UNIVERSITY OF CALIFORNIA SAN DIEGO

SAN DIEGO STATE UNIVERSITY

Effects of Motivationally Enhanced Compensatory Cognitive Training on modifiable risk factors for Mild Cognitive Impairment

A dissertation submitted in partial satisfaction of the requirements for the degree of Doctor of Philosophy

in

Clinical Psychology

by

Zanjbeel Mahmood

Committee in charge:

University of California San Diego

Professor Elizabeth W. Twamley, Chair
Professor Gregory J. Norman
Professor Victoria B. Risbrough

San Diego State University

Professor Paul E. Gilbert
Professor Scott C. Roesch

2022

The Dissertation of Zanjbeel Mahmood is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

_____

_____

_____

_____

_____

Chair

University of California San Diego

San Diego State University

2022

DEDICATION

Always loving you, Mama.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

This research was supported in part by grants to the author from the American Psychological Association (APA), APA Society for Clinical Neuropsychology (Division 40) Education Advisory Committee, American Fellowship from AAUW, VA San Diego Healthcare System Center of Excellence for Stress and Mental Health, Rosenbaum Neuropsychology Dissertation Research Grant, P.E.O International, and the National Register of Health Service Psychologists.

I would like to acknowledge Amber Keller, Dr. Chloe Green, and Hannah Lykins for their time and support for this research project. Without you this project would not have been possible.

Finally, I would like to acknowledge my outstanding graduate mentor, Dr. Elizabeth W. Twamley for her steadfast mentorship and sponsorship. Thank you for encouraging and supporting me through the growing pains of graduate school and championing my success.

VITA

EDUCATION

2022 Doctor of Philosophy, San Diego State University/University of California San Diego Joint Doctoral Program in Clinical Psychology
2019 Master of Science, San Diego State University
2015 Bachelor of Arts, University of California Los Angeles
2013 Associate of Arts, Cerritos College

FIELDS OF STUDY

Major Field: Clinical Psychology
Area of Study: Neuropsychology
Emphasis: Quantitative Methods

PUBLICATIONS

* indicates co-first authors

Peer-reviewed Journal Publications

Mahmood, Z.*, Parrish, E.*, Keller, A. V., Lykins, H., Pickell, D., Granholm, E., & Twamley, E. W. (in press). Modifiable predictors of self-reported and performance-based functioning in individuals with schizophrenia-spectrum disorders and high levels of negative symptoms. *Journal of Psychiatric Research.*

Granholm, E.*, Twamley, E. W.*, **Mahmood, Z.**, Keller, A. V., Lykins, H. C., Parrish, E. M., Thomas, M. L., Perivoliotis, D., & Holden, J. L. (2022). Integrated Cognitive-Behavioral Social Skills Training and Compensatory Cognitive Training for negative symptoms of psychosis: Effects in a pilot randomized controlled trial. *Schizophrenia Bulletin, 48*(2), 359-370.

Clark, J. M. R., **Mahmood, Z.**, Roost, M. S., Williams, R. M., O'Neil, M., Storzbach, D., & Twamley, E. W. (2022). Neuropsychological performance and functional capacity following mild traumatic brain injury in Veterans. *Journal of Head Trauma Rehabilitation.*

Van Patten, R., Nguyen, T. T., **Mahmood, Z.**, Lee, E. E., Daly, R. E., Palmer, B. W., Wu T. S., Tu, X., Jeste, D. V., & Twamley, E. W. (2022). Physical and mental health characteristics of 2,962 adults with subjective cognitive complaints. *International Journal of Aging and Human Development, 94*(4), 459-477.

Van Patten, R., **Mahmood, Z.**, Pickell, D., Maye, J., Roesch, S., Twamley, E. W., Filoteo, J. V., & Schiehser, D. M. (2022). REM sleep behavior disorder in Parkinson's disease: Change in cognitive, psychiatric, and functional outcomes from baseline to 16-47-month follow-up. *Archives of Clinical Neuropsychology, 37*, 1-11.

Van Patten, R., **Mahmood, Z.**, Nguyen, T. T., Maye, J., Kim, H., Jeste, D. V., & Twamley, E. W. (2022). Rates of cognitive and functional impairments in older

adults residing in a continuing care senior housing community. *Journal of the International Neuropsychological Society, 28*, 62-73.

Mahmood, Z.*, Vella, L.*, Maye, J. E., Keller, A. V., Van Patten, R., Clark, J. M. R., Twamley, E. W. (2021). Rates of cognitive and functional impairments in sheltered adults experiencing homelessness. *Psychiatric Services,72*, 333-337*.*

Mahmood, Z.*, Van Patten, R.*, Keller, A. V., Perivoliotis, D., Granholm, E., & Twamley, E. W. (2020). Reducing negative symptoms in psychotic disorders: Feasibility and acceptability of a combined Cognitive Behavioral Social Skills Training and Compensatory Cognitive Training intervention in real-world environments. *Psychiatry Research, 295,* 113620.

Mahmood, Z., Clark, J. M. R., Jak, A. J., Huckans, M., O'Neil, M. E., Roost, M. S., Williams, R. M., Pagulayan, K. F., Turner, A. P., Storzbach, D., & Twamley, E. W. (2020). Predictors of Intervention Adherence in Compensatory Cognitive Training for Veterans with a History of Mild Traumatic Brain Injury. *Journal of Head Trauma Rehabilitation, 36*, 20-24.

Van Patten, R.*, Vella, L.*, **Mahmood, Z.**, Clark, J. M. R., Maye, J. E., & Twamley, E. W. (2020). Accuracy of case managers in estimating intelligence quotients and functional status of people experiencing homelessness. *American Journal of Orthopsychiatry, 90*(5), 586-589.

Mahmood, Z., Van Patten, R., Nakhla, M. Z., Twamley, E. W., Filoteo, J. V., & Schiehser, D. M. (2020). REM Sleep Behavior Disorder in Parkinson's Disease: Effects on Cognitive, Psychiatric, and Functional outcomes. *Journal of the International Neuropsychological Society, 26*(9), 894-905.

Mahmood, Z., Kelsven, S., Cadenhead, K. S., Wyckoff, J., Reyes-Madrigal, F., de la Fuente-Sandoval, C., Twamley, E. W. (2020). Compensatory Cognitive Training for Latino Youth at Clinical High Risk for Psychosis: Study protocol for a randomized controlled trial. *Frontiers in Psychiatry, 10*, 951.

Mahmood, Z., Keller, A. V., Burton, C. Z., Vella, L., Matt, G. E., McGurk, S. R., & Twamley, E. W. (2019). Modifiable predictors of supported employment outcomes in people with severe mental illness. *Psychiatric Services, 70*(9), 782-792.

Mahmood, Z., Clark, J. M. R., Twamley, E. W. (2018). Compensatory Cognitive Training for Psychosis: Effects on negative symptom subdomains. *Schizophrenia Research, 204*, 397–400.

Burggren, A. C., Siddarth, P., **Mahmood, Z.**, London, E., Harrison, T. M., Merrill, D. M., Small, G. W., & Bookheimer, S. Y. (2018). Subregional hippocampal thickness abnormalities in older adults with a history of heavy cannabis use. *Cannabis and Cannabinoid Research, 3*(1), 242–251.

Siddarth, P., Burggren, A. C., Merrill, D. A., Ercoli, L. M., **Mahmood, Z.**, Barrio, J. R., & Small, G. W. (2018). Longer TOMM40 Poly-T Variants Associated with Higher FDDNP-PET Medial Temporal Tau and Amyloid Binding. *PloS One, 13*(12), e0208358.

Mahmood, Z., Hammond, A. M., Nunez, R. A., Irwin, M. R., & Thames, A. D. (2018). Effects of sleep health on cognitive function in HIV+ and HIV- adults. *Journal of the International Neuropsychological Society, 24*(10), 1038–1046.

Thames, A. D., Hammond, A., Nunez, R. A., **Mahmood, Z.**, Jones, F., Carter, S. L., Bilder, R. M., Fisher, S., Bivens-Davis, T., & Jones, L. (2018). Sexual Health Behavior and Mental Health Among Older African American Women: The Sistahs, Sexuality, and Mental Health Wellbeing Project. *Journal of Women's Health, 27*(9), 1177-1185.

Mahmood, Z., Burton C. Z., Vella L., Twamley, E. W. (2018). Neuropsychological predictors of performance-based measures of functional capacity and social skills in individuals with severe mental illness. *Journal of Psychiatric Research, 102*, 201–206.

Thames, A. D., Kuhn, T., **Mahmood, Z.**, Williamson, T. J., Singer, E. J., Bilder, R. M., & Arentoft, A. (2017). Effects of social adversity and HIV on subcortical shape and neurocognitive function. *Brain Imaging and Behavior, 12*(1), 96–108.

Burggren, A. C., **Mahmood, Z.**, Harrison, T. M., Siddarth, P., Miller, K., Small, G., & Bookheimer, S. Y. (2017). Hippocampal thinning linked to longer TOMM40 poly-T variant lengths in the absence of the APOEe4 variant. *Alzheimer's & Dementia, 13*(7), 739–748.

Jones, J. D., Kuhn, T., **Mahmood, Z.**, Singer, E. J., Hinkin, C. H., Thames, A. D. (2017). Longitudinal Intra-Individual Variability in Neuropsychological Performance Relates to White Matter Changes in HIV. *Neuropsychology, 32*(2), 206–212.

Harrison, T. M., **Mahmood, Z.**, Lau, E. P., Karacozoff, A., Burggren, A. C., Small, G. W., & Bookheimer, S. Y. (2016) An Alzheimer's Disease Genetic Risk Score Predicts Longitudinal Thinning of Hippocampal Complex Subregions in Healthy Older Adults. *eNeuro, 3*(3), ENEURO-0098.

Thames, A. D., Kuhn, T., Williamson, T. J., Jones, J., **Mahmood, Z.**, & Hammond, A. (2016). Marijuana effects on changes in brain structure and cognitive function among HIV+ and HIV- adults. *Drug and Alcohol Dependence, 170,* 120-127.

Williamson, T. J., **Mahmood, Z.**, Kuhn, T., & Thames, A. D. (2016). Differential relationships between social adversity and depressive symptoms by HIV-status and racial/ethnic identity. *Health Psychology, 36*(2), 133-142.

Thames A. D., **Mahmood, Z.**, Burggren A.C., Karimian, A., & Kuhn, T. (2015) Combined effects of HIV and marijuana use on neurocognitive functioning. *AIDS Care*, *28*(5), 628-632.

Manuscripts – under review

Maye, J. E., Van Patten, R., Lykins, H. C., Vella, L., **Mahmood, Z.**, Clark, J. M. R., & Twamley, E. W. (under review). Memory, fluid reasoning, and functional capacity in adults experiencing homelessness. *The Clinical Neuropsychologist.*

Manuscripts – in preparation

Mahmood, Z., Pickell, D., Keller, A. V., Muller-Cohn, C., Lykins, H. C., Contreras, I., & Twamley, E. W. Acceptability and feasibility of wrist-worn consumer wearable devices in older adults: A systematic review and meta-analysis.

Kumar, R. G., **Mahmood Z.**, Sol K., Davis-Plourde K., Choi S, Joshi P., White P. G., Jones R. N., Leurgans S. E., Mez J., Dams-O'Connor K., Crane P. K. Memory change among racially diverse older adults with and without lifetime history of traumatic brain injury with loss of consciousness.

Mahmood, Z., Ramsey, M., Kidambi, N., Hernandez, A., Palmer, H., Ancoli-Israel, S., Malhotra, A., Smagula, S., Lee, E. Circadian rest-activity rhythm disruption in schizophrenia.

ABSTRACT OF THE DISSERTATION

Effects of Motivationally Enhanced Compensatory Cognitive Training on modifiable risk factors for Mild Cognitive Impairment

by

Zanjbeel Mahmood

Doctor of Philosophy in Clinical Psychology

University of California San Diego, 2022
San Diego State University, 2022

Professor Elizabeth W. Twamley, Chair

Individuals diagnosed with Mild Cognitive Impairment (MCI) are at a higher risk for conversion to dementia and, therefore, may be particularly motivated/well-suited to participate in interventions to slow cognitive decline. Cognitive and lifestyle interventions targeting modifiable risk factors (e.g., physical activity [PA] and sleep) can slow the rate of cognitive decline. Psychometrically validated subjective indices of PA and sleep offer

a practical and economical method of assessing these cognitively salient lifestyle factors in the context of longitudinal studies of older adults with MCI. Moreover, the burgeoning availability of inexpensive, accurate wearable devices to measure lifestyle behaviors makes valid, unobtrusive objective measurement of these outcomes possible. Thus, this dissertation study examined the efficacy of an 8-week Motivationally Enhanced Compensatory Cognitive Training (ME-CCT) intervention, compared to Goal-focused Supportive Contact (SC), in improving subjectively and objectively measured lifestyle factors in older Veterans with MCI.

Self-reported sleep disturbance and PA levels were examined at baseline, mid-treatment, and post-treatment in 74 Veterans with MCI enrolled as part of a larger randomized controlled trial. Sleep and PA were objectively measured via the Fitbit Charge 2 in a subset of the sample (n=23). Mixed-effects models examined whether (1) ME-CCT, compared to SC, was associated with greater improvements in self-rated PA levels and sleep disturbance; and (2) baseline levels of self-rated PA and sleep disturbance moderated treatment effects on these outcomes. Exploratory analyses examined baseline-level correlates of Fitbit-measured PA and sleep, and the efficacy of ME-CCT in improving objective PA/sleep.

There was no differential treatment-related improvement in either subjective or objective measures of PA or sleep, with no treatment-moderating effect of baseline PA/sleep (*ps*>.05). At baseline, greater self-reported engagement in PA (r_s=0.57, *p*=.005) and less executive dysfunction (*r*=-0.43, *p*=.043) were associated with greater Fitbit step counts. Moreover, higher pain intensity (*r*=-0.49, *p*=.048) was associated with shorter Fitbit sleep duration.

ME-CCT did not differentially improve sleep or PA levels, nor did baseline levels of sleep/PA influence treatment outcomes. The influence of pain intensity and executive deficits, such as planning and organizing, in moderating trajectories in cognitive and health behavior engagement should be considered in current rehabilitation efforts in aging.

Effects of Motivationally Enhanced Compensatory Cognitive Training on improving modifiable risk factors for Mild Cognitive Impairment

Aging in the United States

Age-associated cognitive problems such as Mild Cognitive Impairment (MCI), Alzheimer's disease (AD), and dementia are rising at alarming rates given the rapidly increasing older adult population (> 65 years old) in the United States. AD, the most common form of dementia, affects an estimated 5.7 million Americans today and is considered the costliest disease in the country at $277 billion per year in direct healthcare costs (Alzheimer's Association, 2018). These rapidly increasing prevalence rates are projected to nearly triple by 2050, with costs expected to rise to over $1 trillion. This mounting economic burden is further amplified when considering the costs that extend to family caregivers' increased risk for emotional distress and negative mental and physical health outcomes. The extraordinary human suffering and unsustainable healthcare costs associated with dementia make it one of the most urgent public health concerns of our time.

Mild Cognitive Impairment

MCI is considered an intermediate stage between normal aging and dementia, and is highly prevalent—an estimated 10-20% of older adults aged sixty and above meet diagnostic criteria for MCI, with annual conversion rates to dementia of about 5-15% (Mitchell & Shiri-Feshki, 2009). Moreover, nearly 50% of individuals evaluated for concerning MCI symptoms develop dementia within 3-4 years (Petersen et al., 1999). The etiology of MCI and dementia are viewed as multi-factorial (Huckans et al., 2013) and a range of risk and protective factors contribute toward increased or decreased risk,

respectively. In some individuals, the cumulative and interactive impact of these factors on the brain results in the behavioral manifestation known as MCI, which is characterized by three types of symptoms: a) mild cognitive compromise (measured by objective neuropsychological tests), b) mild functional compromise (evaluated by measures of subjective cognitive complaints, everyday functioning, and functional capacity), and c) commonly associated neuropsychiatric symptoms, such as sleep difficulties, fatigue, and depression (measured by neuropsychiatric symptom questionnaires). Consequently, individuals with MCI represent a heterogeneous population and may present with a wide variety of cognitive, functional, and neuropsychiatric problems (Ellison et al., 2008; Monastero et al., 2009). Efforts to improve accuracy of diagnosis and prediction of conversion to dementia have resulted in the characterization of MCI into four subtypes based on the type of cognitive impairment displayed: amnestic vs. non-amnestic, and single domain impairment vs. multi-domain impairment (Jak et al., 2009; Petersen, 2004). Impairment can be seen in virtually all cognitive domains including memory, language, attention, visuospatial functioning, and executive functions (Arnáiz & Almkvist, 2003). These cognitive impairments are more modest in severity in MCI compared to the substantial cognitive deficits witnessed in frank dementia. Similarly, the functional compromise experienced in MCI is milder and does not preclude independent functioning; however, there may a need for greater effort, compensatory strategies, or accommodations that maintain capacity for independence in everyday activities.

MCI in Veterans

Veterans are at increased risk of cognitive decline, and older Veterans diagnosed

with posttraumatic stress disorder (PTSD) are twice as likely to have a diagnosis of dementia as individuals without PTSD (Yaffe et al., 2010). Hence, the Department of Veterans Affairs (VA) is faced with providing healthcare for an increasing number of elderly Veterans who are beginning to exhibit signs of cognitive decline. Considering the varied costs associated with dementia and the mounting challenge faced by the VA in providing healthcare for Veterans evidencing signs of cognitive decline, there is an urgent need for interventions that can significantly impact disease risk and progression.

Current State of AD Treatment

With no known cure for AD, current treatment guidelines have focused on lowering the rate of conversion to dementia through pharmacological, and various interventions, at the MCI stage. Current estimates suggest a 50% decrease in AD diagnoses if onset is delayed by 5 years through successful interventions (Alzheimer's Association, 2010); however, there remains a general lack of interventions that can considerably impact disease risk and progression (Cummings et al., 2014; Kane et al., 2017).

Pharmacological interventions. Administration of medications, such as acetylcholinesterase inhibitors, or other compounds such as Vitamin E, rofecoxib, and piracetam, does not have a considerable impact on disease risk or progression (Farlow, 2009; Kane et al., 2017; Jelic et al., 2007). Furthermore, the limited drugs authorized for use in dementia are plagued by many adverse side effects (ADI, 2018; Cummings et al., 2021; Pariente et al., 2016; Han et al., 2019). Given this lack of pharmacologic efficacy for MCI, non-pharmacologic interventions, namely cognitive interventions, have been receiving increased attention over the past decade (Li et al., 2011; Petersen et al.,

2009), especially considering the stable and robust relationship between intact cognitive functioning and independent everyday functioning.

Cognitive interventions. The phenomenon of age-related decline in neuroplasticity is well-documented; however, emerging evidence suggests that the aging brain is malleable, even in adults with MCI (Akhtar et al., 2006; Schreiber & Schneider, 2007), and cognitive function can be facilitated via cognitive training (Park & Bischof, 2013). Results from a large-scale cognitive training randomized controlled trial (Advanced Cognitive Training for Independent and Vital Elderly [ACTIVE]) provide the strongest evidence to date in support of neuronal plasticity in late-life; the study demonstrated intervention-related long-term improvements in cognitive function and maintenance of independence in instrumental activities of daily living (Ball et al., 2002; Rebok et al., 2014; Willis et al., 2006). Each intervention arm of the study, however, focused on a different cognitive domain (processing speed, memory, or reasoning) and improvements evidenced within trained domains did not generalize to non-targeted domains. Findings from other focused cognitive intervention trials in at-risk and MCI populations are more mixed but, overall, support the role of cognitive interventions as a potential tool to delay or slow age-related cognitive decline (Kane et al., 2017; NASEM, 2017).

Although the ACTIVE trial provides compelling evidence in support of single-domain-focused cognitive interventions, recent studies examining the efficacy of more comprehensive cognitive training protocols for MCI demonstrate a stronger association of multi-domain as opposed to single-domain cognitive interventions (see Huckans et al., 2013 for review). This emerging pattern underscores the need for rehabilitative

efforts to appreciate the heterogeneity of cognitive impairments noted in MCI. Compensatory cognitive training (CCT) is one such comprehensive cognitive training approach with potential to improve or delay progression of cognitive decline in patients with MCI. The CCT model is closely aligned with the top-down theoretical orientation wherein higher-order processes such as reasoning and problem solving are directly targeted, with the assumption that lower-order functions are trained concurrently (Best & Bowie, 2017; Minzenberg & Carter, 2012). This contrasts with bottom-up restorative training models, which propose that efficient higher-order neurocognitive function cannot be attained without first optimizing deficits in lower-order cognitive systems (e.g., basic attention; Minzenberg & Carter, 2012; Vinogradov et al., 2012). In considering the utility of these different cognitive intervention frameworks in MCI populations, it is important to consider that improvements in cognition are generally considered intermediary outcomes in cognitive training trials, with the primary focus to stave off functional disability associated with cognitive decline. The hierarchical relationship between CCT-targeted core cognitive processes is proposed to be proximal to patient psychosocial recovery outcomes than foundational cognitive processes trained within a bottom-up framework (Keshavan et al., 2014). Therefore, strategy-based training models may be better suited to target real-world functioning, especially given the greater emphasis on generalization of learned skills to community behaviors to promote training-related functional transfer (Best & Bowie, 2017; Medalia & Choi, 2009; Twamley et al., 2012). The efficacy of CCT, in particular, for age-related cognitive compromise may be partially due to its reliance on cognitive functions that are typically well-preserved in patients with MCI (e.g., visual processes and semantic memory; Ally, et al.,

2009; Bäckman & Nilsson, 1996; Belleville et al., 2006). Moreover, CCT-associated increased activation in brain networks subserving memory and improvements in structural and functional brain network organizations (Chapman et al., 2015; Hampstead et al., 2011; Dresler et al., 2017) suggest that CCT can positively affect age-related functional and structural brain changes.

Indeed, CCT-associated improvements have been found across various functionally relevant cognitive domains in patients with MCI, including prospective memory (Kinsella et al., 2008), list learning (Belleville et al., 2006; Rapp et al., 2002), face-name associations (Belleville et al., 2006; Hampstead et al., 2008), and object-location associations (Hampstead et al., 2012). Moreover, CCT-associated improvements have been found in subjective memory ability and knowledge and practice of memory strategies in everyday life (Kinsella et al., 2008; Rapp et al., 2002; Troyer et al., 2008), as well as quality of life, with higher levels of well-being reported by MCI patients after completing CCT (Belleville et al., 2006).

Multimodal interventions. It is theorized that multimodal interventions for MCI and AD may be more successful than single component interventions in producing benefits (Clare et al., 2015; Eggenberger et al., 2015), as simultaneously targeting multiple risk factors for age-related cognitive decline creates potential for a synergistic protective effect. A large-scale randomized controlled trial (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability [FINGER]) underscores the utility of a comprehensive, multimodal intervention, which combines physical activity, diet changes, and cognitive training. The results from this trial demonstrated improvement or maintenance of multidomain neuropsychological performance in adults at risk for MCI or

AD, including within cognitive domains highly relevant for everyday activities (executive functioning, processing speed, and complex memory tasks; Ngandu et al., 2015). Greater appreciation of the complex etiological profile of MCI and dementia necessitates the consideration of modifiable risk and protective factors associated with MCI and dementia.

Modifiable risk and protective factors.

MCI is an etiologically heterogeneous syndrome characterized by cognitive impairment in advance of dementia. Notably, the risk and protective factors associated with MCI are similar to those associated with conversion to dementia (Gomar et al., 2011; Li et al., 2011; Ravaglia et al., 2008; Schmand et al., 2012; Yu et al., 2012). The extant literature supports the role of lifestyle factors, such as sleep (Ju et al., 2014; Westerberg et al., 2012; Yaffe et al., 2014) and physical activity (Hamer & Chida, 2008; Buchman et al., 2012; Sofi et al., 2011; Baumgart et al., 2015), in the prevention of cognitive impairment. These modifiable protective factors are of particular interest to clinicians working with individuals with MCI because they can serve as the focus of preventive interventions and rehabilitation efforts.

Sleep. Sleep disruption is a hallmark feature of advancing age, characterized by disturbances in sleep architecture (e.g., declines in total sleep time and quantity and quality of non-REM slow wave sleep) and circadian rhythm dysfunction (e.g., fragmented nocturnal sleep, excessive daytime sleepiness), as well as subjective sleep problems (e.g., poorer quality, shorter duration; King et al., 1997, 2008). Both subjectively and objectively measured sleep disturbances are linked to greater cognitive impairment (Jelicic, et al., 2002; Musiek et al., 2015; Yaffe et al., 2014). Moreover,

primary sleep disorders, such as insomnia and sleep apnea, become more prevalent with older age (Vitiello, 2009), further compounding the risk for cognitive impairment and development of dementia. Such sleep impairments are highly prominent and significantly accelerated in MCI and AD (Hita-Yañez et al., 2012, Hita-Yañez et al., 2013; Prinz et al., 1982; Westerberg et al., 2012), suggesting a causal and bidirectional relationship between sleep disturbance and AD pathophysiology.

Supporting this reciprocal relationship is emerging evidence from animal models indicating that greater cortical amyloid-beta (Aβ) burden is causally linked to greater sleep disruptions (Kang et al., 2009; Roh et al., 2012), while manipulating sleep and wake time directly escalates Aβ production and corresponding cortical deposition (Kang et al., 2009). Human studies reinforce this reciprocal model by demonstrating that: (1) subjective and objective measures of sleep quality significantly predict the degree of existing cortical Aβ burden in healthy older adults without MCI (Mander et al., 2015; Spira et al., 2013); and (2) better sleep quality in older adults confers a decreased risk of MCI and AD onset, and longer maintenance of cognitive functioning (Lim, Kowgier, Yu, et al., 2013; Lim, Kowgier, Schneider, et al., 2013). As such, sleep disruption is not only a robust symptom of underlying neurodegenerative processes, but also is an indicator and arbiter of cognitive impairments associated with normal and pathological aging (Mander et al., 2016). Overall, the extant literature supports the restorative function of sleep, positioning it as a promising treatment target to delay onset of MCI and AD (Landry & Liu-Ambrose, 2014).

Sleep's status as a modifiable protective factor against age-associated cognitive decline is underscored by the multifactorial mechanistic links between sleep and

cognitive decline associated with AD pathophysiology, such as impairments in hippocampus-dependent memory (Mander et al., 2015). Pharmacological interventions to treat sleep disturbances in older adults have been plagued by undesirable side effects that may increase risk for further cognitive compromise (Deschenes & McCurry, 2009); accordingly, behavioral/multicomponent therapies (e.g., physical activity, leisure activities, cognitive behavioral therapy) are recommended as first-line treatments to improve both subjective and objective quality of sleep and, consequently, cognitive functioning in the elderly (Porter et al., 2015).

Physical activity. As with sleep, an extensive body of research has demonstrated the protective role of physical activity against risk for and progression of cognitive decline (Buchman et al., 2012; Bherer et al., 2013; Erickson, Raji, et al., 2010; Gopinath et al., 2018). Current guidelines by the Physical Activity Guidelines Advisory Committee (2018) recommend less sedentary time ("Some physical activity is better than none") and that older adults engage in at least 150 minutes to 300 minutes of multicomponent physical activity a week, including aerobic and muscle-strengthening activities as well as balance training (USDHHS, 2018). Adherence to a physically active lifestyle, however, becomes increasingly difficult with age due to progressive decline in physical functions and abilities (Franco et al., 2015; Fougner et al., 2018; Achttien et al., 2019).

Reduced levels of both subjective and objective physical activity levels in older adults are directly linked to greater risk for cognitive decline (Erickson, Raji, et al., 2010; Larson et al., 2006; Richards et al., 2003; Sofi et al., 2011; Weuve et al., 2004). Emerging evidence suggests that physical activity levels decline earlier in individuals

with mild cognitive impairments (Sabia et al., 2017). Moreover, age-related cognitive decline may influence poorer physical activity trajectories, with lower levels of executive functioning and memory associated with accelerated decline in physical activity with aging (Cheval et al., 2020). Not only do physically active adults exhibit better cognitive aging (Jak, 2012), but exercise training interventions demonstrate efficacy in reversing hippocampal volume loss in late adulthood, with concurrent improvements in memory function (Erickson, Voss et al., 2010). Moreover, in a separate investigation, Erickson, Raji, and colleagues (2010) found greater physical activity levels (defined as the number of blocks walked in a week) predicted 9-year follow-up greater volume of frontal, occipital, entorhinal, and hippocampal brain regions, which in turn reduced the risk of cognitive impairment by two-fold. These exercise-generated structural brain changes have been linked to stimulation of neurogenesis and synaptic plasticity vis-à-vis increase in brain-derived neurotrophic factor (Beckinschtein et al., 2011; Gomez-Pinilla et al., 2008). Reductions in oxidative stress and decrease in neuroinflammation secondary to increased serotonin levels have also been purported to underlie the neuroprotective function of physical activity (Jak, 2012). Together, these findings highlight a bidirectional association between cognition and physical activity, not unlike the reciprocal relationship between sleep and cognition detailed above.

Older adults' knowledge of current physical activity guidelines is not associated with higher physical activity levels, nor better physical functioning (Cheung et al., 2019), suggesting that interventions should target physical activity limiting factors, such as lack of motivation (Dacey et al., 2008) and poor awareness of the role of exercise in disease prevention (Schutzer & Graves, 2004), as well as physical activity promoting factors,

such as provision of appropriate exercise recommendations (Chao et al., 2000) and improving self-efficacy (Schutzer & Graves, 2004).

Additional modifiable risk and protective factors. A robust evidence-base implicates several additional modifiable disease-related risk factors for MCI and incipient dementia, including, but not limited to, cardiovascular disease, high cholesterol, high blood pressure, and diabetes mellitus (see Huckans et al., 2013 for review). Research has also uncovered the protective role of positive lifestyle factors (e.g., a Mediterranean diet, engagement in cognitively stimulating activities) against age-associated cognitive decline (Jak, 2012; Verghese et al. 2006; Wilson et al. 2002, 2007, 2012). Importantly, physical inactivity and sleep disturbance/disorders are strongly and intricately associated with various chronic diseases that contribute to late-life cognitive compromise (Booth et al., 2012; Foley et al., 2004). The positive cognitive influence of improved sleep and physical activity, therefore, may be partially mediated via impact on chronic medical risk factors. Furthermore, it is likely that the pro-cognitive effects of sleep and physical activity are also arbitrated by the aforementioned upregulation of growth factors and reduced neuroinflammation (Cotman et al., 2007). Therefore, interventions targeting sleep and physical inactivity may also improve cognitive functioning via improvements in cognitive risk-conferring disease severity. Collectively, the literature points to a highly complex, dynamic interplay among the risk and protective factors for cognitive decline, underscoring the need for multi-component interventions that appreciate the etiological heterogeneity of MCI (Huckans et al., 2013).

Utility of subjective measures of physical activity and sleep.

To adequately test new multi-modal, comprehensive treatments for slowing

cognitive decline, better outcome measures are needed to demonstrate improvements in modifiable protective factors for MCI. The laborious nature, expense, and obtrusiveness of current gold-standard laboratory methods/techniques (e.g., physiological monitoring, polysomnography), complicate and impede the evaluation of lifestyle behaviors, particularly in the context of larger and/or longitudinal investigations. Psychometrically sound self-report measures of physical activity (e.g., CHAMPS physical activity questionnaire for older adults; Stewart et al., 2001) and sleep (e.g., Insomnia Severity Index; Bastien et al., 2001; Morin, 1993) provide more practical alternatives. Moreover, their utility as outcome measures for interventions is underscored by their demonstrated sensitivity to change following intervention (Bastien et al., 2001; Morin et al., 1999; Stewart et al., 2001) and convergence with other subjective and objective behavioral measures (Bastien et al., 2001; Moore et al., 2008; Stewart et al., 2001). Nevertheless, the best practice recommendation is to include both subjective and objective measures of behavioral functioning in older adults, given the lack of convergence of subjective behavioral indices with objective measures and/or relevant health outcomes noted in some studies (Parker et al., 2008; Landry, Best, & Liu-Ambrose, 2015). Moreover, there is evidence to suggest that perceived and objective behavioral functioning may represent related, but unique constructs, with differential associations with objective cognitive functioning (Bastien et al., 2003).

Leveraging consumer technology.

The ever-expanding commercial market for technologies to monitor and improve physical health and performance creates new opportunities for scientific and clinical explorations of health behaviors such as sleep and physical activity. Consumer

wearable devices, such as the Fitbit, provide a low-cost, comfortable, and convenient way to estimate sleep quality and physical activity (de Zambotti, et al., 2018; Evenson et al., 2015). This objective measurement of physical activity and sleep greatly enhances our ability to measure everyday behaviors in real-time, thereby reducing the impact of retrospective bias and cognitive deficits commonly noted in methods relying on subjective recall.

Mounting evidence supports the validity of Fitbit wearable devices for accurate assessment of physical activity levels (e.g., step counts; Evenson et al, 2015; Imboden et al., 2018; Paul et al., 2015). Technical limitations of consumer wearables for sleep assessment, however, are worthy of consideration. A review of currently available validation studies suggests that consumer sleep tracking devices have a high degree of sensitivity and can identify sleep periods with some accuracy, but demonstrate inadequate specificity (de Zambotti et al., 2018; Kolla et al., 2016; Mantua et al., 2016; Peake et al., 2018). Of the varied sleep measures assessed via consumer wearable devices (e.g., wake after sleep onset, sleep stages), total sleep time has garnered support as a valuable and adequate measure of interest (Mantua et al., 2016). The most recent validation study of the Fitbit Charge 2—the proposed model for the current study—found it to be highly sensitive in sleep detection (0.96), and to overestimate polysomnography-determined total sleep time by only 9 minutes. Despite some limitations, the exponential uptake of consumer-based technologies projected over the next several decades underscores the value of examining the utility of these devices within clinical research and care. The inclusion of Fitbits for objective physical activity and sleep monitoring in aging and rehabilitation research addresses several gaps within

the literature, including longitudinal tracking of behavior and the generalizability of findings to a well-characterized older adult population with MCI. Moreover, leveraging consumer wearable technology to assess clinically relevant endpoints can enhance our ability to demonstrate the efficacy of novel therapeutic and/or preventative treatments for age-associated cognitive decline.

Motivationally Enhanced CCT.

Because of the heterogeneity of cognitive impairments noted in MCI populations, comprehensive, multi-modal cognitive training techniques, as opposed to focused, single domain cognitive interventions, are needed to fully address their rehabilitation needs. In addition to improving cognitive functioning, rehabilitation interventions should also include healthy lifestyle strategies and techniques to reduce emotional distress, as these can both protect against the development of dementia (Rosenberg et al., 2006). Motivationally Enhanced CCT (ME-CCT) is a novel psychosocial intervention with potential to modify disease progression given its adherence to a multicomponent approach to MCI rehabilitation (Huckans et al., 2013). ME-CCT is a manualized, low-cost, low-tech, highly feasible group-based behavioral intervention (8 weeks, 2 hours per week, 16 hours total) designed to improve cognitive and everyday functioning in patients with MCI. The intervention is comprehensive (i.e., entails cognitive training, psychotherapeutic, and lifestyle techniques) and multi-modal: it incorporates CCT techniques designed to help patients manage problems with memory, attention, and executive functions (i.e., organization, planning, decision-making, and problem-solving); mindfulness-based stress reduction practice which has been shown to improve cognitive and neuropsychiatric function in various populations (Davis & Hayes, 2011);

psychoeducation on recommended guidelines for physical activity and sleep for optimal brain health, as well as brief motivational interviewing techniques to increase engagement in healthy lifestyle behaviors associated with reduced risk for cognitive decline, MCI, and dementia (Huckans et al., 2013; Arnáiz & Almkvist, 2003).

Evaluating the efficacy of ME-CCT on modifiable lifestyle factors for MCI, and consequent impact on cognitive outcomes, has significant clinical, economic, and public health implications for the dementia epidemic. As such, the current study examined self-reported sleep disturbance and physical activity levels in 74 Veterans with MCI, as well as objectively measured sleep and physical activity via the Fitbit Charge 2 in a subset of the sample (n=23), enrolled as part of a larger randomized controlled trial evaluating the efficacy of group-based ME-CCT compared to Goal-focused Supportive Contact (SC) on neurocognitive and functional performance (Cognitive Rehabilitation for Older Veterans with Mild Cognitive Impairment [I01 CX001592; 01/01/2018-12/31/2022]). SC serves as a robust control, group therapy intervention that provides the same frequency and amount of therapist and other group member contact as ME-CCT, but does not provide training in cognitive strategies, lifestyle strategies, or motivational enhancement. It has a primary focus on setting and achieving short or long-term goals. Focusing on goals is intended to provide “face validity” to potential participants and to enhance treatment attendance and reduce drop-out in this population. Sessions will typically include components of empathy and non-directive reinforcement of health, coping, and symptom management behaviors that grow out of group discussions, with only minimal therapist guidance.

Summary and Aims

MCI is an etiologically heterogeneous syndrome characterized by cognitive impairment in advance of dementia. The impact of these cognitive deficits on daily functioning, however, does not preclude independence; therefore, patients with MCI may be particularly motivated and well-suited to participate in interventions to slow cognitive decline. Cognitive and lifestyle interventions targeting modifiable disease protective factors, such as increasing physical activity and improving sleep quality, can slow the rate of cognitive decline, but measuring physical activity and sleep has been impractical until now. Availability of well-validated and reliable subjective indices of physical activity and sleep in older adult populations offers a practical and cost-efficient method of evaluating these cognitively relevant lifestyle factors in larger, longitudinal studies. Moreover, the burgeoning availability of inexpensive, accurate wearable devices to objectively measure physical activity and sleep makes valid, unobtrusive measurement of these outcomes possible. The objective of the current study was to evaluate the efficacy of ME-CCT, compared to SC, in improving self-reported physical activity and sleep. The current study also examined the moderating role of baseline levels of self-reported physical activity and sleep on treatment effects on these outcomes. Finally, in a subset of the sample (n=23), exploratory analyses examined (1) bivariate associations, at baseline, among Fitbit-measured physical activity and sleep and the objective/subjective cognitive, lifestyle and psychosocial functioning, and clinical measures, as well as the relevant strength of these factors as predictors of Fitbit-measured measured physical activity and sleep, and (2) the efficacy of ME-CCT in improving Fitbit-derived physical activity/sleep outcomes.

Specific Aim 1. Examine ME-CCT efficacy in improving self-reported physical activity levels and sleep.

Hypothesis 1a: Compared to the SC group, participants in ME-CCT will report engaging in more hours of physical activity per week across baseline and follow-up.

Hypothesis 1b: Compared to the SC group, participants in ME-CCT will show improved severity of sleep disturbance across baseline and follow-up.

Specific Aim 2a. Examine baseline physical activity levels as a moderator of treatment-related changes in physical activity.

Hypothesis 2a: The slope for the relation between visit and self-reported hours of physical activity per week will change based on both treatment group status and baseline number of hours of physical activity per week, such that, compared to the SC group, lower self-reported physical activity per week at baseline will be associated with increase in physical activity levels across time in the ME-CCT group.

Specific Aim 2b. Examine baseline self-reported sleep disturbance as a moderator of treatment-related changes in sleep.

Hypothesis 2b: The slope for the relation between visit and severity of sleep disturbance will change based on both treatment group status and baseline severity of sleep disturbance, such that, compared to the SC group, greater self-reported sleep disturbance at baseline will be associated with improvements in sleep disturbance across time in the ME-CCT group.

Exploratory Aims. (a) Examine baseline level associations and predictors of Fitbit-

measured physical activity and sleep, specifically objective/subjective cognitive, lifestyle and psychosocial functioning, and psychiatric symptoms severity; (b) Examine the efficacy of ME-CCT in improving objective physical activity and sleep in models similar to those of aims 1 and 2.

Methods

Participants and Procedures

A total of 89 older participants were recruited in the parent study (clinical trial registration number NCT03225482) through the VA San Diego Healthcare System (VASDHS) and VA Portland Healthcare System (VAPORHCS); however, eleven participants did not meet eligibility criteria, three participants declined to participate in group sessions, and one participant was withdrawn due to an invalid signature on the study HIPAA form, leading to a final sample size of 74 (see Figure 1 for CONSORT Flow Diagram). Inclusion criteria include: 1) Veterans ≥55 years old who are able to provide informed consent; 2) Living independently; 3) Willingness to participate in audio-recorded sessions; 4) Meet criteria for MCI based on previously published criteria (Petersen, 2004, 2011); 5) Concern about a decline in cognitive functioning expressed by a physician, informant, participant or nurse; 6) Cognitive impairment in one or more of the following domains: executive function, memory, attention, language or visuospatial abilities; 7) Normal or minimal impairment in functional activities; 8) Does not meet criteria for dementia. Participants will be excluded for: 1) Current substance use disorder with <30 days abstinence; 2) History of schizophrenia, schizoaffective disorder, or other primary psychotic disorder; 3) History of significant brain injury with loss of consciousness > 30 minutes; 4) Auditory or visual impairments that would prevent ability to participate in the cognitive rehabilitation group or benefit from compensatory strategies.

As part of the parent study, two neuropsychologists determined whether individuals met criteria for MCI using comprehensive criteria (impairment defined as

performance on two or more tests in one cognitive domain that falls ≥ 1 standard deviation (SD) below normative expectations; Jak et al., 2009). Discrepancies were resolved by a third neuropsychologist who reviewed the data; participants were only included if consensus was reached. Eligible individuals were then classified into four MCI subtypes: (1) amnestic MCI-single domain characterized by isolated impairment in memory, (2) non-amnestic MCI-single domain involving impairment in a cognitive domain other than memory (e.g., language, executive function), (3) amnestic MCI-multiple domain involving impairment in memory and at least one other cognitive domain, and (4) non-amnestic MCI-multiple domain characterized by impairment in two or more non-memory cognitive domains.

Participants completed a comprehensive assessment battery at weeks 0, 4, and 8, consisting of self-report questionnaires and performance-based tests of neurocognition and functioning. Performance-based tests were not administered at week 4, however, to reduce practice effects. The neurocognitive battery, specifically, was designed in part to confirm accurate diagnosis of MCI using published criteria (Jak et al., 2009; Petersen, 2004) and, therefore, confirm eligibility criteria. A subset of the randomized sample from the VASDHS site (n=28) was also assigned Fitbit devices as part of their study participation.

Retention and reimbursement. Reminder phone calls were used to reduce the study attrition rate. Furthermore, the participants were compensated $50 after each of the first three assessments, and $75 after the fourth and final follow-up assessment, for a total compensation of $225. Additionally, VASDHS participants were given ownership of the Fitbit Charge 2 device at the end of the study as incentive to participate and

reduce attrition rate.

Subjective measures.

Physical activity. Self-reported physical activity levels were measured via the Community Healthy Activities Model Program for Seniors (CHAMPS) physical activity questionnaire (Stewart et al., 2001). Specifically, the questionnaire assessed the frequency and duration of participation in a comprehensive list of light, moderate, and vigorous activities during a typical week during the previous four weeks. Light intensity activities include walking leisurely, golfing with a cart, light housework, yoga, stretching/flexibility, and general conditioning exercises; moderate-to-vigorous intensity activities include walking briskly, jogging, dancing, golfing, walking, singles/doubles tennis, riding a bicycle/stationery cycle, swimming, water exercises, aerobic exercise, heavy housework, and gardening. The questionnaire takes approximately 15 minutes to compete; reporting of total weekly duration of participation in an activity is made easier via provision of several categories (<1 hour, 1–2.5 hours, 3–4.5 hours, 5–6.5 hours, 7–8.5 hours, and ≥9 hours). In addition to total weekly duration of physical activity, the measure also allows for four total scores to be calculated, including frequency and energy expenditure for activities with metabolic equivalent (MET) values ≥3.0 (i.e., moderate and vigorous activities) and frequency and energy expenditure for all activities (i.e., light, moderate, and vigorous activities); however, total weekly duration of physical activity, across all levels of activity, was examined as the primary outcome in the analyses. The CHAMPS questionnaire has demonstrated adequate reliability and validity in diverse older adult populations, and is sensitive to change in activity levels following behavioral interventions (Cyarto et al., 2006; Harada et al., 2000; Moore et al.,

2008; Stewart et al., 1997; Stewart et al., 2001).

Sleep. Disturbance in sleep was measured via the Insomnia Severity Index (ISI), a psychometrically validated retrospective assessment of severity of sleep disturbance in the last two weeks (Morin et al., 1999; Bastien et al., 2001). It is composed of seven items that evaluate the severity of problems with sleep-onset, sleep maintenance, and early morning awakening problems, as well as satisfaction with current sleep pattern, interference in daily functioning, perceptibility of impairment attributed to the sleep problem, and level of distress caused by the sleep problem. All items are rated on a five-point Likert scale; total scores range from 0 to 28, with higher scores indicating greater severity of sleep disturbance. Moreover, sleep duration was derived from response to a single item assessment of weekly average hours of sleep on a cognitive activity inventory.

Psychiatric & clinical symptom severity. Psychiatric symptom severity, considered as a covariate and moderator of outcomes in analytic models, was assessed as follows: depression symptom severity (Patient Health Questionnaire-9; Kroenke et al., 2001); anxiety symptom severity (General Anxiety Disorder-7 Scale; Spitzer et al., 2006); post-traumatic stress disorder (PTSD) symptomatology (PTSD Checklist DSM-5; Weathers et al., 2013); subjective everyday functioning and cognitive complaints (Quality of Life in Neurological Disorders [Neuro-QOL] Applied Cognition: 1) Executive Function scale, which examines perceived difficulties in planning, organizing, calculating, and working memory and learning, and 2) General Concerns scale, which examines perceived difficulties in everyday cognitive abilities such as memory, attention, and decision making; Cella et al., 2011); recent frequency of engagement in

activities requiring mental exercise, a protective factor known to reduce risk of MCI and dementia. (Cognitive Activity Inventory [CAI]; Wilson, Scherr, et al., 2007; Wilson, Barnes, & Bennett, 2003); pain intensity and interference (Patient Reported Outcomes Measurement Information System - Pain Intensity and Interference Short Forms; Cella et al., 2007). For all measures, higher scores represent greater endorsement of the measured construct.

Objective Measures.

Physical activity and sleep. The Fitbit Charge 2, a non-invasive, water-resistant, wrist-worn device, was used to measure participants' activity levels and sleep, specifically step counts and total sleep time. The Fitbit uses a three-dimensional accelerometer to sense movement. It measures steps taken, distance walked, calories burned, active/inactive minutes, stationary time, heart rate, hours and quality of sleep, as well as stages of sleep. The Fitbit's measurement of self-paced and prescribed intensity exercise has been validated against the Omron HJ-720IT accelerometer and direct observation. Furthermore, there is considerable support for the validity of Fitbit accelerometers in measuring physical activity (step counts) and high sensitivity of the Fitbit Charge 2 to detect sleep (de Zambotti et al., 2018; Evenson et al., 2015). Of the varied sleep measures assessed via Fitbit (e.g., wake after sleep onset, sleep stages), total sleep time has garnered support as a valuable and adequate measure of interest (Mantua et al., 2016), and the Fitbit is considered to overestimate polysomnography total sleep time by only 9 minutes (de Zambotti et al., 2018). Therefore, average total daily sleep time, along with average daily step count, were examined as the primary outcomes in the proposed exploratory analyses.

Upon enrollment, VASDHS participants were assigned to wear a unique Fitbit Charge 2 device on their non-dominant hand. A unique login ID and password was created for each participant to enable us to track their data on the Fitbit website; these data were uploaded during the weekly group sessions. When connected to a compatible device (i.e., study computer), data were automatically uploaded to the users' Fitbit accounts. The research team uploaded participants' data for adherence and assessment purposes each week. These data were then stored on a secure study server. The participants were allowed to keep the Fitbit device at the end of their participation in the study and guided through the procedure for establishing a new username and password, thereby terminating the research team's access to their account.

Fitbit data were collected continuously throughout the study. Fitbit data from baseline assessment (week 0) to first treatment session were aggregated to generate average baseline sleep and physical activity levels. At minimum three and up to 14 non-consecutive days of Fitbit-recorded step counts and total sleep time prior to the start of the intervention were averaged to index baseline levels of physical activity and sleep. Mid-treatment levels of physical activity and sleep were indexed as the average of at least three days of Fitbit-recorded step counts and total sleep time circumscribed to +/- 7 days of a participant's mid-treatment assessment visit. Post-treatment physical activity and sleep levels were indexed as the average of at least three and up to 14 non-consecutive days of Fitbit-recorded step counts and total sleep time within the 7 days leading up to the post-treatment or the 14 days thereafter.

Cognition. Premorbid intellectual functioning was estimated using the Wide

Range Achievement Test-4-Reading (WRAT-4; Wilkinson & Robertson, 2006). All participants completed a comprehensive neuropsychological assessment battery measuring cognition in the following domains targeted in ME-CCT: memory (Hopkins Verbal Learning Test-Revised [HVLT-R; Brandt & Benedict, 2001]; Brief Visuospatial Memory Test-Revised [BVMT-R; Benedict, 1997]); attention/working memory (Wechsler Adult Intelligence Scale, Fourth Edition [WAIS-IV] Digit Span [Wechsler, 2008]; WAIS-IV Coding [Wechsler, 2008]; Delis-Kaplan Executive Function System [D-KEFS] Trails, Number and Letter Sequencing [Delis et al., 2004]); and executive functioning (D-KEFS Trails, Number-Letter Switching [Delis et al., 2004]; D-KEFS Color-Word Interference Test, Inhibition and Inhibition-Switching [Delis et al., 2004]). Furthermore, language was assessed using the Boston Naming Test (Goodglas & Kaplan, 2000) and D-KEFS Verbal Fluency (Delis et al., 2004) for the purpose of diagnostic evaluation to determine study eligibility. Finally, the Neuropsychological Assessment Battery (NAB) Daily Living Memory, Judgment, and Driving Scenes subtests (Stern & White, 2003) were also administered to assess memory skills, problem-solving skills, and driving/attention skills relevant to everyday functioning. A global composite score was calculated by averaging adjusted T-scores across all individual tests in the battery.

Functional capacity. The UCSD Performance-Based Skills Assessment-Brief (UPSA-B; Mausbach et al., 2007) was used as an objective measure of functional capacity. The UPSA-B is a role-play-based test that measures ability to communicate efficiently and accurately and apply financial skills to simple (counting change) and more complex (paying a bill by check) situations. The Medication Management Ability

Assessment (MMAA; Patterson et al., 2002) was administered as a performance-based assessment of participants' capacity to carry out a prescribed medication regimen.

Hypothesis-specific Data Analysis Plan and Power Analyses

Power analysis

Using procedures described by Hedeker and colleagues (1999) for Random Regression Models (the RMASS program provided by Hedeker), the following assumptions were made to estimate the required sample size that would provide a minimum of 80% power across all hypotheses and their expected effect size: the mixed design of two groups (ME-CCT and SC) and time (3 levels, weeks 0, 4, and 8) where the slope is the dependent measure; alpha-level of .05, nature of the hypothesis (one-sided), dropout rate (up to 20%), autoregressive covariance structure (with correlation between sequential assessments set at .60) of the longitudinal data, medium effect size as a between-group difference increasing linearly from 0 at baseline to 0.5 SD units at the last time point. These methods estimated that with a final sample size of 72 participants (90, with a drop-out rate of 20%), the study will have minimum 80% power to yield a statistically significant result for a medium effect size.

Statistical analysis

Baseline differences between treatment groups were examined using parametric or non-parametric statistics for continuous variables, depending upon normality of the distribution, and chi-square tests for categorical variables.

Aim 1. Mixed-effects models were conducted in R (R Core Team, 2017) with lme4 (Bates, Maechler, Bolker, & Walker 2015) and lmerTest (Kuznetsova et al., 2017) packages to examine treatment efficacy by evaluating group differences in the

longitudinal trajectories of the self-reported duration of weekly physical activity, as measured via the CHAMPS, over the intervention period. Maximum likelihood estimation was used and, consistent with the intent to treat approach, data from all randomized participants were included in analyses. The random effect of intercept for individuals was included in all models. Time in weeks was included in the model as a continuous predictor, and treatment group (ME-CCT [1]; SC [0]) was included in the model as a categorical predictor. Participants in the SC group reported, on average, significantly more weekly physical activity at baseline than the ME-CCT group participants (Table 1), so the baseline CHAMPS score (grand-mean centered) was included as a covariate in the model used to test hypothesis 1a. Additionally, models included the fixed effects of group, time, and the group-by-time interaction. Effect sizes are reported as correlation coefficients estimated from *t* statistics and degrees of freedom for regression parameter estimates and interpreted as follows: small = 0.10; medium = 0.30; large = 0.50 (Cohen, 1992). A similar model was run for hypothesis 1b by substituting hours of physical activity per week with self-rated total sleep disturbance severity.

Aims 2a & 2b. Hypothesis 2a was tested using similar mixed-effects models as aim 1, with the inclusion of an additional fixed effect: a three-way interaction term between treatment group status, time, and baseline hours of weekly physical activity. The corresponding parameter estimate for this three-way interaction term was the primary outcome of focus. A similar model was run for hypothesis 2b by substituting hours of weekly physical activity with self-reported total sleep disturbance severity.

Analyses for Exploratory Aims. (a) Pearson/Spearman correlations examined the bivariate associations between the Fitbit-measured baseline average total sleep time and step counts and performance-based measures of neurocognition and functioning, and subjective measures of psychiatric symptom severity and functioning. Analyses were conducted using SPSS version 28.0. (b) Mixed-effects models, as described above for aims 1 and 2, were utilized to examine the efficacy of ME-CCT in improving Fitbit-measured physical activity levels (i.e., average step counts) and total sleep time across visits 1-3.

Results

A total of 74 participants were randomized (see Figure 1), but 16 participants did not attend any group sessions (n=4 [50% ME-CCT] lost to follow-up; n=12 [50% ME-CCT] due to COVID-19-related pause in research activities). Of those who attended at least one session (n=58), 54, or 93%, attended all treatment group sessions; two participants in the SC group attended 1 and 5 sessions, respectively, whereas two participants in the ME-CCT group attended 1 and 7 sessions, respectively. Of the 30 participants enrolled/randomized at the VASDHS site, 28 (93%) accepted the Fitbit; however, data from only 23 participants were available due to study dropout or COVID-19-related disruptions to study participation. All 23 participants had at least three days of Fitbit step count data at baseline to be included in analyses; 17/23 participants had at least three days of Fitbit sleep data and were included in analyses for this outcome.

Sample characteristics. Table 1 shows the baseline demographic, clinical, and outcome measure characteristics. Briefly, the total sample was predominantly White, high school educated, and male. The CBSST-CCT and SC groups did not differ significantly on any variables, except for total weekly duration of self-reported physical activity, as assessed by the CHAMPS; the SC group, on average, reported more weekly physical activity (*Mdn*=15.00) than did the ME-CCT group (*Mdn*=9.50), *U*=423.50, *p*=.006, *r* =-.32.

Aim 1. Examine ME-CCT efficacy in improving self-reported physical activity levels and sleep. Table 2 presents parameter estimates, p-values, and effect sizes for the effects of the group-by-time interaction for the mixed-effects models through the 8-week intervention period. For CHAMPS total scores, there was no

significant group-by-time interaction to indicate that the ME-CCT group showed significantly greater improvement in self-reported physical activity levels compared to the SC group (t[1, 137.83]=0.43, p=.669, r=0.04). Similarly, for ISI total scores, there was no significant group-by-time interaction to support ME-CCT-related differential improvement in self-reported sleep disturbance severity relative to the SC group (t[1, 115.55]=1.21, p=.228, r=0.11; see Figure 2).

Aims 2a. Examine baseline physical activity levels as a moderator of treatment-related changes in physical activity. Table 3 presents parameter estimates, p-values, and effect sizes for the effects of the three-way interaction terms (i.e., group-by-time-by-baseline CHAMPS total score and group-by-time-by-baseline ISI total score for the mixed-effects models through the 8-week intervention period. Hypothesis 2a was not supported; specifically, baseline CHAMPS total scores did not moderate treatment effects on this outcome over time (t[1, 135.88]=0.20, p=.840, r=0.02).

Aim 2b. Examine baseline self-reported sleep disturbance as a moderator of treatment-related changes in sleep. Similarly, hypothesis 2b was not supported; specifically, ISI total scores at baseline did not moderate treatments effects on this outcome over time (t[1, 141.75]=0.39, p=.694, r=0.03).

Exploratory Aims 1a. Examine baseline level associations and predictors of Fitbit-measured physical activity and sleep, specifically objective/subjective cognitive, lifestyle and psychosocial functioning, and psychiatric symptoms severity. At baseline, for Fitbit-measured physical activity (i.e., average daily step counts), bivariate correlations showed that higher CHAMPS total scores were

associated with greater Fitbit step counts (r_S=0.57, p=.005). Moreover, higher scores on the Neuro-QOL Applied Cognition Executive Function scale, which is indicative of greater perceived difficulty with executive functions (e.g., planning, problem-solving), were associated with lower Fitbit step counts (r=-0.43, p=.043). At baseline, for Fitbit-measured total sleep time, greater pain intensity (r=-0.49, p=.048) and pain interference (r=-.49, p=.047) were associated with shorter total duration of sleep. No other significant bivariate correlations were found for ISI total scores or Fitbit-measured physical activity or total sleep time (ps>0.05; see Table 4 for correlation coefficients).

Exploratory Aims 1b. Examine the efficacy of ME-CCT in improving objective physical activity and sleep in models similar to those of aims 1 and 2. Table 2 presents parameter estimates, p-values, and effect sizes for the effects of group, time, and the group-by-time interaction for all mixed-effects models through the 8-week intervention period. For the average Fitbit step counts, there was no significant group-by-time interaction to indicate that the ME-CCT group showed significantly greater improvement in objective physical activity levels compared to the SC group (t[1, 45.05]=0.74, p=.473, r=0.11). Similarly, for the average Fitbit total sleep times, there was no significant group-by-time interaction to support ME-CCT-related differential improvement in objective sleep duration relative to the SC group (t[1, 39.10]=-1.57, p=.125, r=-0.24; Figure 3). Mixed-effects models examining whether the average baseline Fitbit step counts moderated treatment effects on this outcome over time showed that the results were not moderated by baseline objective physical activity levels (t[1, 45.83]=-0.80, p=.429, r=-0.12; Table 3). Similarly, average baseline Fitbit total sleep time did not moderate treatments effects on this outcome over time (t[1,

31.36]=-0.237, *p*=.814, *r*=-0.04).

Discussion

The current study aimed to examine the efficacy of an integrated and multicomponent lifestyle and cognitive intervention, i.e., ME-CCT, in improving subjective and objective physical activity levels and sleep. Moreover, the study also sought to identify the treatment-moderating role of lifestyle factors at treatment outset on study outcomes as well as factors associated with objectively measured lifestyle behaviors. Inconsistent with hypotheses, there was no evidence of ME-CCT related differential improvement in self-reported physical activity levels, as assessed by the CHAMPS, nor self-reported sleep disturbance severity, as assessed by the ISI. Moreover, baseline levels of self-reported physical activity and sleep disturbance severity did not moderate treatment-related effects on these outcomes over the intervention period. Exploratory analyses examining similar hypotheses related to Fitbit-measured physical activity and sleep also did not show a differential positive impact of ME-CCT on either outcome. Despite these null findings, the high Fitbit acceptance rate (93%) and minimal alterations to the study design to integrate this technology within the study framework supports the feasibility and acceptability of wrist-worn consumer wearable technology within clinical research.

Given that the ME-CCT intervention integrates components of lifestyle intervention strategies within its protocol, it is possible that the intervention was not potent enough to change physical activity or sleep, given its primary focus on cognitive training. As depicted in Figure 2, both ME-CCT and SC groups show changes, albeit non-significant, in the expected direction for both self-reported physical activity levels and sleep disturbance. Indeed, the SC group may have had some salutary effects on

physical activity and sleep if participants identified these as goals and received support for working on them. The lack of support for differential ME-CCT-related improvements across measures of behavioral functioning may also be explained, in part, by diminished power given failure to meet intended recruitment goals due to the COVID-19 pandemic. Based on initial power analyses, it was estimated that the current study needed 72 participants (after accounting for 20% attrition) to have 80% power in detecting a medium effect. With an actual post-attrition sample of 54 participants, the study, in fact, had only 60% power to detect a medium effect. Recall bias inherent to self-report measures, and cognitive deficits within this clinical population, may have also led to null findings, although the CHAMPS attempts to circumvent the challenges presented in relying on self-report measures in cognitively vulnerable populations through provision of various response categories. In terms of physical activity, the current sample was reportedly a relatively active group, with only 5% of the randomized sample (4/74 participants) reporting less than 150 minutes of weekly activity at baseline, regardless of intensity, so it is possible that the treatment was not efficacious for individuals who were already physically active.

The use of Fitbit to assess lifestyle behaviors introduced the limits of the underlying technology (i.e., microelectronic triaxial accelerometer and proprietary algorithms) in accurately estimating the outcomes of interest; however, considerable support for the validity of Fitbit accelerometers in measuring physical activity and high sensitivity of wearable devices to detect sleep (de Zambotti et al., 2018; Evenson et al., 2015) bolsters the integration of such technology in clinical research aimed at testing new cognitive and lifestyle treatments to improve age-associated cognitive impairments.

It is also unlikely that the methodological limitations of the Fitbit device impacted the investigation of treatment-related changes, as these limitations equally applied to participants in both treatment arms of the study, thereby reducing concerns about confounding effects. The limited evidence-base supporting the validity and reliability of consumer wearable devices, including Fitbits, in older adults—an age group with greater prevalence of chronic diseases and mobility limitations—underscores the need for further investigation to examine the utility of commercially available devices in health promotion and clinical research.

Although the primary study hypotheses were unsupported, analyses examining factors associated with Fitbit-measured behavioral functioning found that greater perceived executive dysfunction, such as difficulties with planning and organizing, was associated with lower levels of objective physical activity levels. This finding is consistent with an expanding evidence base underscoring the importance of executive functioning capacities (e.g., cognitive flexibility, self-monitoring, goal planning and execution, inhibition of reward seeking through behaviors that minimize energetic costs) in health behavior engagement and mobility in general (Gothe et al., 2014). Although the cross-sectional design of the current study precludes causal conclusions, accumulating evidence suggests that the relationship between lifestyle behaviors and cognitive abilities is likely to be reciprocal. For example, an investigation examining the longitudinal relationship between decline in cognitive functioning and physical activity in adults aged 50-90 found a time-ordered effect: the level of cognitive ability, particularly within the domains of memory and executive functioning, had a stronger influence on engagement in physical activity and its trajectory than the influence physical activity

levels had on subsequent changes in cognitive functioning (Cheval et al., 2020). On the other hand, research by Fanning and colleagues (2017) found that substituting 30 minutes of sedentary time with either moderate-to-vigorous physical activity or sleep bolstered executive functioning and self-regulatory strategy use.

Unlike for Fitbit-derived physical activity, pain intensity and interference emerged as the only modifiable predictors of Fitbit-derived sleep duration, with greater pain intensity/interference associated with shorter average duration of sleep. As with the reciprocal nature of the relationship between physical activity and executive functions explored above, research suggests that this pattern of greater pain and poorer sleep is not simply a co-occurrence but, in fact, an interrelated process (Krause et al., 2019). In addition to sleep disturbance being attributable to the discomfort associated with pain, the link between poor sleep and pain intensity is theorized to involve a complicated distribution/interaction of neurochemical and neuroanatomical alterations. Inflammation is one mechanism that explains the relationship between sleep disturbance and pain in aging (Irwin, 2014). Sleep deprivation also enhances pain responsivity within the somatosensory cortex while blunting activity in the striatum and insula, regions with known involvement in modulating pain processing (Krause et al., 2019). These alterations may be due to cholinergic system dysregulation, considering the known inflammatory suppressive effects of acetylcholine (Rosas-Ballina & Tracey, 2009), which may also explain the interplay between sleep, pain, and neuropsychological outcomes, given the high density of cholinergic receptors in cognitively salient brain regions (e.g., hippocampus; Maurer et al., 2017). Although the average insomnia severity rating of the current sample (M=9.42, SD=6.65) places participants in the

subthreshold insomnia range, their average Fitbit-measured total sleep duration of 5.8 hours (SD=1.12) falls within the range associated with inflammation (Irwin, 2014; Patel et al., 2009). This finding underscores the significance of assessing for pain in determining risk for poor health and cognitive outcomes in aging.

Although no other modifiable predictors of Fitbit-derived behavioral functioning were found, greater duration of self-reported engagement in physical activity on the CHAMPS was moderately and statistically significantly predictive of higher Fitbit-measured average weekly step count. In contrast, both self-reported sleep disturbance on the ISI and sleep duration (derived from a single item assessing weekly sleep duration on the CAI) were modestly correlated with Fitbit-measured sleep duration, though these associations did not reach statistical significance. There may be several explanations for the differences in convergent validity between subjective and objective measures of sleep and physical activity. First, questions on the CHAMPS are presented in categories and framed in terms of duration (in hours) spent engaging in a particular activity on a typical day. The CAI sleep item, on the other hand, specifies the time window as a week in an open-ended format, which requires more cognitive effort and may not accurately index average nightly sleep as is purportedly captured by the Fitbit device. Additionally, prior research notes discordance between subjective and objective measures of sleep that is explained by various factors (e.g., gender, sleep characteristics, cognitive impairment; Van Den Berg et al., 2008), thereby highlighting the influence of systematic bias in self-report, which necessitates a nuanced interpretation of any significant association between these indices (Lauderdale et al., 2008).

The modest associations between subjective and objective indices of behavioral functioning supports the growing understanding of perceived and objective behavioral functioning as related, but unique constructs, and underscores the best practice recommendation to include both subjective and objective measures of behavioral functioning within studies (Parker et al., 2008; Landry, Best, & Liu-Ambrose, 2015). Overall, the emergence of different correlates of Fitbit-derived sleep and physical activity in the current study supports our understanding of a highly complex, dynamic interplay among the risk and protective factors for cognitive decline. These findings underscore the need for a multi-faceted/holistic approach in cognitive aging rehabilitation efforts. In service of a triangulation approach to the assessment of behavioral functioning, in addition to objective and patient self-report, future studies may benefit from inclusion of informant report of lifestyle habits/behaviors to extend our understanding of these factors in cognitive aging.

In addition to some of the limitations of the study considered above, it is worth noting that the current study's sample is predominantly White and relatively highly educated, which may limit generalizability of the study findings. Self-selection bias may have also influenced sample characteristics and, consequently, the external validity of the study's findings. Moreover, emerging evidence suggests that there are limitations of photoplethysmographic green light signaling, technology utilized by the Fitbit Charge 2 and other consumer wearable devices, in accurately measuring health constructs such as sleep and physical activity in individuals with darker skin tones (Colvonen et al., 2020). As such, future studies should consider their population characteristics in selection of consumer wearable devices for inclusion in studies and may benefit from

including multiple devices to examine measurement equivalence.

This is the first study to integrate consumer wearable devices to assess behavioral functioning as a treatment outcome in the context of a randomized controlled trial examining the efficacy of a multicomponent lifestyle and cognitive intervention, i.e., ME-CCT, for older adults with MCI. Although no treatment-related improvements were found on proposed outcomes, cross-sectional findings highlighted the role of perceived executive dysfunction and pain intensity/interference as modifiable risk factors for improved health behaviors and, likely, cognitive health. As commercially available health-tracking devices become more commonplace and technologically advanced, their utility in clinical research should be evaluated. In addition to the aims examined within the current study, this dissertation provides novel data regarding the acceptability and feasibility of consumer wearable technology within an MCI sample in the context of a longitudinal clinical trial. These preliminary findings warrant larger investigations of the utility of commercial technology integration within clinical research, particularly in rehabilitation research efforts with cognitively and medically vulnerable older adults.

Appendix

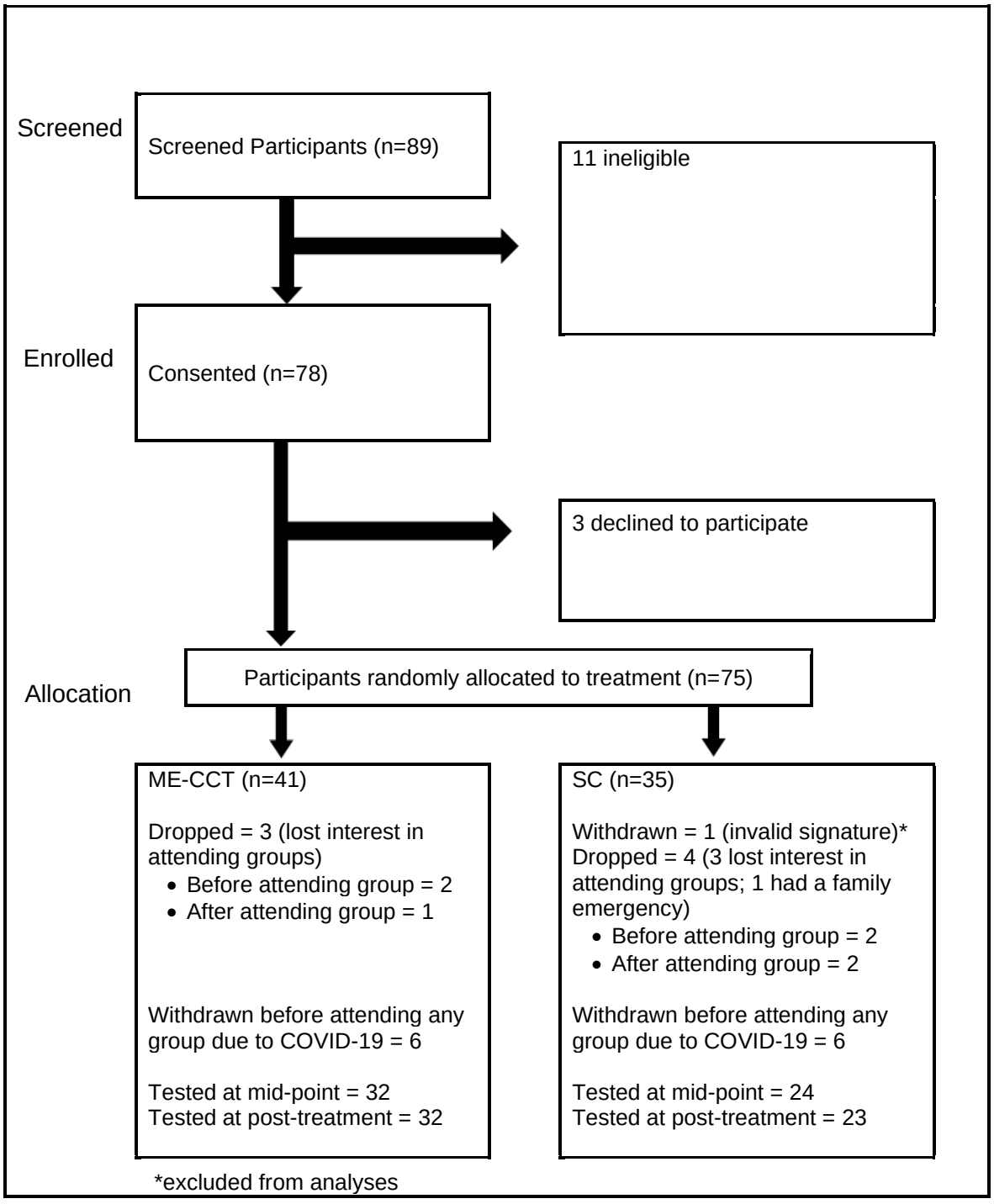


Figure 1

CONSORT Flow Diagram

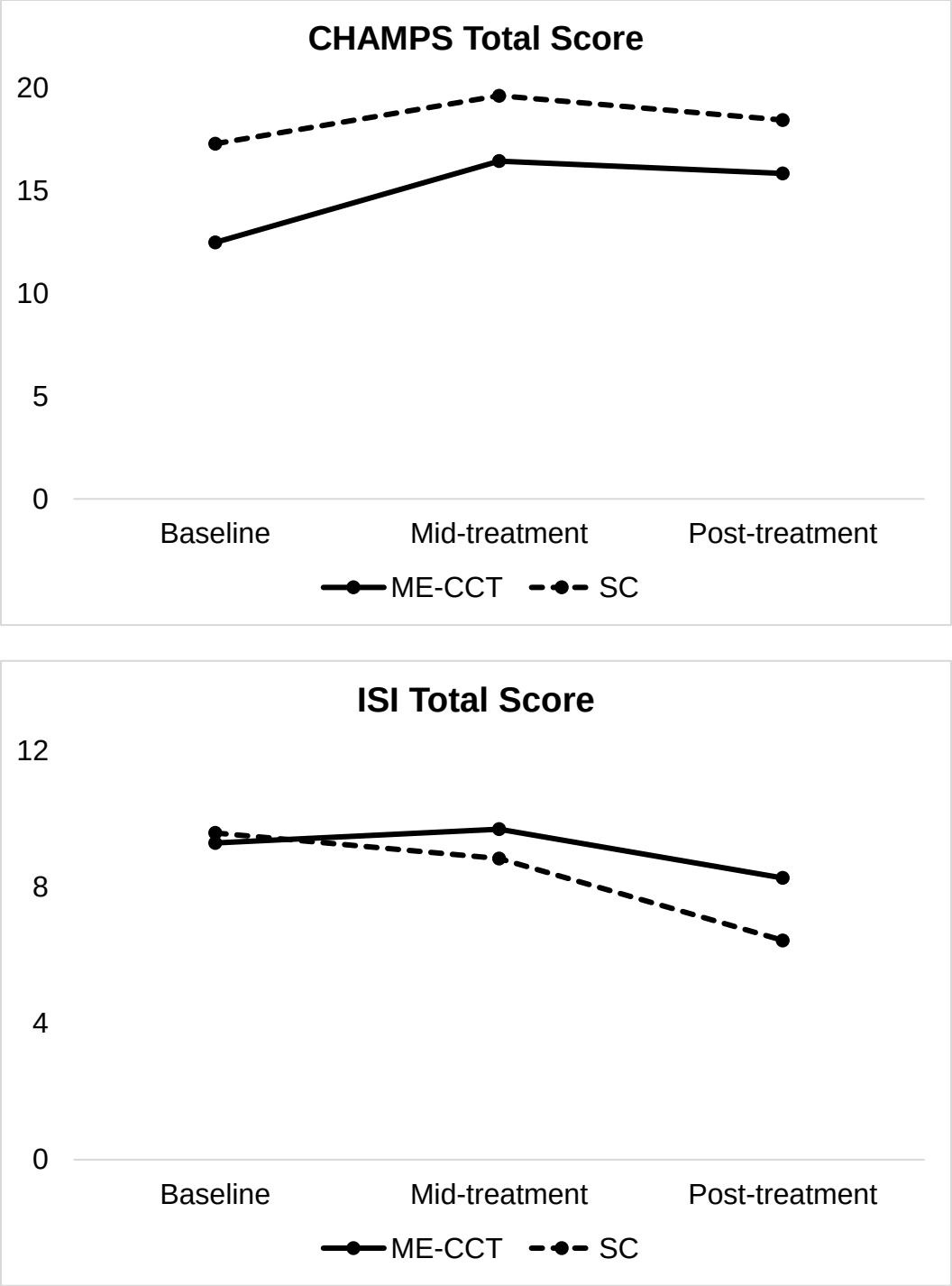
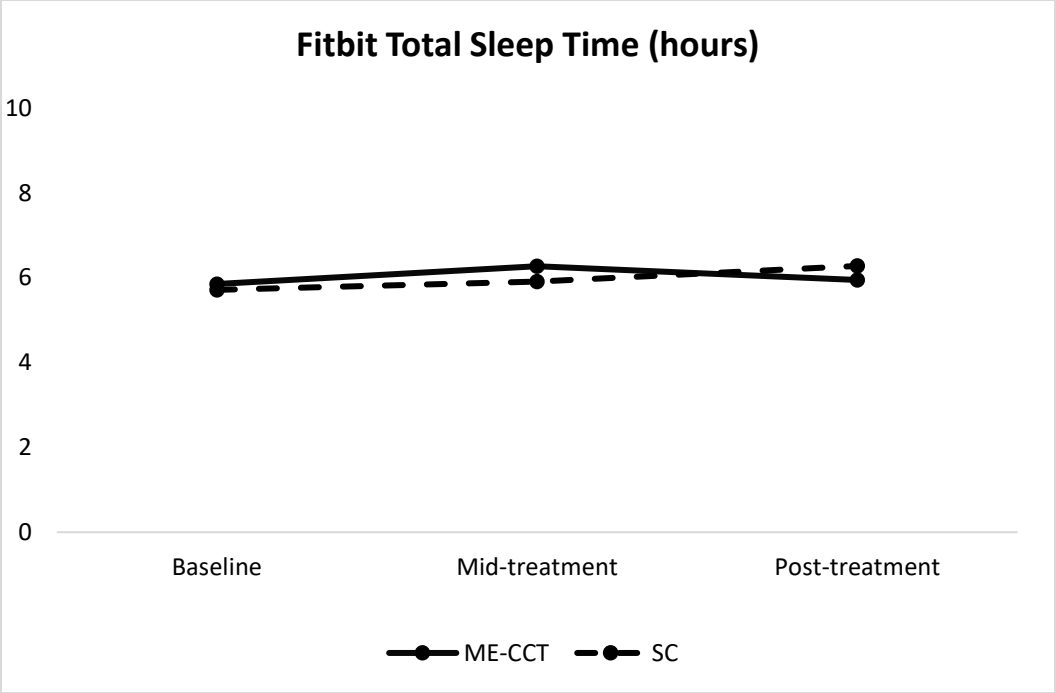


Figure 2

Mean of Self-reported Physical Activity and Sleep Outcomes by Treatment Group



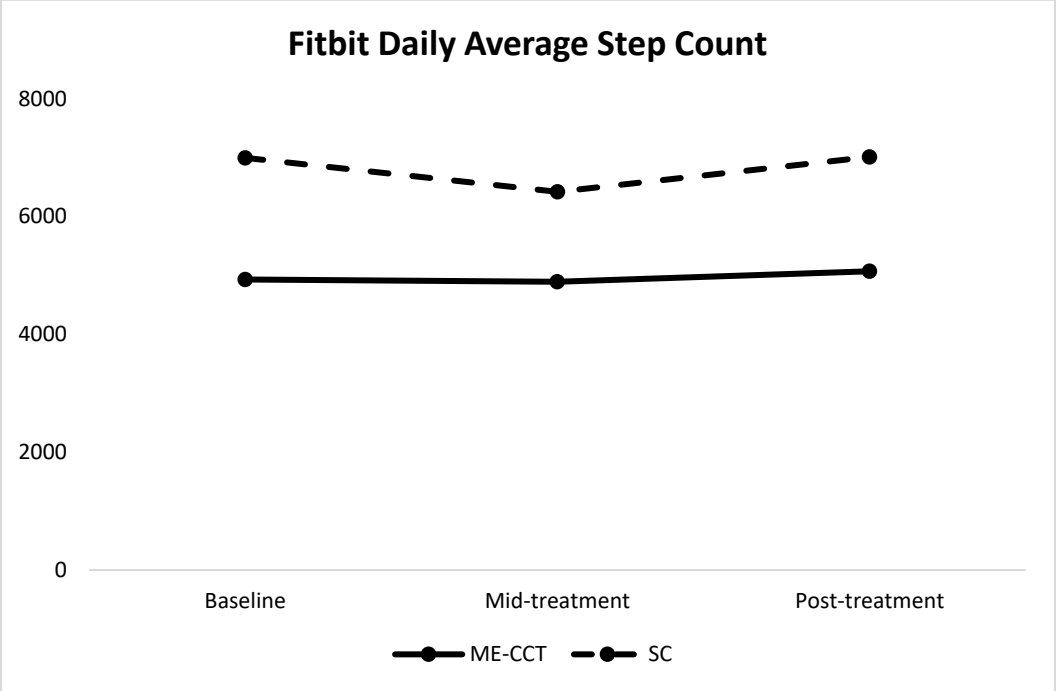


Figure 3

Mean of Fitbit Physical Activity and Sleep Outcomes by Treatment Group

Table 1

Baseline Demographic, Clinical, and Assessment Characteristics

	ME-CCT Mean (SD) (*n* = 41)	**SC Mean (SD) (*n* = 33)**	***t* or χ^2**	***p***	**ES**
Demographic characteristics					
Age (years)	71.10 (8.49)	71.06 (7.14)	-0.02	.984	-0.01
Education (years)	13.98 (2.31)	14.58 (1.90)	1.20	.234	-0.28
Race (%)			*H*=2.28	.632	0.19*
Asian	5	0			
Black/African American	12	9			
Pacific Islander	2	0			
White	80	91			
Gender (% Female)	7	15	1.16	.281	-.13*
Lifestyle factors					
CHAMPS total	12.50 (13.57)	17.31 (10.40)	*U*=423.5	**.006**	-0.32
ISI total	9.29 (6.51)	9.58 (6.92)	0.18	.857	0.04
CAI nightly sleep duration	6.31 (1.98)	6.43 (1.51)	0.27	.791	0.07
Fitbit physical activity**	4931.00 (2839.45)	6997.27 (2401.32)	1.88	.075	0.78
Fitbit sleep***	351.30 (61.60)	343.00 (79.08)	-0.24	.811	-0.12
Clinical characteristics					
PCL-5 total	24.17 (20.83)	18.97 (16.96)	-1.16	.251	-0.27
PHQ-9 total	9.22 (7.20)	6.91 (5.93)	-1.48	.143	-0.35
GAD-7 total	6.49 (5.51)	4.70 (5.14)	-1.43	.157	-0.34
PROMIS pain intensity total	7.78 (3.07)	7.82 (3.31)	0.05	.960	0.01
PROMIS pain interference total	14.83 (7.53)	14.52 (7.82)	-0.18	.861	-0.04
CAI monthly total hours	646.85 (239.75)	685.39 (276.48)	0.64	.523	0.15
MCI subtype (%)			*H*=0.45	1.00	0.03*
Single - amnestic	6	5			
Single - non-amnestic	3	2			
Multi-domain - amnestic	31	25			
Multi-domain - non-amnestic	1	1			
Cognition/Functioning					
WRAT-4 reading subtest	101.24 (12.93)	101.39 (17.58)	0.04	.966	0.01
Global cognition	44.91 (6.42)	43.86 (5.24)	-0.75	.453	-0.18
UPSA-B total	77.07 (11.99)	75.58 (12.54)	-0.52	.602	-0.12
MMAA total	25.71 (5.83)	26.19 (5.45)	0.36	.721	0.09
Neuro-QOL AC					
Executive Function	32.15 (6.61)	33.85 (5.00)	1.22	.225	0.29
General Concerns	24.95 (9.68)	27.09 (7.40)	1.05	.299	0.25

*φ; **ME-CCT: n=12; SC: n=11; *** ME-CCT: n=10; SC: n=7

Bold font denotes $p<.05$. CAI = Cognitive Activity Inventory; CHAMPS = Community Healthy Activities Model Program for Seniors; ISI = Insomnia Severity Index; MCI = Mild Cognitive Impairment; MMAA = Medication Management Ability Assessment; Neuro-QOL AC = Quality of Life in Neurological Disorders, Applied Cognition; PCL-5 = PTSD Checklist; PHQ-9 Patient Health Questionnaire; PROMIS = Patient Reported Outcomes Measurement Information System; UPSA-B = Brief UCSD Performance-Based Skills Assessment; WRAT = Wide Range Achievement Test, 4th edition.

Table 2

Mixed Effects Models – Immediate Post-intervention Estimates for Effects of the Time-by-Group Interaction

Measures	Time x Group			
	B	**SE**	**p**	**r**
Physical activity				
CHAMPS total	0.17	0.40	.669	0.04
Fitbit step count	44.99	60.75	.463	0.11
Sleep				
ISI total	0.16	0.13	.228	0.11
Fitbit total sleep	-5.86	3.73	.125	-0.24

CHAMPS = Community Healthy Activities Model Program for Seniors; ISI= Insomnia Severity Index

Table 3

Mixed Effects Models – Immediate Post-intervention Estimates for the Moderating Effects of Baseline Physical Activity and Sleep on the Time-by-Group Interaction

Measures	Time x Group x Baseline physical activity			
	B	**SE**	**p**	**r**
Physical activity				
CHAMPS total	0.01	0.03	.840	0.02
Fitbit step count	-0.02	0.02	.429	-0.12
	Time x Group x Baseline sleep			
Sleep				
ISI total	0.01	0.03	.694	0.03
Fitbit total sleep	-0.01	0.06	.814	0.04

CHAMPS = Community Healthy Activities Model Program for Seniors; ISI= Insomnia Severity Index

Table 4

Bivariate Correlation Coefficients of Demographic, Lifestyle, Clinical, Cognitive, and Functional Outcomes at Baseline

	Fitbit physical activity (*n* = 23)		**Fitbit sleep (*n* = 17)**	
	r	*p*	*r*	*p*
Demographic characteristics				
Age (years)	0.07	.748	0.29	.255
Education (years)	-0.13	.547	0.43	.083
Race*	0.32	.137	0.09	.720
Ethnicity*	0.11	.628	0.19	.508
Gender*	-0.06	.771	0.20	.432
Lifestyle factors				
CHAMPS total score*	**0.57**	**.005**	-0.02	.928
ISI total score	0.10	.653	-0.37	.150
CAI sleep duration (hours)	-0.45	.059	-0.25	.405
Fitbit physical activity	--	--	0.16	.541
Fitbit sleep	0.16	.541	--	--
Clinical characteristics				
PCL-5 total score	0.29	.175	-0.29	.266
PHQ-9 total score	0.17	.453	-0.27	.303
GAD-7 total score	0.40	.060	0.02	.948
PROMIS pain intensity total score	-0.08	.705	**-0.49**	**.048**
PROMIS pain interference total score	-0.03	.895	**-0.49**	**.047**
CAI monthly total hours	0.14	.533	0.16	.543
MCI subtype*	0.10	.640	-0.24	.350
Cognition/Functioning				
WRAT-4 reading subtest	0.03	.908	0.18	.496
Global cognition	-0.23	.295	-0.02	.936
UPSA-B total score	-0.28	.193	-0.31	.230
MMAA total score	-0.27	.208	-0.04	.893
Neuro-QOL AC				
Executive Function	**-0.43**	**.043**	0.18	.488
General Concerns	-0.20	.351	0.01	.967

*Spearman. Bold font denotes $p<.05$. CAI = Cognitive Activity Inventory; CHAMPS = Community Healthy Activities Model Program for Seniors; ISI = Insomnia Severity Index; MCI = Mild Cognitive Impairment; MMAA = Medication Management Ability Assessment; Neuro-QOL AC = Quality of Life in Neurological Disorders, Applied Cognition; PCL-5 = PTSD Checklist; PHQ-9 Patient Health Questionnaire; PROMIS = Patient Reported Outcomes Measurement Information System; UPSA-B = Brief UCSD Performance-Based Skills Assessment; WRAT = Wide Range Achievement Test, 4th edition.

References

Achttien, R. J., Van Lieshout, J., Wensing, M., Sanden, M. N. V. D., & Staal, J. B. (2019). The decline in physical activity in aging people is not modified by gender or the presence of cardiovascular disease. *The European Journal of Public Health,* 1-7. https://doi.org/10.1093/eurpub/ckz159

Akhtar, S., Moulin, C. J. A., & Bowie, P. C. W. (2006). Are people with mild cognitive impairment aware of the benefits of errorless learning? *Neuropsychological Rehabilitation*, *16*(3), 329–346. https://doi.org/10.1080/09602010500176674

Ally, B. A., Gold, C. A., & Budson, A. E. (2009). The picture superiority effect in patients with Alzheimer's disease and mild cognitive impairment. *Neuropsychologia*, *47*(2), 595-598. https://doi.org/10.1016/j.neuropsychologia.2008.10.010

Alzheimer's Association. (2010). *Alzheimer's and Dementia. 6*(2), 158-194. https://doi.org/10.1016/j.jalz.2010.01.009

Alzheimer's Association (2018). 2018 Alzheimer's disease facts and figures. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *14*(3), 367-429. https://doi.org/10.1016/j.jalz.2018.02.001

Arnáiz, E., & Almkvist, O. (2003) Neuropsychological features of mild cognitive impairment and preclinical Alzheimer's disease. *Acta Neurologica Scandinavica, 107*(s179), 34-41. https://doi.org/10.1034/j.1600-0404.107.s179.7.x

Bäckman, L., & Nilsson, L. G. (1996). Semantic memory functioning across the adult life span. *European Psychologist*, *1*(1), 27-33. https://doi.org/10.1027/1016-9040.1.1.27.

Ball, K., Berch, D. B., Helmers, K. F., Jobe, J. B., Leveck, M. D., Marsiske, M., Morris, J. N., Rebok, G. W., Smith, D. M., Tennstedt, S. L., Unverzagt, F. W., & Willis, S. L. (2002). Effects of cognitive training interventions with older adults: A randomized controlled trial. *JAMA, 288*(18), 2271-2281. https://doi.org/10.1001.jama.288.18.2271

Bastien, C. H., Vallières, A., Morin, C. M. (2001). Validation of the Insomnia Severity Index as a clinical outcome measure for insomnia research. *Sleep, 2*(4), 297-307. https://doi.org/10.1016/s1389-9457(00)00065-4

Baumgart, M., Snyder, H. M., Carrillo, M. C., Fazio, S., Kim, H., & Johns, H. (2015). Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimer's and Dementia, 11*(6), 718-726. https://doi.org/10.1016/j.jalz.2015.05.016

Bekinschtein, P., Oomen, C. A., Saksida, L. M., & Bussey, T. J. (2011). Effects of environmental enrichment and voluntary exercise on neurogenesis, learning and

memory, and pattern separation: BDNF as a critical variable? *Seminars in Cell & Developmental Biology, 22*(5), 536–542. https://doi.org/10.1016/j.semcdb.2011.07.002

Belleville, S., Gilbert, B., Fontaine, F., Gagnon, L., Menard, E., & Gauthier, S. (2006). Improvement of episodic memory in persons with mild cognitive impairment and healthy older adults: Evidence from a cognitive intervention program. *Dementia and Geriatric Cognitive Disorders*, *22*, 486-499. https://doi.org/10.1159/000096316

Benedict, R. H. B. (1997). *Brief Visuospatial Memory Test-Revised (BVMT-R)*. Psychological Assessment Resources.

Best, M. W., & Bowie, C. R. (2017) A review of cognitive remediation approaches for schizophrenia: From top-down to bottom-up, brain training to psychotherapy. *Expert Review of Neurotherapeutics, 17*(7), 713-723. https://doi.org/10.1080/14737175.2017.1331128

Bherer, L., Erickson, K. I., & Liu-Ambrose, T. (2013). A review of the effects of physical activity and exercise on cognitive and brain functions in older adults. *Journal of Aging Research, 2013*, Article 657508 . https://doi.org/10.1155/2013/657508

Booth, F. W., Roberts, C. K., & Laye, M. J. (2012). Lack of exercise is a major cause of chronic diseases. *Comprehensive Physiology, 2*(2), 1143-1211. https://doi.org/10.1002/cphy.c110025

Brandt, J. & Benedict, R. H. B. (2001). *Hopkins Verbal Learning Test Revised (HVLT-R)*. Psychological Assessment Resources.

Buchman, A. S., Boyle, P. A., Yu, L., Shah, R. C., Wilson, R. S., & Bennett, D. A. (2012). Total daily physical activity and the risk of AD and cognitive decline for older adults. *Neurology, 78*(17), 1323-1329. https://doi.org/10.1212/WNL.0b013e3182535d35

Cella, D., Nowinski, C., Peterman, A., Victorson, P., Miller, D., Lai, J., & Moy, C. (2011). The neurology quality-of-life measurement initiative. *Archives of Physical Medicine and Rehabilitation, 92*(10), S28-S36. https://doi.org/10.1016/j.apmr.2011.01.025

Cella, D., Yount, S., Rothrock, N., Gershon, R., Cook, K., Reeve, B., ... & Rose, M. (2007). The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. Medical care, 45(5 Suppl 1), S3-S11.

Chao, D., Foy, C. G., & Farmer, D. (2000) Exercise adherence among older adults: Challenges and strategies. *Controlled Clinical Trials*, *21*(5), S212-S217. https://doi.org/10.1016/S0197-2456(00)00081-7

Chapman, S. B., Aslan, S., Spence, J. S., Hart Jr, J. J., Bartz, E. K., Didehbani, N., Keebler, M. W., Gardener, C. M., Strain, J. F., DeFina, L. F., & Lu, H. (2015). Neural mechanisms of brain plasticity with complex cognitive training in healthy seniors. *Cerebral cortex, 25*(2), 396-405. https://doi.org/10.1093/cercor/bht234

Cheval, B., Orsholits, D., Sieber, S., Courvoisier, D., Cullati, S., & Boisgontier, M. P. (2020). Relationship between decline in cognitive resources and physical activity. *Health Psychology, 39*(6), 519–528. https://doi.org/10.1037/hea0000857

Cheung, C., Talley, K. M., McMahon, S., Schorr, E., & Wyman, J. F. (2019) Knowledge of physical activity guidelines and its association with physical activity and physical function in older adults. *Activities, Adaptation, & Aging,* 1-13. https://doi.org/10.1080/01924788.2019.1591152

Clare L., Nelis, S. M., Jones, I.R., Hindle, J. V., Thom, J. M., Nixon, J. A., Cooney, J., Jones, C. L., Tudor Edwards, R., & Whitaker, C. J. (2015). The Agewell trial: A pilot randomised controlled trial of a behaviour change intervention to promote healthy ageing and reduce risk of dementia in later life. *BMC Psychiatry*, *15*(25). https://doi.org/10.1186/s12888-015-0402-4

Colvonen, P. J., DeYoung, P. N., Bosompra, N. O. A., & Owens, R. L. (2020). Limiting racial disparities and bias for wearable devices in health science research. *Sleep, 43*(10), zsaa159. https://doi.org/10.1093/sleep/zsaa159

Cotman, C. W., Berchtold, N. C., & Christie, L. A. (2007). Exercise builds brain health: Key roles of growth factor cascades and inflammation. *Trends in Neuroscience, 30*(9), 464-472. https://doi.org/10.1016/j.tins.2007.06.011

Cummings, J., Aisen, P., Apostolova, L. G., Atri, A., Salloway, S., & Weiner, M. (2021). Aducanumab: Appropriate use recommendations. *The Journal of Prevention of Alzheimer's Disease, 8,* 1-13. https://doi.org/10.14283/jpad.2021.41

Cummings, J. L., Morstorf, T., & Zhong, K. (2014). Alzheimer's disease drug-development pipeline: Few candidates, frequent failures. *Alzheimer's Research and* Therapy, *6*(4), 37. https://doi.org/10.1186/alzrt269

Cyarto, E. V., Marshall, A. L., Dickinson, R. K., & Brown, W. J. (2006). Measurement properties of the CHAMPS physical activity questionnaire in a sample of older Australians. *Journal of Science and Medicine in Sport, 9*(4), 319-326. https://doi.org/10.1016/j.jsams.2006.03.001

Dacey, M., Baltzell, A., Zaichkowsky, L. (2008). Older adults' intrinsic and extrinsic motivation toward physical activity. *American Journal of Health Behavior, 32*(6), 570-582. https://doi.org/10.5555/ajhb.2008.32.6.570

Davis, D. M., & Hayes, J. A. (2011). What are the benefits of mindfulness? A practice review of psychotherapy-related research. *Psychotherapy, 48*(2), 198-208. https://doi.org/10.1037/a0022062

Delis, D. C., Kramer, J. H., Kaplan, E., & Holdnack, J. (2004). Reliability and validity of the Delis-Kaplan Executive Function System: An update. *Journal of the International Neuropsychological Society, 10*(2), 301-303. https://doi.org/10.1017/S1355617704102191

de Zambotti, M., Goldstone, A., Claudatos, S., Colrain, I. M., & Baker, F. C. (2018). A validation study of Fitbit Charge 2 compared with polysomnography in adults. *The Journal of Biological and Medical Rhythm Research, 35*(4), 465-476. https://doi.org/10.1080/07420528.2017.1413578

Deschenes, C. L., & McCurry, S, M. (2009). Current treatments for sleep disturbances in individuals with dementia. *Current Psychiatric Reports, 11*, 20-26. https://doi.org/10.1007/s11920-009-0004-2

Dresler, M., Shirer, W. R., Konrad, B. N., Müller, N. C. J., Wagner, I. C., Fernández, G., Czisch, M., & Greicius, M. D. (2017). Mnemonic training reshapes brain networks to support superior memory. *Neuron, 93*(5), 1227-1235. https://doi.org/10.1016/j.neuron.2017.02.003

Eggenberger, P., Schumacher, V., Angst, M., Theill, N., & de Bruin, E. D. (2015). Does multicomponent physical exercise with simultaneous cognitive training boost cognitive performance in older adults? A 6-month randomized controlled trial with a 1-year follow-up. *Clinical Interventions in Ageing, 10*, 1335-1349. https://doi.org/10.2147/CIA.S87732

Ellison, J. M., Harper, D. G., Berlow, Y., & Zeranski, L. (2008). Beyond the “C” in MCI: Noncognitive symptoms in amnestic and non-amnestic mild cognitive impairment. *CNS Spectrums, 13*(1), 66-72. https://doi.org/10.1017/S1092852900016175

Erickson, K. I., Raji, C. A., Lopez, O. L., Becker, J. T., Rosano, C., Newman, A. B., Gach, H. M., Thompson, P. M., Ho, A. J., & Kuller, L. H. (2010). Physical activity predicts gray matter volume in late adulthood. *Neurology, 75*(16)*,* 1415-1422. https://doi.org/10.1212/WNL.0b013e3181f88359

Erickson, K. I., Voss, M. W., Prakash, R. S., Basak, C., Szabo, A., Chaddock, L., Kim, J. S., Heo, S., Alves, H., White, S. M., Wojcicki, T. R., Mailey, E., Vieira, V. J., Martin, S. A., Pence, B. D., Woods, J. A., McAuley, E., & Kramer, A. F. (2010). Exercise training increases size of hippocampus and improves memory. *Proceedings of the National Academy of Sciences, 108*(7), 3017-3022. https://doi.org/10.1073/pnas.1015950108

Evenson, K. R., Goto, M. M., & Furberg, R. D. (2015). Systematic review of the validity and reliability of consumer-wearable activity trackers. *International Journal of Behavioral Nutrition and Physical Activity*, *12*, 1-22. https://doi.org/10.1186/s12966-015-0314-1

Fanning, J., Porter, G., Awick, E. A., Ehlers, D. K., Roberts, S. A., Cooke, G., Burzynska A. Z., Voss, M. W., Kramer, A. F., & McAuley, E. (2017). Replacing sedentary time with sleep, light, or moderate-to-vigorous physical activity: Effects on self-regulation and executive functioning. *Journal of Behavioral Medicine, 40*(2), 332-342. https://doi.org/10.1007/s10865-016-9788-9

Farlow, M. R. (2009). Treatment of mild cognitive impairment (MCI). *Current Alzheimer Research, 6*(4), 362-267. https://doi.org/10.2174/156720509788929282

Foley, D., Ancoli-Israel, S., Britz, P., & Walsh, J. (2004) Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation *Sleep in America* survey*. Journal of Psychosomatic Research, 56*(5), 497-502. https://doi.org/10.1016/j.jpsychores.2004.02.010

Fougner, M., Bergland, A., Lund, A., & Debesay, J. (2018). Aging and exercise: Perceptions of the active lived body. *Physiotherapy Theory and Practice, 35*(7), 561-562. https://doi.org/10.1080/09593985.2018.1456584

Franco, M. R., Tong, A., Howard, K., Sherrington, C., Ferreira, P. H., Pinto, R. Z., & Ferreria, M. L. (2015). Older people's perspectives on participation in physical activity: A systematic review and thematic synthesis of qualitative literature. *British Journal of Sports Medicine, 49*(19), 1268-1276. https://doi.org/10.1136/bjsports-2014-094015

Goodglas, H. & Kaplan, E. (2000). *Boston Diagnostic Aphasia Examination-Third Edition*. Pearson.

Gomar, J. J., Bobes-Bascaran, M. T., Conejero-Goldberg, C., Davies, P., & Goldberg, T. E. (2011). Utility of combinations of biomarkers, cognitive markers, and risk factors to predict conversion from mild cognitive impairment to Alzheimer disease in patients in the Alzheimer's disease neuroimaging initiative. *Archives of General Psychiatry, 68*(9), 961-969. https://doi.org/10.1001/archgenpsychiatry.2011.96

Gomez-Pinilla, F., Vaynman, S., & Ying, Z. Brain-derived neurotrophic factor functions as a metabotrophin to mediate the effects of exercise on cognition. *European Journal of Neuroscience, 28*(11), 2278-2287. https://doi.org/10.1111/j.1460-9568.2008.06524.x

Gopinath, B., Kifley, A., Flood, V.M., & Mitchell, P. (2018). Physical activity as a determinant of successful aging over ten years. *Scientific Reports, 8*, 1-5. https://doi.org/10.1038/s41598-018-28526-3

Gothe, N. P., Fanning, J., Awick, E., Chung, D., Wójcicki, T. R., Olson, E. A., Mullen S. P., Voss M., Erickson K. I., Kramer A. F., & McAuley E. (2014). Executive function processes predict mobility outcomes in older adults. *Journal of the American Geriatrics Society, 62*(2), 285-290. https://doi.org/10.1111/jgs.12654

Hamer, M., & Chida, Y. (2008). Physical activity and risk of neurodegenerative disease: A systematic review of prospective evidence. *Psychological Medicine, 39*(1), 3-11. https://doi.org/10.1017/S0033291708003681

Hampstead, B. N., Sathian, K., Bacon Moore, A., Nalisnick, C., & Stringer, A. Y. (2008). Explicit memory training leads to improved memory for face-name pairs in patients with mild cognitive impairment: Results of a pilot investigation. *Journal of the International Neuropsychological Society, 14*(15), 883-889. https://doi.org/10.1017/S1355617708081009

Hampstead, B. M., Sathian, K., Phillips, P. A., Amaraneni, A., Delaune, W. R., & Stringer, A. Y. (2012). Mnemonic strategy training improves memory for object location associations in both healthy elderly and patients with amnestic mild cognitive impairment: A randomized, single-blind study. *Neuropsychology*, *26*(3), 385-399. https://doi.org/10.1037/a0027545

Hampstead, B. M., Stringer, A. Y., Stilla, R. F., Deshpande, G., Hu, X., Moore, A. B., & Sathian, K. (2011). Activation and effective connectivity changes following explicit-memory training for face–name pairs in patients with mild cognitive impairment: a pilot study. *Neurorehabilitation and Neural Repair*, *25*(3), 210-222. https://doi.org/10.1177/1545968310382424

Han, J., Besser L. M., Xiong, C., Kukull, W. A., & Morris, J. C. (2019). Cholinesterase inhibitors may not benefit mild cognitive impairment and mild Alzheimer disease dementia. *Alzheimer Disease & Associated Disord*ers, *33*(2), 87-94. https://doi.org/10.1097/WAD.0000000000000291

Harada, N. D., Chiu, V., King, A. C., & Stewart, A. L. (2000). An evaluation of three self-report physical activity instruments for older adults. *Medicine & Science in Sports and Exercise, 33*(6), 962-970. https://doi.org10.1097/00005768-200106000-00016

Hedeker, D., Gibbons, R., & Davis, J. M. (1991). Random regression models for multicenter clinical trials data*. Psychopharmacology Bulletin, 27*(1), 73-77.

Hedeker, D., Gibbons, R. D., & Waternaux, C. (1999). Sample size estimation for longitudinal designs with attrition: Comparing time-related contrasts between two groups*. Journal of Educational and Behavioral Statistics*, *24*(1), 70-93. https://doi.org/10.3102/10769986024001070

Hita-Yañez, E., Atienza, M., Gil-Neciga, E., & Cantero, J. L. (2012). Disturbed sleep patterns in elders with mild cognitive impairment: The role of memory decline and ApoE ε4 genotype. *Current Alzheimer Research, 9*(3), 290-297. https://doi.org/10.2174/156720512800107609

Hita-Yañez, E., Atienza, M., & Cantero, J. L. (2013). Polysomnographic and subjective sleep markers of mild cognitive impairment. *Sleep*, *36*(9), 1327-1334. https://doi.org/10.5665/sleep.2956

Hox, J. J., Moerbeek, M., & Van de Schoot, R. (2010). *Multilevel analysis: Techniques and applications*. Routledge.

Huckans, M., Hutson, L., Twamley, E., Jak, A., Kaye, J., & Storzbach, D. (2013). Efficacy of cognitive rehabilitation therapies for mild cognitive impairment (MCI) in older adults: Working toward a theoretical model and evidence-based interventions. *Neuropsychology Review, 23*, 63-80. https://doi.org/10.1007/s11065-013-9230-9

Imboden, M. T., Nelson, M. B., Kaminsky, L. A., & Montoye, A. H. K. (2018). Comparison of four Fitbit and Jawbone activity monitors with a research-grade ActiGraph accelerometer for estimating physical activity and energy expenditure. *British Journal of Sports Medicine*, *52*(13), 844-850. https://doi.org/10.1136/bjsports-2016-096990

Irwin, M. R. (2014). Sleep and inflammation in resilient aging. *Interface Focus, 4*(5), 20140009. https://doi.org/10.1098/rsfs.2014.0009

Jak, A. J. (2012). The impact of physical and mental activity on cognitive aging. In M.C. Pardon & M.W. Bondi (Eds.) *Behavioral Neurobiology of Aging*, *10,* 273-291. https://doi.org/10.1007/7854_2011_141

Jak, A. J., Bondi, M. W., Delano-Wood, L., Wierenga, C., Corey-Bloom, J., Salmon, D.P., & Delis, D. C. (2009). Quantification of five neuropsychological approaches to defining mild cognitive impairment. *The American Journal of Geriatric Psychiatry, 17*(5), 368-375. https://doi.org/10.1097/JGP.0b013e31819431d5

Jelic, V., Kivipelto, M., & Winblad, B. (2007). Clinical trials in mild cognitive impairment: Lessons for the future. *Journal of Neurology, Neurosurgery, and Psychiatry, 77*, 429-438. https://doi.org/10.1136/jnnp.2005.072926

Jelicic, M., Bosma, H., Ponds, R. W. H. M., Van Boxtel, M. P .J., Houx, P. J., & Jones, J. (2002). Subjective sleep problems in later life as predictors of cognitive decline. *International Journal of Geriatric Psychiatry, 17*(1), 73-77. https://doi.org/10.1002/gps.529

Ju, Y. S., Lucey, B. P., & Holtzman, D. M. (2014). Sleep and Alzheimer disease pathology – a bidirectional relationship. *Nature Reviews Neurology, 10*(2), 115-119. https://doi.org/10.1038/nrneurol.2013.269

Kane, R. L., Butler, M., Fink, H. A., Brasure, M., Davila, H., Desai, P., Jutkowitz, E., McCreedy, E., Nelson, V. A., McCarten, J. R, Calvert, C., Ratner, E., Hemmy, L. S., & Barclay, T. (2017). Interventions to prevent age-related cognitive decline, mild cognitive impairment, and clinical Alzheimer's-type dementia. *Comparative Effectiveness Reviews,* No. 188.

Kang, J. E., Lim, M. M., Bateman, R. J., Lee, J. L., Smyth, L. P., Cirrito, J.R., Fujiki, N., Nishino, S., & Holtzman, D. M. (2009). Amyloid-β dynamics are regulated by

orexin and the sleep-wake cycle. *Science, 326*(5955), 1005-1007. https://doi.org/10.1126/science.1180962

Keshavan, M.S., Vinogradov, S., Rumsey, J., Sherrill, J., & Wagner, A. (2014). Cognitive training in mental disorders: Update and future directions. *The American Journal of Psychiatry, 171*(5), 510-522. https://doi.org/10.1176/appi.ajp.2013.13081075

King, A. C., Oman, R. F., Brassington, G. S., Bliwise, D. L., & Haskell, W. L. (1997). Moderate-intensity exercise and self-rated quality of sleep in older adults: A randomized controlled trial. *JAMA, 277*(1), 32-37. https://doi.org/10.1001/jama.1997.03540250040029

King, A. C., Pruitt, L. A., Woo, S., Castro, C. M., Ahn, D. K., Vitiello, M. V., Woodward, S. H., & Bliwise, D. L. (2008). Effects of moderate-intensity exercise on polysomnographic and subjective sleep quality in older adults with mild to moderate sleep complaints. *Journal of Gerontology: Medical Sciences, 63*(9), 997-1004. https://doi.org/10.1093/gerona/63.9.997

Kinsella, G. J., Mullaly, E., Rand, E., Ong, B., Burton, C., Price, S., Phillips, M., & Storey, E. (2009). Early intervention for mild cognitive impairment: A randomised controlled trial*. Journal of Neurology and Neuroscience*, *80*, 730-736. https://doi.org/10.1136/jnnp.2008.148346

Kolla, B. P., Mansukhani, S., & Mansukhani, M. P. (2016). Consumer sleep tracking devices: A review of mechanisms, validity and utility. *Expert Review of Medical Devices, 13*(5), 497-506. https://doi.org/10.1586/17434440.2016.1171708

Krause, A. J., Prather, A. A., Wager, T. D., Lindquist, M. A., & Walker, M. P. (2019). The pain of sleep loss: A brain characterization in humans. *Journal of Neuroscience, 39(*12), 2291-2300.

https://doi.org/10.1523/JNEUROSCI.2408-18.2018

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General International Medicine, 16*, 606-613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x

Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in linear mixed effects models. *Journal of Statistical Software, 82*(13), 1–26. https://doi.org/10.18637/jss.v082.i13

Laird, N. M. & Ware, J. H. (1982). Random-effects models for longitudinal data*. Biometrics*, *38*(4), 963-974. https://doi.org/10.1007/978-3-642-11760-2_2

Landry, G. J., & Liu-Ambrose, T. (2014). Buying time: A rationale for examining the use of circadian rhythm and sleep interventions to delay progression of mild cognitive

impairment to Alzheimer's disease. *Frontiers in Aging Neuroscience, 6*, 1-21. https://doi.org/10.3389/fnagi.2014.00325

Landry, G. J., Best, J. R., & Liu-Ambrose, T. (2015). Measuring sleep quality in older adults: A comparison using subjective and objective methods. *Frontiers in Aging Neuroscience, 7*, 1-10. https://doi.org/10.3389/fnagi.2015.00166

Larson, E. B., Wang, L., Bowen, J. D., McCormick, W. C., Teri, L., Crane, P., & Kukull, W. (2006). Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. *Annals of Internal Medicine, 144*(2), 73-81. https://doi.org/10.7326/0003-4819-144-2-200601170-00004

Lauderdale, D. S., Knutson, K. L., Yan, L. L., Liu, K., & Rathouz, P. J. (2008). Self-reported and measured sleep duration: How similar are they? *Epidemiology 19*(6), 838–845. https://doi.org/10.1097/EDE.0b013e318187a7b0

Li, H., Li, J., Li, N., Li, B. Wang, P., & Zhou, T. (2011). Cognitive intervention for persons with mild cognitive impairment: A meta-analysis. *Ageing Research Reviews, 10*(2), 285-296. https://doi.org/10.1016/j.arr.2010.11.003

Lim, A. S. P., Kowgier, M., Yu, L., Buchman, A. S., Bennett, D. A. (2013). Sleep fragmentation and the risk of incidental Alzheimer's disease and cognitive decline in older persons. *Sleep, 36*(7)*,* 1027-1032. https://doi.org/10.5665/sleep.2802

Lim, A. S. P., Yu, L., Kowgier, M., Schneider, J., Buchman, A. S., & Bennett, D. A. (2013). Modification of the relationship of the apolipoprotein E ε4 allele to the risk of Alzheimer disease and neurofibrillary tangle density by sleep. *JAMA, 70*(12), 1544-1551. https://doi.org/10.1001/jamaneurol.2013.4215

Mander, B. A., Marks. S. M., Vogel, J. W., Rao, V., Lu, B., Saletin, J. M., Ancoli-Israel, S., Jagust, W. J., & Walker, M. P. (2015). β-amyloid disrupts human NREM slow waves and related hippocampus-dependent memory consolidation. *Nature Neuroscience, 18*, 1051-1057. https://doi.org/10.1038/nn.4035

Mander, B. A., Winer, J. R., Jagust, W. J., & Walker, M. P. (2016). Sleep: A novel mechanistic pathway, biomarker, and treatment target in the pathology of Alzheimer's disease? *Trends in neurosciences*, *39*(8), 552-566. https://doi.org/10.1016/j.tins.2016.05.002

Mantua, J., Gravel, N., & Spencer, R. M. C. (2016). Reliability of sleeping measures from four personal health monitoring devices compared to research based actigraphy and polysomnography. *Sensors, 16*(5), 646. https://doi.org/10.3390/s16050646

Maurer, S. V., & Williams, C. L. (2017). The cholinergic system modulates memory and hippocampal plasticity via its interactions with non-neuronal cells. *Frontiers in Immunology, 8*, 1489. https://doi.org/10.3389/fimmu.2017.01489

Mausbach, B. T., Harvey, P. D., Goldman, S. R., Jeste, D. V., & Patterson, T.L. (2007). Development of a brief scale of everyday functioning in persons with serious mental illness. *Schizophrenia Bulletin, 33*(6), 1264-1372. https://doi.org/10.1093/schbul/sbm014

Medalia, A., & Choi, J. (2009). Cognitive remediation in schizophrenia. *Neuropsychology Review*, *19*, 353-364. https://doi.org/10.1007/s11065-009-9097-y

Minzenberg, M. J., & Carter, C. S. (2012). Developing treatments for impaired cognition in schizophrenia. *Trends in Cognitive Sciences, 16*(1), 35-42. https://doi.org/10.1016/j.tics.2011.11.017

Mitchell, A. J., & Shiri-Feshki, M. (2009). Rate of progression of mild cognitive impairment to dementia – meta-analysis of 41 robust inception cohort studies. *Acta Psychiatrica Scandinavica, 119*(4), 252-265. https://doi.org/10.1111/j.1600-0447.2008.01326.x

Monastero, R., Mangialasche, F., Camarda, C., Ercolani, S., & Camarda, R. (2009). A systematic review of neuropsychiatric symptoms in mild cognitive impairment. *Journal of Alzheimer's Disease, 18*(1), 11-30. https://doi.org/10.3233/JAD-2009-1120

Moore, D. S., Ellis, R., Allen, P. D., Monroe, P. A., Cherry, K. E., O'Neil, C. E., & Wood, R. H. Construct validation of physical activity surveys in culturally diverse older adults. *Research Quarterly for Exercise and Sport, 79*(1), 42-50. https://doi.org/10.1080/02701367.2008.10599459

Morin C. M. (1993). *Insomnia: Psychological assessment and management*. Guilford Press. https://doi.org/10.1002/smi.2460100113

Morin, C. M., Hauri, P. J., Espie, C. A., Spielman, A. J., Buysse, D. J., & Bootzin, R. R. (1999). Nonpharmacologic treatment of chronic insomnia. *Sleep, 22*(8), 1134-1156. https://doi.org/10.1093/sleep/22.8.1134

Morin, C. M., Belleville, G., Bélanger, L., & Ivers, H. (2011). The insomnia severity index: Psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep, 34*(5)*,* 601-608. https://doi.org/10.1093/sleep/34.5.601

Musiek, E. S., Xiong, D. D., & Holtzman, D. M., (2015). Sleep, circadian rhythms, and the pathogenesis of Alzheimer Disease. *Experimental & Molecular Medicine, 47*, 1-8. https://doi.org/10.1038/emm.2014.121

National Academies of Sciences, Engineering, and Medicine. (2017). *Preventing cognitive decline and dementia: A way forward*. https://doi.org/10.17226/24782

Ngandu, T., Lehtisalo, J., Soloman, A., Levalahti, E., Ahtiluoto, S., Antikainen, R., Bäckman, L., Hänninen, T., Jula, A., Laatikainen, T., Lindström, J.,

Mangialasche, F., Paajen, T., Pajala, S., Peltonen, M., Rauramaa, R., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto, J.,… Kivipelto, M. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): A randomized controlled trial. *The Lancet*, *385*(9984), 2255-2263. https://doi.org/10.1016/S0140-6736(15)60461-5

Pariente, A., de Gage, S. B., Moore, N., & Bégaud, B. (2016). The benzodiazepine-dementia disorders link: Current state of knowledge. *CNS Drugs, 30*, 1–7. https://doi.org/10.1007/s40263-015-0305-4

Park, D. C., & Bischof, G. N. (2013). The aging mind: Neuroplasticity in response to cognitive training. *Dialogues in Clinical Neuroscience*, *15*(1), 109–119.

Parker, S. J., Strath, S. J., & Swartz, A.M. (2008). Physical activity measurement in older adults: Relationship with mental health. *Journal of Aging and Physical Activity, 16*(4), 369-380. https://doi.org/10.1123/japa.16.4.369

Patel, S. R., Zhu, X., Storfer-Isser, A., Mehra, R., Jenny, N. S., Tracy, R., & Redline, S. (2009). Sleep duration and biomarkers of inflammation. *Sleep, 32*(2), 200-204. https://doi.org/10.1093/sleep/32.2.200

Patterson, T. L., Lacro, J., McKibbin, C. L., Moscona, S., Hughs, T., & Jeste, D. V. (2002). Medication management ability assessment: Results from a performance-based measure in older outpatients with schizophrenia*. Journal of Clinical Psychopharmacology, 22*(1), 11-19. https://doi.org/10.1097/00004714-200202000-00003

Paul, S. S., Tiedemann, A., Hassett, L. M., Ramsay, E., Kirkham, C., Chagpar, S., & Sherrington, C. (2015). Validity of the Fitbit activity tracker for measuring steps in community-dwelling older adults. *British Journal of Sports Medicine*, *1*(1), 1-5. https://doi.org/10.1136/bmjsem-2015-000013

Peake, J. M., Kerr, G., & Sullivan, J. P. (2018). A critical review of consumer wearables, mobile applications, and equipment for providing biofeedback, monitoring stress, and sleep in physically active populations. *Frontiers in physiology*, *9*, 743. https://doi.org/10.3389/fphys.2018.00743

Peterson, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine, 256*(3), 183-194. https://doi.org/10.1111/j.1365-2796.2004.01388.x

Petersen, R. C. (2011). Clinical practice. Mild cognitive impairment*. New England Journal of Medicine, 364*(23), 2227-2234. https://doi.org/10.1056/NEJMcp0910237

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokmen, E. (1999). Mild cognitive impairment clinical characterization and outcome. *JAMA Neurology, 56*(3), 303-308. https://doi.org/10.1001/archneur.56.3.303

Petersen, R. C., Roberts, R. O., Knopman, D. S., Boeve, B. F., Geda, Y. E., Ivnik, R. J., Smith, G. E., & Jack Jr, C. R. (2009). Mild cognitive impairment: Ten years later. *JAMA Neurology, 66*(12), 1447-1455. https://doi.org/10.1001/archneurol.2009.266

Porter, V. R., Buxton, W. G., & Avidan, A. Y. (2015). Sleep, cognition, and dementia. *Current Psychiatry Report, 17*(12). https://doi.org/10.1007/s11920-015-0631-8

Prinz, P. N., Vitaliano, P. P., Vitiello, M. V., Bokan, J., Raskind, M., Peskind, E., & Gerber, C. (1982). Sleep, EEG and mental function changes in senile dementia of the Alzheimer's type. *Neurobiology of Aging*, *3*(4), 361-370. https://doi.org/10.1016/0197-4580(82)90024-0

Rapp, S., Brenes, G., & Marsh, A. P. (2002). Memory enhancement training for adults with mild cognitive impairment: A preliminary study. *Aging and Mental Health, 6*(1), 5-11. https://doi.org/10.1080/13607860120101077

Ravaglia, G., Forti, P., Lucicesare, A., Rietti, E., Pisacane, N., Mariani, E., & Dalmonte, E. (2008). Prevalent depressive symptoms as a risk factor for conversion to mild cognitive impairment in an elderly Italian cohort. *The American Journal of Geriatric Psychiatry, 16*(10), 834-843. https://doi.org/10.1097/JGP.0b013e318181f9b1

Rebok, G. W., Ball, K., Guey, L. T., Jones, R. N., Kim, H. Y., King, J. W., Marsiske, M., Morris, J. N., Tennstedt, S. L., Unverzagt, F. W. & Willis, S. L. (2014). Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *Journal of the American Geriatrics Society*, *62*(1), 16-24. https://doi.org/10.1111/jgs.12607

Richards, M., Hardy, R., & Wadsworth, M. E. J. (2003). Does active leisure protect cognition? Evidence from a national birth cohort. *Social Science and Medicine, 56*(4), 785-792. https://doi.org/10.1016/S0277-9536(02)00075-8

Roh, J. H., Huang, Y., Bero, A. W., Kasten, T., Stewart, F. R., Bateman, R. J., & Holtzman, D. M. (2012). Disruption of the sleep-wake cycle and diurnal fluctuation of β-amyloid in mice with Alzheimer's disease pathology. *Science Translational Medicine,* 4(150). https://doi.org/10.1126/scitranslmed.3004291

Rosas-Ballina, M., & Tracey, K. J. (2009). Cholinergic control of inflammation. *Journal of Internal Medicine, 265*(6), 663–679. https://doi.org/10.1111/j.1365-2796.2009.02098.x

Rosenberg, P. B., Johnston, D., & Lyketsos, C. G. (2006). A clinical approach to mild cognitive impairment. *The American Journal of Psychiatry, 163*(11), 1884-1890. https://doi.org/10.1176/ajp.2006.163.11.1884

Sabia, S., Dugravot, A., Dartigues, J., Abell, J., Elbaz, A., Kivimäki, M., & Singh-Manoux, A. (2017). Physical activity, cognitive decline, and risk of dementia: 28 year follow-up of Whitehall II cohort study. *BMJ Psychiatry, 357*, 1-12. https://doi.org/10.1136/bmj.j2709

Schafer, J. L., & Graham, J. W. (2002). Missing data: Our view of state of the art. *Psychological Methods, 7*(2), 147-177. https://doi.org/10.1037/1082-989X.7.2.147

Schmand, B., Eikelenboom, P., & van Gool, W. A. (2012). Value of diagnostic tests to predict conversion to Alzheimer's disease in young and old patients with amnestic mild cognitive impairment. *Journal of Alzheimer's Disease, 29*(3), 641-648. https://doi.org/10.3233/JAD-2012-111703

Schreiber, M. & Schneider, R. (2007). Cognitive plasticity in people at risk for dementia: Optimising the testing-the-limits-approach*. Aging and Mental Health*, *11*(1), 75-81. https://doi.org/10.1080/13607860600735887

Schutzer, K. A., & Graves, S. (2004). Barriers and motivations to exercise in older adults. *Preventative Medicine, 39*(5), 1056-1061. https://doi.org/10.1016/j.ypmed.2004.04.003

Sofi, F., Valecchi, D., Bacci, D., Abbate, R., Gensini, G. F., Casini, A., & Macchi, C. (2011). Physical activity and risk of cognitive decline: A meta-analysis of prospective studies. *Journal of Internal Medicine, 269*(1), 107-117. https://doi.org/10.1111/j.1365-2796.2010.02281.x

Spira, A. P., Gamaldo, A. A., An, Y., Wu, M. N., Simsonsick, E. M., Bilgel, M., Zhou, Y., Wong, D. F., Ferrucci, L., & Resnick, S. M. (2013). Self-reported sleep and β-amyloid deposition in community-dwelling older adults. *JAMA Neurology, 70*(12), 1537-1543. https://doi.org/10.1001/jamaneurol.2013.4258

Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *JAMA Internal Medicine, 166*(10), 1092-1097. https://doi.org/10.1001/archinte.166.10.1092

Stern, R. & White, T. (2003). *Neuropsychological Assessment Battery*. Psychological Assessment Resources.

Stewart, A. L., Mills, K. M., Sepsis, P. G., King, A. C., McLellan, B. Y., Roitz, K., & Ritter, P. L. (1997). Evaluation of CHAMPS, a physical activity promotion program for older adults. *Annals of Behavioral Medicine, 19*(4), 353–361. https://doi.org/10.1007/BF02895154

Stewart, A. L., Mills, K. M., King, A. C., Haskell, W. L., Gillis, D., & Ritter, P. L. (2001). CHAMPS physical activity questionnaire for older adults: Outcomes for interventions. *Medicine and Science in Sports and Exercise, 33*(7), 1126-1141. https://doi.org/10.1097/00005768-200107000-00010

Troyer, A. K., Murphy, K. J., Anderson, N. D., Moscovitch, M., & Craik, F. I. M. (2008). Changing everyday memory behaviour in amnestic mild cognitive impairment: A randomised controlled trial. *Neuropsychological Rehabilitation, 18*(1), 65-88. https://doi.org/10.1080/09602010701409684

Twamley, E. W., Vella, L., Burton, C. Z., Heaton, R. K., & Jeste, D. V. (2012). Compensatory cognitive training for psychosis: Effects in a randomized controlled trial. *Journal of Clinical Psychiatry, 73*(9), 1212-1219. https://doi.org/10.4088/JCP.12m07686

U.S. Department of Health and Human Services, Physical Activity Guidelines Advisory Committee (2018). *2018 Physical Activity Guidelines Advisory Committee scientific report.*

Van Den Berg, J. F., Van Rooij, F. J., Vos, H., Tulen, J. H., Hofman, A., Miedema, H. M., ... & Tiemeier, H. (2008). Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. *Journal of Sleep Research, 17*(3), 295-302. https://doi.org/10.1111/j.1365-2869.2008.00638.x

Verghese, J., LeValley, A., Derby, C., Kuslansky, G., Katz, M., Hall, C., Buschke, H., & Lipton, R. B. (2006). Leisure activities and the risk of amnestic mild cognitive impairment in the elderly. *Neurology, 66*(6), 821-827. https://doi.org/10.1212/01.wnl.0000202520.68987.48

Vinogradov, S., Fisher, M., & de Villers-Sidani, E. (2012). Cognitive training for impaired neural systems in neuropsychiatric illness. *Neuropsychopharmacology, 37*(1), 43-76. https://doi.org/10.1038/npp.2011.251

Vitiello, M. V. (2009). Recent advances in understanding sleep and sleep disturbances in older adults: Growing older does not mean sleeping poorly. *Current Directions in Psychological Science, 18*(6), 316-320. https://doi.org/10.1111/j.1467-8721.2009.01659.x

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., & Schnurr, P. P. (2013). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va. gov, *10*(4).

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale-Fourth Edition*. Pearson.

Westerberg, C. E., Mander, B. A., Florczak, S. M., Weintraub, S., Mesulam, M., Zee, P. C., & Paller, K. A. (2012). Concurrent impairments in sleep and memory in amnestic mild cognitive impairment. *Journal of the International*

Neuropsychological Society, 18(3), 490-500. https://doi.org/10.1017/S135561771200001X

Weuve, J., Kang, J. H., Manson, J. E., Breteler, M. M. B., Ware, J. H., & Grodstein, F. (2004). Physical activity, including walking, and cognitive function in older women. *JAMA, 292*(12), 1454-1461. https://doi.org/10.1001/jama.292.12.1454

Wilkinson, G. S. & Robertson, G. J.(2006). *Wide Range Achievement Test 4 Professional Manual*. Psychological Assessment Resources.

Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Koepke, K. M., Morris, J. N., Rebok, G. W., Unverzagt, F. W., Stoddard, A. M, & Wright, E. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *JAMA, 296*(23), 2805-2814. https://doi.org/10.1001/jama.296.23.2805

Wilson, R. S., Mendes de Leon, C. F., Barnes, L. L., Schneider, J. A., Bienias, J. L., Evans, D. A., & Bennett, D. A. (2002). Participation in cognitively stimulating activities and risk of incident Alzheimer disease. *JAMA, 287*(6), 742-748. https://doi.org/10.1001/jama.287.6.742

Wilson, R. S., Barnes, L., & Bennett, D. (2003). Assessment of lifetime participation in cognitively stimulating activities*. Journal of Clinical and Experimental Neuroscience*, *25*(5), 634- 642. https://doi.org/10.1076/jcen.25.5.634.14572

Wilson, R. S., Scherr, P. A., Schneider, J. A., Tang, Y., & Bennett, D. A. (2007). Relation of cognitive activity to risk of developing Alzheimer disease*. Neurology*, *69*(20), 1911-1920. https://doi.org/10.1212/01.wnl.0000271087.67782.cb

Wilson, R. S., Segawa, E., Boyle, P. A., & Bennett, D. A. (2012). Influence of late-life cognitive activity on cognitive health. *Neurology, 78*(15), 1123-1129. https://doi.org/10.1212/WNL.0b013e31824f8c03

Yaffe, K., Vittinghoff, E., Lindquist, K., Barnes, D., Covinsky, K. E., Neylan, T., Kluse, M., & Marmar, C. (2010). Posttraumatic stress disorder and risk of dementia among US veterans. *Archives of General Psychiatry, 67*(6), 608-613. https://doi.org/10.1001/archgenpsychiatry.2010.61

Yaffe, K., Falvey, C. M., Hoang, T. (2014). Connections between sleep and cognition in older adults. *Lancet Neurology, 13*(10), 1017-1028. https://doi.org/10.1016/S1474-4422(14)70172-3

Yu, P., Dean, R. A., Hall, S. D., Yuan, Q., Sethuraman, G., Willis, B. A., Siemers, E. R., Martenyi, F., Tauscher, J. T., & Schwarz, A. J. (2012). Enriching amnestic mild cognitive impairment populations for clinical trials: Optimal combination of biomarkers to predict conversion to dementia. *Journal of Alzheimer's Disease, 32*(2), 373-385. https://doi.org/10.3233/JAD-2012-120832