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【報告】

Sleep-disordered breathing in healthy participants without sleep apnea syndrome could be found out by commercially available devices in the trial study by small amount participants

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This study aims to uncover the sleep-disordered breathing that does not lead to sleep apnea syndrome with asymptomatic healthy adults in a home-based test using commercially available wearable sensors. The participants underwent an overnight examination at home according to their life cycle. They attached the wearable heart rate sensor WHS-1 and the pulse oximeter PULSOX-300i by themselves which were commercially available wearable devices. The ratio disordered breathing score, a novel parameter, was calculated using the attached software of the wearable heart rate sensor. Estimated sleep time, 3% ODI (oxygen desaturation index) value, and minimum SpO2 (percutaneous oxygen saturation value) were also analyzed based on the transcutaneous oxygen saturation. The questionnaire included gender, date of birth, height, weight, medical history, medication use, smoking habits, estimated bed time and wake-up time, and Epworth Sleepiness Scale was also carried out. Of the 17 healthy participants in the study, 9 had sleep-disordered breathing. There were statistical differences between the sleep-disordered and non-disordered groups in sleep duration, 3% ODI, and minimum oxygen partial pressure. The disordered breathing score did not show significant correlation between the minimum ODI and 3% ODI. However, sleep-disordered breathing score might be a diagnostic marker for disordered breathing at the cutoff value of 0.1. The disordered breathing score from the commercially available wearable sensor could be useful for the early detection of asymptomatic healthy adults with sleep apnea syndrome even as the pulse oximeter, suggesting that persons can easily screen for the syndrome by themselves.

Keywords　sleep apnea syndrome; commercially available wearable sensor; asymptomatic healthy adults; disordered breathing score

I. Introduction

Repeated sleep-disordered breathing (SDB) is a cause or aggravating factor of so-called adult diseases such as hypertension, heart disease, arrhythmia, stroke, and diabetes. In addition, inadequate sleep may cause strong drowsiness during the daytime, possibly leading to accidents due to falling asleep at the wheel and industrial accidents. Sleep apnea syndrome (SAS) is the breathing disorder that causes these symptoms.

The apnea-hypopnea index (AHI) is used as an indicator of SDB, and a value of 5 or higher is defined as SDB[1)]. In a study conducted in the United States, the proportion of SDB patients with AHI ≥ 5 was 24% in men and 9% in women, of which 4% in men and 2% in women were symptomatic SAS patients[2)]. Therefore, it can be said that most of the remaining patients are potential SAS patients who have not yet developed SAS but show SDB, and this percentage is quite high.

SDB can be divided into obstructive sleep apnea (OSA) and central sleep apnea (CSA), but patients with SDB mostly have OSA. Despite increasing awareness of OSA and its effects, only 8% of older adults at high risk for OSA have undergone home or laboratory sleep testing[3)]. Untreated OSA patients are at increased risk of developing cardiovascular diseases such as uncontrolled blood pressure, coronary artery disease,

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congestive heart failure, arrhythmias, and stroke[4]. OSA is also associated with metabolic abnormalities that affect glucose control and the risk of diabetes[5]. Early identification of potential SAS patients can help prevent these diseases. In addition, increased health care utilization has been reported in patients with untreated OSA; reducing the incidence of these diseases through OSA prevention may also reduce the economic losses associated with these diseases[6].

To diagnose OSA, it is necessary to measure breathing during sleep by in-laboratory polysomnography ("polysomnography" or "PSG") or home sleep apnea testing. However, since these tests are rarely performed in the so-called pre-symptomatic state before SAS, a simple instrumental machine that can voluntarily measure SDB, including respiratory arrest during sleep, would be extremely useful for finding the latent patients. Arikawa et al. developed a method to evaluate OSA using a commercially available wearable sensor[7].

This study attempted to determine the SDB that does not lead to SAS in asymptomatic healthy adults using a commercially available wearable sensor.

I. Materials and Methods

1. Participants

This study was conducted under the permission of the Toho University Ethics Committee (permission number: 27009 26058 25058) in healthy participants without subjective symptoms of SAS.

Participants were recruited using the website of the Toho University School of Medicine. They were first explained by a medical doctor who would not participate in the implementation or analysis of this study at all, the content of the study and that it would be conducted in accordance with the Declaration of Helsinki. Subsequently, the study was carried out only for those who agreed in writing to participate in the study. They received a ¥1,000 gift card after the completion of the study.

2. Study design

The participants underwent an overnight examination at home according to their life cycle and questionnaire survey. The test items during sleep included transcutaneous oxygen saturation (PULSOX-300i, Konica Minolta, Tokyo, Japan) via a monitor probe (LM-5C, Konica Minolta) attached to the index finger, heart rate and body position via a wearable sensor (WHS-1, Union Tool Co., Tokyo, Japan) attached to the left anterior chest by themselves. The questionnaire included gender, date of birth, height, weight, medical history, medication use, smoking habits, and Epworth Sleepiness Scale[8]. BMI was calculated from height and weight.

The estimated sleep time, 3% ODI value, and minimum SpO_2 value were analyzed using a software for transcutaneous oxygen saturation analysis (DS-5, Konica Minolta). The 3% ODI value was calculated using the following equation:

3% ODI (/hr) = (total time transcutaneous oxygen saturation decreased by >3%)/(sleep time)

In accordance with the Guidelines for the Diagnosis and Treatment of Sleep Disordered Breathing in Cardiology, sleep apnea was considered to have occurred if the Epworth Sleepiness Scale score was greater than 11 or the ODI 3% was greater than 7[1].

Cyclic variation of heart rate (CVHR) occurs during the night, and R-R interval (RRI) analysis using a Holter electrocardiogram has been reported to be useful in screening for OSA. Arikawa et al. investigated the usefulness of RRI analysis to identify OSA using the wearable heart rate sensor WHS-1 and newly developed algorithm[7]. Using the RRI averages calculated for each time series, tachycardia with CVHR was identified. The ratio of integrated RRIs determined by integrated RRIs during CVHR to overall sleep time was calculated using our newly developed method, indicating that it could distinguish OSA from Non-OSA[7]. We called the ratio disordered breathing score (DBS).

Data are presented as mean ± standard deviation. A spreadsheet software (Microsoft Excel 2013, Ver 15.0, Microsoft, Redmond, WA, USA) was used for calculation of correlations.

II. Results

A total of 18 volunteers, 10 men and 8 women, participated in this study. Of these, 1 male was found to have frequent atrial tachycardia and was excluded from the analysis. The attributes of the 17 participants included in the analysis are shown in Table 1. Age, height, weight, body mass index (BMI), sleep duration, 3% ODI, minimum partial pressure of oxygen, and Epworth sleepiness scale were 39.6 ± 8.7 years, 165.6 ± 8.7 cm, 63.6 ± 13.2 kg, 23.1 ± 3.6 kg/m^2, 305.4 ± 50.7 min, 6.2 ± 4.9%, 85.0 ± 6.1%, and 7.3 ± 2.2, respectively. Also, there were 2 smokers and 1 participant on medication for hypertension.

SDB was judged to have occurred in 7 males and 2 females and not in 2 males and 6 females. The group with SDB might show prolonged sleep duration, higher values of 3% ODI, and lower values of minimum partial pressure of oxygen (Table 1).

Disordered breathing score (DBS) could not be measured in 3 participants due to incorrect treating of the sensor. The corre-

lation of each parameter was examined from the individual values of the participants.

The correlation coefficient between 3% ODI and Epworth sleep coefficient was 0.02361 (Fig. 1), between BMI and 3% ODI was 0.37786 (Fig. 2), and between BMI and minimum SpO_2 was 0.18006 (Fig. 3). The correlation coefficient between DBS and minimum SpO_2 was 0.62779 (Fig. 4), and between DBS and 3% ODI was 0.51947 (Fig. 5).

DBS ≥ 0.1 was found in 7 of the 9 non-sleep apnea-prone patients. When the cutoff value of DBS was 0.10, the sensitivity was 77.7%, and the specificity was 100%.

Table 1 Baseline characteristics of study

	Total	Male	Female
Number	17	9	8
(SDB)	9	7	2
(non-SDB)	8	2	6
Age (years)	39.6 ± 8.7	42.2 ± 10.1	36.6 ± 7.0
(SDB)	43.4 ± 8.3	44.7 ± 9.1	39.0
(non-SDB)	35.3 ± 7.3	33.5	35.8 ± 8.1
Body height (cm)	165.6 ± 9.5	172.4 ± 7.8	157.9 ± 3.6
(SDB)	168.3 ± 11.0	172.3 ± 8.7	154.5
(non-SDB)	162.5 ± 7.0	173.0	159.0 ± 3.2
Weight (kg)	63.6 ± 13.2	71.9 ± 11.6	54.3 ± 8.7
(SDB)	69.4 ± 12.4	71.9 ± 12.4	61.5
(non-SDB)	56.9 ± 11.3	72.0	51.9 ± 7.0
Body mass index (kg/m^2)	23.1 ± 3.6	24.1 ± 3.1	21.9 ± 4.2
(SDB)	24.5 ± 3.7	24.1 ± 3.3	25.9
(non-SDB)	21.4 ± 3.0	24.1	20.5 ± 2.9
Sleeping time (min)	305.4 ± 50.7	312.7 ± 53.8	297.2 ± 51.5
(SDB)	325.8 ± 48.0	320.1 ± 53.6	346.0
(non-SDB)	282.4 ± 45.8	286.8	280.9 ± 49.2
3% ODI	6.2 ± 4.9	9.0 ± 5.0	3.0 ± 2.8
(SDB)	9.6 ± 4.3	10.3 ± 4.6	7.2
(non-SDB)	2.3 ± 1.4	4.4	1.6 ± 0.6
Minimum SpO_2 (%)	85.0 ± 6.1	81.1 ± 5.5	89.4 ± 2.9
(SDB)	83.4 ± 5.8	82.1 ± 5.9	88.2
(non-SDB)	86.7 ± 6.3	77.6	89.8 ± 3.2
Epworth sleepiness scale	7.3 ± 2.2	8.2 ± 2.5	6.3 ± 1.5
(SDB)	7.6 ± 2.2	7.7 ± 2.5	7.0
(non-SDB)	7.0 ± 2.3	10.0	6.0 ± 1.7
Smoker (N)	2	1	1
(SDB)	1	0	1
(non-SDB)	1	1	0
Medication (N)	1	1	0
(SDB)	1	1	0
(non-SDB)	0	0	0

Each value represents the mean ± standard deviation.

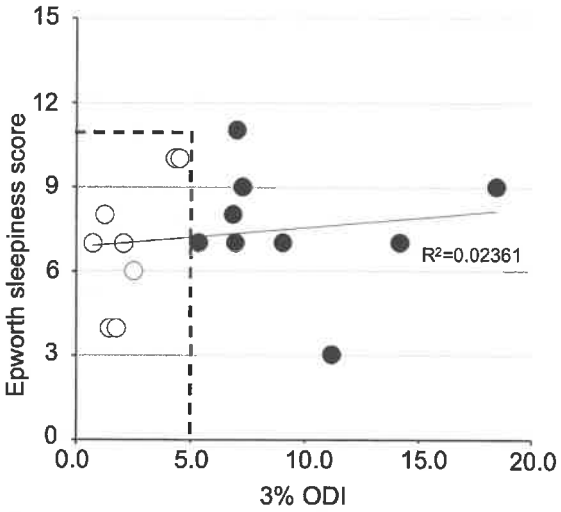

Figure 1. Correlation between 3% DOI and Epworth sleepiness scale.

R^2 represents the correlation coefficient between these two parameters. Broken lines represent borderlines for the presence or absence of sleep-disordered breathing according to the guidelines for the diagnosis and treatment of sleep-disordered breathing in cardiology. Closed circles and open circles represent participants with and without sleep-disordered breathing, respectively. ODI, oxygen desaturation index.

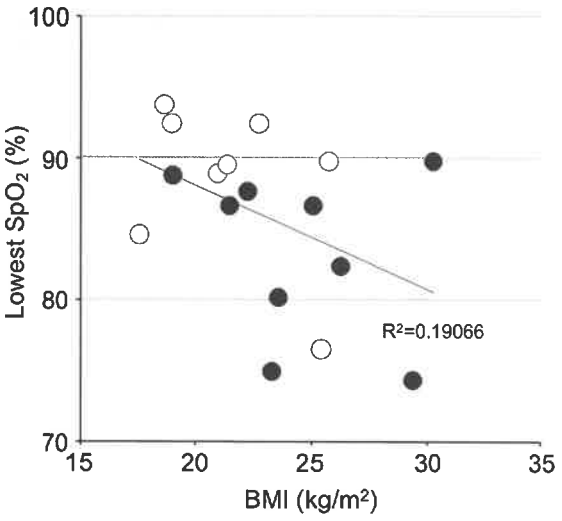

Figure 3. Correlation between BMI and Minimum SpO_2.

R^2 represents the correlation coefficient between these two parameters. Closed circles and open circles represent participants with and without sleep-disordered breathing, respectively. BMI, body mass index

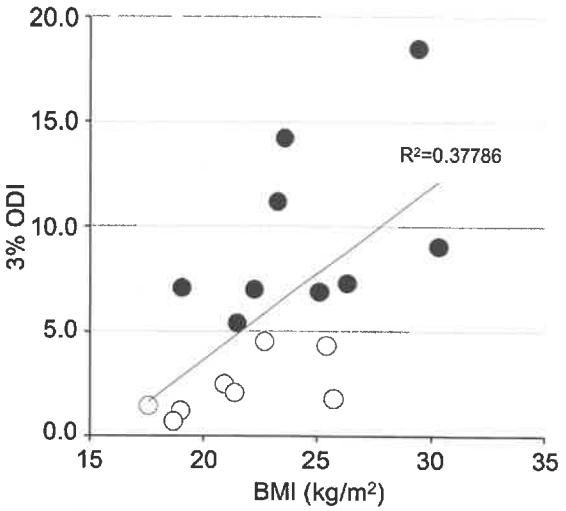

Figure 2. Correlation between BMI and 3% ODI.

R^2 represents the correlation coefficient between these two parameters. Closed circles and open circles represent participants with and without sleep-disordered breathing, respectively. BMI, body mass index, ODI, oxygen desaturation index.

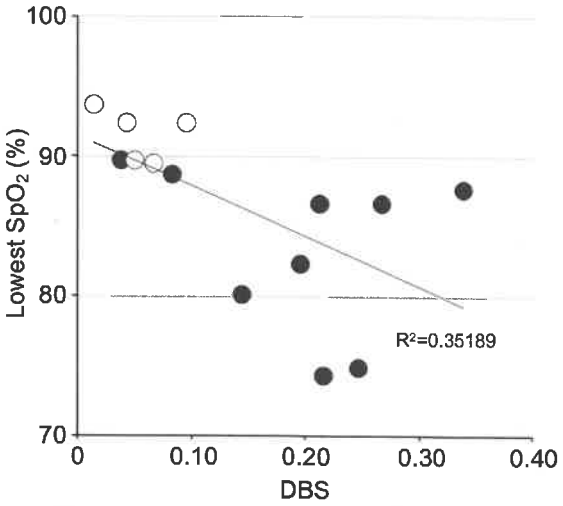

Figure 4. Correlation between BMI and Minimum SpO_2.

R^2 represents the correlation coefficient between these two parameters. Closed circles and open circles represent participants with and without sleep-disordered breathing, respectively. BMI, body mass index

Ⅲ. Discussion

The method of measuring SpO_2 used in this study is commonly used as a simple test for sleep apnea syndrome. In addition to measuring SpO_2, a wearable sensor that can measure heart rate and body position during sleep was attached,

and the disordered breathing state was estimated from the data obtained by the sensor.

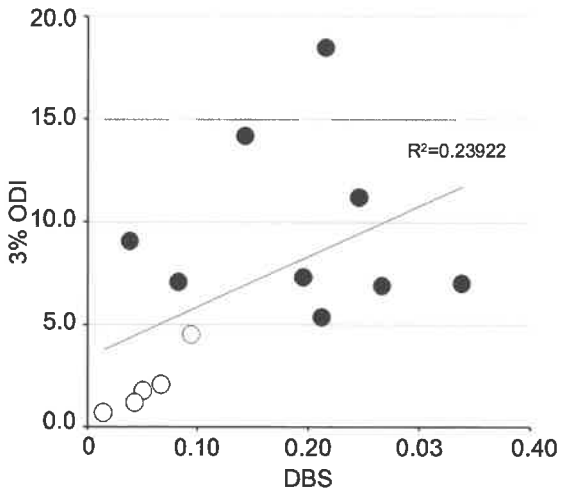

Figure 5. Correlation between DBS and 3% ODI.
R^2 represents the correlation coefficient between these two parameters. Closed circles and open circles represent participants with and without sleep-disordered breathing, respectively. DBS, respiratory disturbance score, ODI, oxygen desaturation index.

One of the important risk factors for OSA is obesity, and weight loss is recommended for treating OSA[1]. However, in this study, there was no statistically significant difference in the BMI and body weight between the disordered breathing-induced group and the non-induced group. In addition, the BMI of the disordered breathing-induced group was 24.5 ± 3.7 kg/m^2), which is generally around the upper limit of standard weight. Therefore, it was inferred that apnea was likely to be induced during sleep even in people within the international standard weight.

According to a survey conducted in 2016, the average sleep time of Japanese people was 7 hours and 40 minutes, but the participants in this study slept less than 5 hours[9]. Many of the participants stated that they had difficulty falling asleep because they slept with the devices installed for the first time, suggesting that their sleep time may have been shortened because of the unusual environment. In addition, the disordered breathing-induced group slept significantly longer than the non-induced group because they unnecessarily repeated onset and offset of sleep due to respiratory arrest. The relationship between sleep apnea and sleep duration needs to be further investigated because it is impossible to evaluate sleep state accurately without an electroencephalogram. The transcutaneous partial pressure of oxygen was used as one of the indices to distinguish the sleep apnea-induced group from the non-induced group. The significant difference between the disordered breathing-induced and non-induced groups suggests that the 3% ODI is an appropriate parameter to separate these two groups.

The correlation of each parameter was examined from the individual values of the participants. In general, a coefficient of determination (contribution ratio: R^2) of 0.4 to 0.7 indicates a significant correlation, and that of 0.7 to 1.0 indicates a strong correlation. In this study, there was little correlation between the 3% ODI, one of the criteria for OSA syndrome, and the Epworth Sleep Scale. The Epworth Sleep Scale is generally used to measure daytime sleepiness and does not apply to asymptomatic patients such as the participants in this study. This result is consistent with other large-scale evaluations with high false-negative rates[4]. The correlation between BMI and 3% ODI was also poor. Although obesity is one of the risk factors for developing OSA, sleep apnea is induced before obesity develops, indicating that the number of potential SAS patients may be larger than expected. Moreover, there was little correlation between BMI and minimum oxygen partial pressure.

In our preliminary analysis by our wearable sensor, disordered breathing was observed when the participants lay on their backs. The results suggest that hypoxia can occur transiently even in healthy participants without sleep apnea, which might be affected by their sleeping positions. The DBS value analyzed by the wearable sensor and its software did not show a high correlation between partial pressure of oxygen or 3% ODI. However, DBS might serve as a diagnostic marker for disordered breathing at the cutoff value of 0.1.

Transcutaneous measurement of arterial oxygen saturation or expiratory airflow has been used as a simple test that can be performed at home[4]. The results of this study indicate that the use of a wearable sensor and its analysis software may increase the sensitivity or specificity of the diagnosis of sleep apnea, which could motivate the implementation of full-scale SAS testing in hospitals. Self-testing using these sensing elements may contribute not only to the detection of SAS but also to the health care economy through the prevention of SAS.

In conclusion, this study revealed that sleep apnea occurs even in asymptomatic people generally considered healthy. This suggests that there are more pre-symptomatic sleep apnea patients than expected and that early screening of these patients is extremely important. As one of such screening methods, analysis using wearable sensors may be useful.

Ⅳ. Limitation

Since this study was conducted with a small number of participants at only one night, it is necessary to recruit a larger number of participants in the future and collect similar data to this study to obtain more accurate data.

Ⅴ. Acknowledgements

We acknowledge Dr. Atsushi Sugiyama, Professor of the Department of Pharmacology, Faculty of Medicine, Toho University, for supporting the study. We also thank Dr. Koichiro Tanaka, who obtained the informed consent of the participants as a medical doctor. All authors deeply thank the participants of this study.

Ⅵ. Conflict of Interest

This study was supported by a research grant from Union Tool Co. Mr. Matsui and Dr. Shinozaki, and Dr. Nakata belonged to the Production Engineering Department of the company and its Product Development Division, respectively. They were not engaged in this clinical study but only Dr. Ando took part in it. He lent the devices to participants and send de-identified numerical data of the clinical study to Mr. Matsui and Dr. Shinozaki. The two analyzed them. All authors were involved putting together this article by the analyzed data after that. Each author has declared that there are no other conflicts of interest in the submitted work.

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