

Mindfulness-Based Interventions for Chronic Pain: A Systematic Review of the Evidence

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Abstract

Objectives: Chronic pain is a common disabling illness that does not completely respond to current medical treatments. As a consequence, in recent years many alternative interventions have been suggested. Among them, mindfulness-based interventions (MBIs) are receiving growing attention. The aim of the present article is to review controlled studies investigating the efficacy of MBIs for the reduction of pain and the improvement of depressive symptoms in patients suffering from chronic pain.

Methods: A literature search was undertaken using MEDLINE,[®] ISI web of knowledge, the Cochrane database, and references of retrieved articles. The search included articles written in English published up to July 2009. The data were independently extracted by two reviewers from the original reports. Quality of included trials was also assessed.

Results: Ten (10) studies were considered eligible for the present review. Current studies showed that MBIs could have nonspecific effects for the reduction of pain symptoms and the improvement of depressive symptoms in patients with chronic pain, while there is only limited evidence suggesting specific effects of such interventions. Further findings evidenced some improvements in psychologic measures related to chronic pain such as coping with pain following MBIs as well.

Discussion: There is not yet sufficient evidence to determine the magnitude of the effects of MBIs for patients with chronic pain. Main limitations of reviewed studies include small sample size, absence of randomization, the use of a waiting list control group that does not allow distinguishing of specific from nonspecific effects of MBI as well as differences among interventions.

Conclusions: However, because of these preliminary results, further research in larger properly powered and better designed studies is warranted.

Introduction

CHRONIC PAIN is a common disabling illness that affects about 20%–30% of the adult population in Western countries¹ and is often related to high rates of comorbid depressive symptoms.² Although current therapeutic approaches, including analgesic and opioid drugs, can provide significant improvements, the most potent drugs only reduce pain by 30%–40% in fewer than 50% of patients.³ In addition, surgical techniques such as implantation of artificial discs in the spine and implantable drug delivery systems provide limited pain reduction in only a subset of patients as well.^{4,5} As a consequence, several psychologic treatments for chronic pain have been suggested.⁶ Among them, mindfulness-based stress reduction (MBSR) and closely derived interventions (mindfulness-based interventions or MBIs) are some of the most studied.

MBSR is a standardized group-based meditation program conceived in the late 1970s from the effort to integrate Buddhist mindfulness meditation with contemporary Western clinical and psychologic practice.^{7,8} In the last 2 decades, MBSR has been proposed as a treatment for many diseases, showing a good efficacy for many mental and physical disorders^{9–11} as well as for healthy people,¹² although results are not always convincing.^{9,13} Note, however, that such a meditation program was originally developed and is still consistently used for patients suffering from chronic pain.^{14,15}

The main feature of MBSR is the cultivation of “mindfulness” (i.e., the development of a particular kind of attention characterized by a nonjudgmental awareness, openness, curiosity, and acceptance of internal and external present experiences, which allows the practitioners to act more reflectively rather than impulsively).^{16–18} MBSR comprises three different techniques including (1) “body scan,” which

involves a gradual sweeping of attention through the entire body from feet to head, focusing noncritically on any sensation or feeling in body regions and using periodic suggestions of breath awareness and relaxation; (2) "sitting meditation," which involves both mindful attention on the breath or on the rising and falling abdomen as well as on other perceptions, and a state of nonjudgmental awareness of cognitions and of the stream of thoughts and distractions that continuously flow through the mind; and (3) "Hatha yoga" practice, which includes breathing exercises, simple stretches, and posture designed to strengthen and relax the musculoskeletal system.⁷ The standard program consists of 8-week sessions with a duration of 2 hours each and homework for 45 minutes a day, 6 days a week,^{7,8} even though several modifications in sessions, homeworks, and total duration can be observed among different courses for different populations of patients. Additionally, interventions inspired by the original program but including specific modifications such as the adjunct of particular exercises or of psychologic techniques are consistently used as well.¹⁹

Preliminary results on the efficacy of MBIs for patients suffering from chronic pain have been established in several independent uncontrolled studies on patients with different types of pain such as low back, upper back, shoulder and cervical pain, headache,^{14,20,21} and fibromyalgia.²² Interestingly, there is some evidence to suggest that results gained in the short term could be maintained in the long term²³ and that MBIs could be useful for older people as well.^{21,24} However, it is worth mentioning that very often initial emphasis deriving from early uncontrolled studies is not yet supported when controlled studies are undertaken.

As a consequence, the aim of the present article is to review controlled studies investigating the efficacy of MBIs for the reduction of pain and/or the improvement of depressive symptoms in patients with chronic pain.

Methods

Literature research

A literature search was undertaken using MEDLINE,[®] ISI web of knowledge, the Cochrane database, and references of retrieved articles. The search included original articles, letters to the editor, and congress abstracts indexed by web-based electronic databases mentioned above or mentioned in retrieved articles published up to July 2009. The search strategy considered only studies published in English. The main search terms were MBSR, mindfulness-based intervention, mindfulness meditation, stress reduction, and chronic pain, in various combinations as needed.

Selection of trials

Included studies had to investigate the efficacy of a MBI, be performed in patients suffering from chronic pain (e.g., low back pain, fibromyalgia, rheumatoid arthritis) with at least 6 months of illness history, provide at least one measure of pain and/or depression, provide quantitative data, have a control group procedure that was either inactive (for instance, a waiting list) and/or active, and oriented to control for nonspecific effects of the MBI group (such as an educational control group). Of note, we considered an intervention as nonspecific (placebo-like) if it could induce the expectancy

of a benefit but it had no additional specific effects.²⁵ Exclusion criteria were as follows: absence of a control group, qualitative reports, speculative reports, and review articles. A summary of included articles investigating the efficacy of MBIs for the management of chronic pain is shown in Table 1. Main features of included interventions are reported in Table 2. Quality of included trials, assessed by the authors using a validated quality scale,²⁶ is shown in Table 3. A flow chart of the review process is shown in Figure 1.

Outcome measures

Our primary outcomes were (1) the reduction of pain and (2) the reduction of depressive symptoms in MBI groups compared to inactive and/or active control groups. Our secondary outcome measures were the improvement of (1) coping with pain, (2) physical function, (3) stress reduction and quality of life, and (4) miscellaneous psychologic changes related to MBIs.

Data extraction and quality assessment

The data were independently extracted by the authors from the original reports. Quality of included trials was independently assessed by the authors using a validated quality scale²⁶ (Table 3). All disagreements were resolved through discussion. A score ≥ 3 was considered to be indicative of a moderate- to high-quality study.²⁶

Results

Characteristics of included studies

The original search retrieved 190 articles. One hundred and seventy-three (173) articles were excluded because their primary focus was not the investigation of a MBI for patients with chronic pain. After the first screening, 17 articles remained. Seven (7) studies were excluded because of the absence of a control group and/or of quantitative analysis (Table 4) and 10 studies could be included in the present review (Table 1). Included studies comprised 6 randomized controlled studies²⁷⁻³² and 4 controlled studies.³³⁻³⁶ Five (5) studies compared MBIs to a waiting list,^{28,30,31,33,35} 1 study compared a MBI + *qigong* to a nonspecific intervention (social support group),²⁷ 1 study compared a MBI to a specific treatment,³⁴ 2 studies compared MBIs to both a waiting list and a specific treatment,^{29,36} and 1 study compared a MBI to both a nonspecific and a specific treatment.³² Four (4) studies focused on fibromyalgia,^{27,28,33,34} 4 studies on various types of chronic musculoskeletal pain such as low back pain,^{29,30,35,36} and 2 studies on rheumatoid arthritis.^{31,32} Six (6) studies included a follow-up at different time points.^{28-32,34}

Primary outcome measures

Efficacy for pain symptoms. Seven (7) of the included studies reported some measures of pain.^{27,29,30,32-34,36} Five (5) of these studies reported an improvement in pain perception in MBI groups that was significantly higher than that observed in the comparison groups.^{30,32-34,36} Among them, three studies suggested that MBIs were better in comparison to a waiting list^{30,33,36}; 1 study suggested that a MBI was better than an educational control group designed to control for nonspecific effects of the intervention, such as the ex-

TABLE 1. SUMMARY OF INCLUDED STUDIES

Study	Meditation/ comparison	Number of subjects (ITT)	Study design	Disease condition	Mean duration of symptoms ^a	Measures of pain	Measures of depression	Further measures	Main findings
Goldenberg et al., ³³ 1994	MBI Waiting list or no treatment	87 42	CT	Fibromyalgia	7.3 ± 9.9 7.9 ± 7.8	VAS pain	-	FIQ, GSI	Mean VAS scores, FIQ and GSI scores significantly improved in the meditation compared to the control group.
Astin et al., ²⁷ 2003	MBSR + <i>qi gong</i> Support group	64 63	RCT- ANSC	Fibromyalgia	5.22 ± 7.31 4.89 ± 4.15	Pain subscale of SF-36	BDI	TPC, FIQ, 6-minute- walk time test	Significant and equivalent improvements from baseline were observed for both groups at the 8th week for pain subscale of SF-36, FIQ, Total Myalgic and BDI scores. No improvement in the 6-minute-walk time test. Benefits were still maintained at the 6-month follow-up in both groups.
Sagula & Rice, ³⁵ 2004	MBSR Waiting list	49 22	CT	Various types of chronic pain	Not reported	-	BDI	STAI, RTL	MBSR group showed significant reductions in depression and state anxiety and advanced significantly more quickly through the initial stages of grieving than the comparison group
Plews-Ogan et al., ²⁹ 2005	MBSR Massage Waiting list	10 10 10	RCT-AC	Musculoskeletal pain	Not reported	VAS	-	Mental Health scale of SF-12	Massage groups showed significantly higher benefits for pain and MBSR group showed significantly higher improvements for Mental Health scores compared to waiting list. Results of active treatments were still maintained at 4-week follow-up.
Septhon et al., ²⁸ 2007	MBSR Waiting list	51 40	RCT	Fibromyalgia	4.5 ± 3.6 4.9 ± 5.2	-	BDI	FIQ, SSQ	Marked reductions in BDI scores were observed in the meditation group but not in the control group. Benefits were still maintained at the 2-month follow-up.
Grossman et al., ³⁴ 2007	MBSR & PMR & gentle stretching	31 16	CT-AC	Fibromyalgia	13.8 ± 6.1 9.9 ± 6.9	VAS, PPS	HADS depression	IPR, QOF	MBSR compared to PMR group displayed significant improvements for VAS, QOL subscales, coping with pain, anxiety, depression, and somatic complaints. Benefits were still maintained at the 3-year follow-up.
Pradhan et al., ³¹ 2007	MBSR Waiting list	31 32	RCT	Rheumatoid arthritis	6 ± 7 11 ± 12	-	BDI	MAAS, DAS28, PWBS, GSI	At 2 months, there were no significant differences between groups in any outcomes. At 6 months there were significant improvements for MBSR compared to control group for GSI, PWBS, BDI, and MAAS score. No impact on disease status was observed.

(continued)

TABLE 1. (CONTINUED)

Study	Meditation/ comparison	Number of subjects (ITT)	Study design	Disease condition	Mean duration of symptoms ^a	Measures of pain	Measures of depression	Further measures	Main findings
Morone et al., 2008 ³⁰	MBSR Waiting list	19 18	RCT	Chronic low back pain in people >65 years	Not reported	Pain subscale of SF-36, MPQ-SF	-	CPAQ, RMQ, SPPB, SF-36	Significant reductions in the MBSR compared to the control group were observed for the Pain subscale of SF-36 as well as for CPAQ. No significant difference for other measures. Positive results were maintained at the 3-month follow-up.
Gardner-Nix et al., 2008 ³⁶	In-site MBI Tele MBI Waiting list	99 57 57	CT	Various types of chronic pain	Not reported	NRS-P	-	PCS	Tele and in-site MBI groups achieved similar results for mental health and pain catastrophizing levels. However, only in-site group obtained significantly higher scores on the physical dimension of QOL and lower scores of usual pain compared to waiting list.
Zautra et al., 2008 ³²	MBI CBT Support group	52 (17) 47 (6) 44 (14) ^b	RCT-AC- ANSC	Rheumatoid arthritis	10.86 ± 10.27 15.02 ± 13.78 11.81 ± 13.92	VAS	6 items of PANAS	DAS28, IL-6, CE, PANAS	CBT group showed the greatest pre to post improvement in self-reported pain control and reductions in the IL-6; both MBI and CBT groups showed more improvement in coping efficacy than support group. Patients with history of depression benefited most from MBI across several measures.

^aYears.

^bSubgroup of patients with depression history.

Scales for Scales: (a) Spielberger CD. State-Trait Anxiety Inventory. Palo Alto, CA: Mind Garden, 1983; (b) Schneider J, Deutsch D. Understanding the transformative potential of grief: Construct validation of the Response to Loss Inventory. Traverse City, MI: Seasons Press; 1997; (c) Ware JE, Kosinski M, Keller SD. A 12-item short-form health survey: Construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220-233; (d) Douglass AB, Bornstein R, Nino-Murcia G, et al. The Sleep Disorders Questionnaire: I. Creation and multivariate structure of the SDQ. *Sleep* 1994;17:160-167; (e) Siegrist J, Broer M, Junge A. Profil der Lebensqualität chronisch Kranker. Handanweisung. Göttingen: Beltz Test, 1996; (f) Schermelleh-Engel K. Questionnaire for Pain Regulation (FSR) [in German]. Frankfurt, Swets: Handanweisung, 1995; (g) Brown KW, Ryan RM. The benefits of being present: Mindfulness and its role in psychological well-being. *J Pers Soc Psychol* 2003;84:822-848; (h) Ryff CD. Happiness is everything, or is it? Explorations on the meaning of psychological well-being. *J Pers Soc Psychol* 1989;57:1069-1081; (i) Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: The PANAS scales. *J Pers Soc Psychol* 1988;54:1063-1070; (j) Reich J, Zautra AJ. Experimental and measurement approaches to internal control in at-risk older adults. *J Soc Issues* 1991;47:143-158; (k) McCracken LM, Carson JW, Eccleston C, et al. Acceptance and change in the context of chronic pain. *Pain* 2004;109:4-7; (l) Roland M, Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain. *Spine* 1983;8:141-144; (m) Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 2000;55:M221-M231; (n) Sullivan MJ, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. *Psychol Assess* 1995;7:524-532.

Definitions of terms in notes (a)-(n). MBSR, mindfulness-based stress reduction; CBT, cognitive behavioral intervention; ITT, intent to treat; RCT, randomized controlled trial; CT, controlled trial; RCT AC, randomized controlled trial with an active control; RCT ANSC, randomized controlled trial with an active control; Global Severity Index (of the Hopkins Symptom Checklist

90 Revised).

TABLE 2. CHARACTERISTICS AND FOLLOW-UP OF MBI INTERVENTIONS

Study	Study duration (weeks)	Session duration (minutes)	Daily homework duration (minutes)	Day-long retreat	Retreat duration (hours)	Main modification to the standard program ^a	Follow-up (weeks from baseline)
Goldenberg et al., 1994 ³³	10	120	N.S.	No	–	N.S.	No
Astin et al., 2003 ²⁷	8	150	N.S.	No	–	Adjunct of 1 hour <i>qigong</i>	No
Sagula & Rice, 2004 ³⁵	8	90	At least 20	No	–	None	No
Plews-Ogan et al., 2005 ²⁹	8	150	N.S.	No	–	N.S.	12
Sephton et al., 2007 ²⁸	8	150	30–45	Yes	N.S.	None	16
Grossman et al., 2007 ³⁴	8	150	N.S.	Yes	7	None	3 years for MBSR group only
Pradhan et al., 2007 ³¹	8	150	45	Yes	N.S.	None	26
Zautra et al., 2008 ³²	8	N.S.	N.S.	No	–	No yoga, teaching of cognitive exercises	26
Morone et al., 2008 ³⁰	8	90	45	No	–	No yoga	22
Gardner-Nix et al., 2008 ³⁶	10	120	N.S.	No	–	N.S.	No

^aAs reported in the background.

MBI, mindfulness-based meditation; N.S., not specified; –, not applicable; MBSR, mindfulness-based stress reduction.

pectancy effect and group support, but less efficacious than a standard cognitive behavioral intervention (CBT)³²; and 1 study suggested that a MBI was better than progressive muscle relaxation.³⁴ On the other hand, 2 studies did not observe any significant difference between a MBI + *qigong* and an educational support group designed to control for nonspecific effects of the intervention²⁷ and between a MBI and massages or a waiting list,³¹ respectively.

More in detail, Goldenberg and colleagues³³ observed that 67% of subjects suffering from fibromyalgia assigned to a MBI showed a significant improvement in perceived pain from baseline as measured by a visual analog scale (VAS) for pain compared to only 40% of subjects of the control group ($p = 0.006$). In addition, subjects assigned to the MBI showed a final 16% decrease of pain compared to controls. In a following study, Gardner-Nix and colleagues compared an in-site MBI for patients suffering from musculoskeletal pain to a waiting list and to a distant-site mindfulness program via videoconferencing at local hospital site.³⁶ A significant improvement from baseline in usual pain as measured by a Numerical Rating Scale for Pain³⁷ was observed only in the in-site group ($p < 0.05$). Also, a significant improvement in a MBI group compared to a waiting list was observed in a

sample of older adults suffering from musculoskeletal pain.³⁰ Mean pain scores changed in the expected direction for the meditation group as compared to the control group at the 8-week follow-up for the McGill Pain Questionnaire Short Form³⁸ and the Pain Scale of the Short Form-36,³⁹ though only the latter difference was significant. On the other hand, in a pilot randomized trial performed in a sample of subjects suffering from musculoskeletal pain randomly assigned to a MBI, massages, or to a waiting list, Plews-Ogan and colleagues²⁹ did not observe any significant difference in pain outcomes for the meditation group at any time. Note, however, that this result could be linked to the very small sample size of this study. Although these studies overall suggest the potential clinical usefulness of MBIs, such findings have to be interpreted with caution because of their several limitations including absence of randomization,^{33,36} small sample size,^{29,30} and the impossibility of distinguishing specific from nonspecific effects of MBIs because of the use of a waiting list as a control group.^{29,30,33,36}

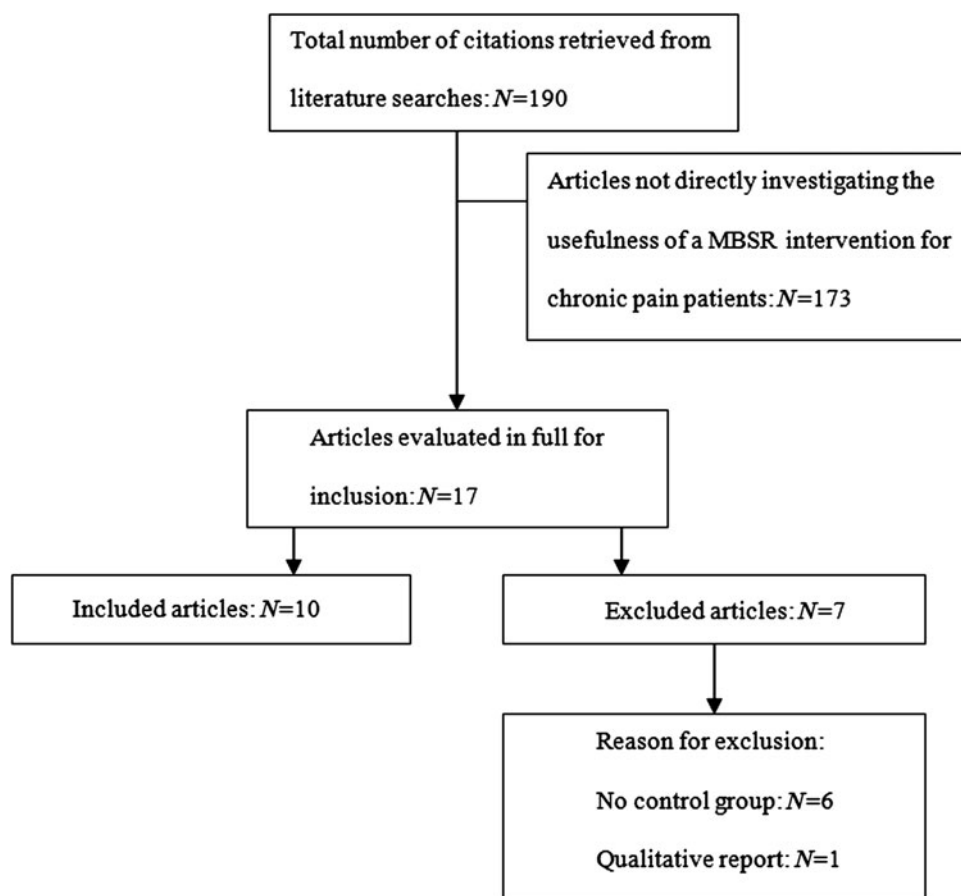
Two (2) further studies showed mixed results in samples of patients with fibromyalgia. In the first nonrandomized study comparing a MBI to a program of progressive muscle relaxation and gentle stretching,³⁴ patients assigned to the

TABLE 3. ASSESSMENT OF STUDIES' QUALITY

Study	Randomization	Appropriate randomization	Dropouts and withdrawals	Blinding	Appropriate blinding	Jadad score
Goldenberg et al., 1994 ³³	No	–	Yes	No	–	1
Astin et al., 2003 ²⁷	Yes	Yes	Yes	Yes	No	3
Sagula & Rice, 2004 ³⁵	No	–	Yes	No	No	1
Plews-Ogan et al., 2005 ²⁹	Yes	Yes	Yes	No	No	3
Sephton et al., 2007 ²⁸	Yes	N.S.	Yes	Yes	No	2
Grossman et al., 2007 ³⁴	No	–	Yes	No	–	1
Pradhan et al., 2007 ³¹	Yes	Yes	Yes	Yes	No	3
Zautra et al., 2008 ³²	Yes	Yes	Yes	Yes	No	3
Morone et al., 2008 ³⁰	Yes	Yes	Yes	No	No	3
Gardner-Nix et al., 2008 ³⁶	No	–	Yes	No	–	1

N.S., not specified.

FIG. 1. Flow diagram of the review process. MBSR, mindfulness-based stress reduction.



MBI achieved a significant reduction from baseline in perceived pain as measured by a VAS for pain ($p < 0.0001$), whereas the control group did not achieve any significant improvement. Also, the sensory and the affective component of perceived pain as measured by the Pain Perception Scale⁴⁰ showed significant reductions in the MBI group ($p < 0.01$ and $p < 0.0001$, respectively) but not in the control group. Interestingly, benefits gained at the end of the trial in MBI subjects were still maintained at the 3-year follow-up. Note, however, that this study was limited by a small sample size

and by the absence of randomization, and opposite results were observed, in fact, in a larger higher quality randomized controlled trial performed in a population of patients with fibromyalgia comparing a MBI + *qigong* to a social support group designed to be structurally equivalent to the meditation program in terms of expectancy effect and group support but excluding the “active ingredient” of formal meditation.²⁷ Although significant improvements from baseline were observed in pain measures in the meditation group, similar results were achieved in the social support group and were maintained in both groups at the 6-month follow-up. However, some concerns could be raised about the integrity of treatment of the this study,²⁷ given that such treatment was not completely manualized and a high attrition rate was observed. Finally, in a randomized controlled study comparing a MBI to CBT and to an educational support group that served to control for the nonspecific effects of the interventions, the authors observed that both active treatments were more efficacious than the educational group in reducing pain levels and enhancing pain control, although the highest improvement was observed in the CBT group.

Considering higher quality randomized controlled trials separately, there is only limited evidence suggesting that a MBI could have a specific effect for patients with rheumatoid arthritis,³² that MBI + *qigong* could have a nonspecific effect for patients with fibromyalgia,²⁷ and contrasting evidence suggesting nonspecific effects of MBIs for patients suffering from musculoskeletal pain.^{29,30} However, higher quality trials are limited by important methodological shortcomings as

TABLE 4. EXCLUDED STUDIES AND REASONS FOR EXCLUSION

Study	Reasons for exclusion
Kabat-Zinn, 1982 ¹⁴	No control group
Kabat-Zinn et al., 1985 ^a	No control group
Kabat-Zinn et al., 1987 ²³	No control group
Kaplan et al., 1993 ²²	No control group
McBee et al., 2004 ²¹	No control group
Morone et al., 2008 ²⁴	Qualitative study
Lush et al., 2009 ^b	No control group

^aKabat-Zinn J, Lipworth L, Burney R. The clinical use of mindfulness meditation for the self-regulation of chronic pain. *J Behav Med* 1985;8:163–190.

^bLush E, Salmon P, Floyd A, et al. Mindfulness meditation for symptom reduction in fibromyalgia: Psychophysiological correlates. *J Clin Psychol Med Settings* 2009;16:200–207.

well, including the application of nonmanualized treatments^{27,32} or lack of adequate power to detect small differences among different treatment groups.^{29,30}

In conclusion, available studies mainly suggest that MBIs could have nonspecific effects related to the expectation of a benefit or of group support^{27,33,36} for pain reduction in patients with chronic pain, while there is only limited evidence suggesting specific effects of such interventions.^{32,34} However, because of several methodological shortcomings of available trials and differences in terms of MBI programs and diseases under investigation, current evidence must be considered with caution and replications in larger, well-designed studies are needed.

Efficacy for depressive symptoms. Six (6) of the included studies reported some measures of depression.^{27,28,31,32,34,35} Four (4) of these studies reported a significant advantage for MBI groups in comparison to control groups.^{28,31,34,35} Among them, 3 studies suggested that MBIs were better in comparison to a waiting list,^{30,33,36} and 1 study suggested that a MBI was better than progressive muscle relaxation.³⁴ On the other hand, 2 studies did not observe any significant difference between a MBI + *qigong* and an educational support group designed to control for nonspecific effects of the intervention²⁷ and between a MBI, CBT, and an educational group,³¹ respectively.

Furthermore, despite MBIs showing some efficacy for reducing depressive symptoms in patients with fibromyalgia in many independent studies,^{27,28,34} current evidence is controversial and it mainly suggests that MBIs could have a nonspecific effect on the reduction of depressive symptoms. A significant advantage for a MBI was observed in comparison to a waiting list control group²⁸ but not in comparison to a social support group designed to control for nonspecific benefits.²⁷ On the other hand, a following study³⁴ showed that a MBI was significantly better than an active treatment (i.e., progressive muscle relaxation) in reducing depressive symptoms in patients with fibromyalgia, as shown by a significant reduction in the depressive subscale scores of the Hospital Anxiety and Depression Scale⁴¹ in the meditation group compared to the control group ($p < 0.03$) that was still maintained at the 3-year follow-up. Note, however, that such studies are limited by methodological shortcomings including small sample size,^{28,34} use of a nonmanualized treatment,²⁷ and absence of randomization.³⁴

In the only study assessing depressive symptoms in patients suffering from musculoskeletal pain³⁵ by means of the Beck Depression Inventory (BDI),⁴² a significant difference in post-test BDI scores emerged between the treatment group when contrasted with the comparison group. However, the use of a waiting list did not allow distinguishing a specific from a nonspecific effect of the MBI in such patients. Finally, pertaining to rheumatoid arthritis, in an early study Pradhan et al.³¹ observed a marginal improvement in depressive symptoms as measured by the BDI in the MBI group compared to the waiting list control group at the 6-month follow-up ($p = 0.08$). In a following study, Zautra and colleagues³² observed a significant improvement in depressive symptoms in their sample, even though no significant difference was observed between the MBI, CBT, and educational support group.

Considering higher quality randomized controlled trials separately,^{27,31,32} current evidence suggests that MBIs could have nonspecific effects but not specific effects on depressive symptoms, although the use of nonmanualized protocols in 2 studies^{27,32} as well as the small sample size of the third study,³¹ possibly related to a false-negative finding, suggest that these findings be considered with caution.

To summarize, studies that investigated the usefulness of MBIs for the reduction of depressive symptoms in patients with chronic pain, including higher quality studies, suggested that they had nonspecific but not specific effects on this outcome. However, because of the heterogeneity of the diseases under investigation and the use of different MBI protocols, further research in larger samples using more standardized MBIs is needed.

Secondary outcome measures

Coping with pain. Some studies suggested that MBIs could have a nonspecific effect in helping patients with fibromyalgia to cope with physical burden related to their illness. The mean Fibromyalgia Impact Questionnaire⁴³ score, in fact, decreased by 11% in participants of the MBI compared to the waiting list control group ($p = 0.05$) in the study performed by Goldenberg et al.,³³ and a similar reduction was reported by Astin and colleagues,²⁷ though similar findings were observed in the social support control group as well. On the other hand, limited evidence for a specific effect of MBIs was supported by Grossman et al.,³⁴ although their findings were limited by a small sample size and by the absence of randomization. Notably, similar findings along with an increase in pain acceptance ($p = 0.008$) were also observed in samples of patients suffering from musculoskeletal pain ($p < 0.01$).³⁶ Additionally, Zautra et al.³² observed that patients with recurrent depression assigned to the MBI group showed a greater shift from pre- to postintervention in their efficacy expectations for coping successfully with pain compared to the CBT and the educational control groups.

Physical function. A single study showed that a MBI could have a significant positive impact on patients with rheumatoid arthritis as shown by an improvement in the Disease Activity Score in 28 joints,⁴⁴ although only the CBT group showed significant reductions in the inflammatory interleukin-6 levels.³² Also, significant improvements were observed in physical function both in the in-site and in the distant-site MBI groups in comparison to the waiting list control group.³⁶

In contrast to the previous findings, however, no improvement in objective measures of physical function such as the number of feet traversed in the 6-minute walk—an objective test often used for patients with fibromyalgia where subjects are asked to walk as far and as quickly as possible within 6 minutes—was observed either in the MBI or in the social support control group in the study performed by Astin et al.²⁷ Additionally, no significant improvement in physical function was observed in older adults suffering from chronic low-back pain³⁰ and in patients suffering from rheumatoid arthritis³¹ in other studies. Note, however, that such negative findings could be related

to the small sample size of these studies,²⁷ and replications in larger studies are needed.

Stress reduction and quality of life. Significant improvements from baseline were observed in MBI groups for measures of stress reduction,³³ anxiety levels, and different domains of the quality of life such as functional status and positive affect in comparison to a progressive muscle relaxation group (all p -values < 0.0001)³⁴ in patients suffering from fibromyalgia. Similarly, some findings suggested that a MBI could be better than a waiting list in reducing psychological distress and enhancing well-being as well as in providing marginal enhancements in mindfulness levels.³¹

Further findings. Further observations suggested a possible nonspecific effect of MBIs on anxiety levels,³⁵ on mental health status,²⁹ and on the grieving process often associated with chronic pain, finding significant support for an improvement in the early phase of grieving (cope/awareness; $p < 0.05$) but not for the second phase (growth).³⁵

When higher quality randomized controlled studies were considered separately, possible nonspecific effects were observed for the ability to cope with pain²⁷ and for the improvement in mental status,²⁹ and a specific effect was observed with respect to physical function in patients suffering from rheumatoid arthritis.³² On the other hand, no significant benefit for physical function in patients with fibromyalgia was observed.²⁷ It is worth noting, however, that these findings must be considered with caution because of a number of methodological shortcomings already considered for the primary outcome measures and because results reported in this section often lack replication. Nonetheless, because of these preliminary findings, further research in larger studies using more adequate methodologies is warranted.

Discussion

The aim of the present article was to review controlled studies investigating the efficacy of MBIs for the reduction of pain and/or the improvement of depressive symptoms in patients with chronic pain. We observed three main findings. First, available studies suggested that MBIs could have nonspecific effects related, for instance, to the expectation of a benefit for pain reduction in patients suffering from fibromyalgia or rheumatoid arthritis, while there is only limited evidence suggesting specific effects of such interventions in these populations of patients. Although MBI groups showed benefits in comparison to waiting list control groups, in fact, when they were compared to active control groups designed to be structurally equivalent to the meditation program in terms of expectancy effect and group support but excluding the active ingredient of mindfulness meditation, they usually showed no significant advantage for the reduction of perceived pain. Of course, it cannot be ruled out that the nonspecific control groups used to control for nonspecific effects of MBIs could provide some specific benefits for pain as well, but such a hypothesis should be more thoroughly investigated in the context of adequate experimental studies.

On the other hand, no significant improvement from baseline and in comparison with other treatment options was

usually found for patients suffering from musculoskeletal pain such as low-back pain or cervical pain. Note, however, that such findings were observed in trials limited by a sample size and performed in very heterogeneous samples of patients, including populations with different sites or types of pain as well as of different ages. As a consequence, further larger properly powered studies are warranted to determine the magnitude of the effects related to MBIs and to more thoroughly investigate whether such effects are larger than those related to nonspecific support groups. Importantly, when we considered higher quality studies separately, results did not significantly change, though such studies were often limited by important methodological shortcomings as well, including the application of nonmanualized treatments or the lack of adequate power to detect small differences among different treatment groups.

A second important finding was that MBIs could be useful for reducing depressive symptoms associated with chronic pain. However, the magnitude of such benefits appeared comparable to that of other nonspecific interventions and did not suggest a possible advantage for MBIs in comparison to such interventions as educational support groups. Notably, in the study performed by Zautra and colleagues, similar results were observed in patients with rheumatoid arthritis who were assigned to a MBI, a CBT, and an educational support group.³² Although it could be suggested that both active treatments showed only a nonspecific effect on the reduction of depressive symptoms, it is noteworthy that, in a previous report, reductions in anxiety as well as enhanced self-efficacy were observed for participants involved in a self-management course for arthritis in comparison to those provided with only an education manual,⁴⁵ hence suggesting that further investigations are needed in order to better explore the nature and the magnitude of the improvements related to the so-called nonspecific treatments and to better differentiate them from the natural history of illness.²⁵

Third, MBIs could be useful to improve specific psychological features associated with chronic pain even without modifying pain itself. Interestingly, reviewed findings showed that patients assigned to MBIs showed an increased pain acceptance and tolerance as well as significant improvements in their stress levels and quality of life, though the frequent use of a waiting list as a comparator does not allow definitive conclusions to be drawn.

Also, it should be noted that very often results gained in the short term were still maintained in the long term. A significant example is represented by the study performed by Grossman et al.,³⁴ who observed that benefits in the group of patients with fibromyalgia who underwent a MBI were still maintained at the 3-year follow-up. Although no comparison was used in the follow-up, most longitudinal studies of female patients with fibromyalgia indicate an absence of spontaneous improvement of symptoms or remission in the natural course of the syndrome.⁴⁶⁻⁴⁸ Thus, it could be hypothesized that, although MBIs do not consistently modify pain perception, they provide beneficial modifications to the relationship of patients with their symptoms, enhancing acceptance and reducing concomitant depressive symptoms. Such an explanation is consistent with the main aim of being mindful, which is not directed at symptom reduction but more fundamentally toward altering how perceptible mental

processes and contents are experienced, toward greater awareness, acceptance, and tolerance of the unavoidable vagaries of life.^{7,14} In addition, acceptance of symptoms could facilitate enhanced psychologic well-being, even in the face of continued symptoms.^{49,50}

Interestingly, there is some evidence suggesting that higher levels of mindfulness could be linked to decreased pain perception and to an overall better functioning.⁵¹ Even though a single study only partially supported an increase of mindfulness levels at postintervention in patients suffering from rheumatoid arthritis,³¹ a challenge for future studies could be linking enhancements of psychologic and physical outcomes to increases in mindfulness levels in patients with chronic pain, a relationship already supported in other populations of patients.^{52,53}

Several limitations have to be taken into account in the interpretation of reviewed findings. A first limitation is represented by the heterogeneity of diseases under investigation, including fibromyalgia, musculoskeletal pain, and rheumatoid arthritis. Even though they all share chronic pain as an important feature of illness, such heterogeneity in patient populations could partially explain the heterogeneity observed in reviewed findings. A second limitation is represented by the differences across the studies in term of comparative control groups. Control groups included waiting lists, nonspecific interventions, as well physical and psychologic interventions of established efficacy. Such differences in comparators along with the heterogeneity of diseases under investigation prevented us from the use of a meta-analytic procedure.

A further limitation is represented by the administration of self-rated scales, which could be influenced by social desirability such as, for instance, the desire to please the investigators. Although such an issue cannot be completely ruled out, it is worth mentioning that the maintenance of clinical benefits at the follow-up suggests that reported improvements did not represent only a momentary emphasis of subjects toward meditation but rather that they could be long-lasting. To overcome such limitations, however, future studies could use specific psychometric scales designed to assess social desirability such as the Marlowe-Crowe Social Desirability Scale,⁵⁴ a strategy already used in previous works about MBSR.⁵⁵ An alternative strategy could be the use, when possible, of external assessments, at least for the measures of depression.

A fourth limitation was that subjects in included studies were often females, white, and belonging to Western countries, thus limiting the generalizability to males, non-Caucasians, and Eastern populations. The last issue is of particular importance, considering that mindfulness could be differently interpreted in Western and Eastern countries.⁵⁶ In addition, current studies were often limited by methodological shortcomings including absence of randomization, small sample size, and the impossibility to perform a meditation trial using a double-blind condition. To overcome such limitations, we considered better-designed studies separately when possible. Also, we assessed the quality of included studies through the use of a standardized scale²⁶ that was not specifically designed to assess the quality of studies about meditative practices. As Orme-Johnson recently pointed out,⁵⁷ the development of a new quality scale designed to assess the quality of studies on meditation is needed. As he

suggested, high-quality meditation research should have high compliance levels, ensure proficient practice, use state-of-the-art measurement methodology, and make sure that control subjects are not inadvertently practicing the same or another form of meditation.

Finally, as already pointed out by other authors (e.g., Toneatto and Nguyen¹³), an important limitation could be represented by differences in the duration and characteristics of included studies. MBI techniques, programs, and lessons/homework duration, in fact, were significantly different across the studies (for this reason, we believed it was more appropriate to call them MBIs rather than MBSR). Even though recent findings suggest that the total length of the program does not seem to significantly influence the outcome,¹⁹ specific modifications to the standard program including, for instance, the exclusion of Hatha yoga practice or the augmentation of *qigong* therapy in some studies, do not allow a precise estimate to be provided of the efficacy of a unique standardized MBI.

Conclusions

In conclusion, there is not yet sufficient evidence to determine whether MBIs could be more efficacious than non-specific interventions such as support and educational control groups for the reduction of pain and depressive symptoms in patients with chronic pain. Further larger and properly powered studies are needed in order to extend current findings, to allow greater comparability across the interventions by using more standardized MBIs and to exhaustively investigate MBIs in more homogeneous samples of patients.

Disclosure Statement

No competing financial interests exist.

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