Word count: 2459
Abstract: 244

Title: Neighborhood Walking Environment and Activity Level Are Associated with Obstructive Sleep Apnea: The Multi-Ethnic Study of Atherosclerosis

Short Title: Walking Environment, Activity Level and OSA

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Each author reports no conflict of interest

Funding: NHLBI N01-HC-95159 through N01-HC-95169 MESA parent study; NHLBI R01 HL071759 (Diez Roux) for MESA neighborhood and NHLBI R01 L098433 (Redline) for MESA Sleep

Prior abstract presentation: American Thoracic Society International Meeting, May 2015; Denver CO

Abbreviations

AHI apnea hypopnea index

BMI body mass index

CI confidence interval

MESA multi-ethnic study of atherosclerosis

OSA obstructive sleep apnea

SES socio-economic status

WE walking environment

Abstract

Background: There has been growing interest in understanding how neighborhoods may relate to cardiovascular risk. Neighborhood effects on sleep apnea may be one contributing mechanism. We investigated whether neighborhood walking environment and personal activity levels are related to obstructive sleep apnea.

Methods: We analyzed data from a subpopulation of the Multi-Ethnic Study of Atherosclerosis (MESA), including subjects who participated in both MESA Sleep and Neighborhood studies (n=1,896). Perceived neighborhood walking environment and subjects' objective activity were evaluated in multivariate, multi-level models for an association with sleep apnea severity as defined by the apnea hypopnea index. Sex, race/ethnicity and obesity were examined as moderators.

Results: Residing in the lowest quartile walking environment neighborhoods (score <3.75) was associated with more severe sleep apnea [mean 2.7 events/hr greater AHI, 95% CI (0.7, 4.6)], after adjusting for demographics, body mass index, co-morbidities, health behaviors, neighborhood socio-economic status and site. Associations were stronger among obese and male individuals. Approximately one standard deviation greater objective activity in men, was associated with a lower AHI [mean -2.4 95% CI (-3.5, -1.3) events/hr]. This association was partially mediated by body mass index ($P<0.001$).

Conclusions: Living in neighborhoods with a low walking environment score is associated with greater sleep apnea severity, especially in male and obese individuals. In men, greater activity level is associated with less severe sleep apnea, independent of body mass index, co-morbidities and socio-economics. Neighborhood-level interventions that increase walkability and enable increased physical activity may potentially reduce sleep apnea severity.

INTRODUCTION

Obstructive sleep apnea (OSA) is strongly associated with hypertension, diabetes, stroke and ischemic heart disease.¹⁻³ Neighborhood built environment features, independently of race and individual socioeconomic status, are also associated with cardiovascular health.⁴⁻⁸ OSA may represent one pathway through which neighborhood factors influence cardiovascular outcomes.

The built environment may lead to OSA by promoting obesity and reducing physical activity. Perceptions of safety, density of fast food restaurants and neighborhood disorder have been associated with body mass index (BMI),⁹⁻¹² possibly by affecting health behaviors and cultivating psychological distress,¹³ leading to obesity¹⁴ and thus promoting OSA. Walkability is negatively associated with BMI.^{15,16} Neighborhood features that promote physical activity, including street connectivity, mixed land-use, and green space,¹⁷⁻¹⁹ may be inversely associated with OSA. Walkability is associated with greater physical activity levels.^{20,21} Exercise interventions have been found to reduce the risk and severity of sleep apnea, independently of inducing weight loss.^{22,23} Recent studies have found an association of walkability with incident diabetes,^{24,25} which has similar risk factors as OSA.

Neighborhood features that limit physical activity may foster sedentary habits.^{26,27} Peripheral edema may be more prominent in those with sedentary lifestyles. Recent data indicate that lower extremity edema may exacerbate OSA by serving as a reservoir of extravascular fluid that can redistribute to the upper airway during sleep, causing airway narrowing.²⁸ Variation in edema has been correlated to inter-individual variation in the apnea hypopnea index (AHI), with greater edema associated with more severe OSA.²⁹ Increased physical activity has been shown to reduce both leg edema and AHI.³⁰

Few studies have investigated the relationship between the neighborhood environment and OSA in adults. Neighborhood disadvantage has been associated with OSA in children.^{31,32} Neighborhood-level crowding, however, has been associated with greater OSA severity in adults, which appears to be mediated by BMI.³⁴ Prior studies have examined associations of the neighborhood built environment with subjective sleep disturbance in adults but did not include objective measures of sleep disorders.³⁵

We hypothesized that living in a neighborhood with lower walking environment scores would be associated with a greater severity of OSA as assessed by the AHI and that this association would be mediated by objective activity level. Furthermore, we hypothesized that greater objective activity level would be inversely associated with OSA severity and mediated by BMI. We explored if sex, obesity and race/ethnicity moderate these associations as walking behaviors and the impact of exercise may differ among these groups.

MATERIAL AND METHODS

Data:

The Multi-Ethnic Study of Atherosclerosis (MESA) is a longitudinal study of cardiovascular disease among adults aged 45-84 years. Subjects were recruited from the community in 6 United States cities (Los Angeles, CA; New York City, NY; Chicago, IL; Winston-Salem, NC; St. Paul, MN and Baltimore, MD).³⁶ The current sample was restricted to those who agreed to participate in the MESA Neighborhood and MESA Sleep ancillary studies (n=1,896), which occurred at the 10-year MESA follow-up (Exam 5 in 2010-2012). The study was approved by the institutional review boards at each site and all participants gave written informed consent (see data supplement).

Neighborhood walking environment (WE) was assessed as part of the MESA Neighborhood Study. Participants completed a 4-item questionnaire during MESA Exam 5, responding on a five-point scale ranging from “strongly agree” to “strongly disagree”. Questions included: “It is pleasant to walk in my neighborhood”, “In my neighborhood it is easy to walk to places”, “I often see other people walking in my neighborhood”, and “I often see other people exercise in my neighborhood.” An identical questionnaire was administered to a random community sample identified via random-digit dialing or list-based sampling. These participants (n=4212), referred to as Community Survey, resided in the same census tracts as MESA subjects in 2011-2012.

The WE scale was calculated by taking the mean of the responses for all respondents from both MESA and Community Survey samples living within a 1 mile buffer of the participant’s home address, excluding the subject’s survey response. The walking environment (WE) scale has been previously validated (Cronbach alpha=0.79).³⁷ A higher score on a range of 1-5 indicates a better walking

environment. We compared those in the WE score <3.75 (25% of sample) to those residing in neighborhoods with a ≥ 3.75 WE score.

Sleep metrics were made through MESA Sleep Ancillary. Eligible participants (not on positive airway pressure, oral appliance or oxygen) were invited to participate and 60% agreed. As described previously, participants underwent in-home full polysomnography with a 15-channel monitor (Compumedics Somte System; Compumedics Ltd., Abbotsville, Australia) enabling scoring of sleep stage and respiratory events. Participants wore an Actiwatch Spectrum actigraph (Philips Respironics, Murrysville, PA) on their non-dominant wrist for one week.³⁸ Our main outcome was the AHI calculated using American Academy of Sleep Medicine hypopnea scoring criterion of 3% or greater desaturation or an arousal.³⁹ Objective activity level was derived from 7-day wrist actigraphy. Activity status for each 30 second epoch was computed using the Actiware-Sleep v. 5.59 scoring algorithm. Sleep periods were identified by technicians using sleep diaries, light levels, event markers, and activity levels.⁴⁰ Activity counts per min divided by 100, approximating the standard deviation, were averaged for periods scored as active (excluding sleep periods and non-wear time) over the 7-day recording.

The socio-demographic and co-morbidity data were obtained from the MESA health and medical history surveys and examination. Subjects reported race/ethnicity (White non-Hispanic, Black non-Hispanic, Hispanic and Chinese), cigarette smoking status (never, current/former), education level (dichotomized by college degree or more) and household income (categorized as < \$ 25,000, \$25-75,000, > \$75,000). Depressive symptoms were based on a Center for Epidemiological Studies Depression scale greater than 16.⁴¹ Diabetes status was categorized based on the 2003 American Diabetes Association criteria (impaired fasting glucose, untreated and treated diabetes).⁴² Hypertension was defined as blood pressure $\geq 140/90$ mm Hg or use of anti-hypertensive medication. Measured weight and height were used to calculate BMI category (<25, 25-29.9, 30-40, >40 kg/m²). To account for

neighborhood SES, a factor scale for neighborhood SES was utilized, generated from census-tract level data from the American Community Survey 5-year estimates from 2007-2011, comprised of information on median household value, percent with college education, percent with managerial/professional occupation, percent with high school diploma and median household income.⁹

Analysis

We dichotomized the walking environment score after identifying a threshold effect for the lowest quartile with our outcome of AHI and a lack of a linear or dose response relationship. We compared those living in neighborhoods with the lowest quartile walking environment ($WE < 3.75$) with the rest of the cohort by sample characteristics, using chi-squared for categorical variables and t-tests for continuous variables.

We then examined the associations of AHI with (a) neighborhood walking environment score and (b) actigraphy-derived activity counts using two linear mixed, two-level models with random effect to account for clustering by census tract as a proxy for neighborhood. Models adjusted for age, race/ethnicity, and sex (except in stratified analyses), and household income, education, study site, cigarette smoking, diabetes, hypertension, depressive symptoms, and neighborhood SES. We excluded observations with any missing covariates. In secondary analyses, multiple imputation was applied to account for missing data (see supplement).^{43,44} BMI was included in selective models. We evaluated for effect modification by sex and obesity ($BMI \geq 30$; when BMI was not identified as a mediator), by adding an interaction term and performing stratified analysis. In exploratory analysis, we evaluate for effect modification by race/ethnicity.

We examined if activity level mediated the association between walking environment and AHI, as well if BMI mediated the association between activity level and AHI. Using methods described by Baron and Kenny,⁴⁵ we fit a series of regression models, see figure 1. We utilized mixed-effects models

with the same clustering by census tract. We calculated the mediated effect point estimate using methods described by MacKinnon using boot-strapping to calculate the 95% confidence intervals.⁴⁶

RESULTS

Of the 1,896 MESA subjects with sleep and neighborhood data included in the analysis, the mean age was 68.5 (standard deviation [SD] 9.1) and BMI was 28.6 kg/m² (SD 5.5) with racial/ethnic and geographic diversity (table 1). The median walking environment (WE) score for subjects' neighborhood was 3.9 (interquartile range 3.75-4.15). The median AHI was 14.4 (interquartile range 6.9-27.2). Of those residing in neighborhoods with a lower walking environment scores (WE<3.75), a significantly greater proportion were black, hypertensive, diabetic, obese, had a household income < \$25,000 and from the Baltimore, MD site and had an AHI ≥ 30; a lower proportion were white, college educated, had a household income >\$75,000 and from the St. Paul, MN site.

Living in the lowest quartile walking environment neighborhoods was associated with higher AHI, [mean 3.21 more events/hr, 95% Confidence Interval (CI) (1.13, 5.29)] in adjusted models, (table 2, model 1). The association was attenuated after adjusting for BMI, but remained significant (model 2). Obesity (BMI≥30) and sex appeared to modify the association between WE and AHI (*P*_{int}=0.05 obesity, *P*_{int}=0.06 sex), with a significant association between walking environment and AHI among obese subjects and men (table 2). Stratified exploratory analyses indicated that the association between low WE and AHI was strongest among black participants (e-Table 1).

Living in the lowest quartile WE neighborhood was not associated with activity level in mixed-level models, and activity level did not mediate the association between low WE and AHI. Higher activity level was associated with lower AHI; approximately one standard deviation greater activity was associated with an average decrease in AHI by 3.3 events/hr, (table 3). This association was attenuated after adjusting for BMI and low WE score but still statistically significant. The effect of activity on AHI differed by sex (*P*_{int}=0.04), with the association observed among men [AHI mean difference -3.61, 95%

CI (-5.41, -1.81)], but not women. Similarly, a significant association was seen among black and Hispanic subjects but not among white or Chinese-Americans (e-Table 2) when stratified.

The association of activity level with AHI was partially mediated by BMI. The mediated effect of BMI was -0.86 events/hr, 95% CI (-1.17, -0.55), (figure 1); i.e., BMI explained 21% of this association.

Sensitivity analyses using imputed data for the sample with missing covariate data showed modest attenuation of the main effects. For the fully adjusted models, the mean AHI change associated with low WE was 1.89 events/hr 95% CI (0.02, 3.80) and with activity level was -1.92 events/hr, 95% CI(-3.01,-0.82), (e-Tables 3 and 4).

DISCUSSION

This study provides novel data linking the neighborhood walking environment with sleep apnea. We found that living in the least walkable neighborhoods was associated with greater OSA severity, specifically in men and obese subjects. The association persisted after adjusting for co-morbidities and socio-demographics. The mean difference of a 2.7 AHI associated with neighborhood is comparable to 5-10% weight loss or 20% of the effect of using mandibular advancement device or undergoing uvulopalatopharyngoplasty, depending on baseline severity.⁴⁷⁻⁴⁹ Living in a less walkable environment may promote a sedentary lifestyle and favor vehicular transportation.²⁷ Reduced walking may promote peripheral edema, which has been identified as a risk factor for sleep apnea.²⁸ Although higher neighborhood walkability has not been associated with less sitting time,⁵⁰ greater walkability may encourage greater physical activity, promote social interaction and time spent outdoors.⁵¹

Greater objectively recorded activity level was associated with lower AHI independent of the walking environment. This association was only partially mediated by BMI, suggesting a beneficial effect of physical activity on OSA independently of BMI. This supports prior studies demonstrating reduction in AHI and a decrease in incident OSA with exercise interventions that did not result in weight loss.^{22,23,30,52} Potential mechanisms include reduction in dependent edema and rostral fluid shift to the pharynx during the night.³⁰ Additionally, exercise may lead to a reduction in visceral adipose tissue, which may also reduce OSA risk.⁵³ The stronger association between activity level and AHI in men may be due to sex differences in the distribution of fluid, including a male predisposition to accumulate neck fluid volume when supine.

A stronger association between walking environment and lower AHI was observed in men as compared to women. Neighborhood attributes may also have less of an impact on walking behavior in women due to a greater underlying fear of crime than men.¹⁷

There was limited power to detect modification of associations by race/ethnicity. However, stratified analyses suggested that associations were strongest in blacks (for both WE and activity level) and Hispanics (for activity level). These data suggest the potential beneficial role of environmental and behavioral interventions in minority groups at increased risk for OSA.

No association was observed between walking environment and objective activity level; accordingly there was no evidence of mediation by activity level as hypothesized. The walking environment score reflects perceived environment for walking and may only roughly reflect actual walking/exercise behavior.⁵⁵ Misclassification of physical activity level with use of wrist actigraphy may bias the association toward the null.

The strengths of this study include the diversity of the subjects (both in racial/ethnic background and geography), the large sample size gathered from the community, and the use of objective sleep and activity measures. A well-validated neighborhood walking environment scale was used, which provided information unbiased by the participant's own response, reducing the effect of same source bias.^{9,11,25} This study confirms prior findings of the relationship of neighborhood features to sleep disturbance,³⁵ but with objective measures of sleep apnea and with actigraphy to provide an objective measure of wake-time activity.

The limitations of the study include the cross-sectional and observational nature of the study, limiting evaluation of causality and the direction of association. The use of mediation analysis with cross-sectional data should be viewed cautiously.⁵⁹ We also only captured a one week snapshot of activity, considering current neighborhood and BMI, and did not account for prior neighborhoods and factors leading to the development of obesity and OSA. Our walking environment measure did not include geographical information systems data on street connectivity, population density, or

recreational facilities to better assess walkability²⁰ and perhaps walking behavior. In addition, the sample of MESA participants in our cohort had a mean age of 68.5 years and our findings may not be generalizable to younger individuals.

CONCLUSIONS

This study provides strong evidence that neighborhood walking environment is associated with sleep apnea severity, with associations strongest in men and among obese individuals and black individuals. Urban planning may be an important tool of public health to improve cardiovascular and sleep health, potentially reducing OSA and health disparities. Being more active during the day may reduce the severity of OSA. Public health measures that increase walking behaviors could potentially reduce the severity of sleep disorders and resulting cardiovascular disease. Further studies are needed to assess for longitudinal changes in OSA severity as neighborhood walkability evolves. Ultimately, large scale public health studies are needed to evaluate if neighborhood-level interventions aimed at improving walkability and activity levels lead to reductions in OSA severity and improved sleep health.

Acknowledgements

The authors thank the other investigators, the staff, and the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at <http://www.mesa-nhlbi.org>. MEB had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. DJ, KM contributed substantially to data analysis and interpretation. SG, SRP, SRR, ADR contributed substantially to the study design, data interpretation, and the writing of the manuscript.

Funding

This research was supported by the National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health through contracts N01-HC-95159 through N01-HC-95169 and by grants UL1-TR-000040 and UL1-TR-001079 from NCRR. Additional funding for MESA Neighborhood ancillary study from the NHLBI R01 HL071759 (Diez Roux) and for MESA Sleep ancillary study from the NHLBI R01 L098433 (Redline).

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Tables

Table 1: MESA Neighborhood and sleep cohort characteristics n=1896

	ALL subjects n=1896	WE ≥ 3.75 n=1424	WE < 3.75 n=472
BMI [*] mean (SD)	28.6 (5.5)	28.3 (5.4)	29.6 (5.7)
Age mean (SD)	68.5 (9.1)	68.3 (9.0)	69.0 (9.3)
% Men (n)	45.6 (864)	45.5 (648)	45.8 (216)
% Race[*] (n)			
White	35.7 (677)	41.0 (584)	19.7 (93)
Chinese-American	12.2 (231)	12.6 (180)	10.8 (51)
Black	28.4 (538)	22.5 (321)	46.0 (217)
Hispanic	23.7 (450)	23.8 (339)	23.5 (111)
% College education ^{*,¥} (bachelor degree and above) (n)	39.6 (750)	44.0 (626)	26.3 (124)
% Hypertension ^{*,¥}	57.0 (1080)	54.4 (774)	64.8 (306)
% Diabetes ^{*,¥}	39.9 (750)	38.6 (545)	44.0 (205)
% Depression (CES-D ≥ 16) [¥]	14.5 (269)	14.4 (201)	14.8 (68)
% Obese (BMI ≥ 30) ^{*,¥}	34.7 (656)	32.2 (457)	42.3 (199)
% Smoker [¥]	45.7 (860)	45.6 (646)	45.9 (214)
% Household income (n)^{*,¥}			
< \$25,000	26.6 (489)	24 (335)	34 (154)
\$25-75,000	45 (829)	44 (612)	48 (217)
> \$75,000	28.4 (524)	32 (444)	18 (80)
% Site (n)[*]			
Wake Forest (Winston-Salem, NC)	14.9 (282)	13.4 (191)	19.3 (91)
Columbia (NYC, NY)	18.5 (351)	19.1 (272)	16.7 (79)
Johns Hopkins (Baltimore, MD)	14.3 (271)	11.4 (162)	23.0 (109)
U Minnesota (St. Paul, MN)	17.1 (324)	20.7 (295)	9.0 (29)
Northwestern (Chicago, IL)	19.0 (360)	20.7 (295)	13.8 (65)
UCLA (Los Angeles, CA)	16.2 (308)	14.7 (209)	21.0 (99)
Neighborhood Scales			
Neighborhood Walking Environment (WE) Score median (IQR)	3.9 (3.75, 4.15)	4.0 (3.9, 4.3)	3.6 (3.5,3.7)
Actigraphy Data			
Activity counts median (IQR) (per min during active intervals)	218.2 (172.1, 275.6)	219.1 (173.4, 275.5)	216.3 (168.4, 275.6)
PSG Data			

% Apnea Hypopnea Index (AHI) ≥ 15 (n)	47.8 (894)	47.6 (672)	48.4 (223)
AHI (hypopnea defined as 3% desaturation or cortical arousal) median (IQR)	14.4 (6.9, 27.2)	14.3 (6.8, 26.6)	14.6 (7.2, 29.2)
% AHI ≥ 30 *	20.8 (390)	19.7 (278)	24.3 (112)

* Significant difference between lowest quartile neighborhood walking environment and all other quartiles, $p < 0.05$ via Chi-squared test for categorical variables, Wilcoxon rank-sum test for continuous

‡ missing values: smoking (n=14), education (n=4), BMI (n=4), depression (n=35), hypertension (n=5), diabetes (n=18), household income (n=54), actigraphy-derived activity counts (n=81), and neighborhood SES (n = 46). See data supplement for details of imputation.

Table 2: Mean difference in AHI in by low walking environment (WE score < 3.75) in adjusted models, presented as β (95% confidence interval), * n=1732

	Model 1 N=1732	Model 2 N=1730	Model 3A (men) n=787	Model 3B (women) N=943	Model 4A (BMI$\geq$ 30) n=598	Model 4B (BMI<30) n=1132
WE score < 3.75	3.21 (1.13, 5.29)	2.73 (0.74, 4.63)	3.74 (0.24, 7.24)	0.81 (-1.46, 3.07)	5.21 (1.42, 9.01)	1.02 (-1.25, 3.29)

* All models adjusted for age, race/ethnicity, sex (except model 3), BMI (except models 1 & 4), education, site, diabetes, hypertension, depression, smoking status, household income and neighborhood socio-economic status with two-level mixed effects linear model with random effect for census tract

Table 3: Mean difference in AHI by activity level, standardized by approximately one standard deviation of actigraphy measured counts per minute. Data presented as β (95% confidence interval), n=1781 in adjusted models *

	Model 1 N=1781	Model 2 N=1781	Model 3A (men) n=820	Model 3B (women) n=908	Model 4[‡] N=1656
Activity Count (per min/100)	-3.32 (-4.43, -2.20)	-2.40 (-3.48, -1.32)	-3.61 (-5.41, -1.81)	-0.81 (-2.09, 0.47)	-2.12 (-3.25, -1.00)

* All models adjusted for age, race/ethnicity, sex (except model 3), BMI (except model 1) site, diabetes, hypertension, depression, smoking status, household income, education, and neighborhood socio-economic status with two-level mixed effects linear model with random effect for census tract

[‡] Lowest quartile neighborhood walking environment score included in model 4

Figure 1: Mediation analysis demonstrating that the association of activity level on AHI is mediated by BMI. Activity level is associated with both BMI (**A**) and AHI (**C**). BMI is also strongly associated with AHI (**B**). The mediated effect is $C - C'$ or the difference in the point estimate of activity level on AHI without and with adjustment for BMI.