Protocol for single case experimental design for yoga and sleep quality and inflammation: A two-hit model of sleep intervention

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ABSTRACT

Background: Poor sleep quality is a neglected clinical condition in the elderly that could predispose them to morbidities and even mortality. Several lines of clinical evidence support the potential of Meditative Movement Interventions (MMIs) in the alleviation of sleep-related disturbances in the elderly population. However, further studies are needed to provide more definitive evidence regarding the effectiveness of yoga-based MMI.

Objective: The primary objective of this study is to evaluate the effectiveness of a repeated course of a yoga-based meditative intervention in a home environment to improve the sleep quality of elderly subjects.

Method: A single-case experimental design with multiple baselines will be used to assess the effectiveness of Yoga-based meditative movement as an intervention for the alleviation of poor sleep quality in the elderly. A concomitant study will also be conducted to test the effectiveness of walking as an intervention using the identical design. We will recruit 6 participants with self-rated poor sleep quality (PSQI-) with external validation using actigraphy. Each participant will be randomly allocated to a different baseline phase (i.e., 7, 10, or 14 days), which will then be followed by a daily 45-min intervention over 12 weeks. The walking group will undergo daily walking.

Conclusion: This single-case, multiple-baseline, between-case intervention randomization design will be the first report, wherein yoga-based intervention would be longitudinally monitored for changes in the objective measure of sleep quality.

Trial registration: The registration number for this trial is CTRI/2021/02/031466.

1. Introduction

Though previously considered a part of normative aging [1], progressive age-associated deteriorations in sleep quantity and quality [2-5] have now been recognized as relevant determinants of healthy aging [6]. Neglect of these sleep-associated abnormalities could lead to age-related co-morbidities [7] spanning varied adverse health outcomes, including mood disturbances, cognitive impairment, physical effects, immune system dysfunction, and social and public health burden [6,8-10]. Altogether, these health ailments could ultimately affect the overall quality of life of the elderly [11]. An increased risk of mortality remains the most adverse consequence of poor sleep quality [8-10].

Inadequacy of sleep in older adults could be ascribed to multiple factors, including changes in circadian rhythms [12], co-morbid chronic medical conditions [12,13], and psychosocial manifestations of aging [14]. Biologically, sleep disturbance has been demonstrated to significantly affect heightened systemic inflammation, even in a general population, followed for over 5 years [15]. This association holds special clinical relevance considering that inflammation is one of the major hallmarks of biological aging and vulnerability to age-associated diseases [16,17].

Over recent years, the rise in the aging population has led to an appreciation of the concept of healthy aging [6]. Aligning with the same, the inter-relationship between sleep and biological aging has also grabbed significant clinical attention [18]. Evidence points to an association between longevity and regularity in patterns of sleep and slow-wave sleep. Nevertheless, the oldest old individuals have been reported to exhibit strictly regular sleep patterns, evidenced by sleep diary records and actigraphy recordings [19].

Although cognitive-behavioral therapy remains the first line of recommended treatment for insomnia in the elderly, it is limited by the requirement of a large number of sessions along with economic and logistical barriers like the non-availability of clinicians to provide the therapy [20]. In this scenario, pharmacological strategies provide an easier alternative for the alleviation of sleep complaints in the elderly [21]. However, long-term use of these drugs has been associated with serious adverse health effects like developing tolerance or dependence, rebound insomnia, residual daytime sedation, cognitive impairment, and motor incoordination that pose concerns over their use [22]. Recent trends suggest increasing use of alternative interventions by the elderly.

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https://doi.org/10.1016/j.conctc.2022.101028
Received 29 April 2022; Received in revised form 7 October 2022; Accepted 26 October 2022
Available online 31 October 2022
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such as Meditative Movement Techniques (MMIs), which integrate physical activity and meditation (tao chi, qi gong, and yoga), have also been indicated to alleviate sleep problems in the elderly [11]. Compared with active therapy or usual care/wait-list controls, MMI interventions have significantly influenced sleep quality (standardized mean difference, −0.70; 95% confidence interval, −0.96 to −0.43). Given the rising popularity, comparable ready availability, and cost-effectiveness of the intervention as compared to cognitive behavioral therapy, MMIs could be a preferred choice of clinicians and therapists. However, the evidence derived from these meta-analyses remains inconclusive because of the varying studying quality and MMI modalities [11]. Yoga and meditation offer one of the most popular and promising, but under-researched MMI for sleep complaints in the elderly [23]. The mechanical explanation for yoga’s beneficial influence on sleep regulation in older people is based on a number of insights. In elderly, practice of specific mindfulness-based meditations such as Vipassana, has been reported to improve their Slow Wave and Rapid Eye Movement sleep, which has been further attributed to intense brain plasticity events and modulation of the hypothalamic pituitary-adrenal (HPA) axis [24–26]. However, these observations have been mainly derived from cross-sectional studies. Several other studies have shown that the practice of yoga could reduce the circulating concentrations of a variety of pro-inflammatory cytokines, in particular basal TNF-α and IL-6 levels [27–31]. Further, the regular practice of yoga has also been shown to limit the level of TNF-α and IL-6 augmentation to a physical challenge of both moderate and intense exercise [31]. These pluripotent cytokines are the common biochemical denominators of sleep regulation [32,33]. The modulatory influences of yoga on lowering of inflammation markers could also be attributed to decline in sympathetic nervous system tone, and increased vagal activity [34]. Overall, Yoga’s ability to modulate the levels of inflammatory markers is especially pertinent in the context of age-related changes in sleep quality, which are themselves characterized by the phenomena of inflammaging [35–40]. It has also been postulated that yoga could also favorably alter circadian activity rhythms as a behavioral non-photosensitizer [41].

Effects of Mindfulness Meditation have been reported on the elderly using subjective variables, however, the outcomes studied were subjective and assessed for the short-term [42]. As a behavioral target, sleep-based assessments need repeated measurements over shorter time intervals [43]. Recent clinical recommendations also favor a relatively longer intervention time for mind-body interventions to promote sleep quality [44]. Capturing such minute changes in sleep quality over time could be addressed using Single Case Experimental Designs (SCEDs) [45,46] with objective methods, e.g., polysomnography or actigraphy, which along with sleep diaries would be better choices [47]. Most importantly, these studies remain limited by the lack of established fidelity of the yoga-based interventions [48]. The Single-case experimental design also provides an optimal platform to overcome the limitations related to fidelity and for assessing causal relationships between interventions and outcomes [45,46]. SCED studies also aid in the visualization of more accurate functional relationships between interventions and outcomes by providing continuous feedback on the treatment progress of individual participants [49]. Polysomnography, the golden standard for sleep assessment is, however, not considered suitable for long-term studies requiring multiple assessments in a geriatric population, on account of its intrinsic, and intrusive features [50]. These features have posed limitations in the use of intrusive longitu- dinal studies on sleep quality [51]. On the other hand, inferential methods like sleep diaries and questionnaires [51] and questionnaires like the PSQI [52], though more suitable for such long-term designs [53], and have the advantage of being relatively cheap and easy to use, may not be accurate due to the tendency in the elderly to underestimate or over-estimate sleep [47]. In such a scenario, actigraphy has been currently accepted as a valid, and practical alternative to PSG [54,55], allowing for long-term continuous sleep assessments in home settings and could be adapted to optimize sleep-related behaviors and reduce reactivity to contextual psychological stressors [56].

There remains a scarcity of high-risk population-specific research evidence on sleep interventions. Additional studies with rigorous research designs are needed to establish the efficacy of these interventions in improving sleep quality and their potential use as an intervention for various populations [57,58].

We hereby hypothesize that regular practice of yoga-based techniques of meditative movement will aid in the attainment of regularity in sleep patterns which in turn, would also align with the optimization of circulating levels of inflammatory modulators, and psychological health.

The overall aim of this work is to test the potential efficacy of a meditation-based yoga intervention to target the simultaneous alleviation of impaired sleep quality and inflammatory physiology in the elderly. This would be correlated with the study of the effectiveness of walking as an intervention, given as a cross-over intervention. We further hypothesize that expected improvements in these key mediators of health would be further reflected in their cognitive and psychological functions. This is the most significant objective of such a rigorous design and analysis where generalizability is not of great concern; rather, SCEDs are crucial when functional and causal relationships are hoped to be established with the potential for replication.

Studies reveal the effectiveness of walking as an intervention in improving the sleep quality of the elderly [59]. Walking, considered a physical activity, is easily acceptable by the elderly as it can be sustained and does not require special instructions [60]. The practice of daily walking effectively enhances sleep quality in older adults [61,62]. Therefore, it is proposed to have a single-case experimental design with between-case intervention randomization with six subjects with yoga for the first group and walking as an intervention for the second group.

2. Methods

2.1. Design, method, and procedure

This study is a prospective, multiple-baseline, single-case experimental design with four repeated measure phases in which each participant will serve as their control. The efficacy of the intervention will be evaluated using a single-case experimental design with between-case intervention randomization, in a concurrent multiple-baseline design across participants with replication (A-B and maintenance). Here, A refers to the baseline, B is the intervention period, C is the maintenance/washout period and D is the follow-up period [45]. We would adopt 2 levels of randomization to increase the internal validity of the study: between-case and multiple baseline randomization. The latter enables different, staggered, intervention start positions, and guards against biases associated with preferential case placement within the study. We will randomly assign six participants to different baseline durations of the SCED using a simple randomization method [63]. Additionally, the between-case intervention randomization design will be used to randomly allocate the two interventions to cases. This is comparable to the ‘independent sample, matched pairs group’ design. Randomization at the intervention phase helps to prevent biases arising from the choice of two different interventions; this is essential to conduct valid statistical tests [64]. Conventionally, a minimum of three baseline observation days are required to establish stability for the dependent variable. However, more observations are preferred as the SCED method is based on assessing the dependent variables (in this case, actigraphy) repeatedly for each of the participants across phases. Further, as recommended, to meet the standards of the design, a minimum of three participants [45] and at least five data collection points within each phase [65], will be considered in the study design. Such a design that includes a minimum of three phases or more is considered strong in terms of statistics [66]. This is strengthened by having multiple subjects in the multiple baseline design (MBD). All participants will
receive a yoga-based or walking intervention (B). A washout period will follow the intervention phase and then conclude with the follow-up phase.

Another strength of the design is that it is possible to determine if the intervention (changes in dependent variables) works for a particular participant alone [67]. Moreover, juxtaposing two interventions to infer the effectiveness of one intervention is possible in SCED [68].

Replication adds strength to the design [69]. Further, we have also added randomization which strengthens the scientific rigor of the study [70]. The study will be conducted and reported as per the Single-Case Reporting Guidelines In BEachavioural Interventions (SCRIBE) 2016 Statement [71]. The research proposal, study design, and methodology have been approved by the Ethics Committee of SVYASA.

It is, therefore, proposed to have a multiple baseline design (MBD) with two interventions, a total of six participants, and between-case intervention randomization. This design makes it possible to establish the causal relationships between the intervention and the expected outcomes [46]. There is, additionally, a comparison of data between two different interventions – yoga and walking. Phase repetitions are equated with sample size in the conventional design, and having many phase repetitions increases the power of the statistical test and also the internal validity. Such a design which includes a minimum of three phases or more [66] and is strengthened by having multiple subjects in the multiple baseline (MB) design, is considered strong in terms of statistics. The participants will receive a yoga-based intervention or walking intervention assigned randomly, followed by a washout period without any intervention, and conclude with a follow-up phase.

2.2. Participant recruitment

We will recruit six community-dwelling, individuals with self-reported sleep disturbances (Pittsburgh Sleep Quality Index > 5), age range 60–80 years (both male and female), from the district of Bengaluru, Karnataka, India. Participants will also be screened for willingness to comply with SCED restrictions, home-based assessments, and sample visits. Participants will be given detailed information about the study and asked to give their consent for the study. The institutional ethics committee has approved the study. All six participants will be recruited parallelly to strengthen internal validity and minimize environmental influences [45]. Potential participants will complete the Pittsburg Sleep Quality Index (PSQI). Participants who demonstrate insomnia severity stability, as indicated by similar scores on the PSQI across the baseline period or an increasing severity trend (i.e., when slope ≥ 0), will shift to the intervention phase. As part of the consenting process, participants will permit their data to be included in publication with their identity blinded.

2.3. Inclusion and exclusion criteria

Participants with uncontrolled diabetes and hypertension would be excluded; also excluded if they have severe chronic co-morbidities, severe painful conditions, severe arthritis; frail health (based on medical opinion), diagnostic criteria for mental illness, severe depression, recent surgery or fractures, addictions including caffeine, use of medications for sleep disorders. Also, those with a history of sleep disorders other than insomnia, on medication affecting sleep, history of alcohol or drug abuse, use of prescription drugs, or clinically significant drugs will be excluded.

2.4. Procedure

The six participants would be randomly assigned to different baseline durations of the SCED using a simple randomization method (Fig. 1) [63]. Adding randomization strengthens the scientific rigor of the study [70]. Principally a minimum of three baseline observation days are required to establish stability for the dependent variable [72]; however, more observations are preferred. Hence, subjects will go through the 5 series of measures at baseline (phase A). During the baseline data collection period, (A), participants will be encouraged to undertake their usual sleep behavior and data would be extracted from sleep assessments completed 7, 14, 21, 28, and 35 days before the intervention. This would be followed by an intervention phase of a Yoga-based Meditative Movement and an intervention of walking and relaxation (randomly assigned to subjects), for three months [68].

Measurements will be taken at 1–6 data points of the Intervention phase (Table 1). Participants will complete a minimum baseline of 3 weeks, during which they will complete the actigraphy, PSQI, and a weekly sleep diary. The best way of evaluating the sleep-wake cycle over an extended period is in the home environment [49]. Hence, the actigraphy device would be given to the subjects to take home and worn for 72 h. Previously validated algorithms will be used to analyze sleep and wake cycles [4]. Actigraphy scores will be plotted and visually inspected. This will be followed by a Withdrawal/washout Phase (C) where both groups will be followed for three months without any intervention, to understand the hangover effect of the intervention (5 data points will be taken) and for the washout effect of the intervention. The last is the follow-up phase (D) of 5 data points to observe the sustenance effect of

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**Figure 1. Study design.**
the intervention. All the participants will receive 1–5 baseline data points each, 1–6 intervention data points followed by 5 Withdrawal/washout Phases, and 5 follow-up data points. There will be a total of four phases ending with the follow-up assessments. This is the ABCD design through which it is hoped to demonstrate that the intervention has a lasting effect.

Simultaneous enrolment is done to minimize external influences and improve internal validity [45].

2.5. Details of intervention

1. Yoga: Movement-based meditation
   - Beginning with breathing exercises, loosening, and stretching exercises – 5 min
   - Cyclic Meditation – 35 min
   - Naadanusandhana – 5 min

   Naadanusandhana – for the healing and calming resonance effect of Omkar chanting – 5 min.
   ‘Akaara’, ‘Ukaara’, ‘Makaara’ chanting is taken up – 3 × 3 times of each syllable (A-U-M), followed by combined AUM chanting 3 times.

2. Walking: 45 min [73].

2.6. Intervention

Randomized controlled trials on sleep quality studies with yoga as an intervention remain limited due to the lack of internal validity and doubts of fidelity of the intervention and the need to be tested for specific participants. To circumvent the same, we propose to include cyclic meditation, a movement-based meditation technique of yoga derived from ancient texts, to be practiced as a combination of preset physical postures (asanas) and relaxation procedures [74]. The stimulations are of varying intensities and are suited to release stress at different levels. This leads to deep relaxation. The components include three types of relaxation – Instant, Quick, and Deep Relaxation techniques alternating with stimulating exercises in standing and sitting postures [75]. The yoga intervention will consist of individual and in-person sessions, five sessions per week for 3 months.

Walking is also positively associated with improvement in sleep quality, whether it is done in the morning or evening [61,76]. Habitual exercises, including walking, are known to improve the sleep quality of the elderly and are found to reduce sleep onset latency and increase sleep efficiency and total sleep time [73]. Walking even 30 min a day was found to improve sleep quality in older adults [77].

2.7. Primary outcome measure

2.7.1. Study measures

The interventions will be primarily evaluated by objective assessments which would include actigraphy registration along with subjective evaluations done with the administration of PSQI and a sleep diary.

3. Material, measures, and instruments

3.1. Actigraphy

Sleep quality will be objectively assessed using the MW8 actigraphy system (CamNtech; Cambridge, United Kingdom). The data obtained will be compared with the self-reported sleep indices based on questionnaires. The Motion Watch 8 is an accelerometer that can give acceleration data ranging from 0.01G to 8G and has a frequency between 3 and 11 Hz. Participants will wear the medical-grade device on their wrist (of the non-dominant arm) to measure sleep quality by quantifying and analyzing the motor activity of limbs in the 24-h period for a minimum of three consecutive 24-h periods [78]. Although actigraphy is still not recommended by AASM in the diagnosis and management of sleep disorders or evaluation of their severity, it is acceptable for use as an adjunct in sleep studies [55]. The recorded data will be transferred to a computer; the movements are analyzed through specialized software (Motionware 1.3.17) that provides objective measures of sleep, such as sleep onset latency (SL), the number of awakenings (NWAK), wakefulness after sleep onset (WASO), and sleep efficiency (SE). Research comparing previous Actigraphy devices to polysomnography (the clinical benchmark for sleep measurements) found comparable performance in measuring total sleep time [79].

3.2. Subjective sleep outcomes

3.2.1. Sleep diaries

Participants will be asked to maintain sleep diaries, which will include information on the time of going to bed for the evening, sleep onset latency, Wake After Sleep Onset (WASO) as the estimated sum of time in minutes of wake during the night after initial sleep onset until the wake-up time in the morning and getting out of bed; also, their sleep quality, use of caffeine, and frequency and duration of day time napping the previous day. Sleep onset and sleep maintenance endpoints will be analyzed using data from the sleep diaries completed daily by each study participant. Subjective Sleep Onset Latency (SSOL) refers to the estimated time in minutes from the attempt to sleep until sleep onset. Subjective total sleep time (STST) will be derived from the minutes spent asleep during their time in bed. Subjective sleep efficiency (SSE) is the proportion of STST per subjective time in bed [80].

3.2.2. Pittsburgh Sleep Quality Index (PSQI)

The researchers propose to use the 19-item PSQI version, an 19-item which is a self-report of the participant’s sleep over the previous seven days. It is a comprehensive measurement of seven domains which are the component scores. The components measured subjectively are: sleep

| Timepoint               | Measures                                                                 |
|-------------------------|--------------------------------------------------------------------------|
| Baseline assessment     | Demography, Sleep tracking device (actigraphy), Pittsburg Sleep Quality Index (PSQI), Daily sleep diaries, Perceived Stress Scale (PSS), Geriatric depression scale (GDS), Loneliness (UCLA-Loneliness), Brief Resilience Scale (BRS) |
| Weekly baseline phase (3–5 weeks) | Sleep tracking device (actigraphy), Pittsburg Sleep Quality Index (PSQI), Daily sleep diaries, Perceived Stress Scale (PSS), Geriatric depression scale (GDS), Loneliness (UCLA-Loneliness), Brief Resilience Scale (BRS) |
| Intervention phases 1–6 | Sleep tracking device (actigraphy), Pittsburg Sleep Quality Index (PSQI), Daily sleep diaries, Perceived Stress Scale (PSS), Geriatric depression scale (GDS), Loneliness (UCLA-Loneliness), Brief Resilience Scale (BRS) |
| Washout phase 1–5       | Sleep tracking device (actigraphy), Pittsburg Sleep Quality Index (PSQI), Daily sleep diaries, Perceived Stress Scale (PSS), Geriatric depression scale (GDS), Loneliness (UCLA-Loneliness), Brief Resilience Scale (BRS) |
| Follow-up 1–5           | Sleep tracking device (actigraphy), Pittsburg Sleep Quality Index (PSQI), Daily sleep diaries, Perceived Stress Scale (PSS), Geriatric depression scale (GDS), Loneliness (UCLA-Loneliness), Brief Resilience Scale (BRS) |
quality, sleep latency, sleep duration, sleep efficiency, disturbances in sleep, sleep medications used, if any, and daytime dysfunction. The sum of scores for these seven components yields one global score [81].

3.3. Sample collection

A blood sample (15 ml) will be collected by using the blood collection tubes; a normal clotting tube (SST II Advance, BD Biosciences) for serum and EDTA (all BD Biosciences), on the morning of the following day. All samples will be kept at room temperature and will be spun within 1 h at 700 × g at room temperature. Cell-free plasma or serum will be aliquoted and stored at −80 °C until analysis. Before analysis, all thawed samples will be centrifuged through a polypropylene centrifuge tube containing a 0.22 μ nylon membrane (Spin-X column; Corning, Corning, NY, USA) to remove debris.

3.4. Multiplex immunoassay

Sleep regulatory molecules, IL-2, 6, 10, TNF-alpha, and CRP will be assessed through a Luminex-based immune assay (Luminex Corporation, Austin, TX). The serum will be assayed according to the manufacturer’s protocols: LX - as part of a Luminex Custom Multiplex panel consisting of IL-2, IL-6, CRP, TNF alpha, and IL-10. The dynamic range of each assay is defined by the highest and lowest concentrations of calibrators specified in each kit. Reproducibility is reported as the percent coefficient of variation.

3.5. Generalization measures

We will also collect data on measures to assess whether any of the effects of the intervention generalize to behaviors and outcomes other than the objective and subjective indices of sleep quality. For example, in this study, measures will be administered to assess whether any treatment effects generalize to psychosocial measures of resilience, loneliness, depression, and perceived stress outcomes other than pain intensity and pain interference. These generalization measures were deemed important to strengthen the external validity of the research findings [46].

3.6. Psychosocial measures

3.6.1. Brief resilience scale

The brief resilience scale (BRS) assesses the individual’s ability to cope with stress and recover from stress [82]. The BRS has 6 items wherein items 1, 3, and 5 are positively worded, and the remaining three items - 2, 4, and 6 are negatively worded. Items 2, 4, and 6 are reverse coded and scored. The mean of the six items gives the BRS score. The participants are asked to indicate the extent to which they agree with each item of the scale: 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree.” [83].

3.6.2. UCLA scale for loneliness

The UCLA scale is a 20-item subjective questionnaire to measure the participant’s feelings of loneliness and social isolation. Participants are required to rate each item on a scale from 1 (Never) to 4 (Often). Items 1, 5, 6, 9, 10, 15, 16, 19, 20 are all reverse-coded and scored [84].

3.6.3. Geriatric depression scale

A measure of self-reported depression in older adults, the shortened version (GDS-5), of the Geriatric Depression Long-Scale (GDS-L), comprises 15 items. Subjects have to respond in a “Yes/No” format. These 15 items are found to have a high correlation with depressive symptoms in previous validation studies [85]. The time taken to complete the questionnaire is between 5 and 7 min, therefore, considered suitable for the elderly who may tire easily or are unable to concentrate for long. Ten of these questions indicate the presence of depression when answered in the affirmative; the remaining five responses are indicative of depression when answered in the negative.

3.6.4. Perceived Stress Scale

A widely accepted psychological instrument, the Perceived Stress Scale (PSS) is used for measuring the perception of stress. It measures the degree to which life events are perceived as stressful. The ten items in the questionnaire help to measure or understand the extent to which the participants find their lives predictable, within their control, and if they are weighed down. However, the questions are clear, simple, and easy to follow and understand. These items pertain to the feelings and thoughts of the respondents.

Scoring: PSS scores are obtained by summing up all scale items, where items 4, 5, 7, & 8 are reverse coded and scored [86].

3.7. Data analysis

The multiple baseline design combined with the intervention withdrawal will be used to observe the effects on the dependent variables (sleep indices, inflammatory markers, and psychological variables) whilst Cyclic Meditation [87] will be considered an independent variable, between-case standardized mean differences on insomnia severity to compute the treatment effect size and perform visual analysis on subject-level data using the Conservative Dual-Criterion method [89]. Results will be presented as a time-series graph. The visual inspection will be completed according to the criteria by Kazdin [89]. Further, to control for the serial dependency of the repeatedly collected data we will perform an intervention time series analysis (ITSA) using autoregressive residuals.

4. Discussion

To the best of our knowledge, this is the first study to design and develop an integrated yoga module in a single case experimental design to observe the efficacy in the sleep quality of the elderly, with a longitudinal, multi-time point approach. Another unique aspect of the proposed research is the inclusion of inflammation markers as outcome variables (correlation between sleep and inflammation, noted through the effect on cytokines (inflammation markers) have been established [36]) as well as certain subjective measures of sleep. Based on the notion that yoga interventions could be optimized to modulate sleep-related behaviors and reduce reactivity to contextual stressors, we would also address the impact of the intervention on several generalization parameters such as resilience, loneliness, depression, and perceived stress.

This study is strengthened by the methodological rigor added by the single-case, multiple-baseline design, and inclusion of actigraphy-based objective assessment of sleep. The longitudinal assessments would provide access to details of the individual responses and trajectories of change. Being a SCED, the study would also address the need for individual-level intervention which is considered to overcome the time-varying social and psychological influences and hence, could not be based on group statistical inferences. The estimates of a group cannot be applied to an individual and such a generalization can be counterproductive at best and a threat to the individuals at worst [90].

The design will also take care of the fidelity of the intervention which has been projected as an important limitation of yoga-based research. Further, the repeated demonstrations of the observed effects in the multiple baseline design would help in establishing confidence in the intervention-induced effects rather than those produced by co-occurring factors. The individual set-up of the intervention also discriminates against other investigating MBIs.

Given the small sample size, this study is limited by the lack of generalizability. However, to enhance the generalizability of the intervention, we have aimed at replicating the SCED, with the same intervention on three subjects. Another limitation related to the single-case designs is related to the assessments, as repeated exposure to the
assessment measure could affect the response. Hence, to eliminate the same, we have planned for repeated assessments of the dependent variable(s) across different phases of the design.

Overall, the SCED design will provide intensive rigor to the study based on repeated measurements taken at multiple time points. Such an evaluation of the intervention will help to determine the efficacy of yoga in improving the sleep quality of individual participants and customizing the yoga module to suit individual requirements. Given the high prevalence of sleep-related disturbances in elderly populations, results from this study could be of great translational importance. If found effective, the cost-effectiveness and ease of the intervention would also provide a feasible alternative for the elderly who are not able to participate in alternate non-pharmacological interventions such as cognitive behavioral therapy.

Funding acknowledgment

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

References

[1] K. Varemchuk, Sleep disorders in the elderly, W.B. Saunders, Clin. Geriatr. Med. 34 (2) (2018) 205–216, https://doi.org/10.1016/j.cger.2018.01.008, May 01.
[2] E.D. Chinoy, D.J. Fry, D.N. Kussinovsky, P.G. Meyer, K.P. Wright, Age-related changes in slow wave activity rise time and NREM sleep EEG with and without zolpidem in healthy young and older adults, Sleep Med. 15 (9) (2014) 1037–1045, Sep, https://doi.org/10.1016/j.sleep.2014.05.007.
[3] C. Schmidt, P. Prigge, C. Cajochoen, Age-related changes in sleep and circadian rhythm: impact on cognitive performance and underlying neuroanatomical networks, 0, Front. Neonat. (2012) 118, https://doi.org/10.3389/FNEUR.2012.00118.
[4] N. Stanley, The physiology of sleep and the impact of ageing, Eur. Urol. Suppl. 3 (6) (Jan. 2005) 17–23, https://doi.org/10.1159/000565005/600001.X.
[5] J.R. Cooke, S. Ancoli-Israel, C, in: P.J. Vinken, G.W. Bruyn (Eds.), Abnormal Sleep in the Elderly, vol. 98, 2011, https://doi.org/10.1186/S12913-016-1520-5.
[6] A. Sowa, B. Tobiasz-Adamczyk, R. Topa, M. Janelsins, M. Janelsins, L.J. Peppone, C. Kamen, Yoga for the treatment of insomnia in elderly cancer patients: a systematic review and meta-analysis, J. Alternative Compl. Med. 21 (9) (Sep. 2015) 509–518, https://doi.org/10.1089/acm.2014.0251.
[7] R. Pattanasathit, S. Sathiamma, S.P. Talakkad, P. Nityananda, R. Trichur, L.J. Peppone, K. Kamas, Practitioners of aipasana meditation exhibit enhanced slow wave sleep and REM sleep states across different age groups, undefined 8 (1) (Jan. 2010) 34–41, https://doi.org/10.1111/j.1479-8425.2009.00416.X.
[8] R.P. Nagendra, T.N. Sathyaprabha, B.M. Kuttty, Enhanced dehydroepiandrosterone levels are positively correlated with N3 sleep stages in long-term meditation practitioners, Sleep Sci 15 (2) (2012) 179–187, https://doi.org/10.5935/1984-0063.20120039.
[9] J.K. Kirocl-Glaser, et al., Yoga’s impact on inflammation, mood, and fatigue in breast cancer survivors: a randomized controlled trial, J. Clin. Oncol. 32 (10) (2014) 1040–1049, Apr, https://doi.org/10.1200/JCO.2013.51.8866.
[10] J.K. Kirocl-Glaser, et al., Stress, inflammation, and yoga practice, Feb, Psychosom. Med. 72 (2) (2010) 113–121, https://doi.org/10.1037/a0018957.
[11] J.E. Bowe, et al., Yoga reduces inflammatory signaling in fatigued breast cancer survivors: a randomized controlled trial, Psychoneuroendocrinology 43 (2014) 20, https://doi.org/10.1016/j.psyneuen.2014.01.019.
[12] C. Estevez, The role of yoga in inflammatory markers, 100421, Mar, Brain Behav. Immun. Health 20 (2022), https://doi.org/10.1016/j.bbihh.2022.100421.
[13] A. Vijayaraghava, V. Doreswamy, O.S. Narasipur, R. Kunnaw, N. Srinivasamurthy, Effect of yoga practice on levels of inflammatory markers after moderate and strenuous exercise, CO88, J. Clin. Diagn. Res. 9 (6) (2015), https://doi.org/10.17925/JCDR.2015.1285.0621. Jan.
[14] Suppl J.M. Clinton, C.J. Davis, M.R. Zielinski, K.A. Jettew, J.M. Krueger, Biochemical regulation of sleep and sleep biomarkers, S38, J. Clin. Sleep Med. 7 (5) (2011), https://doi.org/10.5096/JCSM.2011.0600.
[15] D.M. Djalilova, P.S. Schulz, A.M. Berger, A.J. Case, K.A. Kupary, A.C. Ross, Impact of yoga on inflammatory biomarkers: a systematic review, Biol. Res. Nurs. 21 (2) (Mar. 2019) 198–209, https://doi.org/10.1177/1099800418764671.
[16] M. Nadeli, et al., Serum and gene expression profile of cytokines following strenuous exercise, CC08, J. Clin. Diagn. Res. 9 (6) (2015), https://doi.org/10.5935/1984-0063.20150039.
[17] M. Atienza, J. Ziontz, J.L. Cantert, Low-dose inflammation in the relationship between sleep disruption, dysfunctional adiposity, and cognitive decline in aging, Sleep Med. Rev. 42 (Dec. 2018) 171–183, https://doi.org/10.1016/j.smrv.2018.08.002.
[18] L. Bedovsky, T. Lange, H. Haack, The sleep-improve crosstalk in health and disease, Physiol. Rev. 99 (3) (2019) 1325–1380, Jul, https://doi.org/10.1152/physrev.00010.2018.
[19] 1042 Joseph M. Dzierezwski, et al., Sleep inconsistency and markers of inflammation, 16 Sep, Front. Psychol. 11 (2020), https://doi.org/10.3389/FPSYCO.2020.01042.
[20] M.R. Irwin, M.R. Opp, Sleep health: reciprocal regulation of sleep and innate immunity, Nature Publishing Group, Neurosychopharmacology 42 (1) (2017) 129–136, https://doi.org/10.1038/npp.2016.148, Jan, 01.
[21] C. Franceschi, P. Garagnani, P. Parini, C. Gialian, A. Santoro, Inflammaging: a new immune–metabolic viewpoint for age-related diseases, 2018 14:10, Nat. Rev. Endocrinol. 14 (10) (2018) 576–590, https://doi.org/10.1038/s41574-018-0059-4, Jul.
[22] K.M. Mustian, M. Janein, L.J. Peppone, C. Kamen, Yoga for the treatment of insomnia among cancer patients: evidence, mechanisms of action, and clinical recommendations, Oncol Hematol Rev 10 (2) (2014) 164, https://doi.org/10.17925/OHR.2014.10.2.164.
A. Krasny-Pacini, J. Evans, Single-case experimental designs to assess intervention effectiveness in rehabilitation: a practice guide, Elsevier Masson SAS, Ann. Phys. Rehabilitation Med. 61 (3) (2018) 164-179, https://doi.org/10.1016/j.rehab.2017.12.002. May 01.

M.A. Lobo, M. Moeyaert, A.B. Cunha, I. Babik, Single-case design, analysis, and quality assessment for intervention research, J. Neurol. Physiol. Ther. 41 (3) (2017) 187-197, https://doi.org/10.1097/NPT.0000000000000187.

L. Ward, S. Stebbings, K.J. Sherman, D. Cherkin, G.D. Baxter, Establishing key elements of meaningful equivalence in single-case designs for health sciences researchers: a versatile clinical trials companion, Ther. Practice in Special Education, 271, 2016, pp. 165-179. Jul. 10.1177/1053451615615947.

R. Tanious, P. Onghena, Randomized single-case experimental designs in healthcare research: what, why, and how?, Dec, Healthcare 7 (4) (2019), https://doi.org/10.3390/HEALTHCARE7040163.

T. RL et al., The single-case reporting guideline in BEhavioural interventions (SCBRBE) 2016 statement, Aug, Neuropsychol. Rehabil. 27 (1) (2016) 1-15, https://doi.org/10.1080/09602011.2016.1190533.

R.L. Tate, S. McDonald, M. Peredics, L. Togher, R. Schulte, S. Savage, Rating the methodological quality of single-subject designs and n-of-1 trials: introducing the single-case experimental design (SCED) scale, Neuropsychol. Rehabil. 18 (4) (May 2008) 385-401, https://doi.org/10.1080/10503990802009201.

H. Hori, A. Iemouchi-Sugita, R. Yoshimura, J. Nakamura, Does subjective sleep quality improve by a walking intervention? A real-world study in a Japanese workplace, e101055, Oct, BMJ Open 6 (10) (2016), https://doi.org/10.1136/BMJOPEN-2016-010555.

D.S. Nishoum, N. Aras, S. Mukherjee, Possible roles of cyclic meditation in regulation of the gut-brain Axis, 6047, Dec, Front. Psychol. 12 (2021), https://doi.org/10.3389/FPSYG.2021.768031.BIBTEX.

M. Tg and Suma, “Effect of cyclic meditation on sleep quality, psychological well-being and quality of life among working professionals during the lockdown period”, Int. J. Sci. Res., doi:10.22155/25911600214502. Feb. 05.

M. Karpaa, et al., Long-term efficacy and tolerability of lomexilam compare with placebo in adults with insomnia disorder: results from the phase 3 randomized clinical trial SUNRISE 2, Sleep 43 (9) (Sep 2020) 1-11, https://doi.org/10.3390/SLEEP.Z3A123.

P. Fontil, M. A. J. Gervais, R. Taylor-Gervais, H.J. Lim, Nature and science of sleep relationships between the pituitary sleep quality index and the eponymous sleepiness scale in a sleep laboratory referral population, Nat. Sci. Sleep (2013) 5, https://doi.org/10.2147/NSS.S40608, –15.

L. da Silva-Sauer, T.R.G. Lima, J. Koga, E.K.G. da Fonseca, A. de La Torre-Luque, X. Yu, B. Fernandez-Calvo, Psychological resilience moderates the effect of perceived stress on late-life depression in community-dwelling older adults, Apr, Trends Psychol. (2021) 1-14, https://doi.org/10.1007/s42781-020-00073-3.

B.W. Smith, J. Dahlen, K. Wiggins, E. Tooley, P. Christopher, J. Bernard, The brief resilience scale: assessing the ability to bounce back, Int. J. Behav. Med. 15 (3) (Jul. 2008) 194-200, https://doi.org/10.1007/s10919-008-922297.

D.W. Russell, UCLA loneliness scale (version 3): reliability, validity, and factor structure, J. Pers. Assess. 66 (1) (1996) 20-40, https://doi.org/10.1207/s15327572paa6601_2.

J.J. Sheikh, J.A. Yesavage, 9/geriatric depression scale (GDS) recent evidence and development of a shorter version, Clin. Gerontol. 5 (1-2) (Nov. 1986) 165–173, https://doi.org/10.1300/J018v05n01_04.

S. Cohen, T. Kamarck, R. Mermelstein, A global measure of perceived stress, J. Health Soc. Behav. 24 (4) (1983) 385–396, https://doi.org/10.1177/002215658302400403.

S. Parra, S. Telles, Positive impact of cyclic meditation on subsequent sleep, Med. Sci. Monit.: Int. Med. Res. 21 (1) (2015) 122, https://doi.org/10.12659/MSM-8662/100016. Jul.

S. Patra, S. Telles, Positive impact of cyclic meditation on subsequent sleep, Med. Sci. Monit.: Int. Med. Res. 21 (1) (2015) 122, https://doi.org/10.12659/MSM-8662/100016. Jul.

S. Cohen, T. Kamarck, R. Mermelstein, A global measure of perceived stress, J. Health Soc. Behav. 24 (4) (1983) 385–396, https://doi.org/10.1177/002215658302400403.

S. Parra, S. Telles, Positive impact of cyclic meditation on subsequent sleep, Med. Sci. Monit.: Int. Med. Res. 21 (1) (2015) 122, https://doi.org/10.12659/MSM-8662/100016. Jul.

S. Patra, S. Telles, Positive impact of cyclic meditation on subsequent sleep, Med. Sci. Monit.: Int. Med. Res. 21 (1) (2015) 122, https://doi.org/10.12659/MSM-8662/100016. Jul.

S. Patra, S. Telles, Positive impact of cyclic meditation on subsequent sleep, Med. Sci. Monit.: Int. Med. Res. 21 (1) (2015) 122, https://doi.org/10.12659/MSM-8662/100016. Jul.