HHS Public Access

Author manuscript

Occup Environ Med. Author manuscript; available in PMC 2024 July 12.

Published in final edited form as:

Occup Environ Med. ; 81(6): 302–307. doi:10.1136/oemed-2023-109262.

Lack of association of impaired upper airway sensation with the presence or absence of obstructive sleep apnoea or chronic rhinosinusitis in World Trade Center responders

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Abstract

Objective—Examine sensory function of the upper airway in four groups of subjects recruited from the World Trade Centre General Responder Cohort (WTCGRC), with/without obstructive sleep apnoea (OSA), and with/without chronic rhinosinusitis (CRS).

Methods—Upper airway sensory function was determined using 2-point discrimination (2-PD) and vibration threshold (VT) in 163 WTCGRC subjects with both OSA and CRS (cases), OSA or CRS alone and without OSA or CRS (controls). Presence of OSA was determined from clinical sleep studies or home sleep testing. Presence of CRS was determined by nasal symptom

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Contributors ADR, AL, HRC, IGU, REdlH and SSR contributed to the subject recruitment. AEM, JS, IGU, REdlH, IA, DMR, KB and S-eL analysed the data and edited the manuscript. JS acts as guarantor.

Competing interests CDC/NIOSH: U01OH011481 provided support for the present manuscript to JS, IA, KB, IGU, DMR, S-eL, REdlH, AEM, AL, ARD, HRC and SSR. DMR and IA report grants, personal fees, non-financial support and other from Fisher Paykel Healthcare outside the submitted work. In addition, DMR and IA have patents for modifications of CPAP that result in royalties paid through New York University.

Ethics approval The study protocol was approved by the Institutional Review Boards of Rutgers (Pro20170001426) and the ISMMS (HS#18-00097). Participants gave informed consent to participate in the study before taking part.

questionnaire. The relationship between the presence of OSA and CRS and upper airway sensory impairment was assessed using linear regression analysis with each of 2PD and VT sensory threshold values as the dependent variable; OSA, CRS and their interaction were the independent variables. Age, gender and body mass index were covariates in the statistical model. The primary analysis was comparison of OSA+CRS versus controls (no OSA and no CRS) evaluated by linear contrasts.

Results—There were no differences in 2-PD or VT in those with OSA+CRS, OSA and CRS alone or controls. However, both 2-PD and VT were significantly higher in the WTCGRC controls compared with values seen in historical controls using the same methodology (median 2-PD 13.0; CI (11.0 to 13.5) vs 10.5; CI (8 to 11); VT: mean±SEM (9.3±0.6 vs 2.2±0.1)).

Conclusion—While no differences were found in upper airway sensation between cases of OSA and CRS versus controls in the WTGRC population, there was evidence of impaired upper airway sensation in the WTGRC overall.

INTRODUCTION

Following the WTC attack on 11 September 2001, a diverse population of workers were exposed to vast amounts of dust while working in rescue, recovery and debris removal.[1] The World Trade Centre Health Program (WTCHP) has performed long-term health surveillance on more than 90 000 responders for effects from these exposures.[2]

New and persistent upper airway (UA) diseases (rhinosinusitis, gastro-oesophageal reflux disease and obstructive sleep apnoea (OSA)) have been consistent findings in the WTC General Responder cohort (WTCGRC). A statistically significant association between time of arrival at the site and respiratory symptoms has been demonstrated.[1] In the Role of Nasal Pathology in WTC Responders (WTCSNORE) study, we documented a prevalence of 43% of chronic rhinosinusitis (CRS).[3] Many responders did not consistently use respiratory protective equipment, exposing them to highly alkaline and corrosive dust, including calcium sulphate (gypsum) and calcium carbonate (calcite), known chemical irritants to UA mucus membranes and large airways, that may have led to progression to CRS.[4]

OSA is a chronic condition with recurrent episodes of partial or complete UA collapse during sleep, main risk factors being obesity and male gender. Prevalence of OSA in general populations ranges from 5% to 50%.[5 6] The consequences of untreated OSA include excessive daytime sleepiness, impaired quality of life, depression and cardiovascular and cerebrovascular morbidity and mortality.[7 8] In WTCSNORE, we recruited subjects who did not have a diagnosis of OSA and had no significant snoring prior to 9/11; we also oversampled current non-snorers to reduce selection bias from snorers seeking therapy. Despite this, there was a 75% prevalence of OSA, significantly higher than any other epidemiological cohort reported in the literature with similar characteristics including weight, snoring and sleepiness levels.[3 5 6] We also found that CRS was an independent risk factor for OSA.[3] To explain this association, we initially hypothesised that nasal inflammation and nasal congestion from CRS increase nasal resistance and compromise UA patency, thus providing a potential mechanism for OSA. However, we were unable to demonstrate a difference in OSA prevalence between subjects with high versus low

nasal resistance[9] suggesting other mechanisms that impair mechanoreflexes to negative inspiratory pressure such as neuropathy, and fibrosis may impact UA function and reduced UA sensitivity.[10-12] Both the afferent and efferent limbs of UA reflexes are needed to maintain UA patency. Loss of sensation would lead to failure of UA muscle activation and contribute to UA collapse. An impaired afferent limb of UA reflexes relating to CRS might reduce the ability to perceive and/or process UA loading contributing to failure of reflex muscle activation of the UA. Additionally, UA sensory dysfunction is reported in OSA.[12 13]

We hypothesised that subjects with both CRS and OSA would have decreased sensation in the UA compared with control subjects with neither CRS nor OSA, while subjects with CRS without OSA, and OSA without CRS would have intermediate values. To test this hypothesis, we examined the role of UA sensory function (2-point discrimination (2PD) and vibration sensitivity threshold (VT)) in four groups of subjects: with/without OSA and with/without CRS.

METHODS

Study design: case control study

Cases were OSA positive, CRS positive.

Controls were OSA negative, CRS negative.

Subjects were recruited from the WTCHP at the Environmental and Occupational Health Sciences Institute clinic of Rutgers Health (Pro20170000631) and from Icahn School of Medicine at Mount Sinai (ISMMS) who had agreed to be contacted for future research.

We performed UA sensory testing (2PD and VT) during a single visit. A research assistant measured the subject's height, weight and neck circumference and subjects completed several brief questionnaires (Sleep and Snoring, Epworth Sleepiness Scale (ESS)[14] and Nasal Symptom).[15 16] Self-reported data on WTC exposure level was obtained from the General Responder Cohort Date Centre and classified as very high, high, intermediate or low.[17]

2PD and VT were performed in random order in the UA and at two non-pharyngeal control sites (on the lower lip and on the hand) in a seated position. During a training period, repeated testing was performed by research assistants on different days on the same subjects to confirm reliability and validity of the results obtained.

2 Point discrimination

2PD was measured using standard techniques described by Kimoff *et al*[12] (1) on the dorsum of the hand on the skin overlying the first interosseous muscle, (2) on the lower lip and (3) in the oropharynx along the margin of the soft palate lateral to the uvula on both the right and left sides. A series of two-point probes with fixed interprobe distances ranging from 2 to 28 mm were used, applying the largest interprong distance for the given site. Each application of a probe lasted 2 s with enough pressure to slightly indent the skin or mucosal lining. Testing in the oropharynx was performed under direct visualisation with the aid of a

bright headlamp. The patient was asked to actively open the mouth and protrude the tongue. The testing stimulus was randomly alternated between one and two points and the subject indicated one versus two points either by holding up fingers or verbally (for testing on the hand). If the subject correctly reported the number of points on at least three of five trials, the next smaller interprobe distance was used. The smallest interprobe distance at which the subject correctly identified one versus two points in three of five trials was taken as the 2PD threshold for that site. If a subject was unable to correctly identify one versus two points even at the largest interprobe distance, this distance was assigned as the threshold value.

Vibratory sensation threshold

VT was performed during wakefulness using standard techniques[12 13] with the subject seated, with a clinical testing device (Vibratron II; Physitemp, Clifton, New Jersey) that has been previously used in both adults and children with OSA.[12 13] The device was modified slightly (length of the post extended) to allow access to the oropharynx. The unit consists of a controller and vibrating post capable of delivering a vibrating stimulus at 120 Hz. The amplitude of vibration is determined by varying the voltage at the controller unit. VT was first determined on the subject's hand to familiarise the subject and ensure sensory normality. Similar to 2PD, testing was performed over the lower lip and the oropharyngeal mucosa. For testing of the oropharyngeal mucosa, the transducer was fixed to a stand of adjustable height placed in front of the participant. The position of the stand was adjusted so that the probe was against the oropharyngeal mucosa at the upper portion of the anterior tonsillar pillar with sufficient pressure to slightly (1 mm) indent the mucosa; position of the probe was maintained throughout testing. Direct visualisation with a headlamp ensured that the vibrating probe was always in proper position, applied with the appropriate pressure, and not in contact with any other oral structures. VT was determined using the method of limits.[12 13] Once the probe was in contact with the testing site, the intensity of vibration was increased progressively at a rate of 0.1 vibration units/s from zero until the patient detected the vibration. Stimuli were presented in ascending or descending order, with the participant providing a response after each presentation. A stimulus series was continued until the response changed. At that point, a new series begins in the opposite order. The point at which the participant's response changed provided information about the perceptual threshold. Participants were instructed to say, "I feel it" and "I don't feel it" when testing vibration on the hand, and to raise a hand when they felt vibration in the palate. Ascending and descending trials were performed on the hand. Only ascending trials were performed in the oropharynx as descending trials have been shown to be more likely to elicit a gag reflex.[12] The subject was asked to report the initial detection or extinction of vibration verbally or by holding up a finger. The mean of six detection and extinction values was used to yield the vibratory detection threshold for the hand, and the mean of the three detection values was used to yield the vibratory detection threshold for the palate.

OSA evaluation

1. If the subject had a sleep study within the past 6 months or was scheduled for one as part of clinical care, the raw study data were extracted from the clinical record, deidentified, coded by study ID and evaluated for OSA by trained sleep

technicians at ISMMS using American Academy of Sleep Medicine (AASM) guidelines.

2. Subjects who completed the sensory testing and did not have an in-lab sleep study (either within the last 6 months or scheduled) were given a home sleep monitor worn on the forehead (Sleep Profiler, ABM, Carlsbad, California) to use for one night for an evaluation of sleep apnoea. The Subjects were given a mailer to return the device. The sleep study was scored and reviewed by investigators at ISMMS (DMR, IA). For both in-lab and home sleep test, presence of OSA was defined as an Apnoea+Hypopnoea Index (AHI4) of ≥5 or Respiratory Disturbance Index (RDI)>15 as we had done previously.[3]

Subjective assessment of nasal symptoms

Participants were asked to complete a nasal symptom questionnaire. Presence of ≥3 symptoms of rhinitis present for >8 weeks and unrelated to an infection, with or without associated symptoms of sinusitis, pharyngitis or laryngitis, with onset or worsening after 9/11 classified a subject as having CRS. Current medication use for chronic symptoms, including nasal steroids or use of saline irrigations, was documented.

Statistical analysis

Sample size and power considerations—Based on data from Kimoff *et al*[12] comparing VT in OSA subjects and controls (4.0±1.2 vs 2.2±0.38), the effect size in terms of Cohen's d was 2.0. To compare OSA+CRS versus controls (no OSA no CRS), 50 subjects per group were determined to test a much smaller effect size d=0.57, about 30% of the effect size found in Kimoff *et al*,[12] with 80% power (alpha=5%, two-sided, for each of VT and 2PD). However, due to the COVID-19 pandemic, subject recruitment for the study was stopped after a total of 163 OSA (yes vs no) × CRS (yes vs no) subjects were recruited, and sleep studies were completed only in 157 subjects. With resultant 53 OSA+CRS subjects and 26 controls, our study has 80% power (alpha=5%, two sided) to test an effect size d=0.68, per a post-hoc power analysis.

Data analysis

The mean values of the 2PD and VT sensory threshold between subjects in the 4 groups were compared using linear regression analysis with each of 2PD and VT sensory threshold values as the dependent variable, OSA (yes/no), CRS (yes/no) and interaction of OSA and CRS as the independent variables. Age, gender and body mass index (BMI) were controlled as covariates in the statistical models. The primary analysis was the comparison of OSA+CRS versus Controls (no OSA and No CRS) evaluated by linear contrasts.

Variables studied between the two study locations were compared using two-sample t-test (or Wilcoxon test) for continuous variables and χ^2 test for discrete categorical variables.

RESULTS

We recruited 163 subjects (age 57.3±7.6 years, BMI 29.8±5.0 kg/m^2 (mean±std)). We had sleep study data on 157 subjects, and UA sensation testing data on 147. Final analyses with

regard to UA sensation results were performed on the 147 subjects. 69% of the 157 subjects who had sleep studies had OSA and 49% of all 163 recruited subjects had CRS. The median AHI was 7.0/hour (range of 0–75); RDI 17.47/hour (range of 2–101); ESS 5 (range of 0–22) (see table 1).

When we examined subjects based on their OSA and CRS status (table 2), patients who had OSA and CRS had a higher BMI than without OSA and or CRS. Similarly, those with OSA and CRS were sleepier than those without either OSA or CRS. Of note, those with CRS alone manifested greater sleepiness than those with OSA alone. As expected, AHI, RDI and CRS scores in those with OSA and CRS had significantly higher values than those without OSA and/or CRS (table 2). VT and 2PD in the UA (table 2, figures 1 and 2) or in the control locations (hand, and lip) did not differ among the groups (table 2). No differences were noted controlling for BMI (data not shown). Very few of our subjects (n=21) had either high or very high levels of WTC exposure,[17] and we did not find an association between exposure levels and impairment in either vibration or tactile sensation (data not shown).

DISCUSSION

Our study did not demonstrate differences in UA sensory perception in subjects with/without OSA and CRS. Kimoff[11 12] and others[18-21] previously demonstrated an oropharyngeal sensory impairment and mucosal inflammation in OSA,[18 22] with only slight reversibility with Continuous Positive Airway Pressure (CPAP).[12] Nerve demyelination in UA tissue[23] and changes in UA mucosal nerve endings consistent with a pattern of injury and repair[24] have also been reported. Their findings unlike our study support the presence of an UA sensory neuropathy in OSA, but do not distinguish between causal damage (as could happen from CRS) or changes secondary to OSA, as from mechanical trauma associated with snoring or vibration, tissue traction and from obstructive events, or oxidative stress related to hypoxiareoxygenation or systemic inflammation.[25-27]

There were significant differences between subjects in our population compared with the population that Kimoff *et al*[12] studied, who were recruited from a sleep clinic, were younger (mean age 41), more obese (mean BMI 33) and had more severe OSA (mean AHI of 48) than ours. Additionally, the control values in their subjects for mean VT (2.2 vs 9.7) and median 2-PD (10.5 mm vs 13 mm) were much lower than in our population (better sensitivity) despite similar methodology. In fact, the values obtained for 2-PD in our overall population were in the range seen in the OSA population in the Kimoff study (online supplemental table 1). A study by Jobin *et al*[21] using similar methods to Kimoff also showed impaired UA VT and 2-PD in those with OSA. These subjects also had very severe OSA (mean AHI of 57/hour) and were obese (mean BMI of 32.4 kg/m^2). A study by Guilleminault *et al*[18] showed higher values for 2-PD in OSA than in subjects with upper airway resistance syndrome (UARS) and controls and no differences between UARS and controls. Interestingly, control, snorers and UARS subjects had 2-PD values ranging from 1.0 to 2 mm and those with OSA ranging from 3 to 5 mm. Similar results were also observed by Jeong *et al*[20] in children using the same device with greater impairment noted in children with obesity.[13] These values are much lower than the values obtained by Kimoff or us in controls but were obtained with a different device which may explain this result.

A device similar to the one used by Guilleminault and Jeong was used by Heiser *et al*,[19] and revealed a range of 5±2.4 mm in controls and 11.5±5.4 mm in patients with OSA. Finally, similar to our study, a study examining vibration sensation in men and women without and with snoring and OSA showed no difference in vibration sensation in any of these groups in men.[28] However, the vibration sensation was tested with a different device than the one we used. These findings suggest that results could be very dependent on the methodology of measurement, the severity of OSA, BMI and sex. Indeed, a recent systematic review and meta-analysis of UA sensation in OSA found that for all of the studies that performed 2-PD and VT, data on validation using objective measures such as pharyngeal nerve conduction velocities, airflow stimuli and cough reflex were unavailable.[29] We ensured reliability and validity of our measurements across different researchers by performing repeated measurements in the same test subjects across multiple days.

Other methods of testing UA sensation, including airflow, chemical, gustatory, olfactory, temperature and neurosensation have also been studied in patients with OSA.[19-21 28-32] Overall, while these studies reported a significant correlation between UA sensory impairment and increased OSA severity, the results were significantly heterogeneous.[29]

There is less evidence of impaired UA sensation in patients with CRS. A loss of smell has been reported in patients with CRS and has been attributed to inflammation and release of cytokines.[33] Impairment of olfactory neuronal function from chronic inflammation has also been suggested in animal studies.[34]

While our findings suggest that the presence of CRS and OSA has no effect on UA sensory tactile and vibration sensory perception among the participants, the reasons for these negative results may be due to the population studied.

The WTCGRC were exposed to potential neurotoxic heavy metals and complex hydrocarbons in WTC dust and fumes which provide biological plausibility for the hypothesis that WTC exposure increases the risk of neuropathy.[35] The latter may in turn explain the substantially higher values in both UA vibration and tactile sensory thresholds in our subjects, compared with the controls in the Kimoff study and the similarity of those values to those seen in subjects with OSA in their study (see online supplemental table 1).[12] Thus, this population may have impaired UA and sensory perception as a result of WTC-related exposures, even in the absence of CRS and OSA that may mask any effect from having either or both diseases. There may be a ceiling effect to 2-PD and vibration sensory impairment and therefore differences between those with and without OSA and or CRS may not have been observed.

That our results for the UA are likely accurate is confirmed by the absence of difference in the 2-PD test results in the lip and the hand between our controls and the Kimoff study controls (online supplemental table 1). Additionally, we saw no differences in the VT and 2-PD test results between the two sites where testing was performed by different researchers (online supplemental table 2). Finally, in our population, while there was a significant correlation between the 2-PD in the lip to the UA (correlation coefficient $r=0.17$, $p<0.05$), the correlations between those two sites or between the lip and the hand were much closer

for VT (r=0.38, p<0.0001, and r=0.48, p<0.0001, respectively); VT was, however, higher in our study in the lip and hand and significantly higher in the UA compared with those found in the Kimoff study. This may have been due to the modification of the probe length in order to allow it to reach the posterior pharynx. While these findings suggest a possible impairment in vibration sensation in the WTC population involving the extremities and the UA, the modification of the probe length for VT sensation testing may have impacted this finding. There was, however, in addition an impairment to tactile sensation in the UA, suggesting the presence of impaired UA sensation in this population irrespective of the presence of OSA or CRS.

Peripheral neuropathy symptoms are reported in the WTC population and are associated with exposure intensity.[35 36] Neurotoxins can affect primarily large myelinated fibres, thereby affecting vibration sense with relatively little impairment in the detection of tactile stimuli.[37] Thus, the greater impairment in vibration sense relative to 2-PD in our population as compared with the healthy population in Kimoff's study may be due to exposure to neurotoxins from WTC dust. We, however, did not find an association between exposure levels to dust and impairment in either vibration or tactile sensation. This may have been because very few of our subjects (n=24) had high or very high levels of exposure subjects.

Study limitations

Our study has a number of limitations.

We did not have a healthy control population (unexposed to WTC dust) and therefore the conclusions drawn regarding abnormal UA 2-PD and VT testing results in our population are based on historical controls from another study. However, the aim of our study was to determine the mechanism of OSA in the WTC responder cohort and to understand the relationship between CRS and OSA. We therefore did not recruit non-WTC exposed controls. Additionally, the normal peripheral tactile sensation and the corelation of both vibration and tactile sensation at multiple anatomical sites and at our two locations of testing suggest that our testing was reliable and valid.

Additionally, we used a questionnaire to determine the presence or absence of CRS. Therefore, whether CRS was WTC related or not could not definitively be ascertained.

We used tactile and vibration sensation testing of the UA and did not examine other forms of sensations such as chemical, olfactory, gustatory or temperature because of the differences between patients with OSA and controls shown in prior studies and because we were seeking to understand the high prevalence of OSA and the relationship between CRS and OSA in our WTC population. It is likely that other UA sensory pathways are involved in this population, especially gustatory and olfactory,[38] given the high prevalence of CRS and the effect of CRS on these pathways.

In addition to CRS symptoms, it is possible that laryngeal sensation is impaired as a result of the inhalational exposure. By focusing only on the oropharynx in this study, a potentially important relationship with impaired laryngeal sensory function and risk of OSA may have been missed. Laryngeal afferents and subglottic receptors are known to play an important

role in maintaining UA dilator muscle tone.[39 40] Additionally impairement in sensory inputs may be heterogenous throughout the UA as suggested by the absence of correlation between impaired laryngeal sensation and oropharyngeal sensation in one study.[26] That same study demonstrated impaired laryngeal sensory function in OSA, which in a subset of patients correlated with OSA severity but did not correlate well with the severity of impairment measured in the oropharynx.

We had unequal number of study subjects in each group due to the high prevalence of OSA and CRS in our population.

Finally, we did not fully meet our study recruitment target based on power analysis due to the COVID-19 pandemic. However, we believe our study results would not have been different had we met our recruitment targets as differences in UA tactile and vibration sensation between subjects with and without either OSA or CRS were negligible.

Strengths of the study and future directions

This is the largest study to date examining UA sensation in a population with OSA, and the only study examining UA sensation in those with CRS.

Future studies examining directly the association of WTC exposures on olfactory and gustatory sensation could provide insight into the possible neurotoxic effects of WTC dust in this population. Additionally, objective measures of afferent neural function including sensory nerve conduction studies and muscle responses to pressure stimuli at other UA sites and UA EMG studies[41] could be performed to assess for denervation or myopathic changes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors would like to acknowledge the contributions of Carlos Osorio, David Kim, Sidra Farooqi and Reagan Schoenholz in the recruitment of study participants.

Funding

This study was funded by CDC/NIOSH: U01OH011481.

Data availability statement

Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information.

REFERENCES

1. Herbert R, Moline J, Skloot G, et al. The world trade center disaster and the health of workers: five-year assessment of a unique medical screening program. Environ Health Perspect 2006;114:1853–8. [PubMed: 17185275]

2. Moline JM, Herbert R, Levin S, et al. WTC medical monitoring and treatment program: comprehensive health care response in aftermath of disaster. Mt Sinai J Med 2008;75:67–75. [PubMed: 18500708]

3. Sunderram J, Weintraub M, Black K, et al. Chronic rhinosinusitis is an independent risk factor for OSA in world trade center responders. Chest 2019;155:375–83. [PubMed: 30739642]

4. McGee JK, Chen LC, Cohen MD, et al. Chemical analysis of world trade center fine particulate matter for use in toxicologic assessment. Environ Health Perspect 2003;111:972–80. [PubMed: 12782501]

5. Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the Hypnolaus study. Lancet Respir Med 2015;3:310–8. [PubMed: 25682233]

6. Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177:1006–14. [PubMed: 23589584]

7. Baldwin CM, Griffith KA, Nieto FJ, et al. The Association of sleep-disordered breathing and sleep symptoms with quality of life in the sleep heart health study. Sleep 2001;24:96–105. [PubMed: 11204058]

8. Marin JM, Agusti A, Villar I, et al. Association between treated and untreated obstructive sleep apnea and risk of hypertension. JAMA 2012;307:2169–76. [PubMed: 22618924]

9. Ayappa I, Laumbach R, Black K, et al. (in press) Nasal resistance and inflammation: mechanisms for obstructive sleep apnea from chronic rhinosinusitis. J Clin Sleep Med.

10. Boyd JH, Petrof BJ, Hamid Q, et al. Upper airway muscle inflammation and denervation changes in obstructive sleep apnea. Am J Respir Crit Care Med 2004;170:541–6. [PubMed: 15151922]

11. Kimoff RJ. Upperairway myopathy is important in the pathophysiology of obstructive sleep apnea. J Clin Sleep Med 2007;3:567–9. [PubMed: 17993035]

12. Kimoff RJ, Sforza E, Champagne V et al. Upper airway sensation in snoring and obstructive sleep apnea. Am J Respir Crit Care Med 2001;164:250–5. [PubMed: 11463596]

13. Tapia IE, Kim JY, Cornaglia MA, et al. Upper airway vibration perception in school-aged children with obstructive sleep apnea. Sleep 2016;39:1647–52. [PubMed: 27253764]

14. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness scale. Sleep 1991;14:540–5. [PubMed: 1798888]

15. de la Hoz RE, Shohet MR, Chasan R, et al. Occupational toxicant inhalation injury: the world trade center (WTC) experience. Int Arch Occup Environ Health 2008;81:479–85. [PubMed: 17786467]

16. Storaas T, Steinsvåg SK, Florvaag E, et al. Occupational rhinitis: diagnostic criteria, relation to lower airway symptoms and IGE sensitization in bakery workers. Acta Otolaryngol 2005;125:1211–7. [PubMed: 16353405]

17. Wisnivesky JP, Teitelbaum SL, Todd AC, et al. Persistence of multiple illnesses in world trade center rescue and recovery workers: a cohort study. Lancet 2011;378:888–97. [PubMed: 21890053]

18. Guilleminault C, Li K, Chen N-H, et al. Two-point palatal discrimination in patients with upper airway resistance syndrome, obstructive sleep apnea syndrome, and normal control subjects. Chest 2002;122:866–70. [PubMed: 12226025]

19. Heiser C, Zimmermann I, Sommer JU, et al. Pharyngeal chemosensitivity in patients with obstructive sleep apnea and healthy subjects. Chem Senses 2013;38:595–603. [PubMed: 23821728]

20. Jeong K-H, Yang Y, Choi HR, et al. Assessment of change in palatal sensation in obstructive sleep apnea patients by using two-point palatal discrimination. Clin Exp Otorhinolaryngol 2016;9:226–32. [PubMed: 27095515]

21. Jobin V Champagne V Beauregard J, et al. Swallowing function and upper airway sensation in obstructive sleep apnea. J Appl Physiol (1985) 2007;102:1587–94. [PubMed: 17185498]

22. Dematteis M, Lévy P, Pépin J-L. A simple procedure for measuring pharyngeal sensitivity: a contribution to the diagnosis of sleep apnoea. Thorax 2005;60:418–26. [PubMed: 15860719]

23. Woodson BT, Garancis JC, Toohill RJ. Histopathologic changes in snoring and obstructive sleep apnea syndrome. Laryngoscope 1991;101:1318–22. [PubMed: 1766303]

24. Friberg D, Gazelius B, Hökfelt T, et al. Abnormal afferent nerve endings in the soft Palatal mucosa of sleep apnoics and habitual Snorers. Regul Pept 1997;71:29–36. [PubMed: 9299639]
25. Larsson H, Carlsson-Nordlander B, Lindblad LE, et al. Temperature thresholds in the oropharynx of patients with obstructive sleep apnea syndrome. Am Rev Respir Dis 1992;146:1246–9. [PubMed: 1443879]
26. Nguyen ATD, Jobin V Payne R, et al. Laryngeal and velopharyngeal sensory impairment in obstructive sleep apnea. Sleep 2005;28:585–93. [PubMed: 16171271]
27. Svanborg E. Impact of obstructive apnea syndrome on upper airway respiratory muscles. Respir Physiol Neurobiol 2005;147:263–72. [PubMed: 16054444]
28. Hagander L, Harlid R, Svanborg E. Quantitative sensory testing in the oropharynx: a means of showing nervous lesions in patients with obstructive sleep apnea and snoring. Chest 2009;136:481–9. [PubMed: 19542255]
29. Wallace ES, Carberry JC, Toson B, et al. A systematic review and meta-analysis of upper airway sensation in obstructive sleep apnea - implications for pathogenesis, treatment and future research directions. Sleep Med Rev 2022;62:101589. [PubMed: 35121222]
30. Sunnergren O, Broström A, Svanborg E. Soft palate sensory neuropathy in the pathogenesis of obstructive sleep apnea. Laryngoscope 2011;121:451–6. [PubMed: 21271605]
31. Yenigun A, Degirmenci N, Goktas SS, et al. Investigation of smell and taste function in patients with obstructive sleep apnoea syndrome. J Laryngol Otol 2019;133:376–9. [PubMed: 31006404]
32. Guglielminotti J, Tesniere A, Rackelboom T, et al. Cough reflex sensitivity is decreased in female obese patients with obstructive sleep apnea. Respir Physiol Neurobiol 2007;158:83–7. [PubMed: 17412652]
33. Kern RC. Chronic sinusitis and anosmia: pathologic changes in the olfactory mucosa. Laryngoscope 2000;110:1071–7. [PubMed: 10892672]
34. Victores AJ, Chen M, Smith A, et al. Olfactory loss in chronic rhinosinusitis is associated with neuronal activation of C-Jun N-terminal kinase. Int Forum Allergy Rhinol 2018;8:415–20. [PubMed: 29193850]
35. Marmor M, Shao Y, Bhatt DH, et al. Paresthesias among community members exposed to the world trade center disaster. J Occup Environ Med 2017;59:389–96. [PubMed: 28157767]
36. Colbeth HL, Zeig-Owens R, Webber MP, et al. Post-9/11 peripheral neuropathy symptoms among world trade center-exposed firefighters and emergency medical service workers. Int J Environ Res Public Health 2019;16:1727. [PubMed: 31100846]
37. Gilman S. Joint position sense and vibration sense: anatomical organisation and assessment. J Neurol Neurosurg Psychiatry 2002;73:473–7. [PubMed: 12397137]
38. Altman KW, Desai SC, Moline J, et al. Odor identification ability and self-reported upper respiratory symptoms in workers at the Post-9/11 world trade center site. Int Arch Occup Environ Health 2011;84:131–7. [PubMed: 20589388]
39. Sant'Ambrogio G, Tsubone H, Sant'Ambrogio FB. Sensory information from the upper airway: role in the control of breathing. Respir Physiol 1995;102:1–16. [PubMed: 8610203]
40. Horner RL, Innes JA, Murphy K, et al. Evidence for reflex upper airway dilator muscle activation by sudden negative airway pressure in man. J Physiol 1991;436:15–29. [PubMed: 2061830]
41. Saboisky JP, Butler JE, Luu BL, et al. Neurogenic changes in the upper airway of obstructive sleep apnoea. Curr Neurol Neurosci Rep 2015;15:12. [PubMed: 25704006]

WHAT IS ALREADY KNOWN ON THIS TOPIC

- Chronic rhinosinusitis (CRS) and obstructive sleep apnoea (OSA) are highly prevalent among World Trade Center (WTC) General responders. There is an association between the presence of CRS and OSA. However, the mechanism of this association is unclear and may be related to impairment in upper airway sensory function that can be seen with both diseases.

WHAT THIS STUDY ADDS

- This study showed an upper airway sensory impairment in the WTC general responder cohort irrespective of the presence or absence of either OSA or CRS.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- Further studies examining the presence of neuropathy in this population are warranted.

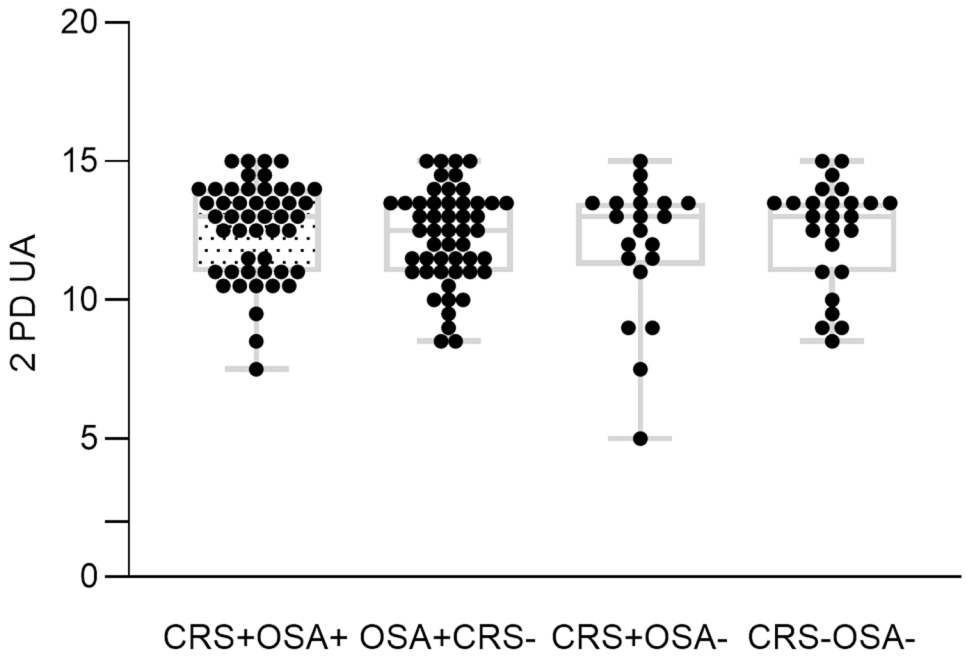

Figure 1.

Box and whisker plots showing median, 25th–75th percentiles values (box) and minimum and maximum values (whiskers) of comparison of upper airway (UA) 2 point discrimination (2PD) (in mm) between chronic rhinosinusitis (CRS) positive obstructive sleep apnoea (OSA) positive, OSA positive, CRS negative, CRS positive OSA negative, and CRS negative and OSA negative World Trade Centre subjects.

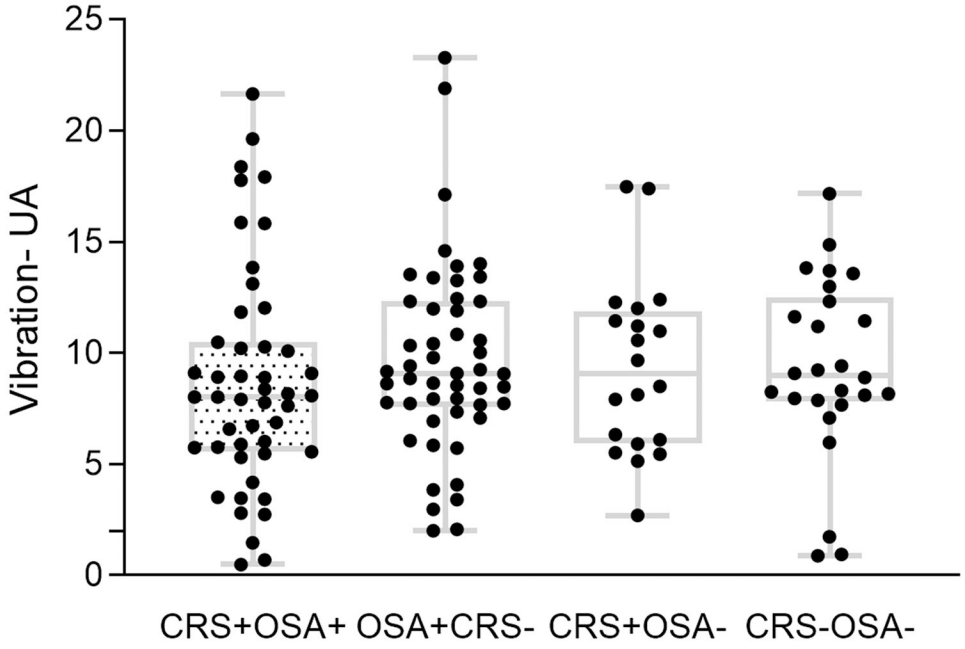

Figure 2.

Box and whisker plots showing median, 25th–75th percentiles values (box) and minimum and maximum values (whiskers) of comparison of upper airway (UA) vibratory threshold (VT) (in units) between chronic rhinosinusitis (CRS) positive obstructive sleep apnoea (OSA) positive, OSA positive, CRS negative, CRS positive OSA negative, and CRS negative and OSA negative World Trade Centre subjects.

Table 1

Characteristics of the study population

Variable	N	Mean±std or %
Age (years)	163	57.3±7.6
BMI (kg/m^2)	162	29.91±5.0
OSA (%)	108	68.8
AHI4/hr	157	11.9±14.3
RDI/hr	157	22.6.±17.5
ESS	162	6.7±4.9
CRS (%)	80	49.1
CRS score	163	2.60±2.1
Exposure	154	
Low	23	14.9
Intermediate	107	69.5
High	21	13.6
Very high	3	2.0

AHI4/hr, Apneoa+Hypopnoea(4%) per hour of sleep; BMI, body mass index; CRS, chronic rhinosinusitis; ESS, Epworth Sleepiness Score; OSA, obstructive sleep apnea; 2PD, two-point discrimination; RDI, Respiratory Disturbance Index; VT, vibration threshold.

Table 2

Group comparisons for variables studied

Variable (mean±std)	OSA positive CRS positive (n=53)	OSA positive CRS negative (n=55)	CRS positive OSA negative (n=23))	OSA negative CRS negative (n=26)
Age (years)	56.1±7.2	58.6±7.4	57.3±8.7	56.9±8.5
BMI kg/m^2	31.2±5.3 *	30.7±5.5 *	27.8±2.8	27.7±3.8
AHI4/hr	16.9±14.5 *	15.9±16.1 *	2.0±1.1	2.3±1.3
RDI/hr	29.9±16.6 *	28.1±18.5 *	8.7±3.2	8.2±3.8
CRS score	4.3±1.3 *	0.9±0.8	4.7±1.2 *	0.7±0.8
ESS	7.1±5.2 *	6.6±4.6 *	9.0±5.5 *	4.7±3.8
2PD UA (mm)	12.6±1.8	12.3±1.7	12.0±2.5	12.4±1.9
VT UA (units)	8.7±5.0	9.7±4.3	9.4±3.9	9.3±4.1
2PD lip (mm)	2.9±0.9	2.9±1.0	2.9±1.1	2.9±0.9
VT lip (units)	3.6±1.3	3.5±1.2	3.5±1.2	3.4±1.1
2PD hand (mm)	18.5±6.4	17.0±6.5	16.5±6.0	18.2±6.6
VT hand (units)	1.9±0.8	1.7±0.8	1.9±0.7	1.6±0.6

* P<0.05 compared with controls (OSA negative CRS negative).

AHI4/hr, Apnoea+Hypopnoea(4%) per hour of sleep; BMI, body mass index; CRS, chronic rhinosinusitis; ESS, Epworth Sleepiness Score; OSA, obstructive sleep apnoea; 2PD, two-point discrimination; RDI, Respiratory Disturbance Index; VT, vibration threshold.