Contemporary Clinical Trials 39 (2014) 22–27

Contents lists available at ScienceDirect

Contemporary Clinical Trials

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

Mindfulness-based intervention for prodromal sleep disturbances in older adults: Design and methodology of a randomized controlled trial

David S. Black [a,*], Gillian A. O'Reilly [a], Richard Olmstead [b], Elizabeth C. Breen [b], Michael R. Irwin [b]

[a] Department of Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, CA, USA
[b] Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience & Human Behavior, University of California, Los Angeles, USA

ARTICLE INFO

Article history:
Received 2 April 2014
Received in revised form 17 June 2014
Accepted 24 June 2014
Available online 1 July 2014

Keywords:
Mindfulness
Sleep problems
Inflammatory markers
Older adults
Randomized controlled trial
Design and methodology

ABSTRACT

Sleep problems are prevalent among older adults, often persist untreated, and are predictive of health detriments. Given the limitations of conventional treatments, non-pharmacological treatments such as mindfulness-based interventions (MBIs) are gaining popularity for sleep ailments. However, nothing is yet known about the impact of MBIs on sleep in older adults with prodromal sleep disturbances. This article details the design and methodology of a 6-week parallel-group RCT calibrated to test the treatment effect of the Mindful Awareness Practices (MAPs) program versus sleep hygiene education for improving sleep quality, as the main outcome, in older adults with prodromal sleep disturbances. Older adults with current sleep disturbances will be recruited from the urban Los Angeles community. Participants will be randomized into two standardized treatment conditions, MAPs and sleep hygiene education. Each condition will consist of weekly 2-hour group-based classes over the course of the 6-week intervention. The primary objective of this study is to determine if mindfulness meditation practice as engaged through the MAPs program leads to improved sleep quality relative to sleep hygiene education in older adults with prodromal sleep disturbances.

Sleep problems are a significant health issue among older adults. Approximately 50% of older adults have difficulties initiating or maintaining sleep [1,2]. Sleep problems increase the risk for health ailments in older adults. Chronic inadequate sleep can adversely affect quality of life by impacting functional capabilities including memory, learning, and attention [1–3]. Sleep problems are also prospectively linked to significant psychological and physical morbidity [4]. Older adults who report sleep problems experience more symptoms of anxiety and depression than those who report no sleep problems [2,5]. Physical health consequences of sleep problems include increased risk for cardiovascular disease, respiratory disorders, and metabolic disorders [6–8]. In addition, sleep disturbances predict physical decline with age and are associated with increased risk for all-cause mortality [3]. The effects of inadequate sleep are cumulative [9], making those with sleep disturbances particularly vulnerable to compounding health problems. The burden of sleep problems on the older adult population represents a significant public health concern that requires low-cost and readily accessible treatment approaches that have the capacity to impart lasting effects.

Sleep problems are undertreated in older adults [10,11]. Moreover, among those who receive treatment, pharmacological therapies are often provided, even though sleep medications are associated with a host of adverse side effects and dependency syndrome [10,11]. As such, non-pharmacological interventions for sleep problems are gaining popularity.

* Corresponding author at: Department of Preventive Medicine, University of Southern California, 2001 N. Soto Street, Ste. 302D, MC 9239, Los Angeles, CA 90032, USA. Tel.: +1 323 442 8223.
E-mail address: davidbla@usc.edu (D.S. Black).

http://dx.doi.org/10.1016/j.cct.2014.06.013
1551-7144/

Moreover, treatments for insomnia symptoms such as Cognitive Behavioral Therapy for Insomnia (CBT-I) can be somewhat effective, yet they require a highly trained therapist, are not routinely implemented due to complexity issues, and are typically only delivered in a clinical setting [12]. These limiting factors indicate the need for approaches that can be more readily delivered in the community. Mindfulness-based interventions (MBIs) are particularly promising non-pharmacological treatments, and have gained substantial popularity in recent years for use with a variety of health-related issues, including sleep problems. MBIs train participants in the systematic and secular practice of continually attending to moment-by-moment experiences, thoughts, and emotions from an open, non-judgmental perspective [13,14].

The one review on MBIs and sleep to date indicates that mindfulness-based interventions (MBIs) can improve some sleep parameters in younger and mid-age adult samples, yet the data remained insufficient to draw concrete conclusions [15]. Many MBIs for sleep have been fraught with methodological limitations that limit interpretation of findings, such as underpowered sample sizes, lack of control conditions, sleep problems as a secondary outcome to a primary condition such as cancer and anxiety, and a generalizability restricted to clinical populations [16–19]. As such, a major gap remains in the research regarding the effect MBIs on sleep disturbances in older adults with prodromal sleep disturbances.

Sleep problems may also have adverse effects on inflammatory processes [20,21]. Evidence indicates that disturbances in sleep quality and quantity are associated with increases in peripheral markers of inflammation [9,21]. The impact of sleep problems on inflammation may have implications for health issues. Many of the inflammatory markers that can increase as a result of sleep problems have been linked to health problems such as cardiovascular disease [8,9]. As older adults are prone to both increased risk for diseases associated with inflammation and sleep disturbances, treatments that can beneficially impact inflammation as well as sleep parameters have potential to improve health outcomes in this population.

Initial evidence indicates that MBIs and movement forms of meditation such as Tai Chi can modulate inflammatory biomarkers. For example, findings from our RCT of a movement meditation Tai Chi versus stress and health education showed that meditation reduced levels of an upstream pro-inflammatory transcription marker (i.e. NF-κB) in older adults at immediate post-intervention [22]. While these findings indicate promising potential for meditation practices to reduce inflammatory response factors, more research is needed to specifically understand the impact of MBIs on biological markers of inflammation in older adults.

Understanding the impact of MBIs on sleep may elucidate a new non-pharmacological approach for the treatment of prodromal sleep disturbances in older adults in the community setting. This article describes the methodology and design of a randomized controlled trial that aims to test whether participation in a MBI results in improved sleep parameters and reduced pro-inflammatory transcription factor (i.e. NF-κB) compared to a sleep hygiene education (SHE) control condition in older adults with sleep problems. This research effort is novel as it compares two community-based treatment offerings, MBI vs SHE, in a randomized controlled trial. This study is also the first MBI trial to target sleep disturbances in a sample comprised solely of older adults.

1. Study objectives

The primary aim of this study is to determine if an ongoing curriculum-based MBI that is available to the general community, Mindful Awareness Practices (MAPs), leads to greater improvements in sleep quality, represented by reductions in global Pittsburgh Sleep Quality Index (PSQI) score, compared to SHE in older adults with sleep disturbances. We anticipate that SHE will improve sleep, but that MAPs will lead to greater improvements in PSQI scores. In order accomplish this aim, we will test the treatment effect of MAPs in comparison to SHE on PSQI scores. Secondary aims are to test if MAPs versus SHE leads to relative improvements in sleep-related daytime impairments (i.e., insomnia, fatigue, depressive, stress, and anxiety symptoms) as well as levels of Nuclear Factor (NF)-κB. NF-κB is a transcription factor that regulates genes responsible for the inflammatory response.

2. Study design

In older adults with sleep problems, this single-site, parallel-group randomized controlled trial with a pretest and immediate posttest design will test the relative effect of the MAPS to SHE program for improving sleep and secondary outcomes of daytime impairment. Participants will be randomized into one of two experimental conditions: (1) the MAPs course at the University of California, Los Angeles or (2) sleep hygiene education (SHE). Both study conditions will be comprised of a standardized 6-week group-based intervention administered at the UCLA Westwood Medical Campus. The UCLA Institutional Review Board has approved all study procedures. This trial will be registered at clinicaltrials.gov.

3. Participants

Participants will include older adult community volunteers between the ages of 55 and 90 (an average age of 65 is expected). Participants will be recruited over a six-month period through advertisement in the local newspaper and flyers posted at our university medical center and affiliated clinical institutes located in Los Angeles, CA. Trained data collectors will screen all interested participants via a 15-minute telephone interview to ascertain sleep problems and study eligibility. Participants will be compensated up to $50 in gift cards and will receive parking vouchers for each visit at the medical center. Eight visits will be requested, including 1 pretest assessment, 6 intervention sessions, and 1 post-test assessment.

4. Power analysis

A priori power analysis was conducted in Gpower, and is based on previous research showing that MBIs and psychoeducational interventions can have between-group medium-sized effects on self-reported sleep quality (e.g., PSQI) in adults with sleep problems [23]. Given 80% power, $p < .05$ (two-sided), 2 treatment groups with 2 assessment points, and a .60 test–retest r (PSQI) [24], the estimated final sample size

needed to detect a significant effect is 42. Based on our previous research with older adults, an attrition rate of ~10% is anticipated, making our target enrollment 47.

5. Eligibility requirements

Inclusion criteria: Participants will be eligible for the study if they experience active insomnia symptoms as indicated by a PSQI score > 5 [25], are 55 years of age or older, and agree to randomization to conditions. Those who are eligible will be community-based volunteers who will self-enroll based on their sleep disturbances. Exclusion criteria: Participants will be ineligible for the study if they have an inflammatory disorder, illness, or infection (e.g., autoimmune disease, type 1 diabetes, Hepatitis C, cancer, acute infection in past 2 weeks), significant current practice of any form of mediation (>15 min per day), [26], cognitive impairment (Mini-Mental State Examination, MMSE < 26), [27], current unresolved sleep apnea diagnosis, inability to speak English, current smoking and/or substance dependence, class II or greater obesity (BMI > 34.9), and depression (Patient Health Questionnaire, PHQ-9 > 14). Class II obesity and depression are set as exclusion criteria to prevent confounding, due to the association between depression and sleep disturbance [28] and because of the effect of both depression and obesity on inflammatory markers [29,30]. Trained study staff will complete the eligibility assessments at initial contact to participants over the phone in a one-to-one interview. During this initial contact, PSQI and illness exclusions will be assessed to ensure eligibility. The MMSE and BMI measures will be completed during a one-to-one visit by trained data collectors at a follow-up assessment. Participants that remain eligible from the MMSE and BMI assessment will complete the baseline survey at the same visit. The remaining eligibility criteria will be collected by self-report.

6. Randomization

Using a computer-generated randomization table, a treatment-blinded statistician (R.O.) will randomize enrollees to treatment conditions. The randomization procedure will use a computer generated 1:1 ratio. Group assignment will be concealed from participants and study staff during all study phases.

7. Interventions

Intervention phases will occur during a six-week period. Participants in each condition will attend weekly 2-hour group-based classes for a total of 6-weeks. Treatment fidelity will be assessed by check box lists that teachers in each condition will use to report the components of the standardized lessons that are delivered.

7.1. Mindful Awareness Practices (MAPs)

MAPs is a weekly, 2-hour, 6 session, group-based manualized course in mindfulness meditation which is available for community residents to take in-person within the Los Angeles area or online. A certified teacher with over 20 years of mindfulness practice will deliver the program curriculum to participants. Session titles by week include: (1) Introduction to mindfulness, (2) Listening, embodiment and obstacles, (3) Working with pain, (4) Difficult emotions and cultivating positive emotions, (5) Thoughts and mindful interactions, and (6) Loving kindness and class wrap-up. Mindfulness exercises embedded in the curriculum include mindful sitting meditation, body scan meditation, eating meditation, daily life meditation, relational mindfulness, appreciation meditation, loving-kindness meditation, walking meditation, standing meditation, movement meditation, and practices to develop positive emotions. An average of 10 to 30 min of mindful experiential practice is engaged in during each class in addition to the teacher-delivered didactic material and group discussion. Participants are also provided with a textbook on mindfulness accompanied by a meditation compact disc [31]. Mindfulness practice is assigned as homework beginning with 5 min daily and advancing to 20 min daily at program's end. The MAPs curriculum will not include any sleep-specific content.

7.2. Sleep hygiene education (SHE)

SHE is a weekly, 2-hour, 6 session, group-based manualized course in sleep hygiene and sleep education developed by the lead author (DSB) that matches the MAPs condition for time, attention, group interaction, and expectancy of beneficial effects. A trained health educator with a Master of Public Health degree will deliver the program curriculum to participants. Active components of the SHE seminar include increasing knowledge of sleep biology, characteristics of healthy and unhealthy sleep, sleep problems, stress biology and stress reduction, relaxation methods for improving sleep, self-monitoring of sleep behavior, and weekly tips for better sleep. Educational and behavioral change content is based on the National Sleep Foundation's tips for better sleep, including changing poor sleep habits, avoiding stimulants such as coffee and tea near bedtime, exercise and relaxation, adequate exposure to natural light, establishing a relaxing bedtime routine, and modification of sleep environment to be relaxing and not distracting [32]. Practice of the sleep hygiene behaviors and reading on healthy sleep is assigned as homework each week of the intervention to match the homework assigned in the MAPS condition.

8. Assessments and measures

All assessments and classes will be completed at the UCLA Medical Center at the Cousins Center for Psychoneuroimmunology. Eight visits to the study site will be requested, including 1 pre-treatment assessment visit, 6 intervention sessions, and 1 post-treatment assessment visit. Pre- and post- treatment visits will include body measure assessment (i.e., height, weight, waist and hip circumference), administration of self-report questionnaires, and blood draw via venipuncture. Measures will be completed prior to the intervention and immediately post-intervention.

8.1. Sleep quality

For the primary outcome, self-reported sleep quality will be measured with the Pittsburgh Sleep Quality Index (PSQI) [25], a validated 19-item self-report questionnaire that assesses sleep disturbances over the past month. The questionnaire assesses

seven domains including subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep-related medication use, and daytime dysfunction, which are quantified into a global score (range: 0–21). Lower scores indicate better sleep quality.

8.2. Sleep-related daytime impairments

For the secondary sleep-related daytime impairment outcomes, insomnia symptoms, depressive symptoms, anxiety symptoms, perceived stress, and fatigue symptoms will be assessed using self-report measures. Insomnia symptom will be measured with the Athens Insomnia Scale (AIS) [33], a validated 8-item self-report questionnaire that assesses sleep difficulty. A sum score is calculated (range: 0–24), with lower scores indicating less sleep difficulty. Depressive symptoms will be measured with the Beck Depression Inventory-II (BDI-II) [34], a validated 21-item questionnaire that assesses depressive symptom severity over the past two weeks. A sum score is calculated (range: 0–64), with lower scores indicating less depression. Anxiety symptoms will be measured with the Beck Anxiety Inventory (BAI) [35], a validated 21-item questionnaire that assesses anxiety severity over the past month. A sum score is calculated (range: 0–63), with lower scores indicating less anxiety. Perceived stress will be measured with the Perceived Stress Scale (PSS) [36], a validated 10-item questionnaire that assesses the degree to which one appraises life situations as stressful over the past month. A sum score is calculated (range: 10–50), with lower scores indicating less stress. Fatigue symptoms will be measured with the Fatigue Symptom Inventory (FSI) [37], a validated 14-item questionnaire that assesses fatigue. Two sub-scales are yielded from the FSI, FSI-Interference and FSI-Severity. FSI-Interference (a sum score of 9 items, range: 0–90) assesses the degree to which fatigue has interfered with daily life over the past week, with lower scores indicating less interference of fatigue on daily life. FSI-Severity (a sum of 4 items, range 0–40) assesses the severity of fatigue experienced over the past week, with lower scores indicating less severe fatigue.

8.3. Blood draw and inflammatory assay

For the secondary inflammatory signaling outcome, blood will be collected via venipuncture between 8:30 AM and 11:30 AM by a certified phlebotomist while the participant is in a normal sitting and upright resting state. Whole blood samples will be collected by venipuncture into Cell Preparation Tubes with sodium citrate anticoagulant (BD, Franklin Lakes, NJ), held at room temperature and processed within 2 h to obtain peripheral blood mononuclear cells (PBMC) according to the manufacturer's protocol. Nuclear extracts will be prepared using 6–10 million PBMC, then stored at −80 °C as previously described [38]. Total protein concentration of each nuclear extract will be determined using a Pierce 660 nm Protein Assay (Thermo Scientific, Rockford, IL). Concentrations of activated NF-κB p65 in pristine aliquots of nuclear extracts will be determined using the TransAM NF-κB p65 ELISA kit (Active Motif, Carlsbad, CA) with recombinant NF-κB p65 (0.3–10 ng/well) as the reference standard. Each extract will be assayed in triplicate at 1–4 μg total protein per well. A positive control (stimulated Jurkat cell extract) provided by the manufacturer will be included in each assay at 2.5 μg/well. NF-κB concentrations will be expressed as ng p65/μg total protein.

8.4. Covariates

Demographic covariates to be measured will include age, gender, ethnicity, education, income, occupation, and marital status. Biobehavioral covariates will include substance use, BMI, and waist-to-hip ratio. Treatment compliance/fidelity will be assessed in both conditions with a standardized teacher-completed checklist of activities completed during each treatment session.

9. Statistical analyses

Analyses will be performed in SPSS v21 (IBM Corp., Armonk, NY). Between-group change in mean PSQI score at post-intervention will be the primary outcome in the intent-to-treat population. Between-group contrasts in outcomes across the intervention period will be tested using generalized linear mixed modeling (MIXED command) with pairwise comparisons, adjusted for pre-intervention levels of the outcome. Other covariates that have at least a marginally significant correlation ($p < .10$) with both the predictor and outcome variable will be adjusted for in the models if substantively relevant. Estimated mean differences and bias corrected effect sizes (Hedge's g) with their 95% confidence intervals will be provided. We will assess whether data provide evidence of benefit of MAPs versus SHE on sleep quality (PSQI) and secondary daytime impairment/inflammatory signaling outcomes. Value comparisons of baseline PSQI scores between those with and without missing data at post-intervention will be compared with t-tests.

10. Discussion

This article describes the design and methodology of a parallel group randomized controlled trial powered to test PSQI between-group differences between MAPs and SHE at post intervention. The primary aim of the study is to determine if the MAPs program leads to improvements in prodromal sleep disturbances in older adults. Secondary aims include determining if the MAPs program leads to improvements in sleep-related daytime impairments. An additional secondary aim is to determine if MAPs reduces levels of the NF-κB inflammatory transcription factor relative to a highly active and standardized sleep hygiene education condition.

Sleep problems are more prevalent among adults >55 years of age than any other age group [3]. The health care utilization and cost burden associated with sleep disorders and related health issues highlight the importance of treating sleep problems in this population [39]. The direct cost of sleep disorders in the U.S. is estimated to be $15.9 billion per year due to medical and non-medical expenditures [40]. Indirect costs of sleep problems include a range of consequences such as reduction or loss of productivity, motor vehicle accidents, hospitalization, increased medical costs, psychological morbidities such as depression, and increased alcohol consumption [40]. The prevalence, health-related consequences, and costs of

sleep problems among older adults highlight the need for treatments aimed at improving sleep for this population.

Previous studies suggest that mindfulness training, alone or in combination with Cognitive Behavioral Therapy, can improve sleep in adults with a disease (i.e., cancer) or with primary insomnia [16,41–43]. While these studies have shown some initial and promising results, they also point to gaps in knowledge and the need of further research. Specifically, no studies have examined the impact of MBIs on prodromal sleep disturbances or sleep problem solely in older adults, even though this population reports the highest prevalence of sleep problems. Furthermore, there have been no studies that have evaluated whether treatment of sleep disturbances is associated with improvements in markers of inflammation, which is of particular importance in the aging population [44].

This study has several strengths. The trial will include a control condition matched for time, attention, demand characteristics, teacher training effects, and social support effects (both conditions will be implemented in group-based settings). An objective biological measure, NF-κB, will be assayed. This will allow us to examine whether changes in sleep are associated with change in NF-κB. Psychosocial measures will be collected via validated instruments for all participants, enabling comparisons of intervention condition effects on several factors important for health and quality of life in older adults. Finally, potential participants will be screened for sleep problems at baseline using a validated measure, which will supply a sub-clinical community-based sample at risk for various morbidities.

This study has some limitations. Participants will be screened via a validated tool for clinical sleep disorders, such as sleep apnea, to determine study eligibility, but this will be by self-report. Due to funding constraints, only self-reported sleep measures will be used. Objective sleep assessments (e.g., actigraphy) will not be administered. However, perceived sleep quality measured by self-report will provide a clinically relevant understanding of the impact of the MAPs program on sleep quality. PSQI scores will be used as both an eligibility criterion and as an outcome, so there is a possibility of regression to the mean. This study will not include a non-treatment control condition. The study will attempt to blind participants to condition but given the nature of behavioral intervention research, it is likely that participates will figure out the treatment intent after the treatment begins. There is potential for cross-contamination as both classes are to be delivered at the UCLA Medical Center. However, treatment groups will be intentionally separated by days in the week to protect against this threat. This study will enroll community-based volunteers, which limits the generalizability of findings to the broader older adult population who are disinclined to volunteer. The study will lack long-term follow-up assessments, so there will be no evaluation of treatment durability.

In conclusion, we have described in detail the significance, rationale, study design, and methodology of a parallel-group randomized controlled trial aimed at improving sleep in older adults with persistent sleep problems. We anticipate that this trial will contribute valuable experimentally-driven evidence to test the efficacy of MBIs for improving prodromal sleep disturbances in older adults. Given that sleep problems often go untreated in older adults, and that untreated sleep problems increase the risk for physical and psychiatric morbidity and all-cause mortality [3,4,6–8], delivering effective treatment for sleep problems is an important public health priority to improve the health and quality of life of the aging population.

Acknowledgments

Supported by UCLA Older Americans Independence Center (AG028748), UCLA Clinical and Translational Science Institute (UL1TR000124), and the National Institute of Mental Health (5T32-MH019925) to D.S.B; R01-AG034588; R01-AG026364; R01 CA160245-01; R01-CA119159; R01 HL095799; R01 DA032922-01; P30-AG028748 to MRI; UCLA CTSI UL1TR000124; the Cousins Center for Psychoneuroimmunology; this work was partially supported by the National Cancer Institute of the National Institutes of Health (T32CA009492) to G.A.O.

References

[1] Crowley K. Sleep and sleep disorders in older adults. Neuropsychol Rev 2011;21:41–53.
[2] Ancoli-Israel S, Ayalon L. Diagnosis and treatment of sleep disorders in older adults. Am J Geriatr Psychiatry 2006;14:95–103.
[3] Dew MA, Hoch CC, Buysse DJ, Monk TH, Begley AE, Houck PR, et al. Healthy older adults' sleep predicts all-cause mortality at 4 to 19 years of follow-up. Psychosom Med 2003;65:63–73.
[4] Foley DJ, Monjan AA, Brown SL, Simonsick EM, Wallace RB, Blazer DG. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep 1995;18:425–32.
[5] Brassington GS, King AC, Bliwise DL. Sleep problems as a risk factor for falls in a sample of community-dwelling adults aged 64–99 years. J Am Geriatr Soc 2000;48:1234–40.
[6] Zee PC, Turek FW. Sleep and health: everywhere and in both directions. Arch Intern Med 2006;166:1686–8.
[7] Li F, Fisher KJ, Harmer P, Irbe D, Tearse RG, Weimer C. Tai chi and self-rated quality of sleep and daytime sleepiness in older adults: a randomized controlled trial. J Am Geriatr Soc 2004;52:892–900.
[8] Miller MA, Cappuccio FP. Inflammation, sleep, obesity and cardiovascular disease. Curr Vasc Pharmacol 2007;5:93–102.
[9] Simpson N, Dinges DF. Sleep and inflammation. Nutr Rev 2007;65: S244–52.
[10] Kamel NS, Gammack JK. Insomnia in the elderly: cause, approach, and treatment. Am J Med 2006;119:463–9.
[11] Montgomery P, Dennis J. A systematic review of non-pharmacological therapies for sleep problems in later life. Sleep Med Rev 2004;8:47–62.
[12] Morin CM, Bootzin RR, Buysse DJ, Edinger JD, Espie CA, Lichstein KL. Psychological and behavioral treatment of insomnia: update of the recent evidence (1998–2004). Sleep 2006;29:1398–414.
[13] Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol 2003;84:822.
[14] Daubenmier J, Lin J, Blackburn E, Hecht FM, Kristeller J, Maninger N, et al. Changes in stress, eating, and metabolic factors are related to changes in telomerase activity in a randomized mindfulness intervention pilot study. Psychoneuroendocrinology 2012;37:917–28.
[15] Winbush NY, Gross CR, Kreitzer MJ. The effects of mindfulness-based stress reduction on sleep disturbance: a systematic review. Explore (NY) 2007;3:585–91.
[16] Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int J Behav Med 2005;12:278–85.
[17] Heidenreich T, Tuin I, Pflug B, Michal M, Michalak J. Mindfulness-based cognitive therapy for persistent insomnia: a pilot study. Psychother Psychosom 2006;75:188–9.
[18] Ong J, Sholtes D. A mindfulness-based approach to the treatment of insomnia. J Clin Psychol 2010;66:1175–84.
[19] Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 2004;29:448–74.

[20] Irwin MR, Carrillo C, Olmstead R. Sleep loss activates cellular markers of inflammation: sex differences. Brain Behav Immun 2010;24:54–7.
[21] Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. Arch Intern Med 2006;166:1756–62.
[22] Black DS, Irwin M, Olmstead R, Ji E, Crabb Breen E, Motivala S. Tai Chi intervention and inflammatory signaling (NF-κB) in lonely older adults: a randomized controlled trial. Psychother Psychosom 2014 [in press].
[23] Gross CR, Kreitzer MJ, Reilly-Spong M, Wall M, Winbush NY, Patterson R, et al. Mindfulness-based stress reduction versus pharmacotherapy for chronic primary insomnia: a randomized controlled clinical trial. Explore (NY) 2011;7:76–87.
[24] Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Test–retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. J Psychosom Res 2002;53:737–40.
[25] Buysse DJ, Reynolds Iii CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
[26] Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–13.
[27] Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.
[28] Riemann D, Berger M, Voderholzer U. Sleep and depression, results from psychobiological studies: an overview. Biol Psychol 2001;57:67–103.
[29] Miller GE, Rohleder N, Stetler C, Kirschbaum C. Clinical depression and regulation of the inflammatory response during acute stress. Psychosom Med 2005;67:679–87.
[30] Carlsen H, Haugen F, Zadelaar S, Kleemann R, Kooistra T, Drevon CA, et al. Diet-induced obesity increases NF-κB signaling in reporter mice. Genes Nutr 2009;4:215–22.
[31] Smalley SL, Winston D. Fully present: the science, art, and practice of mindfulness. Da Capo Press; 2010.
[32] Thorpy M. Sleep hygiene. National Sleep Foundation; 2013 [Retreived from http://sleepfoundation.org/ask-the-expert/sleep-hygiene].
[33] Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. J Psychosom Res 2000;48:555–60.
[34] Beck AT, Steer RA, Ball R, Ranieri WF. Comparison of Beck Depression Inventories-IA and-II in psychiatric outpatients. J Pers Assess 1996;67:588–97.
[35] Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988;56:893.
[36] Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983:385–96.
[37] Hann DM, Jacobsen PB, Azzarello LM, Martin SC, Curran SL, Fields KK, et al. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. Qual Life Res 1998;7:301–10.
[38] Richlin VA, Arevalo JM, Zack JA, Cole SW. Stress-induced enhancement of NF-kappaB DNA-binding in the peripheral blood leukocyte pool: effects of lymphocyte redistribution. Brain Behav Immun 2004;18:231–7.
[39] Ozminkowski RJ, Wang S, Walsh JK. The direct and indirect costs of untreated insomnia in adults in the United States. Sleep 2007;30:263.
[40] Hossain JL. The prevalence, cost implications, and management of sleep disorders: an overview. Sleep Breath 2002;6:85–102.
[41] Hubbling A, Reilly-Spong M, Kreitzer MJ, Gross CR. How mindfulness changed my sleep: focus groups with chronic insomnia patients. BMC Complement Altern Med 2014;14:50.
[42] Ong JC, Shapiro SL, Manber R. Combining mindfulness meditation with cognitive-behavior therapy for insomnia: a treatment-development study. Behav Ther 2008;39:171–82.
[43] Ong JC, Shapiro SL, Manber R. Mindfulness meditation and cognitive behavioral therapy for insomnia: a naturalistic 12-month follow-up. Explore 2009;5:30–6.
[44] Irwin MR, Olmstead R, Carrillo C, Sadeghi N, Breen EC, Witarama T, et al. Cognitive behavioral therapy vs. Tai Chi for late life insomnia and inflammatory risk: a randomized controlled comparative efficacy trial. Sleep 2014 [in press].