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Sleep and olfaction among older adults

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Abstract

Background—Sleep and olfaction are both critical physiological processes that tend to worsen with age. Decline in olfaction can be an early indicator of neurodegenerative diseases whereas poor sleep quality is associated with reduced physical and mental health. Given associations with aging-related health declines, we explored whether variations in sleep were associated with olfactory function among older adults.

Methods—We assessed the relationship between sleep characteristics and olfaction among 354 community-dwelling older adults. Olfaction was measured using a validated field and survey research tool. Sleep characteristics were measured using wrist actigraphy and self-report of sleep problems. We fit structural equation models of latent constructs of olfaction based on olfactory task items and let this be a function of each sleep characteristic.

Results—Actigraph sleep quality measures were associated with odor identification, but not with odor sensitivity. Longer duration sleepers had worse odor sensitivity compared to medium (5 to 8 hours) sleepers but sleep duration was not associated with odor identification. Reported sleep problems and reported usual duration were not associated with olfaction.

Conclusions—Diminished sleep quality was associated with reduced capacity to identify odors. Determining whether this is a causal association will require further study and longitudinal data.

Keywords

Olfaction; sleep; actigraphy; aging

Introduction

Olfaction is critical for human health and is involved in psychosocial functioning, nutrition, social ties, memory, emotion, mood, and overall well-being [1]–[3]. Olfactory dysfunction

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can be harmful via decreased nutritional status, worse emotional and physical well-being, increased depressive symptoms, and social isolation [4]–[8].

Olfaction has been shown to progressively decline after age 57 [9], [10], with up to 80% of those over age 80 showing impairment [11]. Olfactory dysfunction is an early indicator of neurodegenerative diseases including Alzheimer's, Parkinson's, and Huntington's disease [11] and also predicts mortality among cognitively intact older adults [12]–[15]. Olfactory impairment is also more prevalent among men, smokers, African-Americans, Hispanics, those with lower SES and lower cognition scores, and stroke victims [13], [16], [17]. As olfaction is an indicator of neural degeneration, aging, and death, determining the underlying mechanisms of these relationships is important to understanding health trajectories.

Like olfaction, sleep is a physiological process crucial to brain health. Older adults experience increased sleep disturbances including more wake after sleep onset (WASO), greater sleep fragmentation, and poorer self-reported sleep quality including insomnia symptoms[18], [19]. Deep sleep and REM sleep also decline with age [20]. Though findings are inconsistent about sleep duration and mortality (see Kurina et al., 2013 [21]), sleep disturbances have consistently been associated with chronic disease, overall physical and mental health, cognitive function, and mortality [18], [22]–[26].

Given the relationships of olfactory decline and sleep with aging-related health problems, we sought to explore whether variations in sleep were associated with olfactory dysfunction among older adults.

Previous studies have investigated the relationship between sleep and olfaction in humans, including olfactory function and memory consolidation of odors during sleep [27]–[30] and memory consolidation during sleep using olfactory cues [31]–[34]. However less attention has been given to whether variations in sleep are associated with olfactory function more generally. Two experimental studies found that sleep deprivation was associated with worse ability to identify odors among adults [27], [35], consistent with neuroimaging studies showing that sleep deprivation leads to decreases in the cerebral metabolic rate for glucose in the prefrontal cortex, including the orbitofrontal region which is highly involved in olfactory processing [36]. However, the relationship between sleep and olfactory function has not been assessed in a population setting among older adults, the group that experiences increased prevalence of olfactory dysfunction and disordered sleep.

The current analysis examines the relationship between actigraph and self-reported measures of sleep duration and quality with objectively-assessed olfactory function among a subsample of a national study of older adults.

Methods

Study Sample

The National Social Life, Health, and Aging Project (NSHAP) is a nationally representative sample of community-dwelling older adults born between 1920 and 1947 and their

consenting spouses, regardless of their age. Survey data and biomeasures were collected via in-person at-home interviews.

In Wave 2 (2010/2011), the NSHAP population was divided into six subgroups to allocate participants to additional modules. [37] Four subgroups (*n*=2,304) were selected to receive the Olfactory Function Field Exam (OFFE) which was developed to measure olfactory function in survey research [38]. Two subgroups (n=1,117) were selected to participate in the sleep module. A total of 572 individuals were selected to receive both the OFFE and the sleep module. There were 354 participants aged 62-90 who consented to both modules and provided complete data (see Figure 1).

Measures

Olfaction—The OFFE includes measures of odor identification and sensitivity. Odor identification was assessed using a field survey version of a validated test [39]. Participants were presented with five odor filled felt tip pens and were instructed to identify each odor from a selection of four word/picture options. The number of correctly identified odors yielded a score from 0 to 5.

The odor sensitivity module of the OFFE assessed participants' capacities to detect *n*-butanol, a common testing odorant. Participants were presented with three felt tip pens and asked to select the one pen that contained *n*-butanol. Six sets with increasing concentrations of *n*-butanol in one pen were presented. Scores of 0-6 represent how many concentrations were correctly detected. This screening test is reliable and highly correlated (r = 0.92) with psychophysical olfactory sensitivity testing among older adults [40]. A detailed protocol of olfactory data collection, including interviewer training, has been described elsewhere [41].

Sleep—Sleep characteristics were collected via self-report and wrist actigraphy. Actigraphs (Actiwatch Spectrum model, Phillips Respironics) were worn by study participants for a 72-hour period. Participants were asked to push an event marker each night when they started trying to sleep and when they awoke. The event markers, activity counts, and ambient light data (recorded by the actigraph) were used to manually determine the main rest interval for each 24-hour period. Actiwatch software calculated sleep metrics from the pattern of activity counts within each rest interval. We used metrics frequently derived from actigraphy: total sleep duration – the sum of 15-second epochs scored as sleep during the main sleep interval; wake after sleep onset (WASO) –total minutes awake during the main sleep interval; and fragmentation – an index of restlessness expressed as a percentage. Averages of each were calculated from the three nights. A detailed protocol of sleep data collection, including quality control measures, has been described elsewhere [42].

Self-reported sleep duration was assessed via a question asking how many hours participants slept each night. Sleep problems similar to insomnia symptoms (i.e., frequency of trouble falling asleep, trouble waking, waking too early, and restorative sleep) were combined to create a troubled sleep scale. The scale ranges from 0 to 8, with higher scores indicating more insomnia symptoms, as described in detail elsewhere [43].

Cognitive function—Cognitive function was measured using the Montreal Cognitive Assessment (MoCA) [44] adapted for survey administration (MoCA-SA) [45], [46]. The MoCA was developed to assess mild cognitive impairment (MCI) across key cognitive domains and was shown to have a 90% sensitivity in detecting clinically diagnosed MCI [44]. The instrument is more sensitive to variation in cognitive function than screeners designed to identify severe impairment, such as the Mini-Mental State Exam. The MoCA-SA is highly correlated (r=0.973) with the full MoCA [45], [46].

Additional covariates—Demographic and control variables included age, gender, body mass index (BMI), race/ethnicity (white, Hispanic, black, other), current smoking, depressive symptoms, medications, and a comorbidity index. BMI was calculated from direct measures (kg/m^2). Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression scale, which assesses frequency of depressive feelings over the past week. Medications were physically brought to the interviewers and recorded. We include indicators for current usage of antidepressants and hypnotics. Comorbidities were summarized using a modified version of the Charlson Comorbidity Index (CCI) [47], as implemented in NSHAP [48].

Statistical Analysis

To assess the relationship between sleep characteristics and odor identification, we fit a generalized structural equation model to the five observed olfactory identification items assuming a single latent construct of odor identification through a logistic regression (i.e., a 1-parameter item-response model). This model was then extended by specifying odor identification to be a function of each sleep characteristic separately, first only adjusting for age and sex and then adjusting for additional covariates. Due to evidence in the literature of a U-shaped relationship between sleep time and some health outcomes, we also tested a three-level categorical variable for sleep time [21], [49]. The beta coefficient of the main independent variable (the particular sleep characteristic) represents the average change in performance on the odor identification construct, for each additional unit change of the sleep characteristic. The same analysis was performed for odor sensitivity.

As a secondary analysis, we assessed potential mediation of the relationship between sleep characteristics and odor identification via cognition. To assess potential mediation, we augmented the structural equation models to allow us to consider possible mediating effects of cognition using the widely implemented product method [50].

All analyses took into account the study design and sampling weights to account for probabilities of selection and nonresponse [51]. All data were analyzed using Stata Version 13.0 (StataCorp LP, College Station, TX).

Results

Table 1 summarizes the demographic, health, and sleep characteristics of the olfaction-sleep sub-sample. Actigraph total sleep time averaged 7.2 hours, WASO averaged 37.5 minutes, and the fragmentation index averaged 14.2%. Average self-reported sleep was 7.4 hours and the average troubled sleep scale was 2.7. Just over half were able to identify all five odors

(51.4%), however only 7.1% were able to detect the weakest concentration of *n*-butanol. The distribution of covariates in the olfaction-sleep sub-sample was generally similar to the larger study population (see Table S1).

Table 2 presents the coefficients for the sleep characteristics in the age and sex adjusted (Model 1) and fully adjusted (Model 2) structural equation models for both odor identification and odor sensitivity. The outcome for each is the latent variable construct of the particular odor scale, where a higher score indicates better performance. In the age and sex adjusted models, both WASO and fragmentation were significantly inversely associated with odor identification. In the fully adjusted models, each additional minute of WASO was associated with a 0.013 worse odor identification score ($p<0.01$), and each additional percent of fragmentation associated with a 0.039 worse odor identification score ($p=0.09$).

Neither the troubled sleep scale, self-reported sleep duration, nor actigraph total sleep time were associated with odor identification in adjusted models. Modeled as a categorical variable, there was no evidence of a U-shaped relationship between actigraph-measured total sleep time and odor identification.

Neither WASO, fragmentation, self-reported sleep duration, nor the troubled sleep scale score were associated with odor sensitivity. Modeled as a continuous variable, actigraph total sleep time was inversely associated with odor sensitivity; each additional hour of sleep time was associated with a 0.152 worse odor sensitivity score ($p=0.02$). When modeled as a categorical variable, long sleepers (subjects averaging eight hours or more per night) were less able to detect odors compared to medium (5 to 8 hours) sleepers, with marginal significance ($\beta=-0.426$, $p=0.08$)

We assessed potential mediation by cognition between both WASO and fragmentation with odor identification (Table 3). The indirect association represents the portion of the association between the sleep measure and odor identification that is mediated by cognition. Only small portions of the relationships for WASO and fragmentation with odor identification were mediated by cognition (-0.002, $p=0.14$ and -0.006, $p=0.22$, respectively).

Discussion

In our assessment of sleep and olfaction in community-dwelling older adults, we found a positive association between two actigraph measures of sleep disruption and worse ability to correctly identify odors, after adjusting for demographics and comorbidities. We did not find an association between insomnia symptoms or sleep duration, measured either by self-report of actigraphy, and ability to identify odors. We also did not find an association between sleep disruption or insomnia symptoms and odor sensitivity. However, we did observe an unexpected inverse association between total sleep time (measured with actigraphy) and odor sensitivity. When considered as a categorical variable, we found that the relationship was primarily driven by poorer odor sensitivity among long sleepers (8 or more hours per night). As a possible mechanism, we considered models controlling for reported neurological conditions (Parkinson's, Alzheimer's, and stroke), but found no difference in the estimated association. We also considered day-time napping behavior, but did not find

that this confounded the observed associations. While the mechanism of the relationship between longer actigraph-measured sleep time and odor sensitivity remains unclear, there have been many reports of worse health outcomes among long sleepers [52].

We believe that this is the first study to assess the relationship between sleep and olfaction in a population of community-dwelling older adults and the first to include objective measures of both. Actigraph estimates of sleep characteristics avoid potential biases of survey sleep questions and are practical to implement in the field [53]. Similarly, the OFFE includes a validated measure of odor identification [39] and a novel survey-modified measure of odor sensitivity [40], [54]. Although only a minority of NSHAP participants received both modularized measures, we did find several significant, and heretofore unobserved, associations.

Our study did have some important limitations. First, the data are cross-sectional, preventing the observation of temporal associations between disrupted sleep, olfaction, and cognition. Second, actigraphy cannot measure dimensions of sleep that may be salient for odor identification or sensitivity, such as sleep architecture. Third, only 354 of 3,196 age-eligible Wave 2 NSHAP participants have both actigraphy and olfaction data, and a larger sample may be needed to detect associations with some of the sleep measures. Finally, NSHAP participants were not asked specifically about sleep apnea, although they were given an opportunity to list additional medical conditions. Only one participant in this sub-sample reported sleep apnea. There is likely to be both unreported and undiagnosed sleep apnea in the sample population, and we were unable to assess the role of sleep apnea in these associations.

Given prior evidence that poor sleep could be a risk factor for cognitive impairment [24], [25], [55] and that odor identification requires both detection and recognition (a cognitive function) [56], [57], we explored whether the observed relationship between poor sleep quality and worse odor identification was mediated by cognition. Unexpectedly, it was not. It may be that the MoCA-SA does not adequately capture the cognitive components relevant to this pathway. Factor analysis has demonstrated that while the full MoCA captures more variability in MCI than screeners such as the Mini-Mental State Exam [58], it may not accurately identify domain-specific areas of cognitive impairment [59]. While impaired olfaction has been associated with global cognition, it has also been associated specifically with perceptual speed and episodic memory [60]. Thus, it is possible that sleep disruption does diminish capacity to identify odors through a cognitive pathway that is not well measured by the MoCA-SA. However, sleep disruption may affect olfactory processing centers independently of cognition. This alternative would suggest that the difference between the relationship of sleep to odor identification versus odor sensitivity is not related to cognition.

Our study is broadly consistent with animal models on the role of sleep in the consolidation of odor memory. Barnes and Wilson found that manipulation via restriction of slow wave sleep in rats impaired memory consolidation relative to odor recognition [61]. Fragmentation and WASO may reflect lack of slow wave sleep. There are experimental studies of sleep restriction: Prehn-Kristensen et al. and Killgore and McBride both found that sleep

deprivation caused reduced capacity to recognize odors by adults [27], [35]. Our findings differ in that we found an association for lack of sleep consolidation (not sleep duration) and odor identification. Also, we are examining routine sleep variation in the population rather than experimentally manipulated sleep.

Further study is needed to understand whether poor sleep quality leads to olfactory decline or vice-versa, or whether underlying physiologic processes explain both, inducing the observed correlation between the two. Longitudinal data would help answer these questions. If sleep disruption is an early indicator of olfactory dysfunction, it will be important to consider whether modifications to sleep routines aimed at improving sleep quality could delay the onset of other aging-related health outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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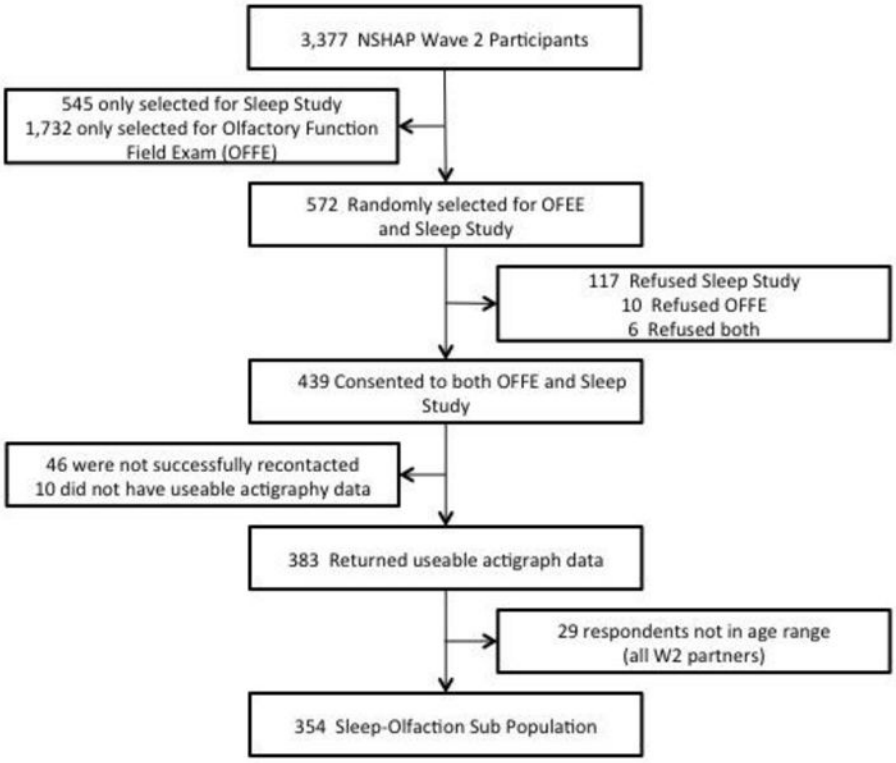

Figure 1.

Table 1

Demographics of the NSHAP Wave 2 Olfaction-Sleep subsample (N=354)

Characteristic	Weighted Value	*N*
Age, mean (sd)	71.7 (7.5)	354
Female	53.6%	354
Race		354
White	82.3%	
African American	6.2%	
Hispanic	6.3%	
Other	5.2%	
Modified Charlson Comorbidity		354
0	48.1%	
1	25.4%	
2	14.0%	
3+	12.4%	
Montreal Cognitive Assessment – Survey Adapted, 0-20 scale, mean (sd)	14.2 (3.5)	354
Body Mass Index, mean (sd)	29.1 (5.50)	345
Current Smoker	13.6%	354
CES-D[1], mean (sd)	7.3 (3.3)	354
Medication Usage		
Antidepressants	17.4%	334
Sleep Aids	8.7%	334
Actigraph-Measured Sleep		354
WASO[2] (minutes), mean (sd)	37.5 (22.6)	
Total Sleep Time (hours), mean (sd)	7.2 (1.4)	
Less than 5 hours, %	5.5 %	
5 to 8 hours, %	70.2%	
More than 8 hours, %	24.3%	
Fragmentation (%)	14.2 (5.9)	
Self-Reported Sleep Duration (hours), mean (sd)	7.4 (1.3)	287
Troubled Sleep Scale[3], mean (sd)	2.7 (2.1)	354
Olfactory Function Field Exam		
Odor Identification (score)[4]		354
0	2.9%	
1	1.3%	
2	6.0%	
3	7.8%	
4	30.7%	
5	51.3%	

Characteristic	Weighted Value	*N*
Odor Sensitivity (score)[5]		354
0	7.1%	
1	8.5%	
2	12.4%	
3	15.9%	
4	23.8%	
5	25.3%	
6	7.1%	

[1] CES-D (range:0-22): Center for Epidemiologic Study Depression Scale

[2] Wake after sleep onset

[3] Troubled Sleep Scale (range:0-8) is a combined metric (0 = Never/rarely, 1 = Sometimes, 2 = Most of the time) from four questions: feeling rested in the morning, trouble falling asleep, trouble waking during the night and trouble waking too early

[4] Odor identification (range: 0-5) is measured via correct identification of five odorants: rose, leather, orange, fish, and peppermint.

[5] Odor sensitivity (range: 0-6) is assessed by participants' capacities to detect n-butanol.

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Table 2

Associations between sleep characteristics and odor identification and olfactory sensitivity among NSHAP Wave 2 olfaction-sleep sub-sample (N=345)

	Model 1[1]			Model 2[2]		
			Odor Identification			
Variable	**Beta coefficient**	**95% CI**	**p-value**	**Beta coefficient**	**95% CI**	**p-value**
WASO	−0.013	(−0.022, −0.003)	<0.01	−0.013	(−0.022, −0.004)	<0.01
Fragmentation	−0.043	(−0.083, −0.003)	0.04	−0.039	(−0.084, 0.006)	0.09
Duration – hours (continuous)	0.027	(−0.111, 0.164)	0.70	0.005	(−0.156, 0.167)	0.95
Duration (categorical)						
<5 hours	−0.291	(−0.829, 0.771)	0.94	0.383	(−0.773, 1.539)	0.51
5-8 hours	-ref-	-ref-	-ref-	-ref-	-ref-	-ref-
>8 hours	0.080	(−0.325, 0.484)	0.69	0.293	(−0.142, 0.727)	0.18
Self-Reported Duration – hours	−0.130	(−0.323, 0.063)	0.38	−0.154	(−0.396, 0.088)	0.21
Troubled Sleep	0.010	(−0.095, 0.114)	0.85	0.064	(−0.065, 0.194)	0.32
			Olfactory Sensitivity			
WASO	−0.003	(−0.008, 0.003)	0.39	−0.003	(−0.009, 0.004)	0.42
Fragmentation	0.003	(−0.027, 0.032)	0.84	0.000	(−0.030, 0.030)	0.99
Duration – hours (continuous)	−0.180	(−0.290, −0.70)	<0.01	−0.152	(−0.275, −0.029)	0.02
Duration (categorical)						
<5 hours	0.214	(−0.388, 0.816)	0.49	0.104	(−0.728, 0.936)	0.80
5-8 hours	-ref-	-ref-	-ref-	-ref-	-ref-	-ref-
>8 hours	−0.532	(−0.991, −0.072)	0.02	−0.426	(−0.897, 0.044)	0.08
Self-Reported Duration – hours	−0.107	(−0.216, 0.002)	0.05	−0.074	(−0.204, 0.055)	0.25
Troubled Sleep	−0.022	(−0.103, 0.059)	0.59	−0.010	(−0.077, 0.096)	0.82

[1]Models are adjusted for age and gender

[2]Models are further adjusted for race/ethnicity, BMI, a modified Charlson Comorbidity Index, Center for Epidemiologic Studies Depression Scale (CES-D), sleep medication and antidepressant usage, and current smoking status.

Table 3

Mediation of the associations between WASO and fragmentation and odor identification by cognition in NSHAP Wave 2 olfaction-sleep subsample

	Beta Coefficient	95% CI	p-value
WASO			
A: Association with cognition	−0.034	(−0.056, −0.012)	<0.01
B: Association of cognition with Odor ID (adjusting for WASO)	0.063	(−0.006, 0.131)	0.07
Indirect association of WASO with Odor ID through cognition	−0.002	(−0.005, 0.001)	0.14
Direct association of WASO on Odor ID (not mediated through cognition)	0.011	(−0.020, −0.002)	0.01
Fragmentation			
A: Association with cognition	−0.083	(−0.152, −0.015)	0.02
B: Association of cognition with Odor ID (adjusting for fragmentation)	0.073	(0.007, 0.140)	0.03
Indirect association of Fragmentation with Odor ID through cognition	−0.006	(−0.012, 0.003)	0.22
Direct association of Fragmentation on Odor ID (not mediated through cognition)	−0.033	(−0.014, 0.002)	0.15