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Improved sleep quality in older adults with insomnia reduces biomarkers of disease risk: Pilot results from a randomized controlled comparative efficacy trial

Judith E. Carroll[a,b,*], Teresa E. Seeman[c], Richard Olmstead[a,b], Gerson Melendez[a,b], Ryan Sadakane[a,b], Richard Bootzin[d], Perry Nicassio[a], Michael R. Irwin[a,b,*]

[a] University of California, Los Angeles—Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, Los Angeles, CA, USA
[b] University of California, Los Angeles, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, Los Angeles, CA, USA
[c] University of California, Los Angeles, Division of Geriatrics, David Geffen School of Medicine, Los Angeles, CA, USA
[d] University of Arizona, Department of Psychology, Tucson, AZ, USA

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KEYWORDS
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Disease risk;
Intervention

Summary
Importance: Sleep disturbances have been linked to increased morbidity and mortality, yet it is unknown whether improving sleep quality in older adult patients with insomnia alters biomarkers of diabetes and cardiovascular disease risk.
Objective: Determine the comparative efficacy of cognitive behavioral therapy (CBT), tai chi chih (TCC), and a sleep seminar control (SS) to reduce multisystem biomarkers of disease risk in older adults with insomnia.
Design: Randomized controlled comparative efficacy trial.
Setting: Los Angeles community.
Participants: A population-based sample of 109 older adults with chronic and primary insomnia.
Intervention: Random assignment to CBT, TCC, or SS for 2-h group sessions weekly over 4 months with a 16-month evaluation (1 year after follow-up).
Main outcome(s) and measure(s): Multisystem biological risk comprised of 8 biomarkers: high-density lipoprotein, low-density lipoprotein, triglycerides, hemoglobinA1c, glucose, insulin, C-reactive protein, and fibrinogen. Using clinical laboratory cutoffs defined as abnormal, a multisystem risk score was computed representing a sum of the deviation around the cutoffs

* Corresponding authors at: Cousins Center for Psychoneuroimmunology, UCLA Semel Institute for Neuroscience and Human Behavior, 300 UCLA Medical Plaza, Suite 3153, Los Angeles, CA 90095-7076, USA. Tel.: +1 310 794 9678/+1 310 825 8281; fax: +1 310 794 9247.
E-mail addresses: jcarroll@mednet.ucla.edu (J.E. Carroll), mirwin1@ucla.edu (M.R. Irwin).

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across the 8 biomarkers. In addition, high risk grouping was classified if subjects exhibited 4 or more biomarkers in the abnormal laboratory range.
Results: An interaction of time-by-treatment-by-high risk group was found ($F(4, 197.2) = 3.14$, $p = .02$) in which both TCC ($p = .04$) and CBT ($p = .001$) showed significantly lower risk scores as compared to SS at 16-months. CBT reduced risk of being in the high risk group at 4-months (odds ratio [OR] = .21 [95% CI, .03—1.47], $p < .10$) and at 16-months (OR = .06 [95% CI, .005—.669]; $p < .01$). TCC reduced the risk at 16-months (OR = .10 [95% CI, .008—1.29]; $p < .05$) but not at 4 months. Of participants who were classified in the high risk category at baseline, improvements in sleep quality, as defined by a clinical severity threshold, reduced the likelihood of being in the high risk group at 16-months, OR = .08 (95% CI, .008—.78); $p = .01$.
Conclusions and relevance: Participants classified as having high multisystem biological risk at entry and assigned to CBT or TCC show improvements in risk scores after one year follow-up. Given that these clinical biomarkers are associated with cardiovascular, metabolic, and inflammatory disease risk, improving sleep quality has the potential to reduce the risk of chronic disease in older adults with insomnia.

1. Introduction

Insomnia symptoms are characterized as impairments in sleep quantity and/or quality that can result from difficulties in falling or staying asleep, frequent arousals, and/or obtaining restorative sleep (CDC, 2011; Colten and Altevogt, 2006; Motivala, 2011). Insufficient sleep and poor sleep quality have been linked to disease risk and mortality (CDC, 2011; Vgontzas et al., 2010; Suzuki et al., 2009; Kojima et al., 2000; Cappuccio et al., 2010; Rod et al., 2014). Not getting enough quality sleep causes repeated disruptions to multiple regulatory systems including metabolic, cardiovascular, and immune (McEwen, 2006; Redline and Foody, 2011; Chen et al., 2014). This is particularly salient in older adults, where the risk for disease and death is elevated, with as many as half of adults over 65 years old reporting insomnia symptoms (Ohayon, 2002). Sleep is a modifiable behavior with established behavioral treatments that improve sleep quality (Irwin et al., 2006; Irwin et al., 2008). Although disturbed sleep has been associated with increased risk for disease and death, it is not clear whether treating sleep problems would reduce laboratory markers of disease risk, particularly among those with elevated levels of such risk markers. Further research is needed to determine whether the treatment of sleep disturbances, such as insomnia, has the potential to aid in the prevention of disease.

There are a number of pathways through which sleep problems likely contribute to poorer health. Among them, inadequate sleep has been associated with adverse effects on levels of glucose, lipids, inflammation, and blood pressure (Motivala, 2011; McEwen, 2006; Chen et al., 2014; Redwine, 2000; Gottlieb et al., 2006; Spiegel et al., 2005; Palagini et al., 2013; Van Cauter et al., 2007; Ju and Choi, 2013; Mullington et al., 2009). Inadequate and fragmented sleep disrupts the normal diurnal rhythm across regulatory systems and interferes with the restorative nature of sleep (McEwen, 2006; Robles and Carroll, 2011). Although each system is important in understanding disease risk, recent work has found that higher multisystem biological risk (a combination of biomarkers representing cardiovascular, metabolic, immune, nervous, and endocrine systems) is a stronger predictor of morbidity and mortality outcomes as compared to the predictive role of each biologic system alone (Gruenewald et al., 2006, 2009; Karlamangla et al., 2006; Seeman et al., 1997, 2001, 2010). Hence, this work is grounded in the hypothesis that the pathway to disease is a dynamic interface between multiple biologic systems that influence the whole and may not be fully captured when measuring individual components. Importantly, multisystem biological risk has been linked to sleep, with shorter sleep duration and poor sleep quality associated with an elevated multisystem risk (Chen et al., 2014; Carroll et al., 2013).

An unanswered question is whether treating sleep disturbances such as insomnia in individuals with elevated markers of disease risk can then reduce such levels, with implications for disease. Cognitive behavioral therapy (CBT) is an effective treatment for insomnia in young and older adults (Irwin et al., 2006; Morin et al., 1999, 2006, 2009; Epstein et al., 2012; Sivertsen et al., 2006) Tai Chi Chih (TCC) has also been proposed as an alternative treatment, with evidence that it improves sleep quality in older adults (Irwin et al., 2007, 2008, 2014; Nguyen and Kruse, 2012; Irwin and Olmstead, 2012). With the exception of our initial findings showing decreases in C-reactive protein following the successful treatment of insomnia (Irwin et al., 2014), we know of no published trials examining the efficacy of an RCT for insomnia in older adults on biomarkers of diabetes and cardiovascular disease risk. An observed reduction in risk via changes in clinical laboratory biomarkers that traditionally signal risk (e.g., LDL cholesterol, hemoglobin A1c, CRP) following the successful improvement of sleep quality would suggest that the treatment of sleep problems among individuals showing initially elevated risk might be included as part of a disease prevention strategy. Following our initial analyses showing that CBT and TCC are efficacious at improving sleep quality in older adults (Irwin et al., 2014), we report on the efficacy of this RCT to reduce multisystem biological risk among individuals classified as higher risk at the beginning of the trial based on several key clinical laboratory biomarkers indicative of disease risk.