)M and IgG KLH-specific antibody responses were measured prior to immunization as well as 3 weeks and 24 weeks postintervention. Participants completed a 10-item measure of positive affect at study entry and postintervention.

**Results:** Participants maintained weekly practice logs documenting participation in yoga, sitting meditation, informal meditation, and body scan. More practice of yoga was associated with higher post-treatment IGF-1 levels and greater improvement in positive affect from study entry to postintervention. Sitting meditation was positively associated with post-treatment IGF-1. Greater use of body scanning was associated with reduced antigen-specific IgM and IgG 3 weeks postintervention but not 24 weeks. No associations were found between MBSR activities and IL-6 levels.

**Conclusions:** Practice of MBSR activities, particularly yoga, could provide benefits for specific aspects of physiologic function and positive affect. Changes in adaptive immunity in older adult MBSR practitioners warrant further study.

## Introduction

**A**GING-RELATED DYSREGULATION of the immune system is associated with a host of adverse effects. Given demographic aging of the population worldwide, the extent to which aging-related physiologic adversities can be mitigated is a question of considerable clinical and public health significance. In this study, the authors examined whether specific components of an intervention to modify states of attentional awareness can influence immune function and inflammatory biomarker levels among older adults. Physiologic recovery

from high-arousal emotional stimuli, negative or positive, is prolonged in people with older, less flexible systems.<sup>1,2</sup> This difficulty in downregulating arousal can result in greater dysregulation of the immune system with harmful physiologic effects, including neuroinflammation and accelerated cellular aging.<sup>3,4</sup> Behavioral interventions designed to modify the response to emotional stimuli could mitigate age-related declines in adaptive immune function and increases in inflammatory biomarkers.<sup>5,6</sup>

One (1) multicomponent behavioral intervention with potential in this regard is Mindfulness-Based Stress

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Reduction (MBSR),<sup>1,7-9</sup> which incorporates meditation practices, specifically yoga, the body scan, sitting meditation and informal meditation, each involving controlled attention to internal and external stimuli. Older adults may be particularly well prepared to practice yoga and meditation, given age-related increases in motivational processes involved in maintaining positive affect via attentional control of emotional experience.<sup>2,3,8</sup> Moreover, the relationship of emotions to immune function underscores the potential benefits of stress-regulating and emotion-enhancing clinical interventions for aging populations.<sup>9,10</sup>

MBSR is intended to cultivate mindful attention to one's moment-to-moment cognitive, affective, and physical experience without evaluation or judgment; such nonjudgmental attention to the physical self may be especially important for older adults, given age-related decrements in physical function and increased consciousness of physical frailty.<sup>10</sup> Improving emotional experiences regarding physical changes appears to affect immune function in older adults.<sup>3,4,11</sup>

In this study, the authors examined the extent to which practicing MBSR-specific activities outside of the weekly MBSR sessions would affect aging-related physiologic outcomes and positive affect among older adults. Several studies have demonstrated that mindfulness meditation and yoga have salutary effects on immune function and affect.<sup>1,7-9,11-14</sup> Yet, there has been surprisingly little research on MBSR's specific components<sup>15</sup> and no study has examined the relative effects of each individual component of MBSR. Presumably, specific MBSR components may contribute differentially to outcomes as might nonspecific treatment components, such as interpersonal support during the group-based training period. Thus, in this study, the relative contributions of MBSR components were examined, specifically yoga, sitting meditation, the body scan, informal meditation, and a nonspecific therapeutic element, interpersonal support, on indicators of physiologic aging and positive affect.

In a prior report, the effects of MBSR on immunological, electrophysiologic, and cognitive outcomes were examined among older adults in a randomized clinical trial of MBSR and a wait-list control group. One of the main findings was that MBSR led to an unexpected significant decrease in antibody titers postintervention. This finding, which appears to contrast with prior findings of increased antibody production among young adults trained in MBSR and then immunized with influenza vaccine,<sup>16</sup> prompted the current investigation. Specifically, further analyses were conducted on the MBSR group and the effects of its specific (yoga, sitting meditation, body scan, and informal meditation) and nonspecific (interpersonal support) components on indicators of physiologic aging (insulin-like growth factor [IGF]-1, interleukin [IL]-6, immunoglobulin [Ig]M and IgG) and positive affect. IGF-1 is a biomarker associated with human longevity<sup>17</sup> and elevated levels of IL-6 cytokines are associated with an activated inflammatory response.<sup>18</sup>

It was hypothesized that more practice time in the MBSR components (yoga, sitting meditation, body scan, informal meditation) would be associated with higher IGF-1, lower IL-6, and improved positive affect, independent of the effects of interpersonal support. There was also interested in exploring the relationship between the specific components of MBSR and the unexpected decrease in IgM and IgG anti-keyhole limpet hemocyanin (KLH) antibody production.

## Materials and Methods

### Participants

Older adults from the community were recruited between December 2006 and October 2009 through advertisements in local newspapers and flyers in primary care offices. To be eligible for the study, participants had to be aged 65 years or older and English speaking. Participants prescribed antidepressant or anxiolytic medications must have had a stable medication regimen for 8 weeks prior to enrollment. Given the didactic and self-directed nature of the MBSR program, individuals with major, uncorrected sensory impairments and cognitive deficits were excluded. Cognitive impairment was defined as a score of 24 or lower on the Mini-Mental State Examination.<sup>19</sup> Potential participants were also excluded for the following mental disorders based on the Structured Clinical Interview for DSM-IV (SCID)<sup>20</sup>: major depression with psychotic features; psychosis; lifetime history of schizophrenia, bipolar disorder, organic brain syndrome, or mental retardation; and alcohol or substance abuse within the previous year. Finally, individuals with allergies to shellfish were excluded from the study as a precaution due to immunization with KLH, which is purified from the mollusc *Megathura crenulata*.

### Initial assessment

A total of 200 subjects met inclusion criteria, provided written informed consent, and underwent initial assessment by one of three masters-level research assistants. Subjects were then randomized to participate in either the 8-week program of MBSR ( $n = 100$ ) or a wait-list control condition ( $n = 100$ ). The current report concerns only the MBSR participants.

Data from the subjects assigned to the MBSR condition were collected: following randomization and before beginning the MBSR program (Time 1); immediately following completion of the 8-week MBSR program (Time 2); 3 weeks later, or 11 weeks following the start of the program (Time 3); and 21 weeks following Time 3, or 5.25 months following the start of the program (Time 4). At Time 2, blood was drawn to establish a pre-immunization baseline and participants were immunized with KLH. Blood was obtained again at Times 3 and 4.

### Mindfulness-based stress reduction condition

Each subject assigned to the MBSR program participated in a group-based (15–20 members) 8-week curriculum that included weekly 120-minute sessions and an "all day intensive" session of 7 hours. The treatment interventions were held between April 2006 and November 2009. No treatment groups were conducted between December and February. The four primary mindfulness practices were incorporated over the course of the program. The MBSR program was designed to accommodate the mobility limitations of older adults who met the inclusion criteria. For example, an individual in a wheelchair could complete mindful Hatha yoga with a variety of modified sitting postures.

### Independent variables

Practice activities. Throughout the intervention phase, participants completed weekly practice logs, indicating their level of home participation in yoga, sitting meditation, body scan, and informal meditation. In the log, participants

reported the number of days per week practicing the four activities. Ratings were averaged across each week of the intervention to yield composite indicators of the average number of days per week participating in each of the four activities and total participation.

**Interpersonal support.** The level of interpersonal support participants experienced during the group sessions was assessed immediately following completion of the 8-week MBSR program (Time 2). Two (2) questions assessed the degree to which participants could confide in the group leader and felt group members were helpful in handling stress; the scale ranged from 1 (not at all) to 4 (very much).

#### Dependent variables

**IGF-1 and IL-6.** Blood obtained by a trained phlebotomist from the antecubital vein of participants on three occasions postintervention (Times 2–4) was used to assay IGF-1 and IL-6 levels. Blood was kept on ice and then centrifuged; serum was stored at  $-80^{\circ}\text{C}$  until assayed for IL-6 and IGF-1 using Quantikine enzyme-linked immunoassay (ELISA) kits from R&D Systems, Inc. (Minneapolis, MN). Absorbance was read at 490 nm with 650-nm wavelength correction 30 minutes after development using an automated Opsy MR Microplate Reader (Thermo Labsystems, Chantilly, VA). The mean minimum detectable limit for IL-6 is 0.039 pg/mL and is 0.026 ng/mL for IGF-1. The intra-assay variability for both assays is  $<5\%$  and the interassay coefficient of variation is  $<10\%$ .

**IgM and IgG antibody response.** At Time 2, participants had blood drawn and were injected with KLH into the deltoid muscle of the nondominant arm in a volume of 0.1–0.2 mL.<sup>21–23</sup> By design, more subjects were assigned into groups receiving 100 and 200  $\mu\text{g}$  of KLH. The final number of subjects receiving 8, 40, 100, 200 and 1000  $\mu\text{g}$  of KLH were 3, 10, 57, 25, and 5, respectively. Participants had blood drawn again 3 weeks (Time 3) and 24 weeks later (Time 4). Anti-KLH antibody titers were assayed by ELISA at three dilutions to determine IgM and IgG levels; the average across dilutions was calculated for analyses.

**Positive affect.** At baseline (Time 1) and following the intervention (Time 2), participants completed the 10-item Positive Affect scale ( $\alpha=0.91$ ) from the Positive and Negative Affect Schedule,<sup>24</sup> which measures positive affect along three dimensions: joy ( $\alpha=0.76$ ), interest ( $\alpha=0.73$ ), and activation ( $\alpha=0.80$ ). Participants indicated the extent to which they had experienced affect states, such as “excited,” during the previous week. Responses range from 1 (very slightly or not at all) to 5 (extremely).

**Data analysis.** Longitudinal changes in IgM, IgG, and positive affect were assessed using residualized change scores, or the residual variation in scores at one time point, after using regression to control for scores at the initial assessment. The study design allowed us to examine changes in IgM and IgG from treatment completion to 3-week follow-up (Time 2 to 3) and from treatment completion to 24-week follow-up (Time 2 to 4), as well as changes in positive affect from baseline to treatment completion (Time 1 to 2). Table 1 shows that IL-6 readings were consistent from Time 2 to 4 ( $F(2,196)=0.26$ ,  $p=0.78$ ); therefore, these three readings were averaged to

TABLE 1. DESCRIPTIVE STATISTICS

Variable	MBSR (n = 100) % or Mean (SD)
<b>Demographics</b>	
Gender: Female	62%
Education: College or greater	86%
Race: White	97%
Age	72.1 (6.7)
<b>Participation, days per week</b>	
Yoga	2.2 (1.3)
Sitting meditation	3.4 (1.5)
Informal meditation	3.1 (1.9)
Body scan	3.6 (1.5)
<b>Nonspecific support</b>	
Rating (1–4)	3.7 (0.5)
<b>IL-6 (pg/mL)</b>	
Treatment completion (T2)	2.6 (2.4)
3-Week follow-up (T3)	2.7 (2.0)
24-Week follow-up (T4)	2.7 (2.7)
<b>IGF-1 (ng/mL)</b>	
Treatment completion (T2)	93.9 (33.3)
3-Week follow-up (T3)	112.9 (42.0)
24-Week follow-up (T4)	111.4 (46.2)
<b>IgM absorption (optical density at 405 nm)</b>	
Treatment completion (T2)	0.49 (0.35)
3-Week follow-up (T3)	0.53 (0.36)
24-Week follow-up (T4)	0.28 (0.17)
<b>IgG absorption (optical density at 405 nm)</b>	
Treatment Completion (T2)	0.22 (0.23)
3-week Follow-up (T3)	0.43 (0.61)
24-week Follow-up (T4)	0.32 (0.45)
<b>PANAS, Positive Affect</b>	
Baseline (T1)	34.4 (7.5)
Treatment Completion (T2)	35.5 (7.3)

MBSR, Mindfulness-Based Stress Reduction; SD, standard deviation; IL, interleukin; IGF, insulin-like growth factor; Ig, immunoglobulin; PANAS, Positive and Negative Affect Schedule.

provide a single indicator of post-MBSR IL-6 levels. IGF-1 ratings were lower at Time 2 than Times 3 and 4 ( $t(99)=6.45$ ,  $p<0.001$ ); however, total participation in MBSR explained similar variance in IGF-1 levels across time points (average  $Z_{r\text{-diff}}=0.45$ ,  $p=0.65$ ). Therefore, three readings were also averaged to yield a single indicator of post-MBSR IGF-1 levels.

Regression was used to examine the association between independent variables (MBSR activities and interpersonal support) and dependent variables (biologic and emotional outcomes). Separate regression analyses were conducted for each predictor, unless otherwise noted. All analyses controlled for participant gender, age, and education level; analyses involving IgM and IgG also controlled for concentration of the injected KLH antigen. Only three data points were missing from the sample (a positive affect rating and two IL-6 ratings), which were replaced with group means in analyses.

## Results

### MBSR-specific treatment effects

Table 2 shows the relationship between participation in MBSR activities and biologic outcomes. As hypothesized,

TABLE 2. PARTICIPATION IN MBSR ACTIVITIES IS ASSOCIATED WITH POST-TREATMENT BIOLOGIC OUTCOMES

Participation	Avg. IGF-1	Pre-KLH exposure		Change 3 weeks post-MBSR		Change 24 weeks post-MBSR	
		IgM	IgG	IgM	IgG	IgM	IgG
Yoga	0.34***	-0.18	-0.03	-0.14	-0.23*	0.04	-0.20*
Sitting meditation	0.29**	-0.15	-0.19	-0.13	-0.10	0.11	-0.18
Informal meditation	0.06	-0.02	-0.24*	-0.11	-0.04	0.07	-0.15
Body scan	0.13	-0.11	-0.28**	-0.32***	-0.24*	0.06	-0.06
Total participation	0.28**	-0.16	-0.28**	-0.24*	-0.20*	0.09	-0.20*

$n=100$ . Table values are standardized  $\beta$  coefficients for regression equations where each participation variable is entered individually, while controlling for gender, education level, and age; IgM and IgG analyses also control for KLH titrations. IGF-1 levels are averaged across readings from all three post-MBSR readings (T2, T3, and T4). Changes in IgM and IgG were calculated as levels at 3 weeks (T3) or 24 weeks (T4) post-MBSR, while controlling for levels recorded prior to KLH exposure (T2). At each time point, IgM and IgG readings were averaged across three dilution levels.

\* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

MBSR, Mindfulness-Based Stress Reduction; KLH, anti-keyhole limpet hemocyanin; IGF, insulin-like growth factor; Ig, immunoglobulin.

total participation in MBSR activities was associated with significantly higher post-MBSR IGF-1 levels; furthermore, effects were specific to yoga and sitting meditation. However, there were no significant findings for IL-6.

The baseline antibody titers to the antigen KLH were expected to be low to undetectable; however, significant pre-existing titers were present at the time of challenge (Time 2). Total participation in MBSR activities was associated with reduced IgM and IgG response to the KLH exposure post-MBSR. In particular, more use of the body scan was associated with reduced IgM and IgG response at 3 weeks post-KLH exposure, and participation in yoga was associated with reduced IgG response at both follow-ups.

As hypothesized, participation in MBSR activities was associated with improvement in positive affect (Table 3). Each of the four activities was associated with total improvement; therefore, a *post-hoc* analysis (not shown tabularly) was conducted using simultaneous regression to determine whether any specific activity accounted for unique variance in improvement. Upon controlling for demographics and all other MBSR activities, yoga ( $\beta=0.22$ ,  $p=0.04$ ) was the lone activity to explain unique variance in total improvement in positive affect.

#### Nonspecific treatment effects

Interpersonal support was associated with post-MBSR IL-6 levels ( $\beta=0.21$ ,  $p=0.04$ ), and reduced immune response 3

TABLE 3. PARTICIPATION IN MBSR ACTIVITIES IS ASSOCIATED WITH IMPROVEMENT IN POSITIVE AFFECT

Participation	Joy	Interest	Activation	Total PA
Yoga	0.27**	0.28**	0.33***	0.34***
Sitting meditation	0.35***	0.24*	0.30**	0.33***
Informal meditation	0.26*	0.19	0.24*	0.26*
Body scan	0.20*	0.18	0.21*	0.25*
Total participation	0.38***	0.31**	0.38***	0.41***

$n=100$ . Table values are standardized  $\beta$  coefficients for regression equations where each participation variable is entered individually, while controlling for gender, education level, and age. Improvement in positive affect is calculated as scores at treatment completion (T2), controlling for baseline ratings (T1).

\* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

PA, positive affect.

weeks post-MBSR (IgM:  $\beta=-0.26$ ,  $p=0.01$ ; IgG:  $\beta=-0.25$ ,  $p=0.01$ ). No other findings involving interpersonal support were significant.

#### Discussion

The effects of specific and nonspecific components of MBSR on IGF-1, IL-6, antibody responses, and positive affect were examined in older adults to address the specificity, indications, and appropriateness of MBSR for this population. To the authors' knowledge, this is the first study to examine the differential effects of the specific components of MBSR (for a summary of key findings, see Table 4).

It was found that increased practice of MBSR activities overall, and yoga and sitting meditation specifically, were associated with significantly increased post-treatment IGF-1 production. The type of yoga incorporated into MBSR typically has the participant focus on breathing and somatic awareness, emotional awareness, and cognitive awareness from moment to moment while being guided from one posture to another. Yoga's potential health benefits have been attributed to reductions in sympathetic nervous system tone<sup>25,26</sup> and increases in vagal activity,<sup>26</sup> both of which may improve endocrine and immune function.<sup>11</sup> Mindfulness can enhance cognition through moment-to-moment attention,<sup>27</sup> and cognitive function has been positively correlated with levels of IGF-1 in healthy elderly.<sup>28</sup> Thus, the current findings indicate improved IGF-1 levels when engaging in focused attention and mindful acceptance of the body while sitting and in motion.

In the randomized trial from which the data reported here were drawn, it was found that MBSR led to an unexpected significant decrease in antibody titers postintervention. In

TABLE 4. SUMMARY OF KEY FINDINGS ON THE SPECIFIC COMPONENTS OF MBSR

Specific component	Key findings
Yoga	Increased IGF-1 Reduced IgG response Most important for positive affect
Sitting meditation	Increased IGF-1
Informal meditation	Least evidence for unique effects
Body scan	Reduced IgM and IgG response

this study, it was shown that greater total participation in MBSR activities was associated with lower IgG levels pre-immunization (Time 2) and a decreased rise in IgM and IgG 3 weeks postimmunization. Body scan in particular was associated with decreased IgM and IgG anti-KLH titers at 3 weeks postimmunization.

These findings suggest that MBSR practice, specifically the body scan, had a deleterious effect on antibody response, or humoral immunity. The body scan is a guided meditation in which the participants are instructed to move their attention from one part of the body to the next, beginning with the feet and ending with the head. It is possible that some element of the body scan was detrimental, although the body scan is intended to involve nonjudgmental attention to bodily sensations as they arise. If participants were unable to suspend judgment, perhaps due to pain or discomfort, this exercise might have negative effects. Without data on implementation fidelity, this is only speculation.

A second possible explanation is that the observed decrease in humoral immunity may have been linked to a favorable rise in cell-mediated immunity, which unfortunately was not tested. There is a balance between the two adaptive immune effector functions, cell-mediated (e.g., cytotoxic responses) versus humoral immunity, which is a function of T helper (Th)1 versus Th2 cells under the regulation of other cell types, particularly T regulatory (Treg) cells.<sup>29</sup> The observed decrease in humoral immunity to KLH might suggest that cell-mediated effector functions are upregulated in MBSR participants.<sup>29,30</sup> In support of this speculation, Irwin et al. observed increased varicella zoster-specific T-cell-mediated responses in older adult (mean age of 70) practitioners of *t'ai chi chih*<sup>31</sup> which, like MBSR, incorporates elements of movement, relaxation, and meditation. Future studies should investigate whether the decrease in antibody response that was observed among those who practiced MBSR more is associated with an increase in cell-mediated immune function, and whether such changes are specific to older adults.

No significant effect was seen of MBSR practice on IL-6 levels. Similar to these results, another study found that participation in yoga sessions did not affect change in IL-6 among expert and novice yoga practitioners; however, expert compared to novice practitioners had lower IL-6, indicating that long-term yoga practice has the potential to minimize inflammatory responses.<sup>11</sup> Although no MBSR activities accounted for variance in IL-6 production, interpersonal support, a nonspecific element of virtually all therapies, accounted for significantly lower IL-6 production. These findings are consistent with research indicating that high interpersonal support buffered the relationship between stress and the inflammatory marker C-reactive protein among middle-aged women.<sup>32</sup>

It was found that the amount of yoga practice made a unique contribution to gains in positive affect. Specifically, engaging in yoga practice 2 additional days per week significantly increased positive affect. Research suggests that the beneficial effect of MBSR on affective experience is related to the amount of time spent engaging in MBSR activities outside of the class.<sup>33–37</sup> The cultivation of nonjudgmental attention is considered to be one of the foundational elements of mindfulness.<sup>38,39</sup> Emotional aging research suggests that older adults are able to successfully regulate emotions by using advanced attentional processes.<sup>3</sup>

Increased practice of yoga may have enhanced older adults' capacities to use attentional strategies to regulate emotions.

Findings should be considered in light of study limitations. The lack of a baseline IL-6 measurement prevented the authors from being able to draw firm conclusions regarding the effect of the intervention on change in IL-6 levels. Furthermore, the effects of MBSR practice on IgM and IgG responses at Time 3 were unexpected, and speculations regarding the observed changes require further study. The control for seasonality is also a limitation of the study, as assessments were not conducted year round. The strengths of the study include its unique attention to the effects of specific MBSR components, the use of both biologic and emotional outcomes relevant to aging, and its focus on possibilities for healthy aging among older adults.

## Conclusions

This study demonstrates associations between specific components of MBSR and specific outcomes. Exploring the differential effects of each component allowed delineation of which was the most effective in driving change in biologic and emotional outcomes. The clinical significance of these findings points to yoga and sitting meditation as the most appropriate practices for promoting health among older adults. Yoga was particularly effective in driving change in IGF-1 and positive affect. The yoga incorporated into MBSR emphasizes nonjudgmental attention and acceptance of the body and mind as one engages in mindful movement, which may be particularly beneficial to older adults experiencing aging-related declines in physiologic functioning.

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## Disclosure Statement

No competing financial interests exist.

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