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Associations between chemical odor intolerance and sleep disturbances in community-living adults☆

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Abstract

Objective: To investigate associations between sleep disturbances and chemical odor intolerance (COI), which is the subjective report of feeling ill from common odors, such as carpet glue or pesticides.

Methods: This cross-sectional study consisted of government employees and their family members ($n = 140$; 61% women, mean age = 46.3 years) derived from a stratified cluster population living in Pima County, Tucson, AZ. Subjects completed a standard survey that included sleep symptoms, a validated measure of COI, and two questions regarding anxiety and depression. Odds ratios (OR) with 95% confidence intervals (CI) were computed to test the association between COI and sleep symptoms. Stratification according to the Mantel–Haenszel method and logistic regression models were used to test for confounding and/or effect modification.

Results: After adjusting for age and gender, subjects with COI were significantly more likely to report difficulty staying asleep (OR = 3.06; CI = 1.17–8.03), insufficient sleep (OR = 3.93; CI = 1.43–10.79), and nightmares (OR = 3.17; CI = 1.14–8.81) compared to persons without COI. Associations between COI, sleep maintenance problems and insufficient sleep were still significant after adjusting for gender and depression; however, the association between COI and nightmares became borderline.

Conclusions: Compared to the non-COI, persons with COI are more likely to report sleep maintenance insomnia and insufficient sleep independent of self-reported depression. Nightmares appear to be related more to depression than to COI.

Keywords: Chemical odor intolerance; Cross-sectional; Depression; Difficulty staying asleep; Epidemiology; Insufficient sleep; Nightmares

1. Introduction

Disturbed sleep is reported frequently by individuals with chemical odor intolerance (COI). COI is the subjective report of feeling ill on exposure to non-toxic low-levels of common outdoor and indoor chemicals, such as auto emissions, pesticides, new carpet odor, drying paint, and perfume [1–5]. It is estimated that mild forms of COI are common (15–30%) in the US general population [2,6]. At its most extreme, COI is the focal symptom of the controversial syndrome multiple chemical sensitivity (MCS) [7–10], prevalence rates of which have been estimated at 4–6% of the population [2,6,11]. In addition to sleep disturbances [12], persons with COI or MCS frequently report unrelated multiple symptoms, such as headaches, myalgias, inability to concentrate, nasal and food allergies and mood changes [13–18]. A key concept that underscores the on-going debate regarding COI and MCS is that these multi-system, polysymptomatic complaints occur at such low-level exposures that they are difficult to quantify and do not appear to follow usual exposure–response relationships [8–10].

In general, women report more COI and MCS [1,2,4,6,15,19] and depression [20,21] than do men.

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A preponderance of MCS studies has shown depression to be the most prevalent premorbid or comorbid psychological complaint [17,22,23]. Although some researchers have suggested that both COI and MCS are psychogenic in nature [9,23,24], COI has been noted to covary weakly with depression. For example, depression failed to account for any of the variance in total COI scores in a non-clinical college sample where 79% of the COI individuals were women [16].

COI has been reported with some frequency in other controversial conditions, including fibromyalgia (FM) [25,26], chronic fatigue syndrome (CFS) [27,28], and Persian Gulf War syndrome (PGWS) [29,30]. It has been suggested that these conditions are related; there is a high degree of multi-organ symptom overlap [19]. Persons with these syndromes have objectively and/or subjectively documented insomnia, particularly sleep maintenance problems, varying degrees of non-restorative sleep, and daytime fatigue [31–39].

Despite consistent reports of disturbed sleep by persons with COI, little systematic research has been done to describe the sleep disturbances of these persons, particularly when compared with the extent to which sleep research has been carried out in companion syndromes. The aims of this study are to identify the proportions of sleep disturbances in persons with and without subjective complaints of COI and determine any independent associations between COI and specific sleep disturbances in a sample of community-living adults.

2. Materials and methods

2.1. Study sample

Subjects ($n = 181$) representing 113 households from a stratified cluster population study of Pima County government employees (Tucson, AZ) completed a standard health questionnaire that included sleep symptoms, an odor intolerance index measure, and two questions on anxiety and depression during a 1992–1993 follow-up investigation [40]. A subset of 140 subjects from this sample, who provided information on the presence of COI and at least one question regarding sleep or sleep aids (77.3% respondent rate) was included in this analysis. Subjects were informed only that this was a continuation of the original environmental health study [40], and not that the odor intolerance index would be used to assess COI in order to reduce the chance for recruitment and/or information bias. Each subject was given written information on the use and confidentiality of this data (informed consent) prior to participating in this follow-up study according to the guidelines set forth by the University of Arizona's Human Subjects' Institutional Review Board.

2.2. Sleep symptoms questionnaire

Subjects completed a standard questionnaire, which has been used extensively throughout the 25-year long Tucson Specialized Center of Research (SCOR) study of airways obstructive disorder [41–43]. This instrument has been shown to be valid and reliable [41], and subjective responses have been consistent with clinical diagnoses in 90% of individuals [42].

In addition to demographics, health behaviors and health histories, this survey included questions for the following sleep symptoms: difficulty initiating or maintaining sleep, early morning awakening with trouble returning to sleep, not enough sleep, daytime sleepiness, nightmares (defined as "dreams which frighten you"), snoring, and use of drugs for sleep. A "Yes" response to current or past sleep symptoms was used to identify persons who were positive for sleep problems, while a "No" response indicated absence of sleep problems. Similarly, a "Yes" to current or past use of medications or alcohol to help them get to sleep was used to identify persons positive for use of drugs for sleep, while a "No" answer indicated the absence of medication or alcohol use for sleep. Frequency of loud snoring utilized a five-point Likert-like scale with 1: "Never" to 5: "Every night". Nominal categories for snoring were dichotomized such that "Every night" and "Most nights" represented frequent loud snoring, and "Some nights", "Rarely" and "Never" represented persons who do not snore.

2.3. Chemical odor intolerance index

Subjects completed a validated measure of COI [44]. Each of five odors (perfume, pesticides, new carpet, drying paint, auto exhaust) was rated on a five-point Likert-like scale with 1: "never" and 5: "almost always". The total summed scores range from 5 to 25. Prior studies from this data set [1,13] identified subjects with COI as "frequently" to "almost always" (range 15–25) feeling ill from the five common chemicals. The odor intolerance index has been used in studies of over 2000 individuals, including college students, community-living elderly, and women with COI or MCS [44]. This self-reported measure has demonstrated strong internal consistency with Cronbach's alpha ranging from 0.80 to 0.92 across samples, as well as discriminant, convergent and group validity [44].

2.4. Anxiety and depression

Standard anxiety and depression measures were not included in this study due to concerns for subject burden. However, two statements, "I experience anxiety", and "I experience depression" were included in the questionnaire. These statements were also rated on a five-point Likert-like scale with 1: "never" and 5: "almost always". Each of these measures was dichotomized with "often" and "almost

always" combined to indicate current anxiety or depression, and "never", "rarely" and "sometimes" combined to indicate the absence of current anxiety or depression.

2.5. Analysis

Chi-square analysis was used to compare proportions of self-reported sleep symptoms among persons with and without COI. Odds ratio (OR) calculations with 95% confidence intervals (CI) were computed in order to determine significant associations between COI and sleep disturbances. Stratification according to the Mantel–Haenszel method and logistic regression models were used to test for confounding and/or effect modification for the association between COI and sleep disturbances [45]. The Fisher's exact test (two-tailed) was used to provide the p-value for OR results [46], with significance set at $p < 0.05$.

3. Results

3.1. Demographic characteristics of the study sample

Demographic characteristics for the study sample are shown in Table 1. Women were significantly more likely than men to be represented in the group having COI (86.2%) than in the non-COI group (54.1%, $p < 0.01$). The non-COI reported significantly more years of education compared to persons with COI (15 versus 13.9 years, $p < 0.05$). No significant differences were noted for age, ethnicity, marital status, smoking or body mass index between the groups. No differences in these characteristics were found between subjects who provided information on sleep symptoms and subjects who did not.

Table 1
Characteristics of the study population

	COI, *N* (%)	Non-COI, *N* (%)
Sex:		
Male	4 (13.8)	51 (45.9)
Female	25 (86.2)	60 (54.1)**
Ethnicity:		
Non-Hispanic White	27 (96.4)	93 (91.2)
Other	1 (3.6)	9 (8.8)
Marital status:		
Married (referent)	18 (62.1)	86 (78.2)
Separated/divorced	5 (17.2)	11 (10.0)
Widowed	1 (3.4)	3 (2.7)
Never married	5 (17.2)	10 (9.1)
Smoking status:		
Never (referent)	16 (55.2)	57 (53.3)
Current	6 (20.7)	9 (8.4)
Past	7 (24.1)	41 (38.3)
Age (years):		
Mean ± SD	46.2 ± 13.9	46.5 ± 11.7
Range	16–71	15–74
Education:		
Mean ± SD	13.9 ± 2.5	15.0 ± 2.6*
Range	10–19	9–21
BMI:		
Mean ± SD	25.7 ± 4.5	26.4 ± 5.5
Range	18–37	18–48

*$p < 0.05$; **$p < 0.01$.

3.2. Chemical odor intolerance and sleep symptoms

The proportion of subjects with sleep symptoms and use of medication or alcohol to promote sleep with and without COI are shown in Table 2. Individuals with COI were three and one-half times as likely to report difficulty staying asleep (OR = 3.55, CI = 1.43–8.79) and over four times more likely to report insufficient sleep (OR = 4.44, CI = 1.68–11.74). The COI were over three and one-half times more likely to report nightmares (OR = 3.71, CI = 1.40–9.90). There were no significant differences between groups for difficulty initiating sleep, early morning awakening with difficulty resuming sleep, excessive daytime sleepiness, frequent loud snoring, or for the use of medication or alcohol to promote sleep. Even after adjusting for age and gender, the associations between COI and difficulty staying asleep (adjusted OR = 3.06, CI = 1.17–8.03), insufficient sleep (adjusted OR = 3.93, OR = 1.43–10.79), and nightmares (adjusted OR = 3.17, CI = 1.14–8.81) were still significant.

3.3. Odor intolerance, anxiety and depression

OR for anxiety and depression associated with COI are shown in Table 3. No significant differences were noted for persons with or without COI for anxiety or depression. The association between COI and depression, however, neared borderline significance ($p = 0.11$).

3.4. Potential confounders in associations between COI and sleep symptoms

The near-borderline significant finding for depression and the larger number of women compared to men with COI suggested that depression and gender could have a confounding effect on the associations between COI and sleep symptoms. Therefore, data were stratified by depression as well as gender. Stratification by depression showed that the OR for the three significant sleep symptoms associated with COI identified in the bivariate analysis were not statistically different in the two strata based on homogeneity tests (Table 4). Moreover, even after adjusting for depression, the association with COI remained significant for difficulty staying asleep (adjusted OR = 3.16, $p < 0.05$), insufficient sleep (adjusted OR = 3.89,

Table 2
Proportion of subjects with sleep symptoms and use of medication or alcohol to induce sleep among persons with and without COI

Sleep symptoms	COI *N* (%)	Non-COI *N* (%)	Crude OR	95% CI	Adjusted OR	95% CI
Trouble falling asleep	11/24 (45.8)	37/103 (35.9)	1.51	0.62–3.71	1.59	0.62–4.11
Trouble staying asleep	15/25 (60.0)	30/101 (29.7)	3.55	1.43–8.79**	3.06	1.17–8.03*
Early morning awakening	12/25 (48.0)	31/100 (31.0)	2.06	0.84–5.01	1.78	0.68–4.61
Insufficient sleep	17/24 (70.8)	35/99 (35.4)	4.44	1.68–11.74**	3.93	1.43–10.8**
Excessive daytime sleepiness	6/23 (26.1)	17/97 (17.5)	1.66	0.57–4.83	1.95	0.61–6.18
Nightmares	10/24 (41.7)	16/99 (16.2)	3.71	1.40–9.90**	3.17	1.14–8.81*
Frequent loud snoring	12/21 (57.1)	46/84 (54.8)	1.10	0.42–2.89	0.79	0.27–2.33
Medication/alcohol use for sleep	9/29 (31.0)	21/111 (18.9)	1.93	0.77–4.83	1.79	0.65–4.92

*$p < 0.05$; **$p < 0.01$.

$p < 0.01$), and nightmares (adjusted OR = 3.14, $p < 0.05$) (Table 4).

Due to the small sample size of males with COI, we were unable to test the associations between COI and sleep symptoms among males and whether they would be different from those among females. However, as for depression, after adjustment for gender, the OR associated with COI were still significant for difficulty staying asleep (adjusted OR = 3.06, CI = 1.19–7.89), insufficient sleep (adjusted OR = 3.77, CI = 1.38–10.33) and nightmares (adjusted OR = 3.27, CI = 1.17–9.13).

When the effect of COI on sleep symptoms was adjusted simultaneously for depression and gender in the multivariate analysis, the adjusted OR associated with difficulty staying asleep (OR = 2.98, CI = 1.14–7.75) and insufficient sleep (OR = 3.40, CI = 1.22–9.45) remained significant. In contrast, the effect of COI on nightmares was no longer significant (adjusted OR = 2.78, CI = 0.96–8.05). Depression was a stronger predictor than COI for the presence of nightmares in the logistic regression model (adjusted OR = 3.67 for the association between depression and nightmares; CI = 1.41–9.54, $p = 0.008$).

4. Discussion

Our findings suggest that persons with COI are significantly more likely to experience sleep maintenance insomnia and insufficient sleep. These associations remained significant after adjusting for age and gender. The sleep maintenance insomnia finding corroborates an existing study of objectively measured disturbed sleep in community-living elderly with COI [12]. Furthermore, COI and its companion syndrome of MCS have been generally attributed to psychiatric symptomatology [9,23,24].

Table 3
Odds ratios for anxiety and depression associated with COI

	COI, *N* (%)	Non-COI, *N* (%)	OR	CI
Anxiety	17/29 (58.6)	57/108 (52.8)	1.29	0.56–2.96
Depression	12/28 (42.9)	29/108 (26.9)	2.02	0.85–4.77

However, our findings do not support the hypothesis that COI and sleep symptoms, such as difficulty staying asleep and insufficient sleep, are associated simply because they are both common among persons with depression. The OR for the associations between COI and these sleep disturbances, in fact, were reduced but still significant after adjustment for depression. The relationship between COI and nightmares is equivocal. While nightmares are associated with COI, results from the multi-variate analysis suggest that this association might be confounded by depression. There are studies suggesting relationships between depression and nightmares, which should be examined further in future studies [47,48].

The findings reported here are as notable for the sleep problems that were ruled out as for those with which COI is associated. Sleep onset problems, early morning awakening with difficulty returning to sleep, snoring, excessive daytime sleepiness, and use of medications or alcohol to promote sleep did not differ between groups. Although sleep onset difficulties and early morning awakening are parts of the spectrum of difficulty initiating and maintaining sleep,

Table 4
Odds ratios for the association between COI and sleep problems stratified and adjusted for depression

	Stratified OR[a]	CI	Adjusted OR[b]	CI
Difficulty staying asleep				
Depression	3.60	0.86–15.01		
No depression	2.86	0.85–9.57	3.16	1.26–7.93*
Insufficient sleep				
Depression	5.83	1.06–32.02		
No depression	2.99	0.85–10.49	3.89	1.44–10.55**
Nightmares				
Depression	3.33	0.81–13.67		
No depression	2.91	0.63–13.32	3.14	1.11–8.86*

*$p < 0.05$; **$p < 0.01$.

[a] Stratified odds ratios are not significantly different in depression and non-depression strata for each of the sleep complaints based on homogeneity tests.

[b] Adjusted odds ratios are significant for each of the sleep complaints.

which are more commonly reported by women [49–51], these complaints are not significantly associated with COI in this study. Snoring and excessive daytime sleepiness are generally related to obstructive sleep apnea, which are associated more with male gender [52]. Our results support the existence of an association between COI and sleep maintenance insomnia, but not sleep apnea, in a polysomnographic study in which older adults with COI demonstrated lower sleep efficiency [12]. The elderly with COI also showed decreased REM percent and a trend toward longer rather than shorter REM onset latency, suggesting that the sleep pattern of these elderly with COI differed objectively from major depressives [12].

Persons with sleep disturbances are more likely to report the use of prescribed medications or alcohol to promote and maintain sleep [53,54]. There are no significant differences between COI and non-COI groups, however, in their reported use of sleep aids or alcohol in this study. Persons with COI are not only less able to tolerate common chemicals, such as perfumes and pesticides, they also report being less able to tolerate prescription medications, alcohol and illicit drugs, and certain foods; these substances reportedly exacerbate their polysymptomatic complaints [2,7,16,27]. This sensitivity to prescription drugs and alcohol could account, in part, for the lower use of sleep aids despite greater reports of sleep symptoms on the part of persons with COI.

Prior epidemiological-based sleep investigations have indicated that women report higher rates of difficulty in initiating and maintaining sleep, as well as nightmares [49]. Advancing age, female gender and comorbid health complaints have also been cited as significant risk factors for insomnia [50]. Environmental research studies have suggested that the rates of COI are much higher for women compared to men [14,16,17]. The higher reports of sleep maintenance insomnia and insufficient sleep by women with COI in this study are consistent with the above-cited epidemiological findings. Future longitudinal studies of COI and sleep will need to be done to determine if COI is a potential risk factor for the sleep disturbances identified in this study, particularly for women. Women also tend to be over-represented in other unexplained illnesses, such as FM and CFS [8,26,27,30], of which COI is a frequent complaint [19]. Insomnia and fatigue have been leading complaints in these female predominant disorders as well [19].

There are several important limitations to this work including the use of self-reported data, nominal data analytic techniques, relatively small sample size, restricted geographical sampling, lack of standard measures of depression, anxiety, and other sleep-related variables and conditions. Studies of this kind, however, using surveys, questionnaires, and statistical analyses based on sound epidemiological methods can provide heuristic approaches in the development of future more rigorous basic- and clinical-sciences studies. The survey questionnaire used in this investigation, adapted from the National Heart Lung Blood Institute (NHLBI) and American Thoracic Society (ATS) questionnaires used in epidemiological research [42,43], is shown to be valid and reliable [41], and responses have been consistent with clinical diagnoses in 90% of individuals [42]. The statistical approaches used in this study are highly relevant to epidemiology and can provide insight into the clinical basis and clinical significance of disorders, and factors that may contribute to the natural course of these disorders.

Skepticism surrounding the nature of MCS in particular and COI in general (ambiguous exposure–response relationships), and the controversy surrounding these unexplained illnesses (litigation issues and chemophobic overtones) have made the study of COI very difficult. Subject selection and recruitment bias were controlled for in this study, however, by recruiting participants for an investigation of "air quality on health" from a community-based pool of adult county workers in lieu of recruiting participants for a study of COI per se. Terms such as COI, chemical sensitivity and MCS were not used in any of the recruitment procedures.

Due to concerns regarding subject burden, sleep diaries and standard measures of anxiety and depression were not included in the data collection. Instead, respondents indicated the degree to which they experienced anxiety or depression. Future studies of COI and sleep problems using validated measures of anxiety and depression in larger samples from the general population are needed to determine the complex interrelationship between these conditions. Validated measures of depression may be able to tease out associations with COI and nightmares, or support greater associations between depression and nightmares. Other issues for future studies should include sleep hygiene and sleep diary data, such as caffeine intake and daytime naps. Although overlap has been reported for FM, CFS and COI [19], screening for these conditions, as well as such parasomnias as restless legs syndrome and periodic limb movements may contribute to a more comprehensive understanding of sleep disturbances in persons with COI. These studies should also over sample men with COI in order to determine any associations between COI and sleep symptoms by gender. Finally, the cross-sectional nature of this investigation cannot infer a cause and effect relationship between COI and specific sleep problems.

These limitations aside, to our knowledge this is the first study to systematically investigate associations between COI and sleep disturbances. Findings from this research can provide a springboard from which future studies of COI and sleep disturbances can be designed and implemented. There are accumulating data suggesting that mild forms of COI are common in the US general population [2,6]. It has also been reported that prevalence rates for both COI and insomnia are higher in women than men, particularly with onset in middle age [49–51]. Low rates for recognition and diagnosis of sleep disorders in both primary care and clinical academic settings [55], in combination with data suggesting that COI

may be a potential risk factor for specific sleep disturbances make associations between COI and sleep important areas for future sleep medicine research.

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