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Tongue Protrusion Strength in Arousal State Is Predictive of the Airway Patency in Obstructive Sleep Apnea

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Contraction of the genioglossus affects either tongue protrusion strength or dilating forces of the upper airway. The upper airway in patients with obstructive sleep apnea (OSA) is thought to collapse during sleep, at least in part because of a sleep related reduction in genioglossus muscle activity. Thus, although tongue protrusion strength by genioglossus activity during sleep contributes to the maintenance of airway patency in patients with OSA, the relationship between tongue protrusion strength in the arousal state and obstructive sleep apnea has not been fully elucidated. Conventional method of tongue protrusion strength cannot be used to evaluate in edentulous subjects and/or subjects with the decreased biting force. In this study, employing a novel measurement method that does not require biting a transducer, we investigated relationships between the tongue protrusion strength and polysomnographic findings. We enrolled twenty normal subjects and 26 subjects with OSA. All subjects completed the measurement of tongue protrusion strength. Each subject with OSA was evaluated by full polysomnography. The degree of tongue protrusion strength was assessed by maximum voluntary contraction against the tongue depressor connected with a strain gauge dynamometer. The tongue protrusion strength was negatively correlated with obstructive apnea time, apnea index (AI) and the percent of sleep stage 2 ($r = -0.61$, $p < 0.0001$, $r = -0.41$ $p = 0.03$ and $r = -0.39$ $p = 0.04$, respectively). Tongue protrusion strength measured in the arousal state is predictive of the airway patency during sleep in OSA.

Keywords: apnea-hypopnea index; apnea index; obstructive apnea time; percentage of sleep stage 2; tongue protrusion strength
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Introduction

In humans, the upper airway (UA), from the posterior end of the nasal septum to the epiglottis, has relatively little bony or rigid support. Thus, there are anatomic and physiologic influences that tend to collapse this portion of the airway that must be offset by UA muscular dilating forces if airway patency is to be maintained (White et al. 2005). On the other hand, obesity and some upper airway anatomical features are associated with negative suction forces within the pharynx during sleep, leading to a decrease of UA patency. In obstructive sleep apnea (OSA), there is an imbalance between UA muscular dilating forces and negative suction forces within the pharynx, which permits occlusion of the UA during sleep (Remmers et al. 1978). Thus, it is generally recognized that muscular dilating forces during sleep in patients with OSA is a critical factor for maintenance of UA patency.

The genioglossus (GG) is one of the main anatomical components of the tongue muscle and affects either tongue protrusion strength or dilating forces of the UA (Remmers et al. 1978). The increased muscular activities of the GG during sleep in OSA have been found to be mainly induced by phasic activation of mechanoreceptors located in the larynx due to complete or partial collapse of the pharyngeal lumen (Akahoshi et al. 2001). Furthermore, the state of central respiratory pattern generator and sleep-sensitive neuromodulators can modify the activity of the hypoglossal motor nucleus that regulates the activity of hypoglossal motor output (Jelev et al. 2001; Fogel et al. 2003). Taken together, the GG activity, which is controlled by both the peripheral and the central neural factors, can provide dilating forces to cancel the collapse of UA in patients with OSA (Jelev et al. 2001; Fogel et al. 2003). Thus, although these components are necessary to maintain the UA patency during sleep, it seems that muscle wasting of the GG in

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patients with OSA may disturb the transient production of the dilating force of the GG by activation of hypoglossal motor output to counter the negative suction forces within the pharynx.

There have been a few reports on tongue protrusion strength during arousal state in patients with sleep disordered breathing (Mortimore et al. 2000; Shepherd et al. 2006). Mortimore and colleagues (1999) have developed a method for measurement of tongue protrusion strength. In order to measure tongue protrusion strength, their method requires that subjects must bite a transducer with their upper and lower front teeth to steady it (Mortimore et al. 1999, 2000; Shepherd et al. 2006). Thus, their method does not enable evaluation of tongue protrusion strength in edentulous subjects and/or subjects with decreased biting force. Therefore, in this study, employing a novel measurement method of tongue protrusion strength which does not require biting a transducer, we hypothesized that tongue protrusion strength in OSA is associated with obstructive apnea. Furthermore, we aimed to evaluate the relationships between the force of tongue protrusion in the arousal state and obstructive apneic events evaluated by polysomnography in patients with OSA.

Methods

Subjects

Twenty-six patients with OSA were enrolled to evaluate tongue protrusion strength. All subjects with OSA were evaluated by full polysomnography at Himeji St. Mary's Hospital. Inclusion criteria for patients with OSA included a full overnight polysomnogram (Sleep Watcher E; Tejin Pharma, Ltd and Compumedics Ltd, Victoria, Australia) with an apnea-hypopnea index (AHI) greater than 5 events per hour. Patients with neuromuscular disease, cognitive disease, and cerebrovascular disease were excluded. Characteristics of patients are shown in Table 1. Twenty healthy subjects were allocated to evaluate tongue protrusion strength. Healthy subjects were originally recruited via public postings in and around Himeji Dokkyo University and Himeji St. Mary's Hospital. All participants provided informed written consent before data collection, and the study was approved by the Institutional Review Boards of Himeji Dokkyo University and Himeji St. Mary's Hospital.

Measurement of the tongue protrusion strength

All measurements were made while the subjects were seated in a comfortable high-backed armchair. The jaw and forehead of each subject were fixed to prevent a change of posture. The range of motion (ROM) of flexure of the cervical spine in each subject was kept at 30 degrees during the measurement of tongue protrusion strength. The distance between the apex of the tongue and the tongue depressor was fixed in absolute term (1 cm) in each subject. The tongue protrusion strength was assessed by maximal tongue protrusion against the tongue depressor connected with a strain gauge dynamometer (dynamometer of tongue muscle; Takei Ltd., Niigata, Japan) (Fig. 1). Peak value during 5 sec maximal voluntary tongue protrusion was evaluated for each participant. The higher value of two consecutive measurements, spaced 2 minutes apart, was defined as the strength of GG. We found the strongly significant correlations between two applications both in healthy subjects ($r = 0.95$, $p < 0.001$) and in OSA patients ($r = 0.84$, $p < 0.001$).

Data analysis

Data are expressed as mean (SD) except where specified otherwise. The Mann-Whitney U test was used to compare normal subjects and OSA patients in tongue protrusion strength. Pearson's correlation coefficient was used to evaluate correlations between variables. A p value of < 0.05 was considered significant.

Table 1. Clinical Characteristics of normal subjects and OSA patients.

	Normal subjects	Patients with OSA	*p* value
Number	20	26	
Height (cm)	164.9 ± 7.8	166.3 ± 7.5	n.s.
Weight (kg)	66.7 ± 18.2	66.9 ± 10.8	n.s.
BMI (kg/m^2)	24.5 ± 6.3	24.1 ± 3.0	n.s.
Age (yr)	37.0 ± 18.8	54.6 ± 13.8	= 0.01
Gender (male/female)	11/9	22/4	-
Tongue protrusion strength (N)	2.48 ± 0.86	2.15 ± 0.8	n.s.
Neck circumference (cm)	-	37.4 ± 3.2	-
Abdominal circumference (cm)	-	89.4 ± 7.1	-
Hip circumference (cm)	-	95.3 ± 8.7	-
AI (events/hr)	-	15.5 ± 17.1	-
AHI (events/hr)	-	29.4 ± 20.1	-
Obstructive apnea time (sec)	-	31.9 ± 45.6	-
Obstructive apnea index (events/hr)	-	20.7 ± 10.2	-
The lowest SpO_2 (%)	-	85.9 ± 6.5	-

Data are mean ± SD. *P*-values were calculated by the Mann-Whitney *U* test.
n.s., not significant; BMI, body mass index; AI, apnea index; AHI, apnea-hypopnea index.

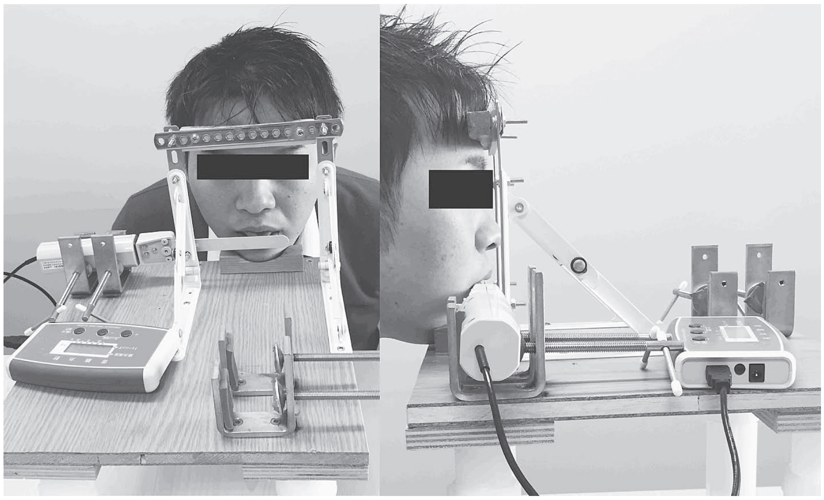

Fig. 1. Measurement of tongue protrusion strength.
Jaw and forehead in each subject were fixed to prevent the change of posture. The range of motion (ROM) of flexure on the cervical spine of each subject was kept at 30 degrees during the measurement of tongue protrusion strength. The distance between the apex of the tongue and the tongue depressor was fixed in absolute term (1 cm) in each subject. The tongue protrusion strength was assessed by maximal tongue protrusion against the tongue depressor connected with a strain gauge dynamometer. Peak value during 5 sec maximal voluntary tongue protrusion was evaluated for each participant.

Table 2. Correlations between strength of the tongue protrusion and clinical characteristics.

	Pearson coefficient	*p* value
BMI (kg/m^2)	0.03	0.87
Age	−0.21	0.29
Neck circumference (cm)	0.04	0.84
Abdominal circumference (cm)	0.09	0.64
Hip circumference (cm)	0.21	0.29
AI (events/hr)	−0.41	0.03
AHI (events/hr)	0.34	−0.19
Obstructive apnea time (sec)	−0.61	< 0.0001
The lowest SpO_2 (%)	0.23	0.25
Sleep stage 1 (%)	0.21	0.29
Sleep stage 2 (%)	−0.39	0.04
Sleep stage 3 (%)	0.19	0.34
Sleep stage 4 (%)	0.18	0.37

Results

Twenty normal subjects and 26 OSA patients completed the experiments without any difficulty or side effects. The clinical characteristics of OSA patients are summarized in Table 1. There was no significant change in tongue protrusion strength between normal subjects (2.48 ± 0.86 Nm) and OSA patients (2.15 ± 0.80 Nm) (Table 1). The relationships between polysomnographic findings and tongue protrusion strength are summarized in Table 2. As shown in Table 2, the tongue protrusion strength was significantly and negatively correlated with obstructive apnea time and apnea index (AI) ($r = -0.61$, $p < 0.0001$ and $r = -0.41$, $p = 0.03$, respectively) (Fig. 2A and B) In addition, the strength of tongue protrusion was significantly associated with the rate of sleep stage 2 ($r = -0.39$, $p = 0.04$) (Fig. 2C).

Discussion

In the present study, tongue protrusion strength in OSA was found to be significantly and negatively associated with obstructive apnea time and AI. In addition, the tongue protrusion strength in OSA showed a significant correlation with the rate of sleep stage 2.

In this study, based on a preliminary experiment in order to assess the reproducibility, we showed for the first time that the tongue protrusion strength was significantly correlated with obstructive apnea time. Since the GG is a primary UA dilator muscle, this finding may suggest that tongue protrusion strength in the arousal state lets us know whether the UA dilating force induced by GG during sleep

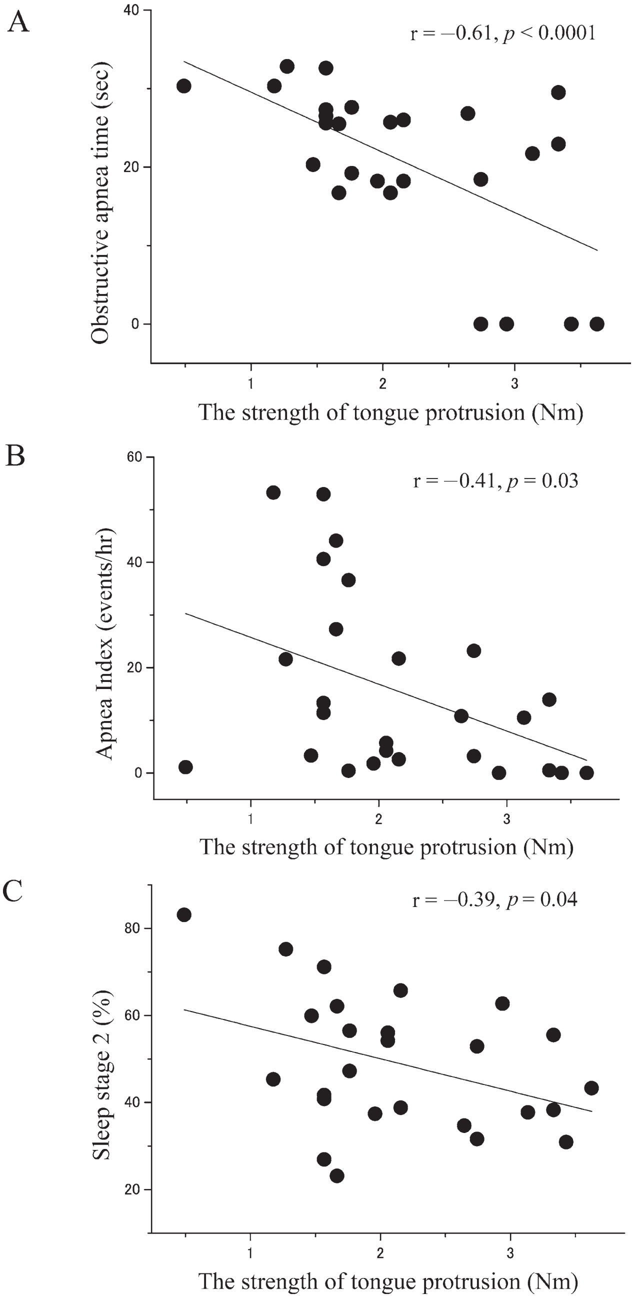

Fig. 2. Relationship between tongue protrusion strength in OSA and polysomnographic findings.
Relationship between tongue protrusion strength in OSA and obstructive apnea time (A), apnea index (B) and sleep stage 2 (C). Each solid regression line represents the function with a significant Pearson coefficient.

cancels the negative suction forces in the pharynx.

There have been a few reports on tongue protrusion strength in patients with sleep disordered breathing (Mortimore et al. 2000; Shepherd et al. 2006). Mortimore and colleague have developed a method for measurement of tongue protrusion strength (Mortimore et al. 1999, 2000; Shepherd et al. 2006). They clearly showed that tongue protrusion strength is significantly correlated with AHI in sleep apnoea/hypopnea syndrome. However, in order to measure tongue protrusion strength, their method required subjects to bite the transducer with their upper and lower front teeth to steady the transducer (Mortimore et al. 1999, 2000) Thus, their method cannot be used to evaluate tongue protrusion strength in edentulous subjects and/or subjects with the decreased biting force. In this study, based on a method for measurement of tongue protrusion strength not necessiting biting a transducer, the tongue protrusion strength in OSA was shown to be significantly and negatively associated with obstructive apnea time and AI but not with AHI. Thus, this finding may suggest that this method for measurement of tongue protrusion strength allows evaluation of the force of tongue protrusion in edentulous subjects and/or subjects with decreased biting force.

In this study, the values of tongue protrusion strength between normal subjects and patients with OSA were consistent with those of a previous study by Mortimore et al. (2000). This suggests that tongue protrusion strength depends on several other factors such as upper airway size and shape, upper airway muscles mechanical efficiency and development of fatigue of upper airway muscles.

There have been the studies concerning muscular dysfunction of GG which resulted from inflammation, denervation and the metabolic change of muscular fibers (Boyd et al. 2004; Kim et al. 2014b). Boyd et al. (2004) showed that inflammatory cells were increased in the muscular layer of patients with OSA, with CD4+ and activated CD25+ T cells predominating. In addition, the most recent study showed that glucose uptake in the GG of patients with sleep apnea was reduced in comparison with obese normal subjects with [18F]-2-fluoro-2-deoxy-D-glucose positron emission tomography imaging (Kim et al. 2014b). Taken together, it can be reasonably assumed that the mechanism of down regulation of maximal strength of GG in the arousal state may be caused by the above-mentioned factors in OSA (Boyd et al. 2004; Kim et al. 2014b).

Recent study revealed increased tongue fat volume in OSA (Kim et al. 2014a). This element may prevent the activation of GG from maintaining the UA patency at supine position during sleep. It must still be clarified whether increased tongue volume causes down regulation of tongue protrusion strength in OSA.

Finally, we found that the tongue protrusion strength was significantly and negatively correlated with the percentage of sleep stage 2. Strong contraction of the GG may lead to up-regulation of peripheral neuromuscular input of the GG, suggesting that this input can activate the central neural system which reflects the shift from sleep stage 2 to 3. However, the effect of transient contraction of the GG during obstructive apnea on the state of sleep stage has not been fully clarified.

In conclusion, the tongue protrusion strength in OSA was found to be associated with obstructive apnea time and AI. This finding may suggest that both UA muscular dilating forces and negative suction forces within the pharynx are needed to improve maintenance of the airway patency in OSA.

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Conflict of Interest

All of the authors declare that they have no competing interests that might be perceived to influence the results and discussion reported in the present manuscript.

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