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Vestibular vertigo is associated with abnormal sleep duration

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Abstract.
BACKGROUND/OBJECTIVE: Several small studies in animals and humans have suggested a relationship between vestibular function and sleep. In this study, we evaluate the association between vestibular vertigo and sleep duration in a large, representative sample of US adults.
METHODS: We used data from the National Health Interview Survey, which administered a Balance Supplement in 2008 in a sample of 20,950 adult respondents. We evaluated the cross-sectional association between vestibular vertigo (based on a well-validated definition) and sleep duration (defined as short <6 hours, normal 6–8 hours, and long >8 hours). We performed multiple and multinomial logistic regression analyses to estimate the odds ratio and relative risk ratio (RRR) of impaired sleep duration compared to normal sleep duration associated with vestibular vertigo. Analyses were adjusted for demographic, lifestyle and health behavior characteristics as well as relevant comorbid conditions.
RESULTS: Thirty percent of individuals with vestibular vertigo reported abnormal sleep duration (15.5% short duration and 14.8% long duration). In adjusted analyses, individuals with vestibular vertigo had a 1.75 (95% CI 1.45–2.11) RRR of having short sleep duration compared to individuals without vestibular vertigo, and a 1.55 (95% CI 1.26–1.91) RRR of having long sleep duration compared to individuals without vestibular vertigo.
CONCLUSION: This study presents epidemiologic evidence to support the association between vestibular function and sleep duration. Individuals with vestibular vertigo had a higher RRR for abnormally short or long sleep duration. Further work is needed to evaluate the causal direction(s) of this association.

Keywords: Vestibular vertigo, vestibular system, sleep duration, National Health Interview Survey

1. Introduction

The vestibular system is responsible for detecting rotational and translational movements of the head and its orientation with respect to gravity, thereby controlling gaze stability, postural control, and locomotion. Recent evidence has also demonstrated that vestibular signals are projected to many subcortical and cortical structures including the insula, parietal operculum, temporoparietal junction, somatosensory cortex, frontal eye fields, hippocampus, cingulate cortex, and intraparietal sulcus (Lopez and Blanke 2011, Dieterich and Brandt 2015, Lopez C 2015). Vestibular influences on processes beyond balance and gait are increasingly being recognized.

Multiple reports have examined the relationship between vestibular function and sleep. Several mechanisms have been proposed to explain the link between the vestibular system and sleep. The vestibular system carries information about the positional location of the head, and may thus play a role in

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sleep initiation and duration (SI Wiener 2005). Additionally, results from animal studies suggest that the vestibular system is involved in regulating circadian rhythms by working in tandem with input from the visual and somatosensory systems (Fuller and Fuller 2006, Martin, Mauvieux et al. 2015). Further, a study of 9 adult patients found that patients with bilateral vestibular loss had abnormal sleep patterns and shorter sleep duration relative to healthy controls (Martin, Moussay et al. 2016). Whether the relationship between vestibular function and sleep holds in a large population-based cohort has not been investigated.

In this report, we use data from the 2008 National Health Interview Survey (NHIS) to examine the association between vestibular function and sleep. We used a well-validated definition of vestibular loss that has been previously applied to the NHIS data (Neuhauser, von Brevern et al. 2005, Bigelow, Semenov et al. 2015). With respect to sleep, the NHIS specifically queried participants about sleep duration, which we used in our analyses. We examined the independent relationship between sleep duration and vestibular vertigo with the hypothesis that those suffering from vestibular vertigo would report aberrant sleep durations (Parsons, Moriarity et al. 2014).

2. Methods

The sample for this cross-sectional study was extracted from the 2008 NHIS, which contained a supplement for dizziness and balance problems (Parsons, Moriarity et al. 2014). In 2008, the National Institute on Deafness and Other Communication Disorders sponsored the first nationally representative survey for balance and hearing disorders, which included a broad range of questions on balance and dizziness problems. More recent iterations of the NHIS (2009–2015) do not include questions on balance problems, and therefore could not be used for investigating the relationship between vestibular vertigo and sleep. The supplemental survey began by asking if the person had experienced balance or dizziness problems within the past 12 months, and those who answered 'yes' were then asked a series of follow-up questions. The NHIS is a multistage area probability design household survey used by the United States National Center for Health Statistics to monitor health status. These data are publically available through the NHIS website, and details on sampling methods and survey design can be found in the "NHIS Survey Description" (Pleis, Lucas et al. 2009). The US Census Bureau conducts these interviews using stratification, multistage sampling, and a probability cluster sampling technique with oversampling of subpopulations to produce generalizable estimates of the civilian, non-institutionalized U.S. population. The study was conducted in accordance with the Declaration of Helsinki, and IRB approval was not obtained because these data are de-identified and publically available.

2.1. Defining vestibular vertigo

We generated a single vestibular vertigo variable based on a definition first developed and validated by Neuhauser and colleagues in the German population (Neuhauser, von Brevern et al. 2005), and subsequently updated and used by several authors to define vestibular vertigo within the NHIS survey (Ward, Agrawal et al. 2013, Bigelow, Semenov et al. 2015). Figure 1 is a flowchart illustrating the development of the case definition variable for vestibular vertigo. Participants, who answered 'yes' to the first question, were then asked a series of questions about the nature of their problem. Participants with a history of stroke, movement disorders, multiple sclerosis, spine injury, muscular dystrophy, glaucoma, diabetic retinopathy, cataracts, and macular degeneration were not included in the vestibular vertigo case definition.

2.2. Defining sleep duration

In the NHIS data, sleep duration was recorded in hour increments. The sleep duration variable was available for all adults 18 years or older in the 2008 survey. Previous studies have categorized sleep duration as short (less than 6 hours), normal (6 to 8 hours), or long (more than 8 hours) per 24-hour period (Nunes, Jean-Louis et al. 2008, Ramos, Wallace et al. 2014, Akinseye, Ojike et al. 2016). Sleeping less than 6 hours or more than 8 hours, has been associated with various adverse health outcomes (Ayas, White et al. 2003, Grandner and Kripke 2004, Grandner, Hale et al. 2010, Akinseye, Ojike et al. 2016). Therefore, we used this same classification for sleep duration in the current study.

2.3. Identifying covariates and possible confounders

Vestibular vertigo has been reported to have an increased prevalence in females, (Neuhauser,

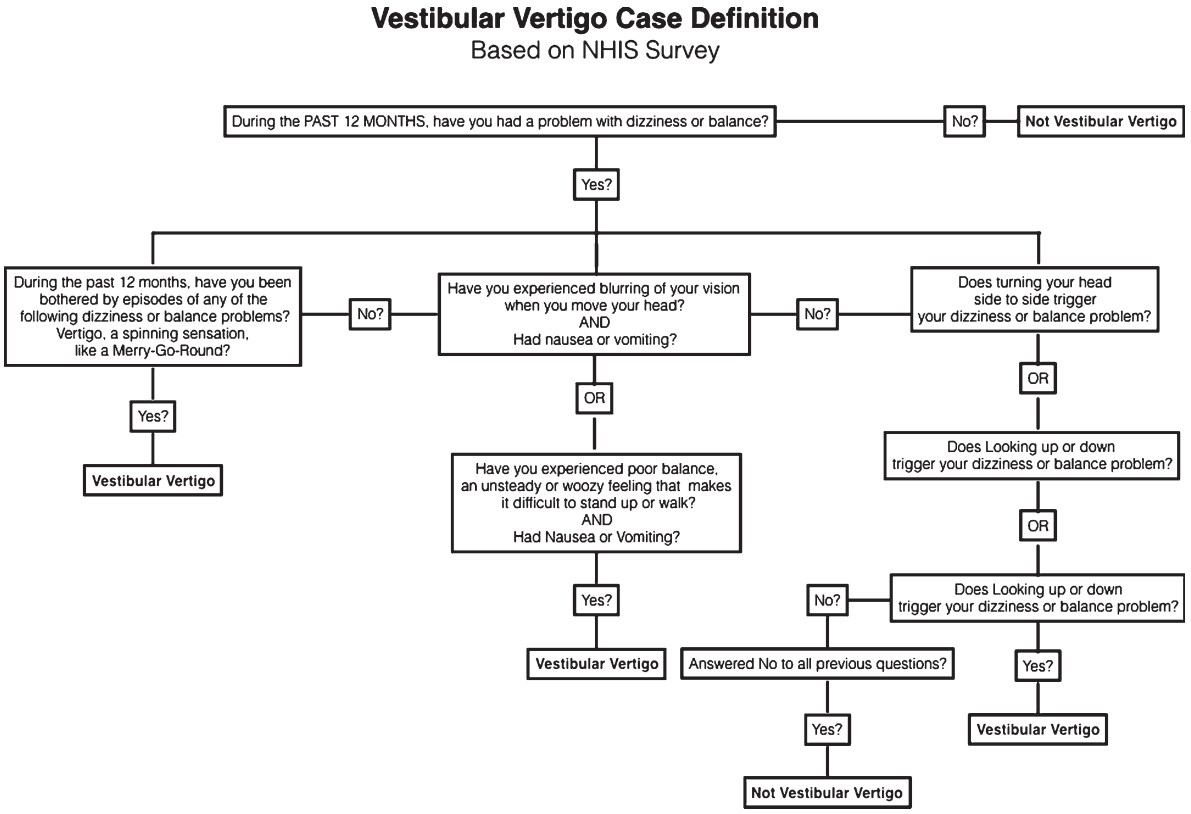

Fig. 1. A flowchart illustrating the case definition for vestibular vertigo from the 2008 National Health Interview Survey. Patients were excluded from the vestibular vertigo definition if they history of any of the following: stroke, movement disorder, multiple sclerosis, spine injury, muscular dystrophy, macular degeneration, glaucoma, diabetic retinopathy, or cataract.

von Brevern et al. 2005, Neuhauser 2007, Bigelow, Semenov et al. 2015) older adults, (Neuhauser, von Brevern et al. 2005, Neuhauser 2007, Ward, Agrawal et al. 2013, Bigelow, Semenov et al. 2015) individuals at lower socioeconomic status, (Agrawal, Carey et al. 2009) diabetics, (Agrawal, Carey et al. 2009, Agrawal, Carey et al. 2010, Buxton and Marcelli 2010) and individuals with psychiatric or cognitive impairment (Bigelow, Semenov et al. 2015). Disturbed sleep patterns have been reported in older individuals, (Pollak, Perlick et al. 1990, Prinz, Vitiello et al. 1990, Bliwise, King et al. 1992, Bliwise 1993) African-Americans, (Nunes, Jean-Louis et al. 2008, Brimah, Oulds et al. 2013) and individuals with diabetes, (Akinseye, Ojike et al. 2016) cardiovascular disease, (Partinen, Putkonen et al. 1982, Qureshi, Giles et al. 1997, Sabanayagam and Shankar 2010, Sabanayagam and Shankar 2012, Akinseye, Ojike et al. 2016) obesity, (Hasler, Buysse et al. 2004, Cizza, Skarulis et al. 2005, Jean-Louis, Williams et al. 2014) visual impairment, (Ramos, Wallace et al. 2014) and psychiatric illness (Bliwise, Friedman et al. 1993). We accounted for these potentially confounding variables in our analyses. Age was categorized into three groups: 18–39 years, 40–59 years, and 60 years or older. Race was classified into five categories: non-Hispanic white, non-Hispanic Black, Asian, Hispanic and other or mixed-race. Education level was classified into three categories: less than high school, graduated high school or has GED, and has an additional degree after high school. BMI was classified into 4 categories based on Centers for Disease Control and Prevention recommended cut-offs (Barlow and Dietz 1998). Details on how the variables for smoking, hypertension, diabetes, asthma, depression, generalized anxiety, panic disorder and chronic fatigue were collected for the NHIS have been previously described (Pleis, Lucas et al. 2009, Bigelow, Semenov et al. 2015).

2.4. Statistical analysis

Analyses were performed on the sample data, and then weighted to produce US population estimates

and prevalence estimates as per NHIS survey sampling design guidelines (Pleis, Lucas et al. 2009). Data that were not within the sampling unit for a specified variable were coded as missing. Prevalence estimates were generated for the overall population and the subpopulation with vestibular vertigo. Simple logistic regressions were used to estimate the crude odds ratio (OR) of each sleep duration category with respect to the others associated with having vestibular vertigo. Multinomial logistic regressions were used to compare the relative risk ratio (RRR) of short and long sleep relative to normal sleep duration associated with vestibular vertigo. Crude (only sleep duration and vestibular vertigo, with normal sleep duration as the baseline) and adjusted (for all covariates) multinomial regression analyses were performed to examine confounders. We checked the fit of our final model using likelihood ratio tests. STATA V.14 was used to perform all analyses (Jones, Jampani et al. 2000).

3. Results

In 2008, 20,950 individuals completed the balance and dizziness supplement. Conditional adult sample response rate for the 2008 survey was 74.2%. Mean age for this population was 45.4 ± 17.3 years and ranged from 18–85 years. Sex distribution was 52.6% female and 47.5% male. Race distribution was 56.4% White, 14.5% African American, 20.3% Hispanic, and 9.10% other races. The prevalence of normal sleep duration was lower in the vestibular vertigo population (69.7% versus 82.2%), while the prevalence of short and long sleep was higher (15.5% versus 7.90% for short sleep, and 14.8% versus 8.80% for

Table 1
US Population Prevalence Estimates of Demographic and Comorbid Conditions from 2008 NHIS Data

Variable Prevalence within US Adult Population	All Respondents		Vestibular Vertigo	
	Per Cent	216 million 95% CI	Per Cent	18 million 95% CI
Sleep Duration				
Short (Less than 6 hours)	7.93%	[7.51–8.39]	15.5%	[13.7–17.5]
Normal (6–8 hours)	83.2%	[82.6–83.8]	69.7%	[66.9–72.3]
Long (More than 8 hours)	8.83%	[8.38–9.31]	14.78%	[12.9–16.9]
Age				
18–39 years	39.6%	[38.6–40.6]	30.2%	[27.4–33.2]
40–59 years	35.5%	[34.7–36.3]	37.9%	[35.0–40.8]
60 or older	24.9%	[24.1–25.7]	31.9%	[29.6–34.4]
Sex				
Male	49.0%	[48.3–49.7]	34.0%	[31.3–36.7]
Female	51.0%	[50.3–51.7]	66.0%	[63.3–68.7]
Race				
White	68.7%	[67.7–69.7]	72.8%	[70.3–75.2]
Black	11.6%	[10.9–12.4]	9.16%	[7.86–10.7]
Asian	4.51%	[4.19–4.85]	2.3%	[1.61–3.30]
Hispanic	13.0%	[12.3–13.8]	12.3%	[10.5–14.4]
Other	2.21%	[1.90–2.57]	3.39%	[2.49–4.62]
Education Level				
Less than High School	15.5%	[14.7–16.2]	19.5%	[17.4–21.8]
High School or GED	27.7%	[26.9–28.6]	29.0%	[26.4–31.8]
More than High School	56.9%	[55.9–57.9]	51.5%	[48.8–54.2]
Body Mass Index				
Underweight	1.57%	[1.38–1.80]	1.64%	[1.10–2.44]
Normal	34.3%	[33.5–35.1]	30.5%	[28.0–33.2]
Overweight	33.3%	[32.6–34.0]	29.3%	[27.0–31.7]
Obese	30.9%	[30.1–31.7]	38.6%	[35.8–41.5]
Ever Smoker	42.2%	[41.3–43.5]	53.31%	[50.7–55.9]
Diabetes Mellitus	8.28%	[7.84–8.75]	15.2%	[13.3–17.3]
Hypertension	29.3%	[28.7–30.3]	43.6%	[40.8–46.5]
Major Depression Disorder	28.2%	[27.4–29.1]	61.6%	[58.8–64.3]
Panic Disorder	7.99%	[7.55–8.44]	25.8%	[23.6–28.1]
Generalized Anxiety Disorder	19.3%	[18.6–20.0]	46.2%	[43.4–48.9]
Chronic Fatigue	2.31%	[2.11–2.54]	10.6%	[9.10–12.2]
Asthma	12.6%	[12.0–13.1]	21.8%	[19.7–24.1]

[§]Chi-squared test. p-values are <0.0001.

Table 2
Multinomial logistic regression models of sleep duration categories, and vestibular vertigo, from the 2008 National Health Interview Survey

Sleep Duration	Simple Logistic[a] Regression	Multinomial Logistic Regression[b] Unadjusted	Multinomial Logistic Regression[b] Adjusted[c]
Short (Less than 6 hours)	2.40 [2.10–2.75] ($p < 0.001$)	2.59 [2.19–3.06] ($p < 0.001$)	1.75 [1.45–2.11] ($p < 0.001$)
Normal (6–8 hours)	0.45 [0.40–0.50] ($p < 0.001$)	1 Base Outcome	1 Base Outcome
Long (More than 8 hours)	1.68 [1.47–1.93] ($p < 0.001$)	2.17 [1.81–2.59] ($p < 0.001$)	1.55 [1.26–1.91] ($p < 0.001$)

[a]Population size is approximately 216 million for these estimates. [b]Population size is approximately 200 million for these estimates. [c]For age, race, education level, income, BMI, smoking history, diabetes, hypertension, asthma, chronic fatigue, depression, panic disorder and generalized anxiety disorder.

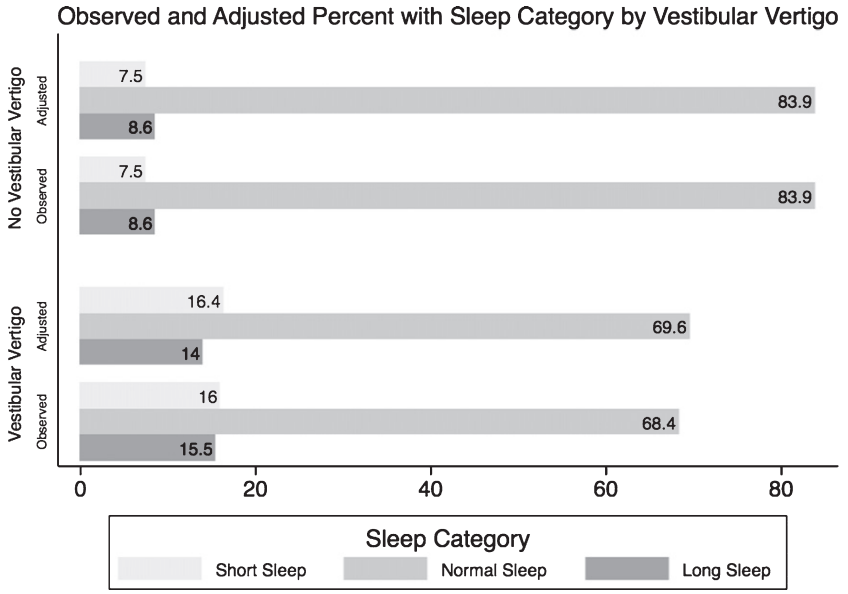

Fig. 2. A graph comparing the observed (crude) and the predicted (adjusted) percentages of each sleep category in normal individuals and in people suffering from vestibular vertigo. *From the Null Multinomial Logistic Regression of Sleep Categories and Vestibular Vertigo only. ^From Extended Multinomial Logistic Regression model including the following covariates: age, race, education level, income, BMI, smoking history, diabetes, hypertension, asthma, chronic fatigue, depression, panic disorder and generalized anxiety disorder.

long sleep). In addition, all health conditions listed in Table 1 have a higher prevalence in the vestibular population compared to the overall US population. Table 1 summarizes findings from 2008 NHIS data on the demographic and associated comorbid conditions of the US population and their prevalence with vestibular vertigo.

Individuals with vestibular vertigo have an adjusted RRR of 1.75 (95% CI 1.45–2.11; p-value < 0.001) of sleeping less than 6 hours a day relative to regular sleep duration, and an adjusted RRR of 1.55 (95% CI 1.26–1.91; p-value < 0.001) of sleeping more than 8 hours a day relative to regular sleep duration, compared to individuals without vestibular vertigo. Table 2 summarizes the unadjusted, and the subsequent adjusted regressions for the ORs and RRRs of the three sleep categories associated with having vestibular vertigo. Figure 2 shows the observed percentages that were presented in Table 1 of each sleep category in individuals with and without vestibular vertigo, and the subsequent adjusted proportion of each sleep category after accounting for all covariates using the multinomial regression analysis.

4. Discussion

Our study estimates that individuals with vestibular vertigo had a 1.75 RRR of having short sleep duration compared to individuals without vestibular vertigo and a 1.55 RRR of having long sleep duration

compared to individuals without vestibular vertigo. The multinomial logistic regression model used in our study allowed us to compare the RRR's of short sleep and long sleep relative to normal sleep associated with vestibular vertigo. We observed a greater RRR for short sleep relative to long sleep duration associated with vestibular vertigo; that is, the relationship between vestibular vertigo and sleep duration was stronger for short sleep duration. After adjusting for variables known to be associated with abnormal self-reported sleep duration, as demonstrated in Fig. 2, individuals with vestibular vertigo reported an 8% higher prevalence of shorter sleep duration than individuals without vestibular vertigo, and a 5% higher prevalence of longer sleep duration.

The effect of abnormal sleep duration on overall health is an evolving area of research. The mechanisms behind abnormally short or long sleep duration are not fully understood. Abnormal sleep duration has been associated with a number of adverse cardiovascular, endocrine, neurologic and psychiatric conditions as well as increased mortality (Bliwise, Friedman et al. 1993, Ayas, White et al. 2003, Grandner and Kripke 2004, Youngstedt and Kripke 2004, Buxton and Marcelli 2010, Sabanayagam and Shankar 2010). A meta-analysis of over 60 studies on sleep duration observed a U-shaped relationship between sleep duration and mortality, whereby mortality risk increases with further deviation from the normal sleep range (Grandner, Hale et al. 2010). Short sleep, in particular, appears to pose a greater risk of morbidity and mortality (Brassington, King et al. 2000). In animal models, short sleep was associated with weight loss, increased energy expenditure, increased plasma norepinephrine, and decreased plasma thyroxine, eventually culminating in death (Rechtschaffen and Bergmann 2002, Rechtschaffen, Bergmann et al. 2002). Short sleep has also been linked to increased falls in older adults (Brassington, King et al. 2000). The link between short sleep and vestibular vertigo may in part account for this association. Long sleep, on the other hand, has been associated with sleep fragmentation, fatigue, and changes in immune function, which also increase morbidity and mortality (Grandner and Drummond 2007).

Several potential mechanisms may explain the association between vestibular vertigo and altered sleep duration. The vestibular system, which senses head position with respect to gravity, may provide important cues for sleep initiation and maintenance. Experiments carried out in simulated hypergravity conditions on knockout mice (het –/–) selectively devoid of otolithic function first introduced the hypothesis that vestibular neuronal input represented by macular signaling activates nuclei throughout the vestibulo-cortical neuraxis including autonomic, limbic and hypothalamic nuclei (Fuller, Jones et al. 2004). Findings from a more recent study by Besnard et al. suggest that vestibular input directly influences the suprachiasmatic nucleus, thereby having a potential regulatory effect on circadian rhythmicity in humans (Martin, Mauvieux et al. 2015).

However, the directionality of the association is an area of evolving research because other studies suggest that abnormal sleep duration may impact vestibular signaling. One study found that sleep deprivation has been shown to alter cortical function within the posterior parietal cortex, which may in turn alter vestibular processing of information, (Drummond, Gillin et al. 2001) while Martin and colleagues reported in their study of adult patients with bilateral vestibular dysfunction that these patients had significantly elevated levels of salivary cortisol compared to healthy controls (Martin, Moussay et al. 2016). In theory, the elevation in cortisol could be attributed to both the stress of disturbed sleep patterns and to vestibular dysfunction, and it has been shown that chronically elevated levels of cortisol may contribute to hippocampal atrophy. This last point was elaborated further in other studies that found correlations between hippocampal atrophy and bilateral vestibular loss (Van Cruijsen, Hiemstra et al. 2007, Aitken, Benoit et al. 2016, Balabhadrapatruni, Zheng et al. 2016, Seo, Kim et al. 2016).

Another hypothesis that could explain the link between sleep duration and vestibular loss are the known vestibular inputs to the autonomic nervous system (Yates 1996, Yates and Bronstein 2005). The vestibular system has been shown to control autonomic functions during rapid eye movement sleep (Morrison and Pompeiano 1970). Krystal et al. reported that electrical stimulation of the vestibular apparatus decreased sleep latency in individuals with sleep latency >14 minutes (Krystal, Zammit et al. 2010). Lastly, in a recent study, Lin and Young found that sleep-deprivation of more than 12 hours resulted in increased asymmetry of oVEMPs, although had no effect on cVEMPs (Lin and Young 2014).

5. Limitations

Our results may be confounded by other possible causes of sleep disturbance that were not available as

part of this historic dataset. We were limited by the variables that were collected during the 2008 NHIS interview, and therefore some confounding variables may have been missed. Furthermore, the directionality of this relationship cannot be ascertained based on cross-sectional data. We are therefore unable to rule out the possibility of reverse causality, wherein sleep disturbance causes vestibular vertigo, and not the other way around. Prospective, longitudinal studies that clearly stratify patients based on established risks for sleep disturbance and vestibular disease are needed to better explain the influence of these two variables on each other.

Given that we performed a cross-sectional analysis looking at a dependent variable that could be affected by many covariates, over-adjustment and under-adjustment are concerns. The importance of under-adjustment was previously underscored by Patel et al. who have demonstrated a 22% decrease in their crude mortality risk after accounting for a variety of possible confounders (Patel, Ayas et al. 2004). On the other hand, with 14 covariates in our final model, we run the risk of over adjusting for variables that may actually be on the causal pathway between vestibular vertigo and sleep, particularly depression, chronic fatigue, and obesity. We tried to overcome this by running several sensitivity analyses, but the independent effect of individual covariates on sleep remains difficult to discern from cross-sectional data. The 2008 NHIS only included one question about sleep that described sleep duration. Sleep quality, encompassing sleep onset latency, sleep interruption, and early awakening, and the effect of sleep quality on daily life were not captured in these data. We therefore are basing our results on one facet of sleep assessment. Future prospective studies should incorporate validated surveys that capture information about sleep quality, such as the Pittsburgh Sleep Quality Index, (Buysse, Reynolds et al. 1989) and impact of poor sleep on activities of daily living, such as the Epworth Sleepiness Scale (Johns 1991) in order to gain true insight into the effect of sleep disturbance on the quality of life of patients with vestibular vertigo. Additionally, the NHIS does not directly capture comorbid sleep conditions such as insomnia, circadian rhythm disorders, and sleep-related breathing disorders. Most notably, obstructive sleep apnea, a common cause of sleep disturbance, is not directly accounted for in this dataset and is therefore approximated using body mass index estimates as a covariate. Future studies investigating the relationship between vestibular dysfunction and sleep should account for these disorders in their data collection and analyses.

Finally, studies examining reliability of subjective sleep duration measures, such as self-reported sleep, reported conflicting results about their agreement with more objective measures such as actigraphy and polysomnography (Akerstedt, Hume et al. 1994, Lockley, Skene et al. 1999, Landis, Frey et al. 2003, Girschik, Fritschi et al. 2012). The majority of studies report generally poor agreement between the subjective questions used in surveys and objective sleep testing, and recommend integrating both objective and subjective measures whenever possible (Argyropoulos, Hicks et al. 2003, Van Den Berg, Van Rooij et al. 2008, van den Berg, Miedema et al. 2009, Segura-Jimenez, Camiletti-Moiron et al. 2015). It is also important to note that short sleep does not necessarily translate into sleep insufficiency, and long sleep may be over-reported to encompass both time spent sleeping and time spent in bed trying to sleep. Responses may be biased towards the null because self-reported sleep may contain considerable error and individuals may misreport how long they actually sleep to durations that they perceive to be more desirable (Coates, Killen et al. 1982, Bliwise, King et al. 1992, Bliwise, Friedman et al. 1993). This is why future studies should aim to utilize data from both subjective and objective sleep assessment tools, and correlate their results.

6. Conclusions

This study presents epidemiologic evidence obtained through robust statistical analyses for an association between vestibular function and sleep duration. Patients with vestibular vertigo have a higher RRR for disturbed sleep patterns, which may contribute to worsening quality of life and may predispose this patient population to other adverse health sequelae. While the mechanisms behind the link between vestibular vertigo and abnormal sleep require further study, increased recognition of sleep impairments among individuals with vestibular vertigo might be useful in the clinical setting.

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