The University of Hong Kong
School of Nursing

Study Proposal

Study Title: The feasibility and preliminary effects of an empowerment-based cognitive behavioural therapy for insomnia on sleep, cognitive function and health-related quality of life in persons with mild cognitive impairment: A mixed-method pilot study

Background

The detrimental impacts of cognitive impairment

Dementia is an irreversible devastating neurodegenerative disorder characterized by memory loss, cognitive deterioration, functional impairment and behavioral changes. Alzheimer's disease is the most common type, accounting for 60-80% of late-life dementia.[16, 17] Dementia imposes not only significant physical and psychological burdens on the sufferers and their families but also enormous service demands on health and social care systems. Because dementia is an incurable and progressive debilitating chronic condition, it is imperative to develop effective means by which to mitigate disease burden at the pre-dementia stage. Mild cognitive impairment (MCI) represents the reversible, intermediate clinical state between normal age-related cognitive decline and dementia, but it does not fulfill the diagnostic criteria for dementia.[3, 18] It is a highly prevalent condition, particularly among the geriatric population. A meta-analysis including 34 epidemiologic studies reported the prevalence of MCI ranged from 8.4% for people aged 65-69 years to 25.2% for those aged 80-84 years.[20] Solid epidemiological evidence suggests that MCI persons are prone to progress to dementia, most often Alzheimer's disease, at a rate of 10 to 15% per year.[18] These data highlight the urgent need to identify effective and safe strategies to halt or even reverse the progression of cognitive impairment in MCI persons.

Insomnia in MCI persons

At present, no pharmacological treatment has proved to be effective in reversing cognitive impairment in MCI persons. Instead, modification of risk factors remains the primary strategy to reshape the cognitive trajectory in these persons. Empirical evidence has linked several lifestyle and vascular risk factors to an increased risk of cognitive decline in MCI and Alzheimer's disease.[22] Accordingly, research evidence is accumulating to support the empirical effects of risk modification interventions in improving the cognitive health of MCI persons, such as engagement in physical, social and cognitive activities.[23-25] Indeed, growing evidence is emerging to suggest insomnia as a new risk factor to be associated with cognitive decline and conversion from MCI to dementia.[5] Insomnia symptoms, including difficulty in falling asleep, waking up during the night and early morning awakening, are highly prevalent among MCI persons but have received the least attention. 27] Epidemiological evidence also suggests that poor sleep is associated with an increased risk of converting from MCI to dementia.[30]

The underlying mechanisms linking sleep to cognition

General and condition-specific mechanisms underlie the connection between sleep and cognition. Generally, sleep serves a restorative function in the brain to maintain normal cognitive function. In particular, slow-wave sleep (i.e., deep sleep) is essential for memory consolidation, a crucial process that stabilizes and fully integrates memory traces into long-term memory. Studies have documented that changing the sleep architecture by reducing the time in slow-wave sleep result in memory loss.[6, 31] Specifically, the underlying mechanisms linking sleep and cognition are related to the deposition of amyloid-β in the brain, the hallmark histopathological change in Alzheimer's disease. APoor sleep increases the level of amyloid-β release over time and augments amyloid-β deposition,[8] thus entailing an increased chance of amyloid plaque accumulation and subsequently contributing to early cognitive decline and conversion to dementia through the disruption of hippocampus-dependent memory.[9] The aforementioned vicious cycle between disturbed sleep and amyloid-β pathology underscores the potential cognitive benefits of interventions to improve sleep among MCI persons.

Sleep promotion in MCI persons: an unaddressed issue

Pharmacotherapy remains the most common sleep aid modality for managing insomnia in adults. However, hypnotic drugs are typically not suggested for long-term use in an older population because of the increased risk for adverse effects, drug-drug interactions, dependence, tolerance and the lack of empirical evidence to support their long-term efficacy in this population.[33] Their common side effect of reducing cognitive performance further compromises their use among the MCI population.[34] Thus, the use of non-pharmacological approaches should be a priority to promote better sleep in this clinical population. Among such strategies, cognitive-behavioral therapy for insomnia (CBT-I) has received the best recognition in the literature.[11, 35]

CBT-I is a multi-component approach that combines various cognitive and behavioral strategies including sleep restriction, stimulus control, cognitive therapy, sleep hygiene and relaxation strategies. The underlying assumption of this non-pharmacological treatment is based on Spielman's 3P Model of Insomnia, which delineates the roles of predisposing, precipitating and perpetuating factors in hampering effective sleep function.[36] CBT-I comprehensively tackles these factors that maintain insomnia over time through the following five key intervention components:

1. Stimulus control: a set of behaviors aimed at strengthening the association between the bedroom and other environmental cues with rapid sleep onset.
2. Sleep restriction: a technique to consolidate sleep by limiting the time spent in bed to the actual time of sleeping. An initial sleep deprivation is induced to increase sleep efficacy and is followed by a gradual prolongation of the sleeping time.
3. Sleep hygiene: teaching lifestyle habits that are more conducive to sleeping and avoiding sleep-incompatible behaviors.
4. Relaxation training: a technique used to induce a complete state of physical and mental relaxation and hence reduce cognitive, emotional and physiological arousal that is non-conducive to sleeping.
5. Cognitive restructuring: a technique to alter faulty beliefs and attitudes that often serve to exacerbate insomnia and replace them with more adaptive substitutes.

The sleep-promoting effects of CBT-I have been widely examined in clinical trials.[12] Because it addresses a variety of perpetuating factors of insomnia, CBT-I was found to be more effective than a single-component approach in tackling insomnia.[11] As such, the international guideline from the American College of Physicians has recommended the wide application of CBT-I to manage chronic insomnia in general adults.[11] Despite such strong recognition of the sleep-promoting effects of CBT-I, its application in people with MCI is minimal. The compromised cognitive ability of this group and, thereby, the resulting challenges in their active engagement may explain such limited application.

Engaging MCI persons in an active learning process: an empowerment approach

The empowerment approach has recently emerged as a novel, effective paradigm for health promotion and education. This person-centered collaborative approach optimizes learning by promoting patient participation during the educational process.[39] The essence of the empowerment model equips the therapist with a step-by-step approach to support the participants in understanding the rationale for behavioral changes; a goal-setting process to help them to stay focused and increase their motivation and autonomy;[14] and a subsequent process to assist the participants in developing an action plan as a roadmap to guide progressive goal attainment. The step of action planning also helps the participants to translate abstract knowledge and beliefs into concrete actions.[14] To the best of our knowledge, such an empowerment-based approach has never been used to compensate for the cognitive impairment in MCI persons that precludes the uptake of CBT-I content. Given the strong relationship between sleep and cognitive impairment, and the inadequacy of current empirical evidence on sleep-promoting interventions for MCI persons, we hypothesize that a multi-component CBT-I intervention featuring an empowerment-based approach would improve the sleep and cognitive function in this highly vulnerable group.

Work done by us

This study is proposed to address the research gap identified by the investigation team. We are currently conducting a randomized controlled trial (RCT) to examine the effects of a new volunteer-supported model to improve cognitive function in MCI persons through the promotion of an active lifestyle. We noticed that sleep problems are highly prevalent among this vulnerable group, and their motivation is low. As such, this team of investigators, which has a strong research track record and expertise in delivering psychosocial interventions, care of persons with MCI and dementia and chronic disease management using the empowerment-based educational model, developed an evidenced-based CBT-I intervention featuring the empowerment approach to improve sleep quality and cognition in persons with MCI. The PI and the Co-I (D. Yu) have successfully used the empowerment model to promote self-care among patients with heart failure. Indeed, the co-investigators have extensive research and clinical experience in working with people with MCI and dementia. The Co-I (D. Yu), a nursing academician specializing in gerontology, has established an online CBT-based website (Sweet Dream) to fight against insomnia in the older population in Hong Kong and has tested the effects of an activity-based intervention for older people with sleep complaints. Another Co-I (A. Wong) is a psychologist with substantial research experience working with people with MCI and dementia. This study proposes to address a neglected area in the literature and to test the effects of an empowerment-based CBT-I for MCI persons on their sleep and cognition.

Research plan and methodology

The proposed study will have two aims:i) to determine the feasibility of an empowerment-based CBT-I in MCI persons; and ii) to examine the preliminary effects of the empowerment-based CBT-I on sleep, cognitive outcomes and HRQoL in persons with MCI. Sleep pattern in terms of time to initiate sleep (sleep latency, SL), number and duration of awakenings after sleep onset (WASO), ratio of total sleep time (TST) to the time spent in bed (sleep efficiency, SE) and sleep quality will be the primary outcomes, and cognitive function and HRQoL will be the secondary outcomes.

Study design

This will be a mixed-method study with a single-blinded parallel-group randomized controlled trial (RCT) and a qualitative study to determine the feasibility and preliminary effects of the empowerment-based CBT-I on sleep, cognitive outcomes and HRQoL in persons with MCI. The study implementation protocol is outlined in Figure 1. A research assistant (RA1) will recruit eligible participants from the elderly community centers operated by two non-governmental organizations in Hong Kong. After collecting the baseline data (T0), RA1 will randomly assign participants into the intervention group and control group with block randomization to ensure even distribution of participants in the two study groups over the study period. A computer-generated random sequence will be used to determine the block size (6, 8 and 10) and respective study group allocation in a 1:1 ratio. To ensure allocation concealment, the group allocation will be determined according to the random sequence codes placed in sealed opaque envelopes. Participants in the intervention group will receive the empowerment-based CBT-I, whereas the control group will receive usual care. To minimize biases, another research assistant (RA2) who is blinded to the group allocation will be responsible for collecting post-test data immediately (T1) and 3 months (T2) post-intervention for both groups. A total of 10 participants, with 3-4 participants from each intervention group, will be invited to take part in a qualitative interview to obtain more in-depth comments about the feasibility and acceptability of the intervention.

Study participants

Adults will be eligible to join the study if they are aged ≥50 years, living in the community, with MCI defined by the following criteria: i) presence of significant cognitive complaints, defined as ≥3 complaints on the Memory Inventory for Chinese;[44] ii) abnormal objective cognitive performance defined as < -1.5 standard deviations from age- and education-matched normal persons on the Montreal Cognitive Assessment Hong Kong version (HK-MoCA);[45] and iii) independence in daily living as evaluated through the clinical interview. Participants are required to have poor sleep quality that can be assessed by the Pittsburgh Sleep Quality Index (PSQI).[46] The PSQI consists of 19 items evaluating seven domains of subjective sleep quality in the preceding month. Each subscale is weighted equally on a 0 to 3 scale. A global score is obtained by summing the scores of the subscales, with a higher score indicating worse sleep quality. MCI persons with a global PSQI score of >5 will be eligible for inclusion. Persons with confirmed dementia,

with known psychiatric conditions, impaired communication, sleep disorders with an organic cause (e.g., sleep apnea, or restless legs syndrome) or due to a medical problem (e.g., pain) and those using hypnotics and other medications known to affect sleep (e.g., steroids, anxiolytics) will be excluded. A total of 60 participants (i.e., 30/study arm) will be recruited for this pilot RCT. The findings of this pilot will provide information for estimating the effect size, which will inform the sample size for a subsequent full-scale RCT.

Intervention group: Empowerment-based CBT-I for MCI

Participants in the intervention group will participate in a 12-week empowerment-based CBT-I comprising face-to-face sessions supplemented with telephone follow-ups. In total, six face-to-face sessions (90 minutes/session) will be conducted in a small group format with 6–8 participants in a group and two 30-minute individual sessions will be scheduled over eight weeks, with the individual sessions arranged in the 4th and 7th week, and this is then followed by two bi-weekly telephone follow-ups. The face-to-face delivery modality is adopted to meet the challenges of mildly impaired cognition faced by MCI persons, whereas the small group format was chosen in accordance with the literature suggesting it has efficacy comparable with the individual format.[50] The group format is more cost-effective, and it can facilitate peer modeling and learning. The face-to-face sessions will cover the following core areas in CBT-I: i) sleep education, ii) sleep hygiene and relaxation, iii) sleep restriction, iv) stimulus control and v) cognitive therapy. The first five sessions will cover these core areas, and a booster session will then follow to summarize the key components of CBT-I and equip the participants with relapse-prevention strategies when sleeping problems recur (Table 1). The content of the CBT-I components complies with the recommendations for managing chronic insomnia by major international sleep associations.[11, 51]

A five-step empowerment approach (Figure 2) will be adopted to implement each face-to-face session to facilitate goal attainment and behavioral maintenance. At the beginning of each session, RA1 will encourage the participants to discuss their usual practice or beliefs about sleep or insomnia related to the core area of that week. The RA1 will make use of various therapeutic communication and counseling skills during the process, which are outlined in Figure 2. Moreover, supportive, non-judgmental and empathetic attitudes will be used to build a rapport with the participants. The RA1 will then deliver a structured educational session about the topic area. The rationales and explicit methods of how to carry out the suggested behaviors will be stated. The content will emphasize assisting participants to understand the linkage between their usual practice (behaviors/thoughts) and the consequences to sleep disruption. The RA1 will then facilitate the participants to identify the discrepancies between their usual practice/dysfunctional beliefs and the recommended best practice for sleep improvement/beliefs that favor better sleep. Easy-to-understand comic stories will be incorporated to illustrate the more abstract concepts about dysfunctional beliefs related to insomnia (for the session on cognitive therapy) and bed-sleep association (for the session on stimulus control). The RA1 will also highlight the possible consequences of these discrepancies on brain health. The RA1 will then assist participants to set self-directed goals related to these areas. During this process, the RA1 will work collaboratively with the participants and ensure that the goals are achievable yet challenging. The RA1 will also work with the participants to develop an action plan for achieving the goals set during each session. After action-planning, a subsequent interactive skill-building session will ensure that participants acquire the skills required to perform specific behaviors. A scenario-based approach will be adopted to train the participants on how to maintain the recommended behaviors. The RA1 will make use of group dynamics by encouraging the discussion among the peers of successful actions, feelings, concerns and perceived barriers to goal achievement. Various memory compensatory strategies will be used to reinforce the educational content, such as memory aids (e.g., memory notebooks, calendars and to-do lists) and mnemonic strategies. Each subsequent session will begin with a discussion of progress in goal attainment and challenges and barriers encountered while implementing the action plan set during the preceding week. The RA1 will also review the key messages delivered in previous sessions.

The RA1 will provide continuous support through telephone calls (two bi-weekly calls) upon the completion of all face-to-face sessions. A telephone record containing the participants' demographic and clinical profile, endorsed dysfunctional beliefs and attitudes about sleep, self-directed goals and action plans will be created to facilitate the telephone support. The RA1 will monitor participants' adherence to the recommended behaviors and goal attainment progress, identify barriers in real-life settings and provide methods of resolving them. The advice and counseling given will be documented to guide subsequent telephone calls.

Control group: Usual care

The control group will receive the standard care provided by the elder community centers. The participants in the control group are required to consent not to participate in any structured cognitive training activities provided by the centers during the study period.

Fidelity monitoring of the study intervention

A step-by-step standard manual with sample dialogue will be developed to guide the RA1 in delivering the intervention. Moreover, the PI will randomly select two groups in the intervention arm for fidelity monitoring and checking. The face-to-face sessions will be videotaped, and the telephone calls will be audiotaped after obtaining the participants' consent. A performance checklist will be developed and used for fidelity checking. Two postdoctoral fellows will be invited to review the videos and complete the checklist. In addition, the attendance of the participants will be recorded. All of these data will be used to interpret the study findings.

Outcome measures

Sleep assessment. Three measures were chosen to evaluate sleep pattern and quality by both subjective and objective means according to the recommendations suggested by the international expert consensus.[52] The 19-item Chinese version of the PSQI will be used to assess subjective sleep quality.[53] It is reliable (Cronbach's alpha = 0.83) and has shown good test-retest reliability and discriminant validity.[53] The Chinese version of the Insomnia Severity Index (ISI-C) (7-item)[54] will be used to assess the perceived insomnia severity, consequences of insomnia and the degree of distress related to insomnia. A five-point Likert scale is used, with higher values indicating higher levels of perceived severity of insomnia, more severe consequences of insomnia and a greater degree of distress associated with insomnia. The ISI-C has good internal consistency (Cronbach's alpha = 0.81), construct and discriminant validity.[54] An Actiwatch, which contains an accelerometer to record the frequency and intensity of body movement, will be used to objectively assess sleep patterns. The parameters of sleep pattern include TST, SL, WASO and the ratio of TST to SE. Participants will be instructed to wear the Actiwatch on their non-dominant wrist during sleep for a consecutive seven-day period.

Cognitive assessments. To detect subtle cognitive changes, a battery of cognitive assessments will be used to evaluate various domains of cognition, including the Cantonese version of the Alzheimer's Disease Assessment Scale–Cognitive subscale (ADAS-Cog)[55] for global cognition, the digit span-forward and backward test for attention and working memory, the Hong Kong List Learning Test for episodic memory, and the Color Trails Test for complex attention, executive function and task switching.

HRQoL. The Chinese Hong Kong version of the Short Form Health Survey (SF-12) will be used to measure HRQoL.[56] It consists of 12 items to form two summary scores to reflect people's physical and mental well-being, with higher scores indicating better HRQoL. Its psychometric properties are satisfactory with evidence of good reliability, content and construct validity.[56]

Data analysis

Statistical analysis of the outcome comparisons will be performed on the basis of the intention-to-treat principle. Variables with skewed data will be transformed appropriately before being subjected to analysis. Baseline characteristics between the two study arms will be compared by t-test, chi-square or Fisher's tests, as appropriate. Repeated measure ANOVA will be used to determine the effects of the intervention by comparing differential between group changes across the 3 time-points. All statistical analyses will be performed using IBM SPSS 25.0. All statistical tests will be two-sided, and a p-value of less than 0.05 will be considered statistically significant. All statistical analyses will be performed using SAS release 9.4 (SAS Institute, Cary, NC). All statistical tests involved will be two-sided with the level of significance set at 0.05.

Ethical Consideration:

This study followed the Declaration of Helsinki on medical protocol and ethics. Ethics approval will be obtained from the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. Patients are voluntary participants in the study. A written informed consent, which will include the research title, purpose, explanation of the research, and the procedures of the study, will be obtained from each eligible participant. Risks and benefits are also explained clearly to the participants.

Participants have the right to withdraw from the study at any time. They will be protected from discomfort and harm during the study. Further, anonymity and confidentiality of the participants will be strictly protected. Their decision of participating in the study will not affect the quality of present or future care they receive in the hospital.

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