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Original Articles

Enhanced Psychosocial Well-Being Following Participation in a Mindfulness-Based Stress Reduction Program Is Associated with Increased Natural Killer Cell Activity

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Abstract

Background: Mindfulness-based stress reduction (MBSR) programs have consistently been shown to enhance the psychosocial well-being of participants. Given the well-established association between psychosocial factors and immunologic functioning, it has been hypothesized that enhanced psychosocial well-being among MBSR participants would be associated with corresponding changes in markers of immune activity.
Objectives: The objectives of this study were to examine changes in psychosocial and immunologic measures in a heterogeneous patient sample following participation in a MBSR program.
Design: A single-group, pretest/post-test design was utilized.
Setting: The intervention was conducted at an academic health center.
Subjects: This pilot study involved 24 participants (aged 28–72 years). Inclusion criteria were as follows: $\geq$18 years of age, English-speaking, and no known autoimmune disorder.
Intervention: The intervention was an 8-week MBSR program.
Outcome measures: Distress and quality of life (QOL) measures included the Brief Symptom Inventory-18 and the Medical Outcomes Survey Short-Form Health Survey, respectively. Immunologic measures included natural killer (NK) cell cytolytic activity and C-reactive protein (CRP).
Results: Patients completed psychosocial assessments and provided a blood sample at baseline (pre-MBSR) and within 2 weeks post-MBSR. Significant improvements in anxiety and overall distress as well as across multiple domains of QOL were observed from baseline to post-MBSR. Reductions in anxiety and overall distress were associated with reductions in CRP. Patients who reported improvement in overall mental well-being also showed increased NK cytolytic activity from pre- to post-MBSR, whereas patients who reported no improvement in mental well-being showed no change in NK cytolytic activity.
Conclusions: Positive improvement in psychologic well-being following MBSR was associated with increased NK cytolytic activity and decreased levels of CRP.

Introduction

The intimate connection between mind and body has gradually become more broadly accepted in Western medicine over the past few decades. Today, it is no longer considered radical for a patient to incorporate a mind–body intervention into a treatment plan to complement "traditional" medical approaches for healing. This shift in medical mindset was highly influenced by the work of Jon Kabat-Zinn and colleagues, and the mindfulness-based stress reduction (MBSR) program in particular.

MBSR is an 8-week standardized program that teaches participants mindfulness practice, or the act of being in the moment. Through mindfulness practice, participants come to identify automatic reactions and reflexive thoughts occurring in response to external and internal events. Empirical data

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indicate that MBSR participants experience enhanced psychosocial and physical functioning.[1–4]

Specific psychosocial improvements include improved quality of life and reductions in psychologic distress.[4,5] Indeed, meta-analyses of MBSR studies concluded that MBSR is associated with robust effects on psychosocial well-being across studies of patients with a wide range of health conditions and disorders.[1,6] For example, it has been demonstrated that mindfulness training can be helpful in reducing the stress that accompanies cancer diagnosis and treatment.[7]

Given that stress is associated with immune dysregulation,[8] it has been proposed that participation in MBSR can lead to not only decreased stress,[1] but also enhanced immune functioning. Findings from a variety of studies provide evidence for the existence of a stress-immunity pathway.[9–13] Psychologic stress may lead to changes in immune functioning via two pathways: (1) through the central nervous system with the activation of the sympathetic nervous system; or (2) through neuroendocrine-immune pathways (i.e., the release of hormones).[14] Indeed, a number of studies have shown that psychologic responses to stressful events can produce immunologic changes in both healthy and patient populations.[15–17] For example, significant declines in natural killer (NK) cell numbers and activity have been observed during periods of high stress (e.g., marital conflict[18,19]). Stress-related alterations in immune functioning have also been observed among patients undergoing diagnosis of,[20] and treatment for,[21] cancer. Among breast cancer patients undergoing surgical treatment, self-reported levels of stress were associated with immune downregulation, including reduced NK cell cytotoxicity, even after controlling for potential confounding variables such as patient age and disease stage.[21] Therefore, based on the body of work demonstrating a stress-immune pathway, interruption of the stress-response (through mindfulness practice) could potentially have physiologic implications for immune functioning. Guided by a psychoneuroimmunologic framework that proposes that psychosocial factors may influence immunologic outcomes via sympathetic nervous system and neuroendocrine pathways,[22] it is proposed that changes in psychologic well-being are likely to be associated with corresponding changes in immunologic functioning.

At present, few studies have directly examined the association between change in psychosocial well-being and immune parameters following MBSR. Several studies have reported improved immune functioning among MBSR participants, but these same studies either showed no association between immune functioning and psychosocial well-being post-MBSR[7,23] or failed to assess this relationship.[24] For example, significant improvements in quality of life and stress symptoms as well as a general shift away from a proinflammatory (or Th1) response to an anti-inflammatory (Th2) type response were identified among breast and prostate cancer patients following participation in MBSR.[7,25] Moreover, significant increases in immunologic functioning (i.e., NK cell activity) were also reported among HIV+ patients following participation in MBSR.[23] An association between immune functioning and psychosocial well-being was not identified in either study. Furthermore, recent research by Witek-Janusek and colleagues[24] showed a re-establishment of NK cell activity and cytokine production levels over time as well as reductions in cortisol levels among 75 early-stage breast cancer patients participating in MBSR compared to non-MBSR controls. However, the relationship between immune functioning and psychosocial well-being was not assessed.

Thus, we conducted a pilot study to examine whether improvement in psychosocial well-being is associated with enhanced immune functioning among a heterogeneous patient population participating in a MBSR program. Specifically, it was hypothesized that immunologic changes would most likely be observed among the MBSR participants who showed improvement in psychosocial functioning.

Materials and Methods

Participants and procedures

A single-group, pretest/post-test design was utilized. Eligible participants were individuals enrolled in an 8-week MBSR program at a university medical center. Eligibility criteria were as follows: 18 years of age or older, English speaking, and able to provide informed consent. Because the primary outcome involved immunologic measures, we excluded individuals with significant immune dysregulation, including known diagnosis of an autoimmune disorder, HIV-positive status, and use of systemic steroid medication within the previous 3 months.

In this pilot study, 53 individuals were approached about participating in the study. Of the 53 who were contacted, 13 individuals (24.5%) were ineligible and 12 individuals (22.6%) declined to participate, leaving 28 individuals (52.8%) who were interested in participating. Of the 28 individuals, 24 individuals (45.3%) were consented and completed study assessments prior to the first MBSR session.

Written informed consent was obtained prior to the baseline assessment. At baseline, participants completed the psychosocial questionnaires and provided a blood sample (20 mL) for immunologic assays. Blood samples were drawn in the evening between 5:30 PM and 9:30 PM. Post-test assessments were obtained within 2 weeks following the final MBSR session. At post-test, participants completed the psychosocial questionnaires and provided another blood sample. During the 8-week program, 5 participants (1 male, 4 females) did not complete the MBSR program, and we were not successful in obtaining follow-up data from those 5 who dropped out. Reasons for dropping out included not being able to complete the 8-week program due to medical reasons ($n = 2$); the program was not as expected ($n = 1$); and the need to reschedule due to personal schedule change ($n = 1$). One participant failed to attend the last three classes and provided no explanation for dropping out of the program. Finally, 1 participant completed 7 of the 8 weeks, but missed the final class due to illness. Due to an extended illness, we were unable to obtain a blood sample from this participant within the 2-week post-MBSR period. Participants did not differ from noncompleters on age or baseline psychosocial and immunologic measures. Therefore, baseline data from the 6 participants who did not complete the program were excluded from the analyses.

Intervention

The 8-week MBSR program, modeled after the program created by Jon Kabat-Zinn,[26] is a standardized, group-based

intervention. Each class was 2.5 hours in length and participants were asked to practice 20–30 minutes of meditation a day at home, 6 days a week.

Measures

Psychosocial functioning and quality of life. Psychosocial distress was measured using the Brief Symptom Inventory-18 (BSI-18).[27] The BSI-18 is highly reliable and valid, yielding three subscale scores: somatization, depression, and anxiety. Internal consistency of each subscale ranges from 0.74 to 0.90. The composite score, the General Severity Index, also demonstrates high levels of reliability and internal consistency. Quality of life (QOL) was measured using the Medical Outcomes Survey Short-Form Health Survey (SF-36),[28] which assesses eight domains of health-related QOL: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. In addition, two component scale values were computed to summarize physical well-being (Physical Components Score) and mental well-being (Mental Components Score, MCS). The SF-36 is widely used in studies of patient populations.[29]

Immunologic measures. Due to the heterogeneous nature of the patient sample, we chose to assess general markers of systemic immune function including natural killer cell cytolytic activity and high-resolution C-reactive protein (CRP). These particular measures were chosen to characterize two components of immunocompetence: nonspecific cell-mediated cytotoxicity (NK cell cytotoxicity) and inflammation (CRP). Of the acute-phase proteins, CRP is of particular interest because it mimics the action of antibodies, but unlike antibodies, this protein has broad specificity for pathogen molecules. CRP is also the most commonly used, acute-phase reactant marker of inflammation in the body. The presence of a systemic inflammatory response (as indicated by increased circulating levels of CRP) has been shown to predict risk of recurrent coronary events after myocardial infarction,[30,31] diabetes risk,[32] and survival in patients with cancer.[33,34] Levels of CRP were assessed on frozen samples using a high-sensitivity, two-site enzyme-linked immunoassay.

NK cells serve as an early defense against certain intracellular infections and are able to recognize and kill a limited range of abnormal cells. NK cells are important in innate immunity and serve as an early defense against certain intracellular infections. NK cells serve as the effectors in antibody-dependent cell-mediated cytotoxicity (i.e., the destruction of antibody-coated target cells) and have the ability to kill certain lymphoid tumor cell lines *in vitro* without the need for prior immunization or activation. NK cells bear no known antigen-specific receptors, but are able to recognize and kill a limited range of abnormal cells.

The functional capability of NK cells can be determined by exposing them to a known NK-specific target that is radioactively labeled. NK cell activity is quantified in this assay by using the K562 cell line, which is known to be NK sensitive. Aliquots of 100 μL of various concentrations of peripheral blood mononuclear cells (PBMC effector cells) were incubated in triplicate with 100 μL of labeled target cells for 4 hours at 37°C with 5% CO_2 (effector-to-target ratios of 50:1, 25:1, 12.5:1, and 6.25:1 were studied). Maximum release of ^{51}Cr was determined by addition of 100 μL of 1% Triton X solution to triplicate wells of K562 cells. At the end of the incubation period, 100-μL aliquots of the supernatants were harvested and counted in a γ counter (Beckman Instruments, Fullerton, CA). NK activity was calculated as [(mean sample activity − mean spontaneous release)/(mean maximum release − mean spontaneous release)] × 100. The results were expressed as percent cytotoxicity.

Lytic units (LU) per 10^7 PBMCs and LU per 10^7 NK cells were calculated according to the method of Bryant et al.[35] NK functional assays do not discriminate between cytotoxicity mediated by a few highly active NK cells versus many NK cells in any one particular sample of PBMCs. Therefore, expressing data as LU per NK cell adjusts for the differences in the percentage of NK cells ($CD3^-CD16^+CD56^+$) in the effector cell population PBMCs.[36] NK cell numbers in the effector cell population were determined by automated flow cytometry at the time of the NK cell assay.[37] The functional data are expressed both as LU per PBMC (LU_{20} PBMC) and LU per NK cell (LU_{20} NK).[38]

Statistical analysis

Data were analyzed using SPSS Version 16.0. Changes in psychosocial and immunologic functioning from pre- to post-MBSR were analyzed using paired samples *t* tests. Correlation analyses between change scores on psychosocial and immune measures were examined to assess if, as hypothesized, immunologic changes would most likely be observed in those individuals who showed the greatest change in psychosocial functioning. Residualized change scores used in the correlational analyses were calculated using the procedure described by Cohen and Cohen.[39] Another way to examine whether change in psychosocial functioning was associated with change in immunologic measures that takes into account baseline values is to conduct regression analyses using the post-MBSR immune variables as the dependent variable, and the pre-MBSR (baseline) immune values and change in psychosocial functioning as the predictor variables. Finally, we divided the sample into two subgroups: Those who reported any positive increase in mental well-being (MCS) from pre- to postintervention and those who reported no change in mental well-being. A 2 (group: positive change versus no change) × 2 (time) repeated-measures analysis of variance (ANOVA) was used to examine change in measures of CRP and NK cytolytic activity (LU_{20} NK and LU_{20} PBMC) from pre- to post-MBSR by group.

Results

Demographic findings

Participants included 12 female and 6 male participants. Diagnoses included chronic pain (44%), symptoms of anxiety and depression (39%), hypertension (11%), and cancer (6%). The mean age of the participants was 50.82 years (standard deviation (SD) = 14.06, range = 28–72). In preliminary analyses, we observed that 1 male participant had outlier results on NK cytolytic activity (ranking higher than 2 SD above the mean), and therefore, we did not include data from that participant in any subsequent analyses. Additional preliminary analyses revealed no associations between participant age and any of the immune measures.

Psychosocial and immunologic measures from pre- to post-MBSR

Psychosocial well-being. Significant decreases in anxiety ($t = 3.40$, $p < 0.01$) and overall distress (i.e., BSI General Severity Index) ($t = 2.55$, $p < 0.05$) were observed from pre- to post-MBSR (Table 1). Significant improvements were also identified on both the QOL Physical Composite Score ($t = -2.41$, $p < 0.05$) and the Mental Composite Score ($t = -2.26$, $p < 0.05$), as well as across multiple aspects of QOL, including role limitations due to physical problems ($t = -2.67$, $p < 0.05$), social functioning ($t = -2.24$, $p < 0.05$), vitality ($t = -2.43$, $p < 0.05$), general health ($t = -3.51$, $p < 0.01$), and mental health ($t = -2.82$, $p = .01$).

Immunologic functioning. No significant change in CRP levels and percentage or absolute NK cells was detected from baseline to post-MBSR. LU_{20} NK and LU_{20} PBMC increased from baseline to post-MBSR, although these changes did not reach statistical significance at the two-tailed level. Pre- and post-MBSR assessments of immunologic measures are presented in Table 1.

Associations between psychosocial and immunologic functioning

Correlational analyses between changes in psychosocial and immunologic functioning. Improvements in the Mental Component Summary (MCS) score were correlated with increased LU_{20} NK and LU_{20} PBMC (rs $= 0.59$ and 0.63, respectively, ps < 0.02). Enhanced mental health was also significantly correlated with increases in LU_{20} NK and LU_{20} PBMC (rs $= 0.69$ and 0.71, respectively, ps < 0.01). Improvement in general health was positively correlated with increased LU_{20} PBMC ($r = 0.54$, $p < 0.05$). Reductions in anxiety and overall distress were significantly correlated with reductions in CRP (rs $= 0.64$ and 0.52, respectively; ps < 0.05).

Regression analyses. An alternative analytic approach for evaluating the relationship between changes in psychosocial and immunologic functioning while adjusting for baseline values of the biological variables is to use linear regression and include the baseline immune measure as a covariate. Results from regression analyses provided a similar account of findings. Specifically, a positive change (improvement) in mental health was positively associated with LU_{20} NK ($\beta = 0.43$, $t = 3.25$, $p < 0.01$) and LU_{20} PBMC ($\beta = 0.50$, $t = 2.83$, $p = 0.013$). Similarly, improvements in the Mental Component Summary (MCS) score were positively associated with post-MBSR LU_{20} NK ($\beta = 0.35$, $t = 2.23$, $p = 0.04$), controlling for baseline values. Improvements in general health were also positively associated with post-MBSR LU_{20} PBMC ($\beta = 0.33$, $t = 2.14$, $p = 0.05$), controlling for baseline values.

Regression analyses also indicated that reductions in depression, anxiety, and overall distress were significantly associated with lower post-MBSR CRP levels, controlling for baseline CRP levels. Specifically, a decrease in depression was associated with lower post-MBSR CRP levels ($\beta = 0.17$, $t = 2.25$, $p = 0.04$). Similarly, decreases in anxiety and overall distress were also associated with lower post-MBSR CRP levels ($\beta = 0.20$, $t = 2.77$, $p < 0.02$ for anxiety; $\beta = 0.17$, $t = 2.25$, $p = 0.04$ for overall distress).

Changes in immunologic functioning among patients with improved psychosocial functioning. Participants who reported any positive increase on the MCS from pre- to post-MBSR assessment were categorized as showing "improvement" in their psychosocial well-being. Of the participants

Table 1. Psychosocial and Immunologic Measures at Pre- and Post–Mindfulness-Based Stress Reduction (MBSR) Assessments

Measure	*Pre-MBSR mean (SD)*	*Post-MBSR mean (SD)*	t-*Test* (p-*value)*
Psychosocial functioning			
Anxiety	6.60 (3.60)	3.65 (4.01)	3.40 ($p = 0.004$)
Depression	6.87 (5.54)	4.80 (4.11)	1.62 ($p = 0.127$)
Somatization	4.93 (4.95)	4.20 (5.05)	1.52 ($p = 0.151$)
General Severity Index	18.40 (10.98)	13.07 (11.47)	2.55 ($p = 0.023$)
Qualify of life			
Physical functioning	67.07 (33.39)	73.06 (27.55)	−1.67 ($p = 0.115$)
Role–physical	30.88 (37.01)	57.35 (42.17)	−2.67 ($p = 0.017$)
Bodily pain	51.13 (32.38)	59.13 (27.61)	−1.70 ($p = 0.109$)
General health	55.38 (26.53)	67.19 (22.60)	−3.51 ($p = 0.003$)
Vitality	39.38 (21.12)	52.81 (16.83)	−2.43 ($p = 0.028$)
Social functioning	52.34 (31.36)	64.84 (22.92)	−2.24 ($p = 0.041$)
Role–emotional	45.10 (40.72)	62.75 (38.88)	−1.77 ($p = 0.95$)
Mental health	56.50 (16.58)	70.13 (13.22)	−2.82 ($p = 0.013$)
Physical composite score	39.97 (13.91)	44.02 (12.46)	−2.41 ($p = 0.029$)
Mental composite score	38.83 (11.68)	45.67 (9.95)	−2.26 ($p = 0.039$)
Immunologic variables			
C-reactive protein (mg/L)	5.22 (8.29)	5.88 (9.29)	−0.88 ($p = 0.39$)
% NK cells	14.41 (5.16)	13.00 (4.33)	1.12 ($p = 0.28$)
# NK cells/μL	268.29 (134.28)	289.18 (111.31)	−0.70 ($p = 0.49$)
NK activity (LU/10^7 NK cells) – LU_{20} NK	320.98 (286.50)	505.44 (474.06)	−1.89 ($p = 0.078$)
NK activity (LU/10^7 PBMCs) – LU_{20} PBMC	46.95 (47.23)	69.40 (73.39)	−1.75 ($p = 0.098$)

SD, standard deviation; NK, natural killer; LU, lytic units; PBMC, peripheral blood mononuclear cells.

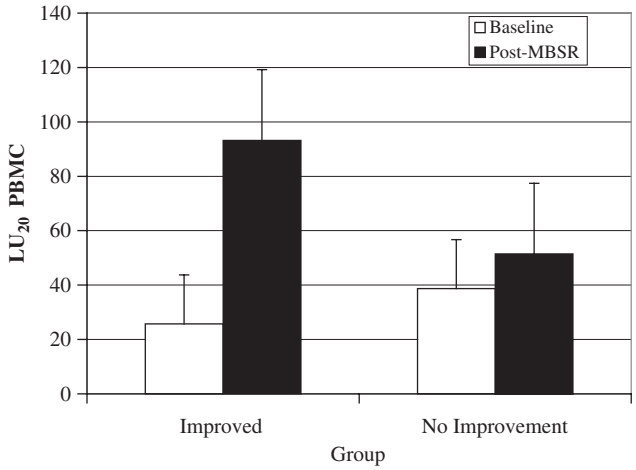

FIG. 1. Change in lytic units $(LU)_{20}$ peripheral blood mononuclear cells (PBMC) among patients who showed improvement versus no improvement in psychosocial functioning following mindfulness-based stress reduction (MBSR).

who were categorized as showing "improvement," the mean increase in MCS scores was 14.46 (SD = 10.36), and the range was 4.72–34.71. Participants whose scores remained the same or decreased from pre- to post-MBSR were categorized as showing "no improvement" in their psychosocial well-being. Of the participants who were categorized as showing "no improvement," the mean change in MCS scores was −4.10 (SD = 4.56), and the range was −0.58 to −12.79.

A repeated-measures ANOVA indicated no effects of group (improved versus no improvement) or time (pre- to post-MBSR) for CRP levels, percentage of NK cells, and absolute NK cells. However, a significant group×time interaction was observed for LU_{20} PBMC, $F(1,16) = 5.29$, $p = 0.036$. Specifically, significant increases in LU_{20} PBMC from pre-MBSR (M = 25.76, SD = 13.70) to post-MBSR (M = 93.20, SD = 82.21) were observed among individuals who reported positive improvement on the MCS score. In contrast, no significant change in NK activity was observed among individuals who reported no improvement in MCS from pre-MBSR (M = 38.70, SD = 38.01) to post-MBSR (M = 51.45, SD = 52.75) (Fig. 1). Individual response data are also presented in a scatterplot (Fig. 2). A similar pattern of results was observed for LU_{20} NK, where significant increases were observed from pre-MBSR (M = 272.88, SD = 203.02) to post-MBSR (M = 632.28, SD = 537.42) among individuals who reported positive improvement on the MCS, but not among those individuals who did not show improvement from pre-MBSR (M = 338.12, SD = 381.97) to post-MBSR (M = 311.63, SD = 241.07), $F(1,16) = 4.29$, $p = 0.056$.

Discussion

Knowledge regarding the intricate relationship between mind and body will continue to advance in the coming years. This broadening understanding will be fueled, in part, by incorporating the assessment of markers of biological functioning within studies of established mind–body interventions, such as MBSR.[4] Given the abundance of empirical data demonstrating that psychosocial well-being is associated with markers of immune functioning, this research sought to expand the MBSR-related literature by assessing whether changes in psychosocial well-being following MBSR participation are associated with corresponding changes in immune functioning.

In the present study, psychosocial functioning of the participants improved from pre- to post MBSR, including significant decreases in anxiety and overall distress as well as significant improvements across various aspects of QOL. This is consistent with data from a number of prior studies that have demonstrated beneficial effects of MBSR on psychosocial functioning.[1,6] In addition, changes in psychosocial well-being were associated with related changes in

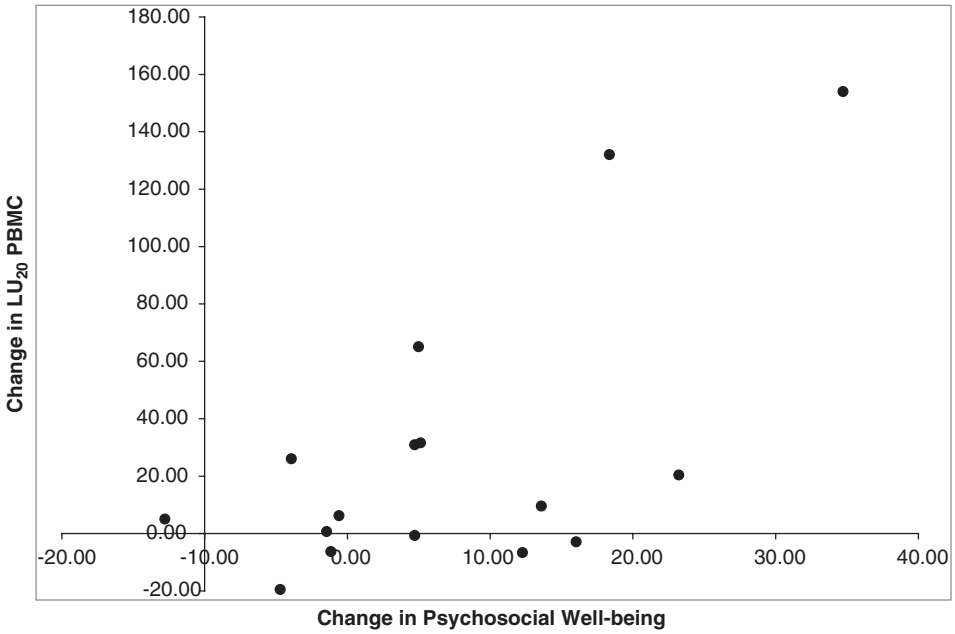

FIG. 2. Scatterplot of the association between change in psychosocial functioning and lytic units $(LU)_{20}$ peripheral blood mononuclear cells (PBMC) among individual patients.

immune parameters, including levels of CRP and NK cytolytic activity.

Specifically, reductions in anxiety and overall distress were significantly correlated with reductions in CRP. This association is consistent with prior findings that have reported that (1) higher levels of anxiety are associated with higher levels of CRP[40]; (2) participation in MBSR leads to reductions in anxiety and psychologic distress[6]; and (3) participation in MBSR was observed to lead to a shift away from a proinflammatory response among patients with cancer.[7] Moreover, the observed association between psychosocial functioning and CRP is also consistent with prior studies that have reported well-established relationships between psychosocial distress and other pro-inflammatory markers, such as interleukin-6.[41,42]

Previous studies also indicate that psychologic distress is associated with reduced NK functional activity,[24] whereas improvements in psychologic functioning have been associated with increased NK functional activity.[43,44] The present finding that improvement in psychologic functioning was associated with enhanced NK cytolytic activity is consistent with prior studies and suggests possible directions for future studies. For example, given that psychosocial distress can not only influence NK cell function but also the trafficking of NK cells into and out of peripheral circulation,[45,46] future studies may be designed to specifically examine whether participation in MBSR is associated with alterations in NK cell trafficking and/or the pattern of leukocyte redistribution between the blood and other immune compartments. In addition, future studies may also investigate whether alterations in innate cellular immunity are reversible with improvement in psychologic functioning following MBSR. Finally, given the beneficial effects of MBSR on physiologic outcomes in various patient populations (e.g., adults at high risk for cardiovascular disease, individuals with diabetes), future studies may propose to examine the hypothesis that participation in MBSR leads to changes in immunologic markers (e.g., reduced inflammation) that are directly relevant to specific disease processes and outcomes (e.g., heart disease).

We acknowledge several limitations of the present study. First, given the pre–post study design, changes in immunologic or psychosocial measures cannot be attributed with certainty to participation in the MBSR program, as there was no comparison group. It is possible that these changes would have occurred naturally, due to external environmental factors or other reasons. Second, due to the heterogeneous nature of the patient sample, we utilized nonspecific measures of immunologic functioning. The clinical implications of the observed changes in immunologic measures are not well-defined. However, it is notable that despite the heterogeneity of the sample, meaningful associations were detected between psychosocial well-being and immune functioning. Third, the present study involved a relatively small sample, and thus, power was limited for detecting statistically significant changes. Fourth, we acknowledge that a meaningful proportion of participants did not complete the final assessment for various reasons. However, the primary purpose of this pilot study was to examine whether changes in psychosocial functioning were associated with changes in immune functioning, and therefore, our focus was necessarily on those participants among whom change in functioning could be determined (i.e., provided pre- and post-assessments). Finally, it is acknowledged that the association between psychosocial well-being and immune functioning could be attributed to other potential confounding factors that were not assessed in the present study, such as sleep quality, changes in existing disease or symptoms, or psychologic comorbidities. In light of prior studies that have reported beneficial effects of MBSR on sleep quality and symptoms,[47] future studies may propose to investigate whether the observed association between psychosocial well-being and assessments of immune functioning is mediated by, or can be attributed to, improvement in these various other factors.

Conclusions

Data from this pilot study suggest that changes in psychologic well-being following MBSR are associated with changes in immune functioning. Future studies to evaluate the hypothesis that enhanced psychosocial functioning leads to corresponding immunologic changes should be conducted using a randomized, controlled design.

Acknowledgments

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Disclosure Statement

No competing financial interests exist.

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