HHS Public Access

Author manuscript

Nurs Res. Author manuscript; available in PMC 2021 March 01.

Published in final edited form as:

Nurs Res. 2020 ; 69(2): 157–164. doi:10.1097/NNR.0000000000000420.

One Year of CPAP Adherence Improves Cognition in Older Adults with Mild Apnea and Mild Cognitive Impairment: A Secondary Analysis of Memories 1

Yanyan Wang, PhD [Research Associate],
University of Texas at Austin School of Nursing, Austin, TX & West China Hospital Sichuan University, Chengdu, China

Cynthia Cheng, PhD, MD [Associate Professor],
Thomas Jefferson University Department of Family and Community Medicine, Philadelphia, PA

Stephen Moelter, PhD [Associate Professor],
University of the Sciences Department of Psychology, Philadelphia, PA

Jamie L. Fuentecilla, PhD [Project Coordinator],
University of Texas at Austin School of Nursing, Austin, TX

Kelly Kincheloe, MSN, RN, FNP-C [Family Nurse Practitioner],
Comprehensive Sleep Medicine, Austin, TX

Alicia J. Lozano, MS [Research Associate],
Virginia Tech College of Science, Blacksburg, VA

Patricia Carter, PhD, RN [Associate Professor],
University of Texas at Austin School of Nursing, Austin, TX

Nalaka Gooneratne, MD [Associate Professor],
University of Pennsylvania School of Medicine, Philadelphia, PA

Kathy C. Richards, PhD, RN, FAAN [Research Professor]
University of Texas at Austin School of Nursing, Austin, TX

Abstract

Corresponding author: Kathy C. Richards, Ph.D., RN, FAAN, University of Texas at Austin School of Nursing, 1710 Red River St. Austin, TX 78712 (nu.krichards@austin.utexas.edu).
Yanyan. Wang, PhD, is Research Associate, **Jamie L. Fuentecilla, PhD**, is Research Coordinator in Memories 2, **Patricia Carter, PhD, RN**, is Associate Professor, and **Kathy C. Richards, PhD, RN, FAAN**, is Research Professor, University of Texas at Austin School of Nursing, Austin, TX.
Yanyan. Wang, PhD, was Associate Professor, West China Hospital, Sichuan University, Chengdu, Sichuan Province, China.
Cynthia Cheng, PhD, MD, is Associate Professor, Thomas Jefferson University, Philadelphia, PA.
Stephen Moelter, PhD, is Associate Professor, University of the Sciences in Philadelphia, Philadelphia, PA.
Kelly Kincheloe, MSN, RN, FNP-C, is Family Nurse Practitioner, Comprehensive Sleep Medicine Associates, Austin, TX.
Alicia J. Lozano, MS, is Research Associate, College of Science, Virginia Tech, Blacksburg, VA
Nalaka Gooneratne, MD, is Associate Professor, School of Medicine, University of Pennsylvania, Philadelphia, PA.

The authors have no conflicts of interest to report.

Ethical Conduct of Research: All procedures were approved by the institutional review boards at George Mason University and University of Pennsylvania.

Clinical Trial Registration: Clinicaltrials.gov NCT01482351, registered on November 30, 2011, the first participant was enrolled on September 1, 2012, link: https://clinicaltrials.gov/ct2/show/NCT01482351?term=NCT01482351&rank=1

Background: Mild cognitive impairment frequently represents a predementia stage of Alzheimer's disease. Although obstructive sleep apnea is increasingly recognized as a common comorbidity of mild cognitive impairment, most apnea research has focused on middle-aged adults with moderate to severe obstructive sleep apnea. Mild obstructive sleep apnea, defined as 5–14 apneas or hypopneas per hour slept, is common in older adults. Little is known about the effect on cognition of adherence to continuous positive airway pressure (CPAP) treatment of obstructive sleep apnea in older adults with mild obstructive sleep apnea and mild cognitive impairment.

Objective: The objective was to explore the effect of CPAP adherence on cognition in older adults with mild obstructive sleep apnea and mild cognitive impairment.

Methods: We conducted a secondary analysis of data from Memories 1, a 1-year quasi-experimental clinical trial on the effect of CPAP adherence in older adults with mild cognitive impairment mild cognitive impairment and obstructive sleep apnea. Those with mild obstructive sleep apnea were divided into two groups based on their CPAP adherence over 1 year: 1) CPAP adherent group (mild cognitive impairment+CPAP) with average CPAP use ≥ 4 hr per night; and 2) CPAP nonadherent group (mild cognitive impairment+-CPAP) with average CPAP use < 4 hr per night. Individuals currently using CPAP were not eligible. A CPAP adherence intervention was provided for all participants, and an attention control intervention was provided for participants who chose to discontinue CPAP use during the 1-year follow-up. Descriptive baseline analyses, paired *t*-tests for within-group changes, and general linear and logistic regression models for between-group changes were conducted.

Results: Those in the mild cognitive impairment + CPAP group compared to the mild cognitive impairment − CPAP group demonstrated a significant improvement in psychomotor/cognitive processing speed, measured by the Digit Symbol Coding Test. Eight participants improved on the Clinical Dementia Rating scale, whereas six worsened or were unchanged. Twelve participants rated themselves as improved on the Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change Scale, whereas three reported their status as worsened or unchanged. The mild cognitive impairment+CPAP group had greater than an 8-fold increased odds of improving on the CDR and greater than a 9-fold increased odds of improving on the Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change Scale, compared to the mild cognitive impairment-CPAP group.

Discussion: CPAP adherence may be a promising intervention for slowing cognitive decline in older adults with mild obstructive sleep apnea and mild cognitive impairment. A larger, adequately powered study is needed.

Keywords

cognition; continuous positive airway pressure; mild cognitive impairment; obstructive sleep apnea

Obstructive sleep apnea (OSA) is characterized by repeated upper airway collapse and/or narrowing that can result in hypoxia and fragmented sleep (Peppard et al., 2013). Continuous positive airway pressure (CPAP), a positive pressure device placed over the mouth and/or nose during sleep, opens the airway, restores oxygenation, and improves sleep. CPAP must be consistently adhered to for efficacy (Wang et al., 2019). The long-term effects of untreated OSA often include impaired cognition, decreased mood and poor quality of life

(Peppard et al., 2013). A growing body of evidence suggests that OSA may accelerate cognitive decline through multiple mechanisms related to OSA severity, such as level of hypoxia and severity of sleep fragmentation (Olaithe, Bucks, Hillman, & Eastwood, 2018). OSA severity is categorized based on the number of obstructive breathing events per hour slept via the apnea hypopnea index (AHI), according to the following criteria: mild, AHI 5–14; moderate, AHI 15–29; and severe, AHI ≥30. Current research focuses primarily on individuals with moderate to severe OSA with 15% of males and 5% of females in North America demonstrating an AHI ≥15 (Young et al., 2009). However, when mild OSA cases are included, the prevalence nearly doubles to 20–30% in men and 10–15% in women, a statistic that demonstrates widespread, and likely under-recognized mild OSA (Young et al., 2009).

Old age is a major risk factor for OSA, however, most prevalence studies and clinical trials are conducted in middle-aged adults with moderate to severe OSA, so little is known about the consequences of untreated mild OSA in older adults, especially in those experiencing mild cognitive impairment (Braley et al., 2018). Mild cognitive impairment (MCI), particularly amnestic MCI, often represents a pre-dementia stage of Alzheimer's Disease, and individuals with OSA are 26% more likely to develop cognitive impairment (Leng, McEvoy, Allen, & Yaffe, 2017; Wilson et al., 2014). We have recently reported a significant positive effect on cognition of adherence to CPAP in older adults with MCI and mild, moderate, and severe OSA (AHI ≥ 10) in Memories 1, a 1-year quasi-experimental trial (Richards et al., 2019), but we did not examine cognitive outcomes related to OSA severity. The purpose of this secondary analysis was to explore the effects of CPAP adherence in cognitively impaired older adults with mild apnea. Little is known about whether CPAP adherence affects cognition and delays progression to Alzheimer's disease in older adults with mild OSA.

Methods

Study Design

We conducted a secondary analysis of Memories 1 data (Richards et al., 2019), including only those participants with mild OSA. Memories 1 was a prospective, quasi-experimental pilot clinical trial that aimed to examine the effect of 1 year of CPAP adherence (≥ 4 hours mean CPAP use over 1 year) on cognitive and everyday function in CPAP naïve older adults with MCI and OSA. In the present study, 17 participants with mild OSA (AHI 10–14) were drawn from the original larger sample: 1) CPAP adherent group (mild MCI+CPAP, ≥4 hr mean CPAP use per night for 1 year, n=7); and 2) MCI, OSA, CPAP non-adherent group (mild MCI-CPAP, <4 hr mean CPAP use per night for 1 year, n=10). The study was approved by the Institutional Review Boards of George Mason University and University of Pennsylvania and registered with ClinicalTrials.gov. Each participant signed an IRB approved consent form granting permission for secondary analysis of their data.

Inclusion and Exclusion

Included subjects were aged 55–89 years; mild OSA; and amnestic MCI (Petersen et al., 1999) which requires five clinical criteria (a) memory complaint, identified as a change from

previous memory, verified by an informant, (b) memory impairment 1.5 standard deviations below normal on the Logical Memory II test, (c) not impaired general cognition (Mini-Mental State Examination, MMSE ≥ 24), (d) cognitive impairment without any repercussions on activities of daily living, and (e) clinical dementia rating (CDR) of 0–0.5 (Rosness, Haugen, & Engedal, 2011)); as well as stable medications; not severe depressed (score of ≤ 28 on the 21-item Beck Depression Inventory II, BDI-II); and had a study partner defined as an informant who lives with the participant or keeps contact with the participant at least 3 times per week. Those with significant neurologic disease, psychiatric disorders, dementia diagnoses, unstable medical conditions, and currently using CPAP were excluded.

Mild OSA Diagnosis

Participants received either a two-night diagnostic and therapeutic polysomnography (PSG), or a split-night diagnostic and CPAP titration PSG in an accredited sleep laboratory for OSA diagnosis. Some participants also had an unattended home sleep study using the Apnea Risk Evaluation System (ARES) (Ayappa et al., 2008). A sleep physician analyzed the results according to the methods and standards of the American Academy of Sleep Medicine (Kapur et al., 2017).

Intervention

CPAP, a form of positive airway pressure ventilation, keeps the airways open during sleep. During titration PSG, an optimal CPAP pressure was identified that normalized the AHI; eliminated snoring, desaturation, and arousals; and restored a normal airflow contour (Kushida et al., 2008). Thus, CPAP treats OSA effectively, but it requires consistent use for at least 4 hours per night (Dzierzewski et al., 2016).

Adherence

Participants received a CPAP adherence intervention from trained project staff, consisting of: (a) OSA education, treatment expectations, and ways to minimize barriers and facilitate CPAP use, (b) promotion of a positive initial CPAP experience, (c) motivational interviewing to reinforce participants' health-related goals and CPAP self-efficacy, (d) anticipatory guidance and follow-up of common CPAP problems, and (e) social support by a study partner. If, at any time during the 1-year study, participants chose to discontinue CPAP, project staff provided an Attention Control Intervention, consisting of health information and conversation, with approximately the same project staff contact and interactions as the CPAP Adherence Intervention. During the 1-year study, hidden sensors in the CPAP units continuously collected data and metadata including precise hours of adherence to prescribed therapy. We defined CPAP adherence as average use of 4 or more hours per night over the 1-year study (Sawyer et al., 2011).

Outcomes and Measures

We chose the cognitive function measures because: (a) they have shown improvement and/or slower cognitive decline after treatment of OSA in other populations (Ancoli-Israel et al., 2008), (b) they have an attention and memory component, and they have been shown to be sensitive to sleep changes, (c) it was expected that older adults with MCI and OSA would

show impairment at baseline and could worsen during the 1-year follow-up, and (d) they were less likely to have floor or ceiling effects. The neuropsychological testers were blinded to participants' adherence and collected outcomes in interviews at baseline and 1 year.

Primary: 1) Memory. Total recall on the Hopkins Verbal Learning Test–Revised (HVLT-R) represented memory. Test–retest reliability was 0.74 (Benedict, Schretlen, Groninger, & Brandt, 1998), and validity was established by a criterion score between 19 and 20 on total recall, with 94% sensitivity and 100% specificity for Alzheimer's disease (Hogervorst et al., 2002). **2) Psychomotor/cognitive processing speed**. The Digit Symbol subtest (DS) from the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) age-adjusted total scaled score (Shirk et al., 2011) was used. Test-retest reliability ranges from 0.85 to 0.90 (Snow, Tierney, Zorzitto, Fisher, & Reid, 1989).

Secondary: 1) Global Cognition. The Montreal Cognitive Assessment (MoCA) represented global cognition. Test-retest reliability was 0.92, and internal consistency was 0.83 (Nasreddine et al., 2005), with 90% sensitivity for MCI (Saczynski et al., 2015). **2) Daytime Sleepiness**. The Epworth Sleepiness Scale (ESS) was used. Respondents are asked to rate the likelihood of falling asleep in different activities. Test-retest reliability was 0.82 and internal consistency was 0.88 (Johns, 1992). **3) Everyday function**. The study-partner used Everyday Cognition (ECog) scale. The ECog reflects cognitively mediated functional abilities. Test-retest reliability was 0.82, and correlations with MMSE, the Clinical Dementia Rating Scale (CDR), and Blessed Dementia Rating Scale were 0.67, 0.74, and 0.74 (Farias et al., 2008). **4) Global progression**. The Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change Scale (ADCS-CGIC) (Schneider et al., 1997) was used. This scale, developed to reveal clinical change according to self and informants, has shown treatment-related effects in recent dementia studies (Barone et al., 2008; Winblad et al., 2007). **5) Progression**. The CDR was used to assess 1-year cognitive progression. The CDR has demonstrated strong inter-rater reliability (kappa values 0.77–1.00 for 6 domains and 0.95 for global rating) and test-retest reliability (kappa values 0.75–1.00 for 6 domains and 0.80 for global rating) (Nyunt et al., 2013).

Sample Size

The sample size estimation for the Memories 1 trial was based on the calculations for the primary endpoints, and no specific post-hoc power estimate was done for the current exploratory secondary analysis. Due to the small sample size available to us (N=17), we can only detect statistically significant large effects. We recognize that due to lack of power this study may generate clinically meaningful effects that are statistically insignificant.

Statistical Analysis

Descriptive statistics were used to characterize the overall sample at baseline and by adherence groups (MCI-CPAP and MCI+CPAP). To assess differences in baseline characteristics between the MCI-CPAP and MCI+CPAP adherence groups, Fisher's exact tests were used for categorical variables; two-sample t-tests were used for comparisons in continuous variables across the two groups. Within-group changes in outcomes from baseline to 1 year were assessed and evaluated for significance using paired t-tests. Change

from baseline to 1 year was examined using unadjusted general linear models for each outcome, where the predictor of interest was adherence group. Using results from the unadjusted general linear models, between-group effect sizes were calculated as the least square mean estimates divided by the mean square error. Finally, separate unadjusted logistic regression models were used to quantify the effect of adherence group on the odds of improvement on the CDR and ADCS-CGIC at 1 year. All statistical tests were two sided, and a P value less than or equal to 0.05 was considered statistically significant. Analyses were performed with SAS software (version 9.4, SAS Institute, Cary, NC).

Results

Sixty-eight participants with MCI+OSA comprised the sample for Memories 1, and 17 of these had mild OSA (mean AHI 12.0 ± 1.87) and were included in this secondary analysis (mean age = 72.1 ± 8.88 yr; 52.9% women; MCI-CPAP = 10, and MCI+CPAP = 7). With the exception of antidepressant use (p=0.01) and PSG whole night baseline lowest oxygen saturation (p=0.02), there were no statistically significant differences in baseline demographics, clinical, cognitive, medications, and sleep characteristics between the mild OSA MCI-CPAP and MCI+CPAP groups (Table 1). We did not adjust for lowest oxygen saturation, given the pilot nature of the study, and the small number of participants. Also, due to the lack of significant difference in depression scores as measured by the the BDI-II, we did not adjust for antidepressant use.

From baseline to 1 year, the MCI+CPAP group showed a statistically significant, clinically relevant increase in psychomotor/cognitive processing speed (DS) (change=1.90, p=0.04), and clinically relevant improvement in daytime sleepiness (ESS) (change= −3.14) without statistical significance (p=0.10). No other within-group changes for memory (HVLT), global cognition (MoCA), and everyday function (ECog) were statistically significant (Table 2).

In the unadjusted general linear models, in the MCI+CPAP group versus the MCI-CPAP group at 1 year, psychomotor/cognitive processing speed (DS) was significantly improved (Parameter Estimate = 1.94, SE = 0.70, 95% CI = 0.44–3.44, $p = 0.01$) with a large effect size (ES) of 1.40. No other variables were statistically significant (Table 3). Unadjusted logistic regression model results are summarized in Table 4. At the 1-year follow-up, 8 participants were improved on the CDR, but 6 were worsened or unchanged. Data for 3 participants were missing, because we could not contact their study partners prior to study closure. The MCI+CPAP group had an over 8-fold increase in odds for improvement on the CDR in comparison with the MCI-CPAP group (OR = 8.33, 95% CI = 0.63–110.00, $p = 0.11$). Twelve participants were self-rated as improved on ADCS-CGIC over 1 year, whereas three rated themselves worsened or unchanged. Data were missing on two participants. The MCI+CPAP group demonstrated an over 9-fold increased odds of improving on the self-rated ADCS-CGIC as compared to the MCI-CPAP group (OR = 9.55, 95% CI = 0.33–278.83, $p = 0.19$). Although the present findings are not statistically significant, they are clinically important.

Discussion

The current study demonstrated that CPAP adherence for 1 year, compared to a non-adherent comparison group, significantly improved psychomotor/cognitive processing speed and attention, in older adults with MCI and mild OSA. Moreover, while not statistically significant in this pilot study, CPAP adherence showed a near significant trend for delaying progression of cognitive decline based on the CDR and self-rated ADCS-CGIC.

A recent meta-analysis in a predominantly middle-aged sample of the effect of CPAP on several cognitive domains showed a small treatment effect on a single cognitive domain, attention, (mean effect size = 0.19) (Kylstra et al., 2013). In contrast to the studies in the meta-analysis, our research focused on a homogeneous sample of older adults with MCI who are more likely to experience a trajectory of cognitive decline, and we followed them for a longer period, one year. Our finding of improved psychomotor/cognitive processing speed is consistent with a recent systematic review that supported information processing speed as a distinct cognitive domain affected by OSA (Kilpinen et al., 2014).

Strengths of this research were a focus on the understudied and prevalent mild OSA population, an extended 1-year follow-up period, and equal attention from project staff to both adherence groups. However, there are a number of limitations. This was an exploratory secondary analysis of a subsample of an existing dataset from Memories 1, and the sample size was only 17. We were not powered to correct for multiple comparisons, or small effects. Thus, any significant findings are likely to be quite clinically relevant. This study used data from three different types of clinical sleep studies for baseline group comparisons. While using clinical sleep study data was pragmatic, and reflected current sleep medicine practice, future, larger studies should standardize sleep diagnostic methods and oxygen saturation variables to allow for more accurate baseline comparisons of the CPAP adherent and the CPAP nonadherent groups. For example, groups should be compared on degree of hypoxemia, as measured by time below 90% and/or 80% oxygen saturation, and any differences should be controlled for in subsequent analysis.

Furthermore, this was not a randomized controlled clinical trial, and the adherent and non-adherent groups might have differed on unknown variables' effects on study outcomes. However, we strongly believe that alternative longitudinal designs for randomized controlled clinical trials incorporating wait-list controls, placebo CPAP, or withdrawal of CPAP, may place older adults with cognitive impairment at increased risk and should be avoided. A survey of geriatricians conducted by our team revealed that the majority would not refer their patients for a placebo-controlled (sham) sleep apnea study for a one-year period due to their concerns regarding untreated sleep apnea, thus we elected to use the current study design.

Future, larger studies should incorporate neuroimaging outcomes, including amyloid and tau positive emission tomography (PET) scans, and examine potential mechanisms for changes in cognition in older adults with mild OSA and MCI, such as white matter hyperintensity volume, sleep fragmentation, and blood pressure. Also, whether a longer nighttime CPAP use, e.g. 6 or 8 hours, has a stronger effect on study outcomes should be examined.

Conclusion

A year of CPAP adherence significantly improved psychomotor/cognitive processing speed in older adults with MCI and mild OSA and shows promise for slowing progression to Alzheimer's disease. A large, definitive trial is needed to confirm our findings, and to examine potential mechanisms for the relationships among mild OSA, CPAP adherence, and cognitive decline.

Acknowledgement:

Research reported in this publication was supported by the National Institutes of Health, National Institute on Aging under Award Numbers NIH-NIA R01AG034682 and NIH-NIA R01AG054435.

References

Ayappa I, Norman RG, Seelall V, & Rapoport DM (2008). Validation of a self-applied unattended monitor for sleep disordered breathing. Journal of Clinical Sleep Medicine, 4, 26–37. [PubMed: 18350959]

Ancoli-Israel S, Palmer BW, Cooke JR, Corey-Bloom J, Fiorentino L, Natarajan L, Liu L, Ayalon L, He F, & Loredo JS (2008). Cognitive effects of treating obstructive sleep apnea in Alzheimer's disease: A randomized controlled study. Journal of the American Geriatrics Society, 56, 2076–2081. 10.1111/j.1532-5415.2008.01934.x [PubMed: 18795985]

Barone P, Burn DJ, van Laar T, Hsu C, Poewe W, & Lane RM (2008). Rivastigmine versus placebo in hyperhomocysteinemic Parkinson's disease dementia patients. Movement Disorders, 23, 1532–1540. 10.1002/mds.21997 [PubMed: 18581467]

Benedict RHB, Schretlen D, Groninger L, & Brandt J (1998). Hopkins Verbal Learning Test-Revised: Normative Data and Analysis of Inter-Form and Test-Retest Reliability. Clinical Neuropsychologist, 12, 43–55.

Braley TJ, Dunietz GL, Chervin RD, Lisabeth LD, Skolarus LE, & Burke JF (2018). Recognition and diagnosis of obstructive sleep apnea in older Americans. J Am Geriatr Soc, 66, 1296–1302. [PubMed: 29744855]

Dzierzewski JM, Wallace DM, & Wohlgemuth WK (2016). Adherence to continuous positive airway pressure in existing users: Self-efficacy enhances the association between continuous positive airway pressure and adherence. J Clin Sleep Med, 12, 169–176. [PubMed: 26350607]

Farias ST, Mungas D, Reed BR, Cahn-Weiner D, Jagust W, Baynes K, & Decarli C (2008). The measurement of everyday cognition (ECog): Scale development and psychometric properties. Neuropsychology, 22, 531–544. [PubMed: 18590364]

Hogervorst E, Combrinck M, Lapuerta P, Rue J, Swales K, & Budge M (2002). The Hopkins Verbal Learning Test and screening for dementia. Dement Geriatr Cogn Disord, 13, 13–20. 10.1159/000048628 [PubMed: 11731710]

Johns MW (1992). Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep, 15, 376–381. [PubMed: 1519015]

Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, & Harrod CG (2017). Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med, 13, 479–504. 10.410.5664/jcsm.6506 [PubMed: 28162150]

Kilpinen R, Saunamaki T, & Jehkonen M (2014). Information processing speed in obstructive sleep apnea syndrome: A review. Acta Neurol Scand, 129, 209–218. 10.210.1111/ane.12211 [PubMed: 24372161]

Kushida CA, Chediak A, Berry RB, Brown LK, Gozal D, Iber C, … Rowley JA (2008). Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. J Clin Sleep Med, 4, 157–171. [PubMed: 18468315]

Kylstra WA, Aaronson JA, Hofman WF, & Schmand BA (2013). Neuropsychological functioning after CPAP treatment in obstructive sleep apnea: A meta-analysis. Sleep Med Rev, 17, 341–347. 10.310.1016/j.smrv.2012.1009.1002 [PubMed: 23063416]

Leng Y, McEvoy CT, Allen IE, & Yaffe K (2017). Association of sleep-disordered breathing with cognitive function and risk of cognitive impairment: A systematic review and meta-analysis. JAMA Neurol, 74, 1237–1245. 10.1210.1001/jamaneurol.2017.2180 [PubMed: 28846764]

Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, … Chertkow H (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc, 53, 695–699. 10.610.1111/j.1532-5415.2005.53221.x [PubMed: 15817019]

Nyunt MS, Chong MS, Lim WS, Lee TS, Yap P, & Ng TP (2013). Reliability and validity of the clinical dementia rating for community-living elderly subjects without an informant. Dement Geriatr Cogn Dis Extra, 3, 407–416. 10.410.1159/000355122 [PubMed: 24348502]

Olaithe M, Bucks RS, Hillman DR, & Eastwood PR (2018). Cognitive deficits in obstructive sleep apnea: Insights from a meta-review and comparison with deficits observed in COPD, insomnia, and sleep deprivation. Sleep Med Rev, 38, 39–49. 10.1016/j.smrv.2017.03.005 [PubMed: 28760549]

Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, & Hla KM (2013). Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol, 177, 1006–1014. [PubMed: 23589584]

Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, & Kokmen E (1999). Mild cognitive impairment: clinical characterization and outcome. Arch Neurol, 56, 303–308. [PubMed: 10190820]

Richards KC, Gooneratne N, Dicicco B, Hanlon A, Moelter S, Onen F, … Johnson J (2019). CPAP adherence may slow 1-year cognitive decline in older adults with mild cognitive impairment and apnea. J Am Geriatr Soc, 67, 558–564. doi: 10.510.1111/jgs.15758 [PubMed: 30724333]

Rosness TA, Haugen PK, & Engedal K (2011). The clinical dementia rating scale could be helpful in differentiating frontotemporal dementia from Alzheimer's disease. Int J Geriatr Psychiatry, 26, 879–880. 10.810.1002/gps.2555 [PubMed: 21744389]

Saczynski JS, Inouye SK, Guess J, Jones RN, Fong TG, Nemeth E, … Marcantonio ER (2015). The Montreal Cognitive Assessment: Creating a crosswalk with the Mini-Mental State Examination. J Am Geriatr Soc, 63, 2370–2374. 10.2310.1111/jgs.13710 [PubMed: 26503296]

Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, & Weaver TE (2011). A systematic review of CPAP adherence across age groups: Clinical and empiric insights for developing CPAP adherence interventions. Sleep Med Rev, 15, 343–356. 10.310.1016/j.smrv.2011.1001.1003 [PubMed: 21652236]

Schneider LS, Olin JT, Doody RS, Clark CM, Morris JC, Reisberg B, … Ferris SH (1997). Validity and reliability of the Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change. The Alzheimer's Disease Cooperative Study. Alzheimer Dis Assoc Disord, 11, S22–S32.

Shirk SD, Mitchell MB, Shaughnessy LW, Sherman JC, Locascio JJ, Weintraub S, & Atri A (2011). A web-based normative calculator for the uniform data set (UDS) neuropsychological test battery. Alzheimers Res Ther, 3, 32 10.1186/alzrt1194 [PubMed: 22078663]

Snow WG, Tierney MC, Zorzitto ML, Fisher RH, & Reid DW (1989). WAIS-R test-retest reliability in a normal elderly sample. J Clin Exp Neuropsychol, 11, 423–428. 10.410.1080/01688638908400903. [PubMed: 2760178]

Wang G, Goebel JR, Li C, Hallman HG, Gilford TM, & Li W (2019). Therapeutic effects of CPAP on cognitive impairments associated with OSA. J Neurology, 10.1007/s00415-019-09381-2

Wechsler D (1981). Manual for the Wechsler Adult Intelligence Scale, Revised. Psychological Corporation, San Antonio, Texas.

Wilson G, Terpening Z, Wong K, Grunstein R, Norrie L, Lewis SJ, & Naismith SL (2014). Screening for sleep apnoea in mild cognitive impairment: The utility of the multivariable apnoea prediction index. Sleep Disord, 2014, 945287 10.1155/2014/945287 [PubMed: 24551457]

Winblad B, Cummings J, Andreasen N, Grossberg G, Onofrj M, Sadowsky C, … Lane R (2007). A six-month double-blind, randomized, placebo-controlled study of a transdermal patch in

Alzheimer's disease—Rivastigmine patch versus capsule. Int J Geriatr Psychiatry, 22, 456–467. 10.410.1002/gps.1788 [PubMed: 17380489]

Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, & Hla KM (2009). Burden of sleep apnea: Rationale, design, and major findings of the Wisconsin Sleep Cohort study. WMJ, 108, 246–249. [PubMed: 19743755]

Table 1

Demographics, clinical, and sleep characteristics of study groups at baseline

Variable	Mild OSA						
	Total (*n* = 17)		MCI+CPAP (*n* = 7)		MCI-CPAP (*n* = 10)		*p*-value
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	
Age	72.1	8.88	68.4	6.60	74.6	9.67	0.14
Sex, female, n (%)[a]	9 (52.9)		2 (28.6)		7 (70.0)		0.15
Race, white, n (%)[a]	10 (58.8)		5 (71.4)		5 (50.0)		0.62
Education, > high school, n (%)[a]	9 (52.9)		4 (57.1)		5 (50.0)		0.14
Married/cohabitate, n (%)[a]	9 (52.9)		6 (85.7)		3 (30.0)		0.07
BMI	29.4 *(n=16)*	6.73	30.0 *(n=6)*	3.30	29.1	8.31	0.78
Diabetes, n (%)[a]	6 (35.3)		3 (42.9)		3 (30.0)		0.64
Cardiovascular disease, n (%)[a]	7 (41.2)		3 (42.9)		4 (40.0)		>0.99
Hypertension, n (%)[a]	9 (52.9)		4 (57.1)		5 (50.0)		>0.99
APOE4, n (%)[a]	4 (23.5)		1 (14.3)		3 (30.0)		0.60
Cholinesterase inhibitors, n (%)[a]	1 (5.9)		0 (0.0)		1 (10.0)		>0.99
Opioid Analgesic, n (%)[a]	2 (11.8)		0 (0.0)		2 (20.0)		0.49
Antidepressants, n (%)[a]	4 (23.5)		4 (57.1)		0 (0.0)		0.01
Sedative/anxiolytics, n (%)[a]	5 (29.4)		2 (28.6)		3 (30.0)		>0.99
Antihypertensives, n (%)[a]	11 (64.7)		3 (42.9)		8 (80.0)		0.16
MoCA	23.7	3.58	23.9	3.02	23.6	4.09	0.88
BDI-II	6.8	5.54	8.0	3.65	5.9	6.61	0.42
ESS	9.4	4.17	9.6	2.88	9.2	5.03	0.85
Self-report Nighttime Sleep duration (hours)	7.2	1.78	7.6	2.15	6.9	1.52	0.49
Self-report Nighttime Number of awakenings	3.6 *(n=15)*	2.47	4.4	2.30	2.9 *(n=8)*	2.53	0.24
ARES baseline sleep[b]							
Apnea-hypopnea index	11.0 *(n=3)*	1.73	*(n=0)*		11.0 *(n=3)*	1.73	--
Lowest oxygen saturation	81.3 *(n=3)*	1.77	*(n=0)*		81.3 *(n=3)*	1.77	--
PSG whole night baseline							
Apnea-hypopnea index	11.9 *(n=8)*	1.74	11.9 *(n=6)*	2.05	11.7 *(n=2)*	0.42	0.80
Lowest oxygen saturation	86.6 *(n=8)*	5.21	88.8 *(n=6)*	3.82	80.0 *(n=2)*	0.00	0.02
PSG split night baseline							
Apnea-hypopnea index	11.7 *(n=6)*	1.90	12.8 *(n=1)*	0.00	11.5 *(n=5)*	2.03	0.59
Lowest oxygen saturation	82.3 *(n=6)*	6.22	87.0 *(n=1)*	0.00	81.4 *(n=5)*	6.47	0.47

Note. MCI = Mild cognitive impairment; +CPAP = Continuous Positive Airway Pressure adherent defined as mean use≥4 hours/night; -CPAP = Continuous Positive Airway Pressure non-adherent defined as mean use <4 hours/night; BMI = Body Mass Index; APOE = Apolipoprotein; MoCA = Montreal cognitive assessment; BDI = Beck Depression Inventory; ESS = Epworth Sleepiness Scale.

The *p*-values are for comparisons between the +CPAP and -CPAP groups.

[a] Percentages are derived using column total in sample.

[b] Source PSG data for AHI and oxygen saturation were missing for 3 participants, we report their ARES data.

Table 2

Descriptive statistics and within group changes in cognitive and everyday function from baseline to 1 year

Cognitive and Everyday Function	Baseline				1 year							
	MCI+CPAP (*n* = 7)		MCI-CPAP (*n* = 10)		MCI+CPAP (*n* = 7)				MCI-CPAP (*n* = 10)			
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	Change	*p*-value	*Mean*	*SD*	Change	*p*-value
Cognition												
Memory HVLT	24.0	5.23	20.3	6.29	22.7	7.54	−1.29	0.42	22.8 *(n=8)*	4.80	1.56 *(n=8)*	0.44
Psychomotor/Cognitive Processing DS	8.0	3.59	8.8	3.47	9.9	3.87	1.90	0.04	8.9 *(n=9)*	3.66	−0.04 *(n=9)*	0.88
Global Cognition MoCA	23.9	3.02	23.6	4.09	24.0	2.58	0.14	0.92	24.7 *(n=9)*	2.78	0.94 *(n=9)*	0.31
Daytime Sleepiness ESS	9.6	2.88	9.2	5.03	6.4	3.15	−3.14	0.10	7.0 *(n=9)*	3.00	−1.79 *(n=9)*	0.17
Everyday Function												
ECog	1.5 *(n=6)*	0.43	1.4	0.58	1.7 *(n=5)*	0.83	0.11 *(n=5)*	0.67	1.5 *(n=9)*	0.82	0.15 *(n=9)*	0.28

Note. MCI = mild cognitive impairment; +CPAP = Continuous Positive Airway Pressure adherent defined as mean use ≥ 4 hours/night; -CPAP = Continuous Positive Airway Pressure non-adherent defined as mean use <4 hours/night; HVLT = Hopkins Verbal Learning Test; DS = Digit Symbol; MoCA = Montreal Cognitive Assessment; ESS = Epworth Sleepiness Scale; ECog = Everyday Cognition.

Change indicates within-group change from baseline to 1 year. The *p*-values rely on comparisons within the +CPAP and -CPAP groups.

Table 3

Unadjusted general linear model results for changes in cognitive and everyday function from baseline to 1 year

Dependent Variable: Cognitive and Everyday Function		Adherence Group (MCI+CPAP *vs.* MCI-CPAP)	Between-Group *p*-value	Between-Group Effect Size[†]
Cognition				
HVLT			0.39	0.47
	PE	−2.16		
	SE	2.40		
	95% CI	[−7.35, 3.03]		
DS			0.01	1.40
	PE	1.94		
	SE	0.70		
	95% CI	[0.44, 3.44]		
MoCA			0.63	0.25
	PE	−0.75		
	SE	1.52		
	95% CI	[−4.01, 2.52]		
ESS			0.46	0.38
	PE	−1.59		
	SE	2.10		
	95% CI	[−6.09, 2.92]		
ECog			0.82	0.13
	PE	−0.06		
	SE	0.25		
	95% CI	[−0.60, 0.48]		

Note. MCI = mild cognitive impairment; +CPAP = Continuous Positive Airway Pressure adherent defined as mean use ≥ 4 hours/night; -CPAP = Continuous Positive Airway Pressure non-adherent defined as mean use <4 hours/night; HVLT = Hopkins Verbal Learning Test; DS = Digit Symbol; MoCA = Montreal Cognitive Assessment; ESS = Epworth Sleepiness Scale; ECog = Everyday Cognition; PE = parameter estimate; SE = standard error; 95% CI = 95% confidence interval.

[†]Effect sizes generated from unadjusted general linear models for change from baseline to 1 year. The p-values are for comparisons between the +CPAP and -CPAP groups.

Table 4

Unadjusted Logistic Regression Model Results for Improvement on the Clinical Dementia Rating (CDR) and the Alzheimer's Disease Cooperative Study Clinical Global Impression of Change Scale (ADCS-CGIC) at 1 year

	Adherence Group (MCI+CPAP *vs*. MCI-CPAP)
CDR (Improved N=8 *vs*. Unimproved N=6)	
OR	8.33
(95% CI)	[0.63, 110.00]
p-value	0.11
ADCS Self (Improved N=12 vs. Unimproved N=3)	
OR	9.55
(95% CI)	[0.33, 278.83]
p-value	0.19
ADCS Partner (Improved N=6 *vs*. Unimproved N=7)	
OR	2.50
(95% CI)	[0.25, 24.72]
p-value	0.43

Note. MCI = mild cognitive impairment; +CPAP = Continuous Positive Airway Pressure adherent defined as mean use ≥ 4 hours/night; -CPAP = Continuous Positive Airway Pressure non-adherent defined as mean use <4 hours/night; CDR = Clinical Dementia Rating; ADSC = Alzheimer's Disease Cooperative Study. Reference group for dependent variable is Unimproved (Worsening/Unchanged) at 1 year. OR = Odds Ratio; 95% CI = 95% Confidence Interval. The p-values are for comparisons between the +CPAP and -CPAP groups.