




Effects of Slow Deep Breathing on Acute Clinical Pain in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Amira E. Joseph, MD¹ , Rajat N. Moman, MD, MA²,
 Ross A. Barman, DO¹ , Donald J. Kleppel, MD¹,
 Nathan D. Eberhart¹, Danielle J. Gerberi, MLIS³,
 M. Hassan Murad, MD⁴, and W. Michael Hooten, MD⁵ 

Abstract

Slow deep breathing (SDB) may help patients with acute pain. The primary aim of this systematic review and meta-analysis is to investigate the effects of SDB on acute pain. Secondary aims include investigating the effects of SDB on acute pain-related physical and emotional functioning. An *a priori* protocol was registered and a database search was conducted by a reference librarian. Randomized controlled trials (RCT) were eligible for inclusion and exclusion criteria included studies of SDB for non-pain indications and studies that applied SDB as a component of an encompassing intervention. The risk or bias was assessed using the Cochrane Collaboration's revised tool for assessing risk of bias in randomized trials. Meta-analysis was conducted using the random effects model. A total of 11 968 studies were screened and seven RCTs met inclusion criteria; five were judged to have low risk of bias. Meta-analysis of post-intervention pain scores demonstrated that SDB was associated with significantly lower pain scores compared with a control group, but with high levels of heterogeneity. Subgroup analyzes demonstrated that trials of burn pain were associated with a larger reduction in pain which partially explains the heterogeneity. Very low certainty evidence suggests that SDB may reduce acute pain intensity. Further research is needed to identify patients who are candidates for SDB and determine the best approach to deliver this therapy.

Keywords

acute pain, systemic review, slow deep breathing

Received July 5, 2021. Received revised December 21, 2021. Accepted for publication January 15, 2022.

Introduction

Controlled breathing has been practiced for hundreds of years.¹ Slow deep breathing (SDB) is an important component of various yoga techniques and mindfulness practices.²⁻⁴ Slow deep breathing interventions have also been used as nonpharmacological adjuncts for a variety of medical conditions,⁵⁻⁷ including acute pain.^{8,9}

The mechanisms responsible for respiratory hypoalgesia have not been fully identified, but cardiovascular and central pain processing systems may play important roles.¹⁰⁻¹² In experimental and clinical studies, acute pain increases inspiratory flow and respiratory rate.^{13,14} However, the effects of SDB on acute experimental pain

¹ Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN, USA

² Washington University School of Medicine, Department of Anesthesiology, Division of Pain Medicine, St. Louis, MO, USA

³ Mayo Medical Libraries, Mayo Clinic, Rochester, MN, USA

⁴ Department of Internal Medicine, Division of Preventive Medicine, Mayo Clinic, Rochester, MN, USA

⁵ Department of Anesthesiology and Perioperative Medicine, Division of Pain Medicine, Mayo Clinic, Rochester, MN, USA

Corresponding Author:

W. Michael Hooten, Department of Anesthesiology and Perioperative Medicine, Division of Pain Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA.

Email: Hooten.william@mayo.edu



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

are mixed. Slow deep breathing is associated with reduced pain intensity in some,^{9,15} but not all,^{16,17} experimental studies. These varied findings could be due, in part, to differences in the experimental pain stimulus, breathing frequency, and pain assessment. In clinical studies, SDB is often combined with other meditative or relaxation techniques which obscures quantifying the independent effects of breathing interventions on acute pain.^{18–20} Knowledge about the independent effects of SDB on acute clinical pain could inform the design of future clinical trials aimed at quantifying the dose effects of various integrative interventions on acute pain.

Systematic reviews exist on studies evaluating the effect of SDB on clinical pain^{5,8} but the quality of these studies have not been systematically evaluated and there is no meta-analysis or related registered protocol to the authors' best knowledge. The primary aim of this systematic review and meta-analysis is to investigate the effects of SDB on acute clinical pain in adults compared to usual care for acute pain. Secondary aims include investigating the effects of SDB on acute pain-related measures of physical and emotional functioning.

Methods

Study Protocol

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed.²¹ An *a priori* protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42020204643).²²

After the protocol was registered, the scope of the systematic review was reduced to investigate only the effects of SDB on acute clinical pain versus the "effects of breathing techniques on pain and pain-related patient-reported outcomes in adult patients with acute, experimental, and chronic pain." No other systematic review or meta-analysis will be performed using this protocol.

In the registered protocol,²² the breathing intervention was defined as "breathing techniques" including "instructed breathing rate, frequency, depth, or volume" which is the working definition of SDB used in this systematic review.

Search Strategy

A comprehensive search of databases was conducted from the dates of inception through August 2020. The literature was searched by a medical librarian, with input from the principal investigator, for the concepts of breathing, pain, and associated variants. Search strategies were created using a combination of keywords and standardized index terms. The databases included EBSCO CINAHL, Ovid EBM Reviews, Ovid Embase, Ovid Medline, PsycINFO, Scopus and Web of Science Core Collection. The reference lists of included studies and systematic reviews were searched and study registries were searched. An unpublished filter was applied to restrict results to randomized trials and, after removal of duplicate citations, 11 968 citations were identified. The search strategy is provided in Supplemental Material 1.

Study Selection Process

Study inclusion criteria included (1) randomized controlled trials (RCT); (2) studies of breathing interventions; (3) adults with acute pain; and (4) all languages. Exclusion criteria included (1) studies of respiration interventions solely for non-pain indications (ie, hypertension, mood disorders, anxiety); (2) studies that apply respiratory techniques as a component of an encompassing intervention (ie, yoga); and (3) studies focusing on heart rate, heart rate variability, blood pressure, and the nociceptive flexion reflex without assessing pain intensity.

In the first review phase, three independent pairs of reviewers screened all titles and abstracts identified by the search strategy. In the second phase, the three pairs of independent reviewers screened the full text of all studies identified in the first review phase. Any disputes were resolved by consensus or involvement of a third party.

Data Extraction

Data were extracted by six independent reviewers in duplicate using a templated electronic database. Based on the *a priori* protocol, abstracted data included measures of pain spanning three domains based on the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMPACT)²³ recommendations, including (1) disability and physical functioning; (2) pain intensity; and (3) pain-related psychosocial functioning. Other abstracted data included (1) author and year of publication; (2) study design; (3) description of the breathing intervention; (4) number of study participants in each arm; (5) intervention used in the comparator group; (6) etiology of acute pain; (7) follow-up period; (8) number of participants lost to follow-up; and (9) participant demographics including age and gender.

Risk of Bias Assessment

The risk of bias in the included studies was assessed by six independent reviewers using the Cochrane Collaboration's revised tool (RoB 2) for assessing risk of bias in randomized trials.²⁴ Reviewer discrepancy was resolved by consensus or by a third reviewer.

Evidence Synthesis

For each trial, the mean, sample size, and standard deviation were recorded for continuous outcomes. The mean difference in pain severity was calculated as the post-intervention mean pain score in the experimental group minus the post-intervention mean pain score in the control group, so that a negative measure implied a reduction in pain due to the intervention. Due to heterogeneity in assessment tools, the standardized mean difference (SMD) was estimated from each study and was combined across studies using the random effects model. The 95% confidence interval (95% CI) was reported and heterogeneity was evaluated using the I^2 statistic.²⁵ Statistical analysis was performed using the "meta" and "metafor" R packages (R version 3.6.3). The certainty in evidence was assessed following the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.^{26,27}

Results

Characteristics of Included Studies

A flow diagram of the study selection process is depicted in Figure 1. Excluded studies are presented in Supplemental

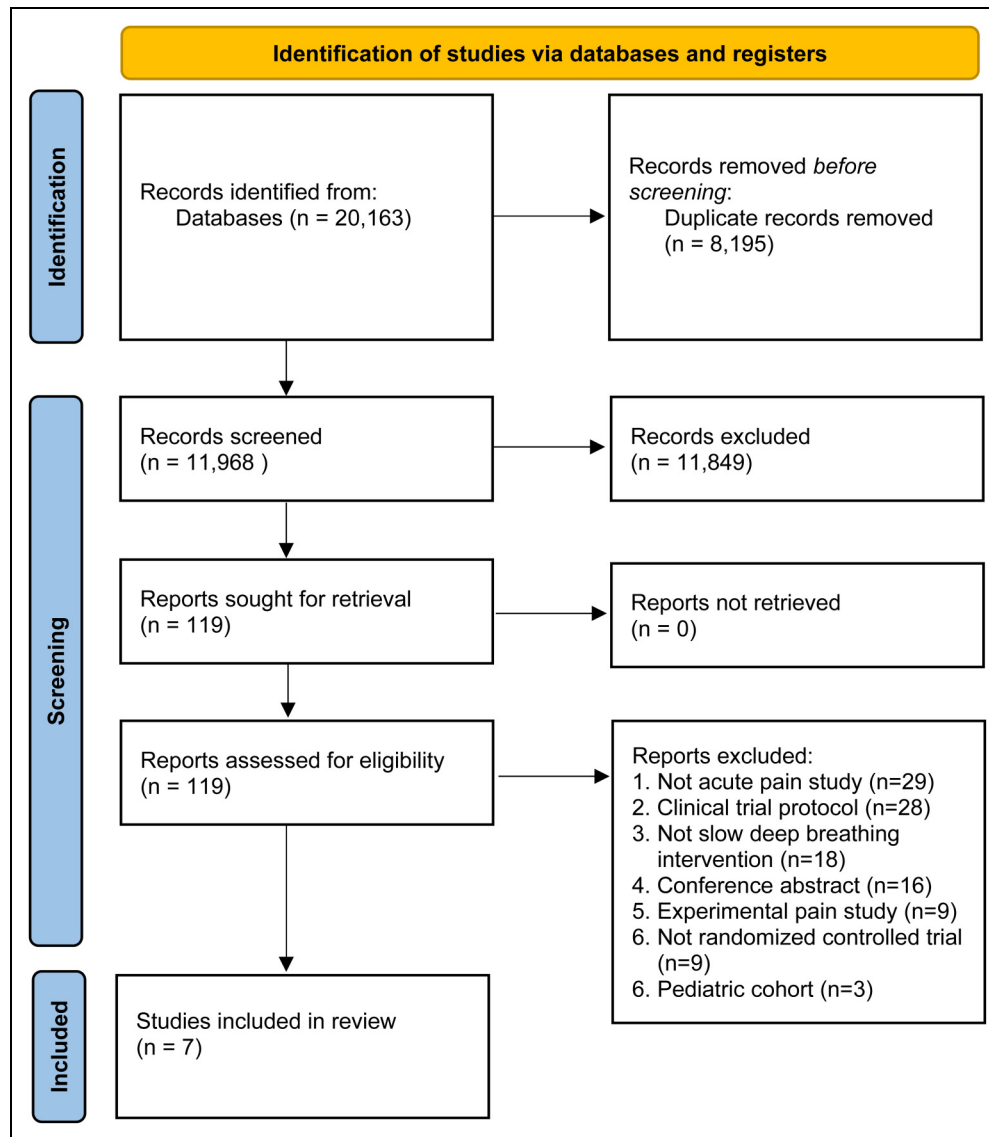


Figure 1. Preferred reporting items for systematic reviews and meta-analyses flow chart for the study selection process.

Table 1. Seven RCTs ($N = 847$) met inclusion and exclusion criteria (Table 1).²⁸⁻³⁴ Two studies involved patients with acute burn pain ($n = 98$),^{29,34} two studies involved patients with acute obstetric labor pain ($n = 390$),^{28,32} and three studies involved patients with acute postoperative pain ($n = 403$).^{30,31,33} Four RCTs assessed physical functioning and psychological distress^{28,30,33} and one study assessed psychosocial outcomes.²⁸

Characteristics of Breathing Interventions

The breathing interventions used in each RCT are described in Table 2. The breathing interventions varied on several parameters including the rate and depth of respiration, frequency of implementation during the acute pain episode and overall duration of use. Five RCTs provided descriptions of the breathing intervention.^{28,29,32-34} In the Hosinzadeh-Karimkoshteh et al.³⁴ and Boaviagem et al.²⁸ RCTs, the inspiratory and expiratory phases were 4 to 5 seconds, respectively. In the other five RCTs,²⁹⁻³³

the duration of the inspiratory and expiratory phases was not described. In the two obstetric labor^{28,32} and two burn pain RCTs,^{29,34} the breathing intervention was performed during labor contractions and dressing changes, respectively. In the Westerdahl et al. RCT,³³ the breathing intervention was used five times daily during the postoperative course, but the frequency of use was incompletely described in the other two acute postoperative pain RCTs.^{30,31} The duration of use was limited to the period of acute labor pain and pain during dressing changes in the obstetric^{28,32} and acute burn^{29,34} RCTs, respectively. In the three acute postoperative pain RCTs, the duration of use was two days,³¹ three days³⁰ and two months.³³

Risk of Bias Evaluation

Five RCTs were assessed to have low risk of bias.^{28,31-34} One RCT had some concerns for risk of bias because of lack of

Table 1. Study Characteristics.

Author	Study design	Participant characteristics	Pain type	Intervention description	Control description	Pain outcomes	Functional outcomes	Comments
Boaviagem, ²⁵ 2017	RCT	I = 67 C = 73 100% female mean age 20	Acute obstetric pain	Inhale slowly 5 sec, exhale slowly 5 sec, deep breath post exhale pauses (1-2 sec) with pursed lip breathing	"Standard Procedures"	VAS: I = 7.7 C = 8.0 No significant difference	State-Trait Anxiety Inventory: I = 45.8 C = 45.5 No significant difference	Foundation funding
Hoseinzadeh-Karimkoshteh, ³¹ 2019	RCT	I = 15 C = 15 63% male mean age 26	Acute burn pain	Inhaled 4 sec, pause 4 sec, IV morphine exhale 4 sec plus IV morphine Performed during dressing change (20 min)	IV morphine	VAS (post 4 dressing changes): #1: I = 4.5; C = 7.9 (P < .001) #2: I = 4.1; C = 7.1 (P < 0.001) #3: I = 3.3; C = 6.2 (P = .004) #4: I = 3.2; C = 5.3 (P = .19)		Funding source not reported.
Lalehgani, ²⁶ 2013	RCT	I = 34; mean age 35.2 C = 34; mean age 34.7	Acute burn pain	Deep and slow inspiratory-expiratory then rest Performed during and after dressing change (15-45 min)	"Routine interventions"	VAS: I = 3.1; C = 4.8 Group difference (P = .04)		Funding source not reported
Levin, ²⁷ 1987	RCT	I = 7 C = 10 100% female Mean age not reported, age range for study inclusion 21-65 yrs	Acute post-operative pain (cholecystectomy)	Rhythmic breathing when "discomfort" experienced POD 1-3	Control received treatment as usual	VAS: pain scores for each group assessed on POD 1 = 1 score POD 2 = 2 scores POD 3 = 2 scores (total = 5 pain scores)	Visual analog distress scale where 0 indicated no emotional distress and 10 indicated worse possible distress Distress scores for each group assessed on POD 1 = 1 score; POD 2 = 2 scores POD 3 = 2 scores (total = 5 distress scores)	Funding source not reported Two additional arms; relaxation group = 9; attention-distraction control = 7 40 subjects; 6 excluded from data analysis and no data reported for 1 subject
Miller, ²⁸ 1990	RCT	I = 15; 80% male C = 14; 79% male Age 40-60 yrs = 31% Age 61-80 yrs = 68%	Acute post-operative pain after cardiac surgery	Slow, rhythmic, deep breathing accompanied by conversation; patients followed until end of POD 2	Conversation only	VAS: I = 38.3; C = 47.1 No significant difference Visual descriptor scale rated 1 (mild) to 7 (severe): I = 4.1; C = 4.6 No significant difference		Funding source not reported

(continued)

Table 1. (continued)

Author	Study design	Participant characteristics	Pain type	Intervention description	Control description	Pain outcomes	Functional outcomes	Comments
Westerdahl, ³⁰ 2014	RCT	I = 159 C = 154 8.5% male median age 67	Acute post-operative pain after cardiac surgery	30 deep breaths 5 times daily for 2 months, this included 3 sets of 10 deep breaths with 30-60 sec pause between sets	"No breathing exercises"	NRS: median pain score at rest = 0; deep breath = 1; cough = 2 No significant differences	Quality of Recovery questionnaire Short Form Health Survey (SF-36)	Multiple sources of grant funding Median pain scores for intervention and control not reported separately
Yüksel, 2017	RCT	I = 125 C = 125 100% female mean age 23	Acute obstetric pain	Deep inhalation and exhalation during second stage of delivery	Standard Care	VAS: I = 88.2 C = 90.5 No significant differences		Funding source not reported

Abbreviations: I, intervention; C, control; RCT, randomized controlled trial; sec, second; min, minute; yrs, years; IV, intravenous; POD, postoperative day; NRS, numerical rating scale; VAS, visual analog scale.

intention-to-treat analysis and concerns about bias in the measurement of outcomes.²⁹ A single RCT had a high risk of bias due to concerns about bias in the measurement of outcomes and an unclear prespecified analysis plan.³⁰ The RoB 2 assessment for each RCT is presented in Supplemental Table 2.

Pain Intensity

All seven RCTs reported mean values for pain intensity and standard deviations of the mean; no standard deviations were imputed. The seven RCTs reported three different pain scales. Five RCTs reported a visual analog scale (VAS) ranging from 0-100,^{28,30-32,34} one RCT reported a VAS ranging from 0-10,²⁹ and one RCT reported a bodily pain subscale of the Short-Form Health Survey (SF-36) ranging from 0-100.³³ In addition to the VAS, a single RCT reported a visual descriptor scale ranging from 1-7 which was anchored with four pain descriptors (eg, no pain, mild, moderate, severe) placed equidistant on a vertical line.³¹ Scores from the visual descriptor scale were excluded from the meta-analysis. The post-intervention scores from seven studies were included in a meta-analysis. Pooled analysis revealed SDB had a statistically significant effect size on acute pain (SMD -0.68, 95% CI -1.19 to -0.18) but high levels of heterogeneity were observed ($I^2 = 90\%$) (Figure 2).

Heterogeneity was investigated using subgroup analyzes based on pain etiology (burn, obstetric labor and postoperative) and RoB (low, some and high) (Figure 2). Two RCTs^{29,34} reported pain intensity in patients experiencing burn pain, and pooled subgroup analysis demonstrated SDB was associated with statistically lower pain scores compared to controls (SMD -2.24, 95% CI -3.49 to -0.98) but high levels of heterogeneity were observed ($I^2 = 77\%$) (Figure 3). Two RCTs^{28,32} reported pain intensity in patients experiencing obstetric labor pain but pooled subgroup analysis demonstrated no significant group differences in pain scores between the SDB and control groups (SMD -0.19, 95% CI -0.53 to 0.15; $I^2 = 62\%$). Three RCTs^{30,31,33} reported pain intensity in patients experiencing postoperative pain but pooled subgroup analysis demonstrated no significant group differences in pain scores (SMD -0.04, 95% CI -0.25 to 0.16; $I^2 = 60\%$).

Subgroup analysis was performed based on RoB (Figure 3). Although the SMD of the five RCTs^{28,31-34} that had low RoB was different from the Lalehgani et al.²⁹ RCT that had some risk of bias,²⁹ the latter RCT was a burn study, which could explain the difference. Therefore, it is not clear whether RoB is a significant moderator of heterogeneity.

Physical and Emotional Functioning

Three studies reported outcomes related to physical and emotional functioning.^{28,30,33} Due to heterogeneity of included measures, meta-analysis was not performed. Westerdahl et al.³³ used the Quality of Recovery questionnaire and the SF-36 to assess physical and emotional function during the postoperative period following cardiac surgery. The Quality of Recovery questionnaire assesses five clinical domains including emotional state, physical comfort, psychological support, physical independence, and

Table 2. Description of Slow Deep Breathing Interventions.

Study	Breathing intervention	Intervention description	Intervention frequency
Boaviagem, ²⁵ 2017	Slow, deep breathing +/- post-exhalation pause	<ul style="list-style-type: none"> • A: Inhale slowly, counting from 1 to 5 • B: Breathe out gradually, counting from 5 to 1 • C: Increase the post-exhalation pause (1-2 s), propelling the lips • A and B performed during initial active phase, addition of C during active and late active phase 	Not specified
Hoseinzadeh-Karimkoshteh, ³¹ 2019	Slow, deep breathing	<ul style="list-style-type: none"> • Inhale for 4 seconds • Pause for 4 seconds • Exhale for 4 seconds during dressing change 	4 dressing change sessions
Lalehgani, ²⁶ 2013	Slow, deep breathing	<ul style="list-style-type: none"> • Place tongue in floor of the mouth • Deep and slow inspiration • Deep and slow exhalation • Rest 	Not specified
Levin, ²⁷ 1987	Rhythmic breathing	Rhythmic breathing exercise instructed via tape recording	Not specified
Miller, ²⁸ 1990	Rhythmic breathing	Slow, rhythmic deep breathing	Estimated frequency varied from 1 to 15 times
Westerdahl, ³⁰ 2014	Deep breathing	<ul style="list-style-type: none"> • Perform 30 deep breaths 5 times a day • Three sets of 10 deep breaths with a 30- to 60-second pause between each set • All performed in a sitting position 	30 breaths, 5 times daily for 2 months after surgery
Yuksel, ²⁹ 2014	Deep breathing	<ul style="list-style-type: none"> • Fill your stomach and then your lungs with air while inhaling • Feel the expansion in your stomach • Make sure the muscles from your stomach to your knee are relaxed while exhaling • Exhale slowly from your mouth 	Not specified

pain. The SF-36 has eight subscales including bodily pain, mental health, physical functioning, emotional role functioning, physical role functioning, social functioning, and vitality. No significant differences between the breathing and control groups were observed for the Quality of Recovery questionnaire or SF-36. Boaviagem et al.²⁸ assessed the effects of the breathing intervention on a validated measure of anxiety but no significant group differences between the breathing and control groups were identified. Levin et al.³⁰ assessed anxiety using a visual analog scale but no significant group differences between the breathing and control groups were identified.

Certainty in Evidence

Using the GRADE approach, there is very low certainty in evidence that breathing interventions had an effect on acute burn pain. The certainty in evidence was downgraded three levels due to concerns about inadequate blinding, inconsistency, and imprecision. There is very low certainty in evidence that breathing interventions lacked an effect on obstetric labor pain. The certainty in evidence was downgraded three levels due to the level of follow-up, inconsistency and imprecision. There is low certainty in evidence that breathing interventions lacked an effect on postoperative pain. The certainty in evidence was

downgraded two levels due to inadequate blinding and imprecision. The certainty in evidence assessment is presented in Supplemental Table 3.

Discussion

This systematic review summarizes the available evidence regarding the effects of SDB interventions on acute pain in adults. The key findings of this systematic review and meta-analysis were that SDB was associated with significantly lower pain scores compared to controls, but high levels of heterogeneity were observed. Subgroup analysis was performed to investigate sources of heterogeneity. This analysis demonstrated that pain etiology was a moderator of heterogeneity, whereas risk of bias was a less clear moderator of heterogeneity. No significant group differences in physical functioning or psychological distress were reported in the three RCTs that assessed these clinical domains. The certainty in evidence for all findings was low to very low. Prior to considering the clinical implications of the study findings, understanding the potential mechanisms governing the effects of SDB on acute pain warrant further explanation.

The physiological and neurobiological mechanisms responsible for respiratory hypoalgesia have not been fully elucidated

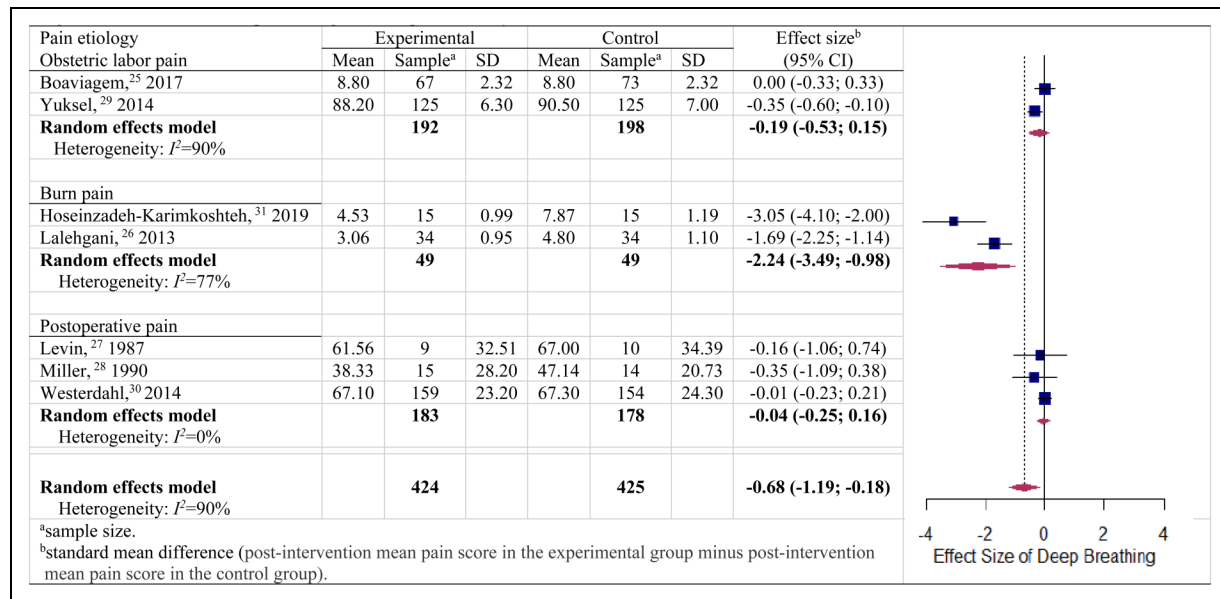


Figure 2. Effects of slow deep breathing on acute pain intensity.

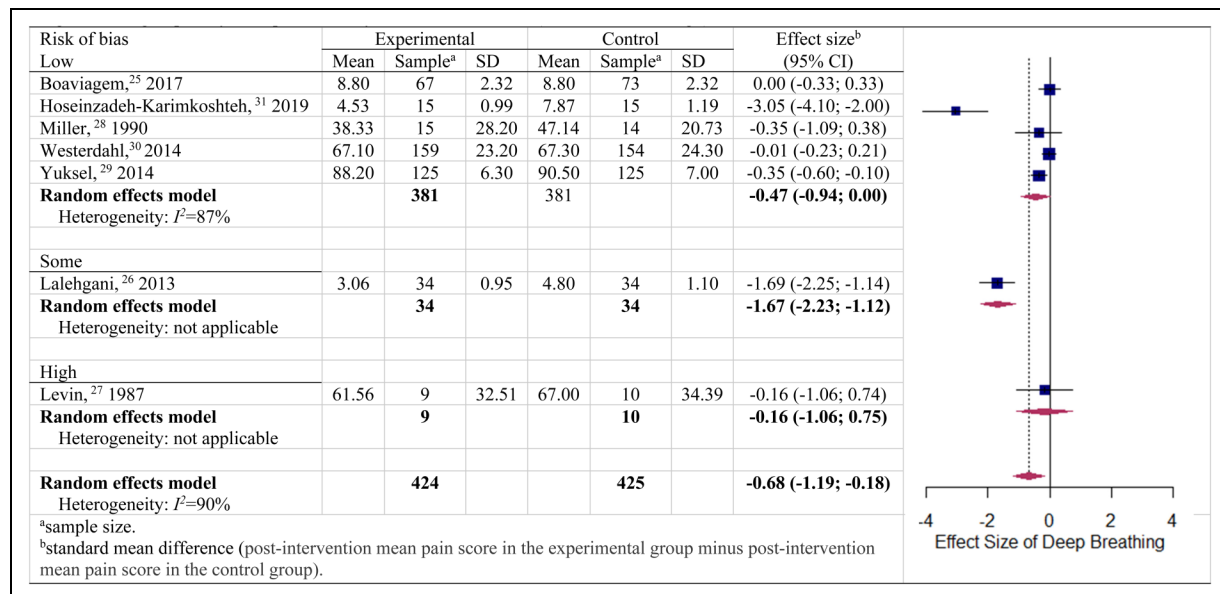


Figure 3. Subgroup analysis of pain intensity based on risk of bias (low, some, high).

but the cardiovascular, specifically the baroreceptor system, and central pain processing systems may play important roles. The baroreceptor system is comprised of a cardiovascular and central branch. Baroreceptors located in the carotid sinuses, aortic arch, and heart chambers detect changes in blood pressure and heart rate that occur during the respiratory cycle.¹¹ These changes are relayed by the vagus and glossopharyngeal nerves to the nucleus of the solitary tract (NST) located in the dorsomedial medulla. Fibers from the NST then project to other parasympathetic and sympathetic brain stem nuclei, and efferent activity in these nuclei influence the sympathetic and parasympathetic tone of the cardiovascular system,

respectively.¹⁰ The baroreceptor system also has a central branch that projects from the NST to limbic and forebrain structures that are involved in processing pain stimuli and modulating the affective dimensions of pain.¹² The baroreceptor system can be posited to influence hypoalgesia by conveying respiratory changes in cardiovascular activity to brain regions responsible for regulating autonomic tone, processing pain stimuli, and modulating pain affect.

Although SDB influences cardiovascular activity, the findings of three recent experimental studies suggest that cardiovascular changes are not responsible for the hypoalgesic effects of SDB.³⁵⁻³⁷ In an experimental heat pain study, 48 healthy

subjects performed 4 breathing patterns including unpaced breathing, paced breathing at the subject's natural breathing frequency, SDB at a frequency of 6 breaths per minute with a low inspiration-expiration ratio, and SDB at 6 breaths per minute with a high inspiration-expiration ratio.³⁷ In response to heat stimuli, pain scores from the three paced breathing groups were significantly lower compared to the unpaced group but cardiovascular changes did not mediate the effects of paced breathing on pain.³⁷ In a second study involving 83 healthy female subjects, baroreceptor activity and heart rate variability were significantly increased in the SDB group compared to the normal paced breathing group but no significant group differences in pain intensity were observed in response to electrocutaneous, thermal or mechanical pain stimuli.³⁵ In a third study involving 44 healthy subjects, pain scores were significantly lower in a SDB group that incorporated an inspiratory threshold load of 10 centimeters water compared to a normal frequency controlled breathing group.³⁶ However, the difference in mean pain scores between the two groups was 2 points on a 100 point numerical rating scale and the clinical effect was small (Cohen's $d = 1.3$). Although SDB increased cardiovascular activity, mediation analysis demonstrated that the effect of SDB on pain intensity was not explained by changes in cardiovascular activity.³⁶ The findings from these three studies suggest that other mechanisms including attentional, emotional, and behavioral modulators may play a role in SDB-related hypoalgesia.^{35,36}

Slow breathing activates the endogenous opioid system but other supraspinal mechanisms may contribute to the hypoalgesic effects of SDB. In a randomized, double-blind, placebo controlled trial, healthy subjects allocated to a SDB group experienced significant reductions in pain intensity and pain unpleasantness but the changes in pain scores were insensitive to naloxone.³⁸ These findings suggest SDB reduces pain independent of the endogenous opioid system which is consistent with observations from mechanism-based studies of mindfulness-meditation.³⁹ More specifically, mindfulness-meditation induced hypoalgesia is associated with activation of the ventral-lateral prefrontal and anterior cingulate cortices and reduced activity in the thalamus.^{40,41} Slow deep breathing may also reduce arousal thereby potentiating a relaxed state and alter pain appraisals which suggests SDB represents an opportunity for distraction.⁴² The activation of forebrain structures by SDB may be particularly relevant to patients with acute burn pain because dressing changes are associated with high levels of anxiety^{43,44} and high levels of pain-related anxiety, in turn, are associated with significant reductions in heat pain thresholds and tolerances.⁴⁵ Thus, pain reductions associated with SDB in acute burn pain may be partly mediated by reductions in pain-related anxiety via activation of brain regions similar to that observed for mindfulness-meditation.

The results of this systematic review and the proposed biological mechanisms have important implications for ongoing research. Although SDB was the basis for the breathing interventions in all RCTs, clinical heterogeneity was identified. As

a result, carefully designed RCTs are needed that include (1) clear description of all the components comprising the SDB intervention; (2) clear description about the frequency and duration of the SDB intervention; (3) incorporation of validated measures of pain affect; (4) inclusion of an active comparison condition (ie, paced breathing at a normal frequency); and (5) inclusion of experimental testing to investigate the effects of SDB on posited peripheral and central mechanisms responsible for respiratory hypoalgesia. Successful completion of high quality RCTs could potentially identify specific patient populations with the greatest likelihood of responding to SDB interventions and drive identification of a dose-response relationship which would have widespread implications in the clinical management of acute pain.

This study has limitations. First, the scope of the systematic review was limited to clinical studies of adults with acute pain. As a result, the findings may not be applicable to pediatric populations or adults with chronic pain. Similarly, the search strategy did not identify RCTs of acute pain associated with minor procedures and, as a result, the study findings may not be applicable to minor procedures typically performed in an ambulatory care setting. Second, the certainty in evidence was low to very low due to methodological limitations of the RCTs identified by the search strategy. As noted, future well-designed RCTs are needed to confirm the efficacy of slow deep breathing for acute pain. Finally, key sources of heterogeneity identified in this study include incomplete descriptions of all the components of the SDB interventions and variations in the frequency and duration of the SDB intervention. However, other unidentified sources of heterogeneity could have influenced the study findings.

In summary, the long-term goal of this area of research is to drive the development, testing, deployment, and dissemination of effective SDB interventions for adults with acute pain. Although SDB has beneficial effects on acute burn pain, the certainty in evidence was very low. The findings of this systematic review, including sources of clinical heterogeneity, could be used to inform the design of future RCTs aimed at confirming the efficacy of SDB for acute pain.

Acknowledgments

None.

Author Contributions

Joseph AE: Study conception and design; data analysis and interpretation; data acquisition; manuscript development. Moman RN: Study conception and design; data analysis and interpretation; data acquisition; manuscript development. Barman R: Data analysis and interpretation; data acquisition; manuscript development. Kleppel DJ: Data analysis and interpretation; data acquisition; manuscript development. Eberhart N: Data analysis and interpretation; data acquisition; manuscript development. Gerber D: Study design, data analysis and interpretation; data acquisition; manuscript development. Murad MH: Study conception and design; data analysis and interpretation; data acquisition; manuscript development. Hooten WM: Study conception

and design; data analysis and interpretation; data acquisition; manuscript development.

Declaration of Conflicting Interests

W. Michael Hooten receives funding from the National Institutes of Health and US WorldMeds. The authors have no other conflicts of interest to report.

Ethical Approval


This systematic review was exempt from ethical review.


Funding

Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN.

ORCID iDs

Amira E. Joseph  <https://orcid.org/0000-0002-9570-1648>

Ross A. Barman  <https://orcid.org/0000-0002-0370-6354>

W. Michael Hooten  <https://orcid.org/0000-0001-5645-6355>

Supplemental Material

Supplemental material for this article is available online.

References

1. Tipton CM. The history of “exercise is medicine” in ancient civilizations. *Adv Physiol Educ.* 2014;38(2):109-117.
2. Blanck P, Perleth S, Heidenreich T, et al. Effects of mindfulness exercises as stand-alone intervention on symptoms of anxiety and depression: systematic review and meta-analysis. *Behav Res Ther.* 2018;102:25-35.
3. Kuppusamy M, Kamaldeen D, Pitani R, Amaldas J, Shanmugam P. Effects of bhrumari pranayama on health - a systematic review. *J Tradit Complement Med.* 2018;8(1):11-16.
4. Jayawardena R, Ranasinghe P, Ranawaka H, Gamage N, Dissanayake D, Misra A. Exploring the therapeutic benefits of pranayama (yogic breathing): a systematic review. *Int J Yoga.* 2020;13(2):99-110.
5. Brandani JZ, Mizuno J, Ciolac EG, Monteiro HL. The hypotensive effect of yoga's breathing exercises: a systematic review. *Complement Ther Clin Pract.* 2017;28:38-46.
6. Atilgan ED, Tuncer A. The effects of breathing exercises in mothers of children with special health care needs: a randomized controlled trial. *J Back Musculoskelet Rehabil.* 2021;4(5):795-804.
7. Ng DL, Chai CS, Tan KL, et al. The efficacy of a single session of 20-minute mindful breathing in reducing dyspnea among patients with acute decompensated heart failure: a randomized controlled trial. *Am J Hosp Palliat Care.* 2021;38(3):246-252.
8. Jafari H, Courtois I, Van den Bergh O, Vlaeyen JWS, Van Diest I. Pain and respiration: a systematic review. *Pain.* 2017;158(6):995-1006.
9. Martin SL, Kerr KL, Bartley EJ, et al. Respiration-induced hypoalgesia: exploration of potential mechanisms. *J Pain.* 2012;13(8):755-763.
10. Norgren R. Projections from the nucleus of the solitary tract in the rat. *Neuroscience.* 1978;3(2):207-218.
11. Radaelli A, Raco R, Perfetti P, et al. Effects of slow, controlled breathing on baroreceptor control of heart rate and blood pressure in healthy men. *J Hypertens.* 2004;22(7):1361-1370.
12. Reyes BA, Van Bockstaele EJ. Divergent projections of catecholaminergic neurons in the nucleus of the solitary tract to limbic forebrain and medullary autonomic brain regions. *Brain Res.* 2006;1117(1):69-79.
13. Green DA, Bowtell J, Turner DL. Electrical percutaneous tibial stimulation modulates within-a-breath respiratory drive in man. *Respir Physiol Neurobiol.* 2008;161(2):214-217.
14. Duranti R, Pantaleo T, Bellini F, Bongianini F, Scano G. Respiratory responses induced by the activation of somatic nociceptive afferents in humans. *J Appl Physiol.* 1991;71(6):2440-2448.
15. Zautra AJ, Fasman R, Davis MC, Craig ADB. The effects of slow breathing on affective responses to pain stimuli: an experimental study. *Pain.* 2010;149(1):12-18.
16. Arsenault M, Ladouceur A, Lehmann A, Rainville P, Piche M. Pain modulation induced by respiration: phase and frequency effects. *Neuroscience.* 2013;252:501-511.
17. Zunhammer M, Eichhammer P, Busch V. Do cardiorespiratory variables predict the antinociceptive effects of deep and slow breathing? *Pain Med.* 2013;14(6):843-854.
18. Evans DR, Eisenlohr-Moul TA, Button DF, Baer RA, Segerstrom SC. Self-regulatory deficits associated with unpracticed mindfulness strategies for coping with acute pain. *J Appl Soc Psychol.* 2014;44(1):23-30.
19. Garland EL, Baker AK, Larsen P, et al. Randomized controlled trial of brief mindfulness training and hypnotic suggestion for acute pain relief in the hospital setting. *J Gen Intern Med.* 2017;32(10):1106-1113.
20. Hanley AW, Gililand J, Erickson J, et al. Brief preoperative mind-body therapies for total joint arthroplasty patients: a randomized controlled trial. *Pain.* 2021;162(6):1749-1757.
21. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the prisma statement. *PLoS Med.* 2009;6(7):e1000097.
22. Joseph A, Moman R, Hooten WM. Breathing exercises and pain: a systematic review. PROSPERO 2020 CRD42020204643. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020204643
23. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: impact recommendations. *Pain.* 2005;113(1-2):9-19.
24. Sterne JAC, Savovic J, Page MJ, et al. Rob 2: a revised tool for assessing risk of bias in randomised trials. *Br Med J.* 2019;366:14898.
25. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21(11):1539-1558.
26. Guyatt G, Oxman AD, Akl EA, et al. Grade guidelines: 1. Introduction-grade evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011;64(4):383-394.
27. Murad MH. Clinical practice guidelines: a primer on development and dissemination. *Mayo Clin Proc.* 2017;92(3):423-433.

28. Boaviagem A, Melo Junior E, Lubambo L, et al. The effectiveness of breathing patterns to control maternal anxiety during the first period of labor: a randomized controlled clinical trial. *Complement Ther Clin Pract*. 2017;26:30-35.
29. Lalegani H, Esmaeeli S, Karimi M, Moghani M, Jivad N. The effect of deep-slow and regular breathing on pain intensity of burn dressing. *J Crit Care Nurs*. 2014;6:223-228.
30. Levin RF, Malloy GB, Hyman RB. Nursing management of post-operative pain: use of relaxation techniques with female cholecystectomy patients. *J Adv Nurs*. 1987;12(4):463-472.
31. Miller KM, Perry PA. Relaxation technique and postoperative pain in patients undergoing cardiac surgery. *Heart Lung*. 1990;19(2):136-146.
32. Yuksel H, Cayir Y, Kosan Z, Tastan K. Effectiveness of breathing exercises during the second stage of labor on labor pain and duration: a randomized controlled trial. *J Integr Med*. 2017;15(6):456-461.
33. Westerdahl E, Urell C, Jonsson M, Bryngelsson IL, Hedenstrom H, Emtner M. Deep breathing exercises performed 2 months following cardiac surgery: a randomized controlled trial. *J Cardiopulm Rehabil Prev*. 2014;34(1):34-42.
34. Hoseinzadeh-Karimkoshteh M, Firouzkouhi M, Abdollahimohammad A. Effect of regular smooth breathing on the intensity of pain caused by dressing change in patients with second-degree burns: a clinical trial. *Med-Surg Nurs J*. 2019;8(2):e92321.
35. Courtois I, Gholamrezaei A, Jafari H, et al. Respiratory hypoalgesia? The effect of slow deep breathing on electrocutaneous, thermal, and mechanical pain. *J Pain*. 2020;21(5-6):616-632.
36. Gholamrezaei A, Van Diest I, Aziz Q, Vlaeyen JWS, Van Oudenhove L. Controlled breathing and pain: respiratory rate and inspiratory loading modulate cardiovascular autonomic responses, but not pain. *Psychophysiology*. 2021;58(10):e13895.
37. Jafari H, Gholamrezaei A, Franssen M, et al. Can slow deep breathing reduce pain? An experimental study exploring mechanisms. *J Pain*. 2020;21(9-10):1018-1030.
38. Wells RE, Collier J, Posey G, et al. Attention to breath sensations does not engage endogenous opioids to reduce pain. *Pain*. 2020;161(8):1884-1893.
39. Zeidan F, Adler-Neal AL, Wells RE, et al. Mindfulness-meditation-based pain relief is not mediated by endogenous opioids. *J Neurosci*. 2016;36(11):3391-3397.
40. Zeidan F, Emerson NM, Farris SR, et al. Mindfulness meditation-based pain relief employs different neural mechanisms than placebo and sham mindfulness meditation-induced analgesia. *J Neurosci*. 2015;35(46):15307-15325.
41. Zeidan F, Martucci KT, Kraft RA, Gordon NS, McHaffie JG, Coghill RC. Brain mechanisms supporting the modulation of pain by mindfulness meditation. *J Neurosci*. 2011;31(14):5540-5548.
42. Zaccaro A, Piarulli A, Laurino M, et al. How breath-control can change your life: a systematic review on psycho-physiological correlates of slow breathing. *Front Hum Neurosci*. 2018;12:353.
43. Carrougier GJ, Ptacek JT, Honari S, et al. Self-reports of anxiety in burn-injured hospitalized adults during routine wound care. *J Burn Care Res*. 2006;27(5):676-681.
44. Weinberg K, Birdsall C, Vail D, Marano MA, Petrone SJ, Mansour EH. Pain and anxiety with burn dressing changes: patient self-report. *J Burn Care Rehabil*. 2000;21(2):155-156. Discussion 157-161.
45. Terry MJ, Moeschler SM, Hoelzer BC, Hooten WM. Pain catastrophizing and anxiety are associated with heat pain perception in a community sample of adults with chronic pain. *Clin J Pain*. 2016;32(10):875-881.