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Original Article

Sleep-related intermittent hypoxia is associated with decreased psychomotor vigilance in Japanese community residents☆

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ABSTRACT

Background: Sleep disordered breathing (SDB) is associated with decreased psychomotor vigilance (hereafter "vigilance") in clinical settings, but this association has yet to be confirmed in the general population. The aim of this study is to determine the associations between SDB and vigilance in a large sample of community-based participants.

Methods: The study sample consisted of 1508 community-dwelling Japanese persons (age: 30–79 years, women: 62.7%, mean body mass index [BMI]: 23.1 kg/m^2). Vigilance was measured by the psychomotor vigilance task (PVT), and SDB was measured by overnight pulse oximetry. We investigated odds ratios for "high mean reaction time (RT)" and "high number of lapses," which we defined as the 75th percentile of each value, across categories of oximetry values (three percent oxygen desaturation index [ODI], 4% ODI, average oxygen saturation, minimum oxygen saturation).

Results: Multivariable-adjusted odds ratios of high mean RT and high number of lapses in severe SDB (3% ODI $\geq$ 30.0 events/h) were 3.0 (95% confidence interval: 1.0–8.9; P for trend = 0.03) and 3.3 (95% confidence interval: 1.2–9.2, P for trend = 0.03), respectively, compared to participants without SDB. Similar associations were observed between PVT metrics and four percent ODI. No significant associations between average oxygen saturation and PVT metrics were observed. Minimum oxygen saturation was significantly associated with the trend of high number of lapses (P for trend = 0.007), but not with high mean RT.

Conclusions: The present study provides evidence that the intermittent hypoxia in SDB is significantly associated with the deterioration of PVT outcome metrics.

1. Introduction

Patients with sleep disordered breathing (SDB) are commonly known to have an increased risk of motor vehicle accidents [1]. The connection between SDB and accidents is thought to originate from neurocognitive dysfunction, impaired vigilance and excessive sleepiness caused by SDB [2]. Out of many components of neurocognitive functions, the ability to sustain attention, or vigilance, is essential when operating any transportation vehicle [3]. To measure vigilance associated with SDB, tests such as Steer Clear, the Oxford Sleep Resistance (OSLER) test, continuous performance tests including driving simulator tasks, digit vigilance test, and the psychomotor vigilance task (PVT) have been utilized.

In clinical studies testing patients with overt obstructive sleep apnea (OSA), many have found that vigilance is significantly associated with SDB measures such as apnea hypopnea index (AHI) [4,5] and hypoxemia [5–7], though others have not [8–10]. Some studies reported that continuous positive airway pressure (CPAP) therapy for SDB improved vigilance measured by PVT [11,12]. On the whole, evidence supports the existence of a

Abbreviations: SDB, sleep disordered breathing; PVT, psychomotor vigilance task; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; RT, reaction time; AHI, apnea hypopnea index; ESS, Epworth Sleepiness Scale; BMI, body mass index.

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relationship between presence of SDB and impairment of vigilance.

However, in epidemiological studies, the evidence is still limited. Blackwell et al. reported that nocturnal hypoxemia (any sleep time with <80% arterial oxygen saturation) was associated with longer completion times for digit vigilance tests in 2909 community-dwelling men aged 65 years and older [13]. A report from the Wisconsin Sleep Cohort Study of 611 participants aged 35–74 years showed a significant association between SDB and impaired psychomotor vigilance in participants aged 65–75 years only [14]. Recently, a type 3 sleep study and PVT were performed on 415 participants aged 40–65 years from Iceland's general population, and a significant relationship between AHI and vigilance was found only in participants with severe OSA (AHI ≥ 30) [15]. Results from previous studies are varied, and the collection and analysis of data from large populations including a wide range of age groups is warranted.

The present study examined 1508 Japanese community residents aged 30–79 years. All study participants were subjected to PVT to measure vigilance and pulse oximetry to evaluate intermittent hypoxemia during sleep. Our aim was to confirm the association between SDB and vigilance by examining participants with a wide range of ages and SDB severity levels in a large population, and to extend the generalizability of the findings from previous studies.

2. Methods

2.1. Study participants

The study sample for the current investigation was derived from the Toon Health Study, which is a prospective cohort study in Toon City, Ehime Prefecture, Japan. The cohort study was initiated in 2009 to characterize the risk factors for cardiovascular disease in a community-based setting, and has been described in detail elsewhere [16,17]. Residents in Toon city responding to newspaper advertisements, posters, or invitations were considered eligible if they were 30–79 years of age. The SDB screening testing began in 2009, and the 10-min PVT testing started in 2010. Of the 1580 participants enrolled in the study from 2010 to 2012, participants undergoing treatment for SDB at the time of the survey (n = 7) were excluded from the current analysis. Those with incomplete data on overnight pulse oximetry (n = 58) or PVT (n = 7) were also excluded. Thus, the data for the remaining 1508 participants were used for analysis.

The study protocol was approved by the Institutional Review Board of the Ehime University Graduate School of Medicine and the Ethics Committee of Juntendo University. Written, informed consent was obtained from all study participants.

2.2. Psychomotor vigilance task (PVT)

To measure their vigilance performance, all participants underwent PVT in the morning at a local health center prior to participating in the home sleep study. PVT is a test that is widely used to measure behavioral alertness [18], and single PVT administration has been reported as a reliable measure of sleepiness [19]. PVT records response times to visual stimuli that occur at random inter-stimulus intervals. We used a portable PVT device (PVT-192, CWE, Inc., Ardmore, PA). When administering the test, we followed the protocol used by Lim and Dinges [20]; the test duration was 10 min, and the inter-stimulus interval was two to 10 s. During the test, participants were instructed to press the button as rapidly as possible whenever they saw the bright red millisecond counter appear on the screen of the device. Responses with a time of ≥500 msec were counted as "lapses." In this study, we chose mean RT and number of lapses to evaluate the association between intermittent hypoxia and vigilance. Higher scores on both measures indicated poorer performance. We defined "high mean RT" and "high number of lapses" as higher than the 75th percentile of the mean RT (mean RT ≥ 320.2 msec) and mean number of lapses (number of lapses ≥ 4), respectively. In sex-stratified analysis, high mean RT and high number of lapses were defined based on the 75th percentile for each gender group; mean RT ≥ 317 msec and number of lapses ≥4 for men, and mean RT ≥ 323 msec and number of lapses ≥4 for women. Similarly, in age-stratified analysis, high mean RT and high number of lapses were defined based on the 75th percentile in each age group; mean RT ≥ 281 msec and number of lapses ≥2 for age 30–44, mean RT ≥ 308.2 msec and number of lapses ≥3 for age 45–59, mean RT ≥ 332.74 msec and number of lapses ≥5 for age 60–69, and mean RT ≥ 393 msec and number of lapses ≥12 for age 70–79.

2.3. Assessment of sleep-disordered breathing

When the participants arrived at a local health center to perform PVT, they were instructed to complete a home sleep study on the following night. Pulse-oximetry equipment (PULSOX-3 Si; Konica Minolta Co., Osaka, Japan) was used to monitor participants overnight. The portable sleep monitor was placed on the left wrist for one night of monitoring at the participant's home. The sensor from the pulse-oximetry equipment was placed on the fourth finger and secured with removable tape. After the overnight study, the oximetry data were downloaded to a personal computer via an interface (PULSOX IF-3; Konica Minolta) and subjected to a computerized algorithm to identify oxygen desaturations of at least three percent. The oxygen desaturation event index (ODI), average oxygen saturation, and minimum oxygen saturation were determined. The following two thresholds were used to define the ODI: ≥3% and ≥4%. To avoid erroneous minimum oxygen saturation values, each oximetry tracing was reviewed by trained staff to remove potential artifacts and to verify the minimum oxygen saturation value reported. Based on the 3% ODI, and 4% ODI, severity of SDB was defined as follows: normal (<5 events/h), mild disease (5.0–14.9 events/h), moderate to severe disease (15.0–29.9 events/h) and severe disease (≥30.0 events/h). Average oxygen saturation and minimum oxygen saturation during the night were categorized into quartiles. As the duration of nocturnal sleep was not recorded, each participant was instructed to complete a sleep diary and provide an estimate of sleep duration.

2.4. Assessment of confounding covariates

Several covariates that may confound the association between SDB and vigilance were assessed. Each participant's medical history was obtained by physicians. Trained dietitians interviewed each participant on health habits including habitual sleep duration, daily alcohol intake and smoking. To assess subjective sleepiness, all participants were instructed to fill in the Japanese-language version of the Epworth Sleepiness Questionnaire [21]. Participants who attended the study in 2011 and 2012 also answered questions about whether they consumed caffeine on the morning of the exam. Height and weight were measured in light clothing to determine BMI.

2.5. Statistical analysis

For comparison of characteristics between men and women, the Mann-Whitney *U* test was performed. Multiple logistic regression analyses were used to assess the independent association between vigilance and SDB severity. The prevalent odds ratios for high mean