PEDIATRIC DENTAL JOURNAL 15(2): 152–164, 2005

Effects of vibration stimulus on lower-jaw-position sensation in patients with cerebral palsy during inhalation of laughing gas

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Abstract To clarify the effects of a vibration stimulus applied during sedation with nitrous oxide (hereafter referred to as laughing gas) on the ability of muscles attached to the lower jaw to sense lower-jaw position and on the sensation of muscle spindles attached to the lower jaw in patients with cerebral palsy (CP) using healthy adult subjects without functional abnormalities of the jaws and oral cavities as control subjects (hereafter referred to as healthy subjects). Experiments were performed under the following conditions: for each subject, before the application of the vibration stimulus (referred to as S_{pre}) and after the application of the vibration stimulus (S_{post}); before the inhalation of laughing gas (LG) and oxygen (air-inhalation condition: referred to as without LG inhalation) and during the inhalation of LG and oxygen (inhalation condition of LG and oxygen under LG-induced sedation: referred to as during LG inhalation). Subjects in the experiments were eight CP patients and eight healthy people as controls. The ability to discriminate lower-jaw position was estimated by asking the subjects to determine whether the diameter of a test stick was larger or smaller than that of a reference stick after performing the following tasks: a) holding a reference stick between the central teeth of their upper and lower jaws for 5 s, and b) replacing the reference stick with a test stick and holding it at the same position for 5 s, and the test stick was then removed. The following findings were obtained.

1) In comparing the ability of healthy subjects to discriminate between S_{pre} and S_{post} during LG inhalation using different test sticks, when the test stick diameter was 9.5 mm (smaller than the reference stick diameter), the rate of mis-estimation (RME) for S_{post} was significantly larger than that for S_{pre} ($P<0.05$). No significant differences were observed for any other test sticks.
2) In comparing the ability of CP patients to discriminate between S_{pre} and S_{post} during LG inhalation using different test sticks, when the test stick diameter was 9.5 mm (smaller than the reference stick diameter), the RME for S_{post} was significantly smaller than that for S_{pre} ($P<0.05$). No significant differences were observed for any other test sticks.

These results suggest the following: the combination of LG for sedation with vibration stimulus further inhibits neuronal functions at the upper level of the central nervous system in CP patients, compared with cases in which each variable is applied separately, and the combination also inhibits the sustained increase in muscle tonus, which is characteristic of CP patients. LG reduces the activity of γ-motor neurons via the upper level of the central nervous system. In addition, tonic vibration reflex (TVR) develops due to the vibration stimulus, which increases the threshold value of sensitive muscle sensation and decreases the activity of γ-motor neurons, and furthermore decreases the activity of muscle spindles attached to the lower jaw. Consequently, a tendency toward increased ability to discriminate lower-jaw position is observed.

Key words
Cerebral palsy,
Laughing-gas,
Lower-jaw-position sensation,
Sedation,
Vibration stimulus

Received on January 24, 2005
Accepted on July 15, 2005

Introduction

Cerebral palsy (CP) is a motor disorder involving the central nervous system caused by nonprogressive pathological changes in the brain that may occur at any stage from the embryonic to early postnatal stages. As symptoms of motor disorders, increased muscle tonus and reflection of voluntary muscles during motions or maintaining postures, as well as the development of involuntary motions, are observed. These symptoms are observed not only in the four limbs but also in various muscles in the jaw-facial and head-neck regions[1,2]. Hence, abnormalities in muscle activities in CP patients become obstacles in daily life activities, preventing social independence. In addition, it is difficult to evaluate occlusion relationships in CP patients with the aim of recovering occlusion functions. Therefore it cannot be claimed on the basis of scientific data that occlusion functions are recovered in CP patients in dental clinical practice.

The activity of γ-motor neurons is involved in the occlusion and lower-jaw-position (LJP) sensation of humans. As a physiological evaluation index of the activity of γ-motor neurons, discrimination ability for LJP is known and its test was developed by Morimoto[3–6]. This test is applied to evaluate not only healthy subjects[7], but also CP patients and patients with dysfunctions in the jaw and oral cavity[5,6]. Yamaguchi *et al.*[8,9] observed an abnormal sensation of the masticatory muscle in CP patients, for example the overevaluation of interincisal distance, compared with healthy adult subjects (hereafter referred to as healthy subjects), on the basis of their investigation using a test of ability to discriminate LJP. They reported that the reason for this sensation was excessive stress due to the increased muscular tonus and overactivation of γ-motor neurons. However, many factors as causes of motor dysfunctions in the oral region of CP patients were still unclarified. Morimoto *et al.*[3] reported that, when muscle spindles in the occlusal muscles of a healthy subject were stimulated to the point of excitement, at 110 Hz from the surface of the skin at the chin of the lower jaw, the ability to discriminate LJP deteriorated for sticks of which diameters are smaller than that of the reference stick. Yoshida *et al.*[10] investigated the effects of a vibration stimulus on LJP sensation in CP patients by applying a vibration stimulus (110 Hz) to their chins at the lower jaw, and reported that the ability to discriminate LJP improved for stick diameters smaller than the reference stick diameter. Based on these findings, we assumed that an increased muscle tonus of the muscles attached to the lower jaw in CP patients affects the LJP sensation. Regarding the inhibition of increased muscle tonus, a method using a vibration stimulus and a method using laughing gas (LG) in an LG-induced sedation method were known[11,12]. Therefore, in this study, we investigated the effects of the inhibition of increased muscle tonus by LG on the LJP sensation.

The LG-induced sedation is a simple and fairly safe method for humans; hence it is used to alleviate anxiety and fear[13–17]. However, in addition to the sedative effect, the method was reported to increase the threshold value of sensation in the oral cavity of patients; for example, alleviating aches and decreasing the vomiting reflex[18–20]. Yoshida *et al.*[21] investigated the effects of LG-induced sedation on muscle sensation accompanied by the extension of the muscles attached to the lower jaw in healthy subjects, and confirmed that the ability to discriminate LJP is decreased by LG. Yoshida *et al.*[11] also investigated these effects in CP patients and confirmed that the ability to discriminate LJP is improved by LG. Furthermore, Yoshida *et al.*[12] reported that the involuntary muscle tonus of the jaw-facial plane in CP patients is inhibited by the inhalation of nitrous oxide gas (hereafter referred to as laughing gas (LG)) during dental practice, on the basis of the frequency analyses of electromyographies.

Under these circumstances, in this study we assumed that the combination of LG used in an LG-induced sedation method and a vibration stimulus may further inhibit the activity of γ-motor neurons in CP patients, compared with the case in which each factor is applied separately. To confirm how these two factors, that is, LG and vibration stimulus, affect the sensation of LJP, and how they affect the muscle sensation from the muscle spindles attached to the lower jaw, we evaluated differences in the LJP sensation using a test of discrimination ability, using healthy subjects without abnormalities in the jaw-facial system as controls. The results obtained are reported here.

Subjects and Methods

Subjects

The subjects in this study were eight patients with CP who visited the Department of Dentistry, Saitama Prefecture Colony Ranzango (four males and four females; average age, 32.0 ± 6.0 years old, hereafter referred to as the CP group), and eight healthy adults as control subjects (four males and four females; average age, 29.0 ± 4.6 years old; hereafter, referred to as the control group). While the subjects of the current study are adult patients with CP, a similar tendency may be observed in infant patients with CP. Therefore, we consider that the findings obtained in this study could also be effective in pediatric dentistry.

Prior to the study, the details of this study were fully explained to the subjects themselves, guardians (parents) and caretakers, and their consent was obtained. Approval for the study was given by the President of Colony Ranzango, the Director of Ranzango Hospital and the Manager of the Dental Department.

The subjects were selected on the basis of the following criteria.

1) They understood and approved of the objectives of the study. (They could communicate well without dysarthria.)
2) The patients showed no significant difference in the severity of CP. (This was evaluated by a specialist at the medical department of Colony Ranzango.)
3) They could breath through the nose and showed no involuntary muscle tonus on the jaw-facial region due to the use of a nasal mask.
4) They had no functional abnormalities of the jaw or oral cavity, and they could eat and swallow solid food normally.
5) During experiments in this study, they could maintain a posture appropriate for a dental chair and could hold their head and jaw positions stably.
6) They had slight systemic involuntary motions, particularly facial motions due to CP, but these symptoms did not pose any problems in this study.
7) They had neither dental prostheses nor defects in the front teeth of the upper jaw.
8) They had no systemic complications.
9) They were not using drugs such as muscle relaxants.

Methods

In a test of the ability to discriminate LJP, a subject was seated on a dental chair in a treatment room of the dental division. The backrest of the dental chair was set at an angle of about 100 degrees from the lower-limb side, and the extension of its headrest was set at the same angle as the backboard. A subject's Frankfurt plane was maintained parallel to the floor, and the subject wore an eye mask to eliminate visual information. The trunk of the subject was fixed with a strap attached to the dental chair. The hips and legs were fixed with sandbags (NAVIS). No particular measures were taken to alleviate the tension of the subject. The test of the ability to discriminate LJP was performed in accordance with the method of Morimoto[3–6]. The reference and test sticks used in the experiments are made of stainless steel (Tokyo Shizai). The reference stick has a diameter of 10.0 mm (124 g). Eight test sticks of different diameters at intervals of 0.5 mm were used; these were categorized into two groups on the basis of their diameters with respect to the reference stick; one group included test sticks whose diameters were smaller than that of the reference stick, and the other included those whose diameters were larger than that of the reference stick. The group of smaller-diameter sticks consisted of those with diameters of 8.0 mm (79 g), 8.5 mm (89 g), 9.0 mm (100 g) and 9.5 mm (110 g). The group of larger-diameter sticks consisted of those with diameters of 10.5 mm (136 g), 11.0 mm (150 g), 11.5 mm (162 g) and 12.0 mm (178 g). The measurement procedure was as follows. First, a subject was instructed to hold the reference stick between the central teeth of his/her upper and lower jaws for 5 s. The reference stick was replaced with a test stick, and the subject was instructed to hold the test stick at the same position for 5 s. Then, after removing the test stick, the subject was asked to determine whether the diameter of the test stick was larger or smaller than that of the reference stick. This procedure was repeated using test sticks of different diameters. Eight test sticks were presented randomly using a table of random numbers. Eight test sticks were presented in each session, and a total of ten sessions were performed for each subject. The rate of mis-estimation (RME), which was used to evaluate the discrimination ability of each patient, was obtained by dividing the total number of incorrect answers by the total number of answers, then multiplying the quotient by 100 to calculate the percentage. The higher the RME, the lower the ability to discriminate LJP, and *vice versa*.

These measurements were performed for each subject before and after the application of vibration stimulus (hereafter, referred to as S_{pre} and S_{post}, respectively)[10]. The application of a vibration stimulus

Table 1 Conditions of optimal sedation for LG-induced sedation

Objective symptoms (items evaluated by the operator)

1. The patient is conscious and able to talk.
2. The patient responds to the operator's questions and instructions.
3. The patient has a non-nervous relaxed look on his/her face.
4. The patient shows a marked reduction in the frequency of blinking his/her eyes.

Subjective symptoms (items evaluated by the subject)

1. The patient has a sense of exhaustion or a sense of slight intoxication.
2. The patient feels warm with his/her palms sweating.

Table 2 Comparison of RME between the first time and the second time for S_{pre} in each CP patient and healthy adult for different test sticks, and results of the significance tests for S_{pre} (between the first and second times)

The patients with CP (A) (Unit: %)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
The first measurement	0.0	1.6	6.3	9.6		6.3	5.0	3.1	0.0
The second measurement	0.0	1.6	6.3	10.2		6.3	6.3	3.8	0.0

mean ± S.D.

A healthy adult (a) (Unit: %)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
The first measurement	0.0	0.0	0.0	1.6		3.8	1.3	0.0	0.0
The second measurement	0.0	0.0	0.0	1.3		3.1	0.7	0.0	0.0

mean ± S.D.

and the site of application were in accordance with the method of Morimoto[3–6]. Stimuli were applied using a stimulator (TMT-18, HEIWA DENSHI) at a frequency of 110 Hz. The application site was at the chin in the lower jaw. A measurement was performed after the stimulator was applied to the chin in the lower jaw of a subject for 3 s to provide vibration. Measurements were also performed before the inhalation of LG and oxygen (air-inhalation condition: hereafter referred to as without LG inhalation) and during the inhalation of LG and oxygen (condition of LG and oxygen inhalation under LG induced sedation: referred to as during LG inhalation)[11]. In a test of the ability to discriminate LJP during LG inhalation, measurements were begun when a subject exhibited the optimal sedation as described in Table 1[11,21]. Table 1 lists optimal sedation conditions. For the inhalation of a mixture of LG and oxygen, a continuous-flow inhalation sedation system, Psychorich T-70 (SEKIMURA), was used. The subjects were instructed to inhale a mixture of 40% LG and 60% oxygen through a nose mask fixed on their face. The flow rate in the sedation system was set at approximately 6 to 8 *l*/min by taking into account the breathing capacity of healthy adults. A test of ability to discriminate LJP during LG inhalation was performed one week after the test and without LG inhalation[11,21].

In this study, the measurements of the ability to discriminate LJP were performed for CP patients and healthy adults for S_{pre} (the first time) and S_{post}. Measurements were also performed on the same subjects on a day one week after the first measurement for S_{pre} (the second time). This confirmed that there was no learning effect in the subjects. Table 2 shows the comparison of RME for S_{pre} between the first and second times for one subject each from the CP group and the control group (the CP patient (A) and healthy subject (a)).

Statistical analysis

As statistical methods, a significance test using the paired *t*-test was performed to compare the RME between the first and second times for S_{pre} in each of the CP patients and the healthy subjects.

To compare the RMEs for both S_{pre} and S_{post} between the control group and CP group, the unpaired *t*-test was used; for the comparison between S_{pre} and

Table 3 Comparison of mean RME for S_{pre} between the control group and the CP group for different test sticks, and results of the significance tests for S_{pre}

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
The control group	0.0	0.0	0.0]**	1.6±1.1]**		3.1±1.5]*	0.8±0.5]*	0.0	0.0
The CP group	0.0	1.6±1.1	6.3±2.4	10.2±4.2		6.3±2.4	5.5±2.1	3.1±1.5	0.0

**: $P<0.01$, *: $P<0.05$ mean±S.D.

Table 4 Comparison of mean RME after vibration stimulus between the control group and the CP group for different test sticks, and results of the significance tests after stimulus

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
The control group	0.0	0.0	0.0	6.3±2.4		5.5±2.1	2.3±1.1	0.0	0.0
The CP group	0.0	0.0	3.1±1.5	5.5±2.1		3.9±1.5	3.1±1.5	1.6±1.1	0.0

mean±S.D.

Table 5 Comparison of mean RME in the control group between S_{pre} and S_{post} for different test sticks, and results of the significance tests for S_{pre} and S_{post}

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
Before the vibrating stimulus	0.0	0.0	0.0	1.6±1.1]*		3.1±1.5	0.8±0.5	0.0	0.0
After the vibrating stimulus	0.0	0.0	0.0	6.3±2.4		5.5±2.1	2.3±1.1	0.0	0.0

*: $P<0.05$ mean±S.D.

S_{post} in both the control group and CP group, the paired *t*-test was used to determine significance.

For the comparison between no LG inhalation and during LG inhalation both in the control group and CP group, the paired *t*-test was used; to compare the control group and the CP group during LG inhalation, the unpaired *t*-test was used in the significance tests.

For the comparison between S_{pre} and S_{post} in both the control group and CP group during LG inhalation, the paired *t*-test was used; for the comparison between the control group and the CP group during LG inhalation for S_{post}, the unpaired *t*-test was used in the significance tests.

Results

Table 2 shows results of comparison and significance tests of RME in CP patient and in the healthy adult for S_{pre} (the first and second times) using different test sticks. No significant differences in RME were observed for any test sticks in either the CP patient or the healthy adult.

Table 3 shows results of comparison and significance tests of the mean RME between the control group and the CP group for S_{pre} using different test sticks. In the cases of test stick diameters of 9.0 mm and 9.5 mm, which are smaller than the reference stick diameter, and those of 10.5 mm and 11.0 mm, which are larger than the reference stick diameter, the mean RME of the CP group was significantly higher than that of the control group ($P<0.01$, and $P<0.05$, respectively). No significant differences were observed for any other test sticks.

Table 4 shows results of comparison and significance tests of the mean RME between the control group and the CP group for S_{post} using different test sticks. No significant differences were observed for any test sticks.

Table 5 shows results of comparison and significance tests of the mean RME between S_{pre} and S_{post} in the control group for different test sticks. In the case of the test stick diameter of 9.5 mm, which is smaller than the reference stick diameter, the mean RME for S_{post} was significantly higher than that for S_{pre} ($P<0.05$), but no significant differences were observed for any other test sticks.

Table 6 Comparison of mean RME in the CP group between S_{pre} and S_{post} for different test sticks, and results of the significance tests for S_{pre} and S_{post}

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
Before the vibrating stimulus	0.0	1.6±1.1	6.3±2.4 *	10.2±4.2 *		6.3±2.4	5.5±2.1	3.1±1.5	0.0
After the vibrating stimulus	0.0	0.0	3.1±1.5	5.5±2.1		3.9±1.5	3.1±1.5	1.6±1.1	0.0

*: $P<0.05$ mean±S.D.

Table 7 Comparison of mean RME in the control group between the absence and presence of LG inhalation for different test sticks, and results of the significance tests

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
In the absence of LG-induced sedation	0.0	0.0	0.0	1.6±1.1		3.1±1.5 *	0.8±0.5 *	0.0	0.0
During LG-induced sedation	0.0	0.0	0.0	2.3±1.4		8.6±3.3	5.5±2.1	2.3±1.5	0.0

*: $P<0.05$ mean±S.D.

Table 8 Comparison of mean RME in the CP group between absence and presence of LG inhalation for different test sticks, and results of the significance tests

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
In the absence of LG-induced sedation	0.0	1.6±1.1	6.3±2.4 *	10.2±4.2 *		6.3±2.4	5.5±2.1	3.1±1.5	0.0
During LG-induced sedation	0.0	0.8±0.5	3.1±1.5	5.5±2.1		3.9±1.5	3.1±1.5	1.6±1.1	0.0

*: $P<0.05$ mean±S.D.

Table 9 Comparison of mean RME during LG inhalation between the control group and the CP group for different test sticks, and results of the significance tests

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
The control group	0.0	0.0	0.0	2.3±1.4		8.6±3.3 *	5.5±2.1	2.3±1.5	0.0
The CP group	0.0	0.8±0.5	3.1±1.5	5.5±2.1		3.9±1.5	3.1±1.5	1.6±1.1	0.0

*: $P<0.05$ mean±S.D.

Table 6 shows results of comparison and significance tests of mean RME between S_{pre} and S_{post} in the CP group using different test sticks. In the case of test stick diameters of 9.0 mm and 9.5 mm, which are smaller than the reference stick diameter, the mean RME for S_{post} was significantly lower than that for S_{pre} ($P<0.05$), but no significant differences were observed for any other test sticks.

Table 7 shows results of comparison and significance tests of mean RME between no LG inhalation and during LG inhalation in the control group using different test sticks. In the case of test stick diameters of 10.5 mm and 11.0 mm, which are larger than the reference stick diameter, the mean RME during LG inhalation was significantly higher than that during no LG inhalation ($P<0.05$). No significant differences were observed for any other test sticks.

Table 8 shows results of comparison and significance tests of mean RME between no LG inhalation and during LG inhalation in the CP group for different test sticks. In the case of test stick diameters of 9.0 mm and 9.5 mm, which are smaller than the reference stick diameter, the mean RME during LG inhalation was significantly lower than that during no LG inhalation ($P<0.05$). No significant differences were observed for any other test sticks.

Table 9 shows results of comparison and

Table 10 Comparison of mean RME during LG inhalation in the control group between S_{pre} and S_{post} for different test sticks, and results of the significance tests for S_{pre} and S_{post}

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
Before the vibrating stimulus	0.0	0.0	0.0	2.3 ± 1.4]*		8.6 ± 3.3	5.5 ± 2.1	2.3 ± 1.5	0.0
After the vibrating stimulus	0.0	0.0	0.0	6.3 ± 2.4]*		8.6 ± 3.3	3.9 ± 1.5	0.0	0.0

*: $P<0.05$ mean ± S.D.

Table 11 Comparison of mean RME during LG inhalation in the CP group between S_{pre} and S_{post} for different test sticks, and results of the significance tests for S_{pre} and S_{post}

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
Before the vibrating stimulus	0.0	0.8 ± 0.5	3.9 ± 1.5	5.5 ± 2.1]*		3.9 ± 1.5	3.1 ± 1.5	1.6 ± 1.1	0.0
After the vibrating stimulus	0.0	0.0	1.6 ± 1.1	1.6 ± 1.1]*		1.6 ± 1.1	0.8 ± 0.5	0.0	0.0

*: $P<0.05$ mean ± S.D.

Table 12 Comparison of mean RME during LG inhalation between the control group and CP group for S_{post} for different test sticks, and results of the significance tests after stimulus

(Unit: %, N: 8)

The interincisal distance (mm)	8.0	8.5	9.0	9.5	10.0 (The reference stick)	10.5	11.0	11.5	12.0
The control group	0.0	0.0	0.0	6.3 ± 2.4]*		8.6 ± 3.3]**	3.9 ± 1.5	0.0	0.0
The CP group	0.0	0.0	1.6 ± 1.1	1.6 ± 1.1]*		1.6 ± 1.1]**	0.8 ± 0.5	0.0	0.0

*: $P<0.05$ mean ± S.D.

significance tests of mean RME between the control group and the CP group during LG inhalation using different test sticks. In the case of a test stick diameter of 10.5 mm, which is larger than the reference stick diameter, the mean RME of the CP group was significantly lower than that of the control group ($P<0.05$). No significant differences were observed for any other test sticks.

Table 10 shows results of comparison and significance tests of mean RME between S_{pre} and S_{post} in the control group during LG inhalation using different test sticks. In the case of a test stick diameter of 9.5 mm, which is smaller than the reference stick diameter, the mean RME for S_{post} was significantly higher than that for S_{pre} ($P<0.05$). No significant differences were observed for any other test sticks.

Table 11 shows results of comparison and significance tests of mean RME between S_{pre} and S_{post} in the CP group during LG inhalation using different test sticks. In the case of a test stick diameter of 9.5 mm, which is smaller than the reference stick diameter, the mean RME for S_{post} was significantly lower than that for S_{pre} ($P<0.05$). No significant differences were observed for any other test sticks.

Table 12 shows the results of comparison and significance tests of mean RME between the control group and the CP group during LG inhalation for S_{post} using different test sticks. In the case of a test stick diameter of 9.5 mm, which is smaller than the reference stick diameter, and that of 10.5 mm, which is larger than the reference stick diameter, the mean RME of the CP group was significantly lower than that of the control group ($P<0.01$ and $P<0.05$, respectively). No significant differences were observed for any other test sticks.

Discussion

Subjects

In addition to dysfunctions in the four limbs, CP patients have dysfunctions in their oral cavity region, for example disturbances in eating, swallowing and chewing due to the discoordination of motions, primarily of the muscles of mastication[1,2]. In particular, it was reported that the causes of the discoordination of motions of the muscles of mastication in CP patients are disturbances in the information-output system linked to the peripheral effector organs due to dysfunctions in the central nervous system[22–24], or the influence of the feedback control for sensing information from the muscles of mastication not working properly[9]. Generally, patients are categorized as either having spastic CP or athetosic CP. However, many patients are classified as having the intermediate type of CP, in which the characteristics of both types are present[1,2], hence, accurate classification is difficult. In addition, some reports state that no differences in the functions such as occlusal pressure or mastication ability are observed between different diseases[25–27]. Therefore, we did not carry out investigations in terms of different diseases.

Methods of study

Sensory receptors controlling the sensation of LJP are considered to be associated with the periodontal membrane[28], jaw joint[29], tendon[30], and muscle spindles of the occlusal muscle[28–31]. Broekhoijsen *et al.*[7] applied a local anesthetic to each sensory receptor of the oral cavity, such as the jaw joint and periodontal membrane, to clarify mechanisms by which LJP is sensed by humans. They found that the sensation of LJP does not change significantly after the application of the anesthetic. Morimoto *et al.*[6] investigated the sensation of LJP in subjects in whom the jaw joint was injured by wounds or abnormal calcification. They found no differences from that in healthy subjects. In another study, Morimoto *et al.*[5] investigated the sensation of LJP in patients with Duchenne muscular dystrophy, whose muscle tissues were severely damaged, and in patients whose muscles attached to the lower jaw on one side were removed; they observed a significant deterioration in the ability to sense LJP as compared with healthy subjects. On the basis of these results, we suggest that the sensation of LJP is affected by muscle spindles rather than by other sensory receptors.

With respect to the presence or absence of a stimulus, discrimination ability determined by the method used in this study reflects the activity of γ-motor neurons, which control the muscle sensation detected by the receptor of the extended muscle spindles of the muscles attached to the lower jaw. The activity of γ-motor neurons can be evaluated by comparing the discrimination ability for S_{pre} and S_{post}. Thus, differences in LJP sensation were examined by comparing the discrimination ability before and after the application of a stimulus to the muscles attached to the lower jaw. The ability to discriminate LJP was measured in accordance with the method by Morimoto[3–6]. Namely, subjects were tested using test sticks of different diameters, and their ability to discriminate LJP for each test stick was measured quantitatively using RME.

Conventionally, studies using LG-induced sedation methods focused mainly on its sedative and analgesic effects[32–34]. On the other hand, attention was directed to a decrease in the muscle tonus by an LG-induced sedation method[33,35,36]. In a study using electromyographic frequency analyses, Yoshida *et al.*[12] observed that the activity of maxillofacial muscles in CP patients was suppressed by LG inhalation in dental practice. Nagao *et al.*[35] applied an LG-induced sedation method to CP patients whose jaws were difficult to position so that they corresponded to interdigitation, and to patients for whom it was difficult to determine the occlusion relationship for other reasons. They reported that this sedation method facilitated the monitoring of jaw position and of the ability to direct the jaws. If LG-induced sedation decreases the tonus of muscles attached to the lower jaw, the activity of spindle muscles is also considered to be inhibited simultaneously, and it is possible that the sensations of occlusion and LJP are affected. Yoshida *et al.*[21] investigated the effect of LG-induced sedation on muscle sensations associated with the extension of the muscles attached to the lower jaw in healthy subjects and identified a reduced ability to discriminate LJP as a result of exposure to LG. These findings suggest that LG increases the threshold of muscle sensation by inhibiting the central nervous system. Furthermore, Yoshida *et al.*[11] investigated the effect of LG-induced sedation on muscle sensations associated with the extension of the muscles attached to the lower jaw in CP patients and identified an increased ability to discriminate LJP as a result of exposure to LG.

Yoshida *et al.*[12] reported that involuntary maxillofacial muscle tonus was decreased by inhalation of LG in dental practice based on electromyographic frequency analyses.

Yoshida *et al.*[11,21] also reported that the appropriate LG concentration in a LG-induced sedation method was 40% based on clinical experience. Ogata[37] treated 107 CP patients who required dental treatment by applying LG inhalation at a concentration of 36–

50%, and reported that, from the patients' responses to a postoperative questionnaire, the most effective LG concentration was approximately 40%. On the basis of these reports, a mixed gas of 40% LG and 60% oxygen was used in this study.

The test of the ability to discriminate LJP during LG inhalation was begun after achieving optimal sedation with LG. As a result, regarding the starting time of the test, all subjects were determined to be in the optimal sedation state less than 5 min after LG inhalation. In general, the solubility of LG in blood and tissue is low (blood/gas dissolution coefficient is 0.47). It was reported that the degree of saturation in blood and tissue reached approximately 90% of the inhalation concentration less than 5 min after the inhalation of the gas, and that the LG-induced sedation state was attained quickly[38].

Results

One point should be noted regarding the results before discussing them. As shown in Table 2, thus, the RMEs for S_{post} in both the CP group and control group are considered temporary values. As already mentioned in the section on Subjects and Methods, the CP patients as the subjects of this study have only cerebral palsy without mental retardation and are capable of responding similarly to healthy adults; we confirmed that the RMEs are reproducible, and they are not due to learning effects.

As shown in Table 3, in the comparison of RME between the control group and the CP group for S_{pre}, the RMEs for test stick diameters other than 8.0 mm or 12.0 mm in the CP group were higher than those of the control group. Yamaguchi *et al.*[8] investigated the ability to discriminate LJP in CP patients using RME and found that CP patients showed more difficulty in discriminating LJP when test stick diameters were smaller than the reference stick diameter than did healthy subjects. In our study, CP patients also had difficulty discriminating LJP when test stick diameters were larger than the reference stick diameter. Yamaguchi *et al.*[8,9] observed an abnormal sensation of masticatory muscles in CP patients, such as the overevaluation of interincisal distance, compared with healthy subjects in their investigation using a test of ability to discriminate LJP. They reported that the reason for this is excessive tonus due to the overactivity of γ-motor neurons. Suzuki *et al.*[39] reported that CP patients overevaluate small changes in the muscle tonus compared with healthy subjects. They speculated that the reason for this in CP patients is the overactivation of γ-motor neurons, which control the muscle spindles, leading to an increase in the frequency of discharge of afferent impulses. Because the sensory property of LJP sensation of the muscles attached to the lower jaw is considered to arise from the sensory property of the muscle sensation of the four limbs[39], a decrease in the ability to discriminate LJP sensation in CP patients is considered to reflect the overactivation of γ-motor neurons controlling the spindles in the muscles attached to the lower jaw.

As shown in Table 4, the RME of the CP group was lower than that of the control group. We speculate that the reason for this is as follows: when stimulus is applied while γ-motor neurons in healthy subjects are continuously overactivated[3,4], the activity of already overactivated γ-motor neurons in CP patients dose not increase, but rather decreases[40–42] resulting in a decrease in RME. We intend to further investigate the details of this mechanism by electromyography.

As shown in Table 5, thus, the ability to discriminate interincisal distances smaller than the reference stick diameter decreases for S_{post} compared with that for S_{pre}, thereby showing the influence of the stimulus. The reason for this is as follows: when sensing the test stick with a 9.5 mm diameter which is smaller than the reference stick diameter of 10.0 mm, the muscle spindles are not in a state of extension. However, the application of a stimulus in this state leads to a sustained overactivation of γ-motor neurons, resulting in a decrease in the ability to discriminate LJP[8,9]. The muscle spindles are not stretched in the cases of test stick diameters smaller than 10.0 mm (reference stick diameter), and they are stretched in the cases of test stick diameters larger than 10.0 mm; we considered that the occurrence and nonoccurrence of stretching of muscle spindles depends on the interincisal distance. Morimoto *et al.*[3] reported a decrease in the ability to discriminate LJP even in healthy subjects for test stick diameters smaller than the reference stick diameter when the spindles of the occlusal muscles were excited by an application of a 110 Hz stimulus on the surface of the skin at the chin of the lower jaw. Thus, the results of our study agreed with those of Morimoto *et al.*

As shown in Table 6, accordingly, the discrimination ability increased for S_{post} compared with that for S_{pre} for test stick diameters smaller than the reference stick diameter, showing the effect of the stimulus. Yamaguchi *et al.*[8] investigated the ability to discriminate LJP in CP patients using RME and found that CP patients showed difficulty discriminating test stick diameters smaller than the reference stick diameter in comparison with healthy subjects; this result agrees with our result for S_{pre}. However, when results were compared between S_{pre} and S_{post}, the discrimination ability in terms of the RME of the CP group improved, contrary to that of the control group. This result shows a contradiction that, in spite of sustained overactivation of γ-motor neurons in CP patients, this overactivation was rather suppressed after the application of the stimulus.

It is generally known that when a vibration stimulus is applied to voluntary muscles, including the muscles attached to the lower jaw, the muscles develop slow tonus called tonic vibration reflex (TVR)[40–42]. This reflex is considered to develop multisynaptic muscle tonus in the upper level of central nervous system. Therefore, if we assume that TVR developed both in the CP group and the control group, the reason for the contradictory results for the two groups may be as follows: in the CP patients, the development of TVR secondarily decreased the activity of γ-motor neurons, resulting in an increase in the threshold of oversensitive muscle sensation by the vibration stimulus. As a result, the discrimination ability of the CP patients improved.

As shown in Table 7, in the above cases of test stick diameters of 10.5 mm and 11.0 mm, the discrimination ability during LG inhalation was lower than that during the absence LG inhalation; thus, the effect of LG inhalation was observed for test stick diameters larger than the reference stick diameter.

As shown in Table 8, in the above cases of test stick diameters of 9.0 mm and 9.5 mm, the discrimination ability during LG inhalation is higher than that during the absence of LG inhalation; thus, the effect of the LG inhalation was observed for test stick diameters smaller than the reference stick diameter.

In this study, we investigated the effects of LG on LJP sensation. Yamaguchi *et al.*[8] investigated the effects of air-inhalation on LJP sensation. In our study using LG, we selected subjects with particular importance placed on the following two points: (1) They could breath through the nose and showed no involuntary muscle tonus in the jaw-facial region due to the use of a nasal mask during experiments. (2) They could maintain a posture appropriate for a dental chair. Yamaguchi *et al.* do not provide such a detailed explanation for the selection of subjects under the condition of air inhalation. Accordingly, because the subjects in our study satisfy these conditions, the severity of CP dysfunctions of the patients in our study is milder than that in Yamaguchi's study. (In our study, the ADL survey of the subjects was not carried out; however, a specialist in Ranzango diagnosed the subjects and evaluated the severity of their CP to be mild.) This difference in the severity of dysfunctions may have lead to the difference in RME by one order of magnitude smaller for CP patients[11].

Regarding the sensory property of the ability to discriminate muscle sensation in the four limbs, it is known that CP patients overevaluate muscle sensations compared with healthy subjects, which this leads to the coordinated motion of the four limbs being more difficult[39]. Regarding oral dysfunctions as well, because CP patients characteristically overevaluate the sensation of muscles attached to the lower jaw, similar to the cases of the four limbs, they are thought to have greater difficulty than healthy subjects in performing intended oral motions smoothly.

Next, let us compare the RMEs obtained between the CP group and control group during LG inhalation, in contrast to those obtained during the absence of LG inhalation.

Morimoto *et al.*[43] reported that healthy subjects opened their mouths wider momentarily before and after reference stick removal during the absence of LG inhalation. That is, the muscle spindles, which were already extended, were further extended.

Regarding the results of the control group shown in Table 7, the RME increased during LG inhalation in the cases of test stick diameters of 10.5 mm and 11.0 mm (larger than the reference stick diameter), compared with that during the absence of LG inhalation, thus indicating a decreased discrimination ability. In general, when the LG-induced sedation method is applied to healthy subjects, the functions of the central nervous system deteriorate and a change in the consciousness accompanying a feeling of euphoria develops, and the healthy subjects are in a state of stable sedation with a decreased tension in the sympathetic nervous system. Therefore, the range of the spontaneous tapping motions of the jaw reportedly increases[33]. On the basis of these findings, we consider that, in healthy subjects, a decrease in the function of the central nervous system occurred due to the inhalation of LG, and the LG affected the spindles of the peripheral muscles attached to the lower jaw, which yielded results different from those during the absence of LG inhalation (in the cases of test stick diameters of 10.5 mm and 11.0 mm). Yoshida *et al.*[21] investigated the effect of LG-induced sedation on muscle sensations associated with the extension of the muscles attached to the lower jaw in healthy subjects and identified a reduced discrimination ability for test stick diameters larger than the reference stick diameter during LG inhalation, compared with that during the absence of LG inhalation, similar to our results shown in Table 7. Thus, their results agree with the results of this study.

Regarding the results of the CP group shown in Table 8, the muscle tonus of the jaw and facial muscles characteristic of CP patients was suppressed during the inhalation of LG in the CP patients, which is different from the results of healthy subjects[12]. In particular, the muscle sensation from the spindles of the muscles attached to the lower jaw approaches the normal state. Accordingly, the discrimination ability increased as shown by the decrease in the RME for test stick diameters of 9.0 mm and 9.5 mm (smaller than the reference stick diameter) during LG inhalation, in comparison to that during the absence of LG inhalation. In addition, an LG-induced sedation method has been widely used for prosthetic treatments and others against involuntary muscle tonus to facilitate the induction of lower jaw position and recording jaw motions by alleviating mental stress in CP patients[35]. Thus, we speculate that because the LJP sensation of the CP patients approaches that of the healthy subjects due to inhalation of LG, the results of RME during LG inhalation differ from those during the absence of LG inhalation (for test stick diameters of 9.0 mm and 9.5 mm).

The effects of LG, in the comparison of RME during LG inhalation between the control group and CP group are shown in Table 9. This indicates that the discrimination ability of the CP group increased due to the inhalation of LG, and the CP patients are affected by LG more strongly than the healthy subjects. Yoshida *et al.*[12] reported that the activity of the muscles of the jaw-facial plane in CP patients was inhibited during the inhalation of LG in dental practice, on the basis of frequency analyses of electromyography. Kaufman *et al.*[36] stated that the amplitude of muscle discharge induced by the Hoffmann (H) reflex of the muscles in the lower limbs in CP patients decreased due to inhalation of LG. They concluded that LG has an inhibitory effect on the activation of motor neurons at the level of the central nervous system.

Table 10 shows the RME of the control group during LG inhalation. We suggest that the discrimination ability of the healthy subjects further decreased due to the combined conditions of LG inhalation and vibration stimulus application compared with the condition of only LG inhalation.

Table 11 shows the RME of the CP group during LG inhalation. We suggest that the discrimination ability of the CP patients further increased due to the combination of LG inhalation and vibration stimulus application compared with the condition of only LG inhalation. In addition, the results shown in Tables 10 and 11 indicate that the presence or absence of a vibration stimulus leads to a further increase or decrease in the discrimination ability. We intend to further investigate this issue in detail using electromyography.

Table 12 shows the comparison of RME during LG inhalation between the control group and the CP group. We suggest that the discrimination ability of the CP patients further increased under the combined conditions of LG inhalation and vibration stimulus application compared with the healthy subjects.

Functional recovery is a major issue in the field of physical therapy. In recent years it is well known that the clinical effects of physical therapy may be increased by the coutilization of drugs which affect the activation of the central nervous system[44–48]. Similarly, we can suggest that the discrimination ability for LJP in CP patients is improved by two conditions, that is, the application of a vibration stimulus and LG of the LG-induced sedation method, and that the functions of the jaw and oral cavity in CP patients, that is, the sensation of LJP, approach those in healthy subjects.

On the basis of these findings, the following conclusions can be reached. By combining the two conditions: LG of a LG-induced sedation method and vibration stimulus application, the neural functions in the upper level of the central nervous system in CP patients are further inhibited compared with those when each condition is applied separately, and an increase in the sustained muscle tonus characteristic of CP patients is also inhibited; the activity of γ-motor neurons is decreased by LG via the upper-level central nervous system[12]. Furthermore, the vibration stimulus induces the development of tonic vibration reflex (TVR), increases the threshold of sensitive muscle sensation, and decreases the activity of γ-motor neurons[40–42], and it also decreases the activity of the spindles of the muscles attached to the lower jaw; as a result, the ability to discriminate LJP sensation tends to increase further. In the future, we intend to investigate these issues in detail using electromyography.

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