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Erectile dysfunction is independently associated with apnea-hypopnea index and oxygen desaturation index in elderly, but not younger, community-dwelling men☆

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ABSTRACT

Objective(s): To examine the association between obstructive sleep apnea (OSA) and other sleep indices using polysomnography (PSG) data and erectile dysfunction (ED) in a representative cohort of men.
Design: Cross-sectional.
Setting: Community-based.
Participants: Aged 40+ years (n = 734; mean age [SD], 60.8 [10.9]).
Measurements: Men with no prior OSA diagnosis who underwent in-home PSG (Embletta X100; 2010-11) and ED assessment (Global Impotence Rating) were selected. Un-adjusted and multi-adjusted regression models of ED were fitted against PSG measures, along with qualifying sociodemographic, lifestyle, and health-related covariates. Mediation effects were examined using the Baron-Kenny method.
Results: Of the men examined, 24.7% (n = 181) had ED, most notably in men older than 65 years (cf. men 35-49 and 50-64years; $P < .001$). There was no significant association between ED and any of the PSG measures for allaged men. Given an observed ageinteraction within OSA categories ($P = .005$), analyses were repeated in age-stratified samples (<65 years; 65+ years). In men younger than 65 years, only severe OSA was found to have an association with ED (2.01; 1.13-4.69) in unadjusted models. For men aged 65+ years, an independent association with ED was found for apnea-hyponea index (AHI; 1.55;1.02-2.36), moderate (AHI:10.0-19.9; 1.79;1.18-2.43), and severe (AHI:20.0+; 4.84;2.56-9.93) OSA, and oxygen desaturation index (ODI; both continuous [1.48;1.03-1.99] and >16 seconds [2.79;1.23-6.32]). The effect of AHI on ED was shown to be primarily mediated through ODI (63.4%, Sobel *P* value = .29).
Conclusions: In younger, community-based men, there appeared no independent relationship between objective measures of sleep and ED. However, there appears a strong, independent relationship between OSA, ODI, and ED in men 65 years and older.

Recent reviews have highlighted a putative role for obstructive sleep apnea (OSA) in the development of erectile dysfunction (ED).[1] Despite a link between OSA and ED being first identified almost 4 decades ago, the available evidence still relies predominantly on clinical trial and patient samples. The few population-based studies report absent,[2] equivocal,[3] or strong effects for OSA on ED.[4] Furthermore, most have relied on self-reported, rather than objectively measured sleep dysfunction (eg, polysomnography [PSG] testing). To date, there are only 2 previous studies that have examined the effect of OSA

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on ED using PSG. Data from a large study of Brazilian men who underwent laboratory PSG testing reported a strong effect of OSA (defined as apnea-hypopnea index [AHI] >15) on the presence of ED. The authors also demonstrated that men who spent less time in rapid eye movement (REM) sleep were particularly at risk for ED; however, no other sleep indices were examined.[5] More recently published data from the Osteoporotic Fractures in Men study reported an aged-adjusted association between PSG-measured OSA and ED,[6] although this occurred in men with a mean age of 76 ± 5 years and used older criteria for scoring desaturations and arousals for hypopneas (4%). Furthermore, it remains unclear which measure of sleep dysfunction (eg, AHI, sleep fragmentation, hypoxemia) any purported effect on ED is mediated through, limiting inferences around underlying mechanisms.

To date, there have been numerous mechanisms proposed to link OSA with ED, including lowering endogenous testosterone production, decreased REM and other sleep disturbances, elevated sympathetic activity, and increased oxidative stress (see Hoyos et al[7] for review). Both OSA and ED share multiple, related comorbidities and risk factors, including cardiovascular disease (CVD), central obesity, diabetes, depression, inflammation, dyslipidemia, low testosterone, smoking, low physical activity, and high alcohol consumption ([1]). The extent to which OSA and other sleep disorders influence normal erectile function, either through direct mediation or as a function of these shared comorbidities, is limited by the few available studies that have been able to concurrently adjust for these confounders.

Herein therefore, we briefly examine the association between OSA and other direct markers of sleep dysfunction on the presence of ED, adjusting for multiple confounders, in a large sample of representative, community-based men who underwent in-home PSG testing.

Participants and methods

Study design and sampling

The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) study comprise surban, community-dwelling men aged at least 40 years randomly selected from the Northern and Western Statistical Local Areas of Adelaide, Australia, using computer-assisted telephone interviews as previously described.[8] Briefly, a total of 2563 age-matched men from existing prospective cohorts (the Florey Adelaide Male Ageing Study[9] and the North West Adelaide Health Study[10]) were harmonized into a dataset incorporating detailed information on sociodemographic, clinical, behavioral, chronic disease, and medication data. To date, there have been 4 major waves of the MAILES study: 2002-2006 (MAILES 1), 2007-2010 (MAILES 2), 2010 (MAILES 3), and the sleep substudy in 2010-2011 (MAILES 4). Comparisons to the 2006 and 2011 Australian Census data showed that MAILES participants matched the target population for most key demographics, although younger groups and never-married men were underrepresented and older participants were overrepresented.[10] The present study involved MAILES men without a prior diagnosis who agreed to participate in overnight, in-home PSG testing (participation rate, 75.2%) and had complete ED measures (n = 734; mean age, 44.8 ± 8.2 years). The study was approved by the North West Adelaide Health Service and the Royal Adelaide Hospital institutional ethics committee, with all participants providing informed, written consent (NHMRC Project Grant No. 627227).

ED assessment

ED was assessed using the single-item Global Impotence Rating measure to categorize participants as having no (*always/usually able to get or keep an erection good enough for sexual intercourse*) or significant (*sometimes/never able to get or keep an erection good enough for sexual intercourse*) ED.[11] The Global Impotence Rating correlates well with the International Index of Erectile Function and the Brief Male Sexual Function Inventory (r = 0.71-0.78, $P < .001$), with similar point-prevalence estimates to that provided by the International Index of Erectile Function (κ = 0.56-0.58).

Sleep measures

Two weeks before overnight PSG testing, participants were sent a brief questionnaire including the Epworth Sleepiness Scale[12] and Pittsburgh Sleep Quality Index.[13] Total sleep time (TST) was defined as the time spent in N1, N2, N3, and REM sleep stages. Wake after sleep onset (WASO) was defined as the time spent in wake after first sleep but before the final awakening. Total sleep period was defined as WASO plus TST. OSA was defined using the 2007 American Academy of Sleep Medicine alternate criteria[14] as an AHI ≥10/hof sleep, with further categorization: mild, AHI of 10-19/h; moderate, 20-29/h; and severe, ≥30/h. The number of oxygen desaturation events of 3% or more per hour (3% oxygen desaturation index [ODI 3%]) was used as the indicator of nocturnal intermittent hypoxia.

Covariate data

Information on age, education, marital, occupational, smoking, physical activity, and disease status was obtained by self-report questionnaire.[8] Anthropometric measures, blood pressure, grip strength, and body composition (by dual energy x-ray absorptiometry) were obtained in-clinic from trained staff. Data from serum total testosterone, sex hormone–binding globulin, estradiol, high-density lipoprotein cholesterol, triglycerides, glucose, and C-reactive protein were all collected using standard pathology protocols in NATA-certified laboratories (see Grant et al[8]). Medication use was determined by self-report and data linkage with the national medication registry.

Statistical analyses

Descriptive analyses of selected independents and outcome measures were conducted using χ^2tests (categorical) and *t*tests (continuous). Binary logistic regression models for ED (none-mild vs moderate-severe) were sequentially built for each of the sleep indices. For multiple-adjusted models, selected independents with an age-adjusted association with the outcome variable of $P \leq .15$ (as per Lemeshow and Hosmer[15]) were included in the final model to account for multiple testing, with nonlinear independents log-transformed. Interaction effects were examined for selected independents with resultant terms included in multiple-adjusted models, where appropriate. Potential mediation effects between selected independents and outcome were examined using the Baron and Kenny method,[16] with the Sobel test used to test whether the indirect effect was equal to zero. Sensitivity analyses were also performed to examine the influence of other confounders on the relationship between the main independent variables and ED. A 2-tailed P value of <.05 was considered to be significant. Statistical analyses were performed using SPSS version 24.0 for Windows (IBM SPSS Inc, Chicago, IL).

Results

Sleep and ED

Overall, 24.7% (n = 181) of those men who underwent overnight PSG testing reported significant ED. Men with ED were also found to have higher AHI (including in both REM sleep and non-REM sleep) and higher levels of severe OSA (AHI ≥ 30). Of the other sleep indices, men with ED also recorded shorter TST, including less time in slow-