

The relationship between oral function and cognitive
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-Effect of tongue and lip motor training for cognitive
function in elderly people-

(口腔機能と認知機能の関係
—高齢者の認知機能に及ぼす舌口唇機能訓練の効果—)

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松本歯科大学大学院歯学独立研究科博士(歯学)学位申請論文

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Department of Hard Tissue Research, Graduate School of Oral Medicine
(Chief Academic Advisor : Professor Mihoko Tomida)

The thesis submitted to the Graduate School of Oral Medicine,
Matsumoto Dental University, for the degree Ph.D. (in Dentistry)

【背景と目的】

超高齢社会を迎えた我が国は、医療費および社会保障費の増加が著しい問題になっている。それと同時に認知症患者数も年々増加し、2025年には700万人に達し、介護や看護をする側の負担が非常に大きくなると予想される。一方で、口腔機能が全身の健康維持に関与しており、脳を活性化させることが報告されてから、歯数の維持が重要視され、現在歯数が多いほど脳機能は低下しにくいことが明確にされた。従って、高齢者の認知機能を維持するためにも、適切な口腔機能の保持が重要であると考えられる。しかし、認知機能に対する口腔機能訓練の効果に関しては未だ不明な点が多い。そこで、口腔機能と認知機能の関連性を明らかにし、さらに口腔機能の1つである舌口唇運動の機能訓練が認知機能に与える影響を調べた。

【対象と方法】

研究対象者100名(65-100歳)に①口腔内検査(現在歯数、義歯の使用の有無)、②認知機能検査(Mini-Mental State Examination: MMSE)、③咬合力検査(オクルーザー)、④咀嚼機能検査(キシリトール咀嚼チェックガム:5段階評価)、⑤舌口唇運動機能検査(オーラルディアドコキネシス:ODK)を実施し、認知機能と口腔機能の関連をSpearmanの順位相関係数を用いた単相関と重回帰分析で調べた。MMSEは、正常、軽度認知障害、軽度認知症、中等度認知症、重度認知症の5段階で評価した。ODKは、1秒間に発音できた「パ」「タ」「カ」の3語の平均回数を健口くん[®](Takei, Co, Japan)を使用して算出した。さらに、MMSEの判定から正常者(non-impairment group: N群)5名、それ以外から(impairment group: I群)10名を選び、舌口唇運動機能訓練(食前にパ、タ、カの各語の連呼(5秒間)を3回)を15ヶ月間実施させた。訓練開始から3ヶ月毎15ヶ月まで②-⑤を行い、訓練前と訓練後をFriedman検定とDunnett-T3 test(等分散でない場合も使用可能)を用いて比較検討し、訓練が認知機能に与える影響を調べた。

【結果】

初回のMMSEの判定では、正常:33名、軽度認知障害(Mild Cognitive Impairment: MCI):25名、軽度認知症:11名、中等度認知症:27名、重度認知症:4名であった。MMSEの点数との関連を調べるために最初に行った単相関においては、MMSEと年齢、現在歯数、咀嚼機能、ODKとの間に相関関係が認められた。さらに、年齢と現在歯数、咀嚼機能、ODK、現在歯数と咬合力、咀嚼機能、ODK、咬合力と咀嚼機能、ODK、咀嚼機能とODKの間に相関が認められた。MMSEを従属変数とした重回帰分析から、MMSEは年齢、ODKの順に関連があった。N群の中の2名の3、6ヵ月後のMMSEの点数は、MCIに該当する点数であったが、訓練9ヶ月以降は正常範囲を維持した。I群の10名のうち2名が入院したため、15ヶ月の経過を追えた

のは8名であった。この8名の訓練開始後15ヶ月のMMSEの点数は、訓練前と訓練開始後3ヶ月に比較して有意に上昇した。咬合力は両群において各測定時での有意差は認められなかった。咀嚼機能において、N群での訓練開始15ヶ月後は訓練前より有意に高値を示した。I群では、各測定時に有意差は認められなかった。ODKにおいて、N群の訓練開始後15ヶ月は訓練前や訓練開始後3ヶ月よりも有意に上昇した。I群では、訓練開始9ヶ月以降のODKは、訓練前に比較して有意に上昇した。また、訓練開始15ヶ月後のODKは、3、6ヶ月後より上昇した。

【結論】

MMSEの点数は、年齢、現在歯数、咀嚼機能、ODKと相関が認められ、年齢、ODKの順に関連が認められた。これらの結果から、加齢とともに認知機能は低下し、舌口唇機能も衰えると考えられた。また、初回のMMSEで認知機能に低下があると判定された全員の認知機能は、舌口唇運動機能訓練15ヵ月後に改善された。さらに、訓練の継続でODKも増加した。しかしながら、咬合力と咀嚼機能には変化が認められなかったため、咬合力と咀嚼力を向上させるには、別の訓練が必要だと考えられた。今回の研究で、高齢者の認知機能は一定ではなく、環境や身体の状態に左右されることもわかった。舌口唇運動機能訓練を継続する事により、舌筋や口輪筋が鍛えられ口腔の動きも円滑となり、そこからの感覚や運動刺激が脳に伝えられることで、認知機能が改善したと示唆された。

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意に上昇した。咬合力は両群において各測定時での有意差は認められなかった。咀嚼機能において、N 群での訓練開始 15 ヶ月後は訓練前より有意に高値を示した。I 群では、各測定時に有意差は認められなかった。ODK において、N 群の訓練開始後 15 ヶ月は訓練前や訓練開始後 3 ヶ月よりも有意に上昇した。I 群では、訓練開始9ヶ月以降の ODK は、訓練前に比較して有意に上昇した。また、訓練開始 15 ヶ月後の ODK は、3、6 ヶ月後より上昇した。

【結論】

MMSE の点数は、年齢、現在歯数、咀嚼機能、ODK と相関が認められ、年齢、ODK の順に関連が認められた。これらの結果から、加齢とともに認知機能は低下し、舌口唇機能も衰えると考えられた。また、初回の MMSE で認知機能に低下があると判定された全員の認知機能は、舌口唇運動機能訓練 15 ヶ月後に改善された。さらに、訓練の継続で ODK も増加した。しかしながら、咬合力と咀嚼機能には変化が認められなかったため、咬合力と咀嚼力を向上させるには、別の訓練が必要だと考えられた。今回の研究で、高齢者の認知機能は一定ではなく、環境や身体の状態に左右されることもわかった。舌口唇運動機能訓練を継続する事により、舌筋や口輪筋が鍛えられ口腔の動きも円滑となり、そこからの感覚や運動刺激が脳に伝えられることで、認知機能が改善したと示唆された。

Introduction

The number of patients with dementia has surpassed six million in Japan, a country with a “super-aged” society. The number of people with dementia will continue to increase in Japan and in many other parts of the world. It is a major social problem because patients with long-term dementia reduce their quality of life and their families, friends, and caregivers induce psychological and physical burdens. Identifying preventive strategies for dementia and strategies for improving cognitive function of dementia patients is essential for super-aged society¹⁾.

Recent studies have explored various non-pharmacological intervention programs and found that cognitive training such as learning therapy can improve cognitive function, which depends on the plasticity of the nervous system^{2,3)}. Some studies have found that enjoyable activities, reading, playing games, dancing, and music therapy, significantly reduced the risk of dementia⁴⁾ and cognitive impairment^{5,6)}. Moreover, these activities have a positive effect on both cognitive function and mental health, including depressive symptoms, among older people⁷⁾. Consequently, home-based training sessions or hands-on activities have been introduced as effective measures against dementia. Music therapy has

been found to improve cognitive function in early stage dementia^{8,9)}. Task such as playing musical instruments can also significantly improve the frontal lobe function in patients¹⁰⁾. However, to play games or musical instruments at home, people need to buy the device or instrument. Therefore, despite showing positive results, costly intervention programs are not widely used in clinical settings¹¹⁾. In summary, few studies have investigated the long-term effects of training or activities on patients with dementia. Therefore, it is necessary to develop individual interventions that are low cost and include personalized training programs and enjoyable content.

Regarding oral functions, numerous prospective studies have reported on an association between oral health and dementia in old age¹²⁾. Particularly, tooth loss was independently associated with the development of cognitive impairment and poor nutrition¹³⁾. Recent research has also demonstrated that the dexterity of the tongue simultaneously improved pronunciation functions¹⁴⁾. Body strength, which is related to tongue pressure is very important for preventing dysphagia (i.e., swallowing disorders) in the elderly¹⁵⁾. As strengthening the tongue has been found to be important for maintaining and improving the health of elderly people, we hypothesized that tongue and lip motor training may improve tongue pressure

and dexterity. Therefore, this study aims to investigate the relationship between the cognitive function and oral function, and to clarify the effects of tongue and lip motor training for elderly people who are healthy or require a minimum amount of care.

Methods

Subjects

One hundred residents of a nursing home (33 men, 67 women) aged ≥ 65 years old volunteered to participate in this study which was investigated the relationship between oral function and cognitive function. We excluded volunteers who were unable to communicate well. All subjects undertook the Mini-Mental State Examination (MMSE), and the oral, occlusal force, masticatory function, and oral diadochokinesis (ODK) examinations. The correlation of these factors were analyzed.

In a second study, we randomly selected five subjects from among those evaluated as having no cognitive impairment in first MMSE, and allocated them to the non-impairment (NI) group (n=5). Next we randomly selected 10 subjects from among those evaluated as having some cognitive impairment in the first

MMSE, and allocated them to the impairment (I) group (n=10), Mild cognitive impairment (MCI, n=5), mild dementia (MD, n=3), and moderate dementia (MOD, n=2).

We did not include persons with severe dementia because it would have been difficult for them to participate in tongue and lip motor training on a daily basis.

The present study was approved by the Ethics Committee of Matsumoto Dental University (No. 258). Informed consent was obtained from all participants. This study followed the Declaration of Helsinki with regard to medical protocol and ethics.

Cognitive evaluation

Cognitive function was measured using the MMSE, an instrument that has been used extensively in clinical and research settings¹⁶⁾. The MMSE consists of 11 simple tasks grouped into seven cognitive domains:

1. Orientation to time
2. Orientation to place
3. Registration of three words
4. Attention and calculation

5. Recall of three words

6. Language

7. Visual construction

A maximum score of 30 was used to assess an individual's cognitive performance based on direct observation. The following five levels were employed to classify cognitive impairment:

1. No cognitive impairment — 28–30 points

2. MCI — 24–27 points

3. MD — 21–23 points

4. MOD — 11–20 points

5. Severe dementia — ≤ 10

Oral examination

A dentist examined the total number of present teeth and the use of dentures.

Teeth with severe decayed teeth and residual teeth were not considered present teeth.

Occlusal force

Subjects were asked to bite the pressure sensitive film (Dental Prescale 50H Type R, GC, Tokyo, Japan) with maximum force. If subjects habitually used their dentures, they bit the film wearing their dentures. Occlusal force was measured in Newtons (N) using a pressure-sensitive film and the associated analytical equipment (OCCLUZER 709, GC, Tokyo, Japan).

Masticatory function

We measured subjects' masticatory function using xylitol check gum (LOTTE Co., Ltd, Tokyo), which changes color during the chewing process. After subjects had chewed the gum sixty times, the color of the gum was observed. Masticatory function was evaluated as per five phases each with a related score:

1. Green (score 1) means very poor mastication
2. Yellow green (score 2) means poor mastication
3. Light pink (score 3) means normal mastication
4. Pink (score 4) means good mastication
5. Red (score 5) means very good mastication.

Oral diadochokinesis

The ODK rapid syllable repetition test was used to evaluate articulatory oral motor skill at sites such as the lips, tongue tip, and tongue dorsum. Subjects were asked to repeat each given syllable Pa, Ta and Ka sequentially and as fast as possible for five seconds. The number of repetitions per second were calculated using an electronic calculator via an internal microphone named Kenkoukun (Takei Scientific Instruments, Co., Ltd., Niigata, Japan). We measured the number of repetitions three times with 10-second intervals in between and calculated the mean value per one second. Furthermore, we calculated the average repetition time of three words and the value was used for the analysis of correlation and comparison.

Training

Subjects performed two kinds of training exercise three times per day before each meal. The first training exercise involved subjects keeping their mouths open for five seconds while holding their lower jaw with their hand and applying upward pressure. This training exercise was performed three times to prepare subjects for the next tongue and lip motor training.

The second training exercise was to pronounce the syllables, Pa, Ta, and Ka.

Subjects rapidly repeated Pa for five seconds three times, with 10-second intervals.

They then did the same for Ta and Ka in turn.

Statistical analysis

At first, to explore the factor correlated with MMSE, the relevance between MMSE, the number of present teeth, masticatory function, occlusal force, and ODK were tested using single correlation with Spearman's rank correlation. Furthermore, the relations between each factor and MMSE were analyzed using a stepwise multiple regression analysis. To evaluate the effect of training, Friedman's one-way repeated measure analysis of variance test was used on the MMSE, occlusal force, masticatory function and ODK times. Thereafter, the Dunnet-T3 test which is available in the case of non-equal variance was used to compare the values of the groups during training. All statistical analyses were conducted using SPSS 23.0 and the results were considered significant at $P<0.05$.

Results

Subject attributes

Age distribution is shown in Table 1 and subject characteristics are shown in Table

2. The mean \pm SD of MMSE scores was 23.36 ± 5.97 points. The subjects evaluated by the MMSE were allocated to groups as follows: 33 subjects in the NIG, 25 subjects in the MCI, 11 subjects in the MD, 27 subjects in the MOD, and 4 subjects in the severe dementia.

Correlations between each factor

As Table 3 shows, the MMSE scores were correlated with age ($r=-0.428$, $P<0.01$), the number of present teeth ($r=0.337$, $P<0.01$), masticatory function ($r=0.426$, $P<0.01$), and ODK ($r=0.436$, $P<0.01$). There were also some correlations between other factors, (Table 3).

Connection with the MMSE score

From the results of the multiple regression analysis with MMSE scores as the dependent variable, cognition function was shown to be strongly related to age ($t=-2.79$, $P<0.01$) and ODK ($t=2.28$, $P<0.05$) (Table 4).

Effects of tongue and lip motor training

Subjects

The mean age \pm SD of five subjects (one man, four women) in the NI group was 74.2 ± 6.8 . Two of the ten subjects selected for I group were hospitalized during the 15-month follow up, and so dropped out of the study. The mean age of the eight remaining subjects (4 men, 4 women) was 78.7 ± 6.5 . There was no significant age difference among the subjects in the two groups.

MMSE scores

In the NI group, the median MMSE scores pre-training was 29, and the scores post after 3, 6, 9, 12 and 15-months of training were 28, 28, 30, 30 and 30, respectively. The Friedman-test results showed a significance level of $P<0.005$. However, the difference between each two periods was not significant as shown in Figure 1A.

In the I group, the median MMSE scores pre-training was 23.5, and the scores post after 3, 6, 9, 12 and 15-months of training were 23, 24.5, 25.5, 27 and 28.5, respectively. The Friedman-test results showed a significance level of $P<0.005$ for the I group. The scores post 15 months of training were significantly higher than the pre-training scores and the scores three months after training started ($P<0.05$), as shown in Figure 1B. Moreover, four subjects in the I group

who were evaluated as having MCI before training improved in no cognitive impairment after 12 months of training. Two subjects in the MD moved up to the MCI and two subjects in the MOD moved up to the MD after 15 months of training.

Occlusal force

In the NI group, the median scores for occlusal force before training was 369.7 N, and the scores after 3, 6, 9, 12 and 15-months of training were 176.9, 236.4, 255.8, 196.5 and 231.6 N, respectively. The Friedman–test results showed $P<0.05$ for the NI group, but, the differences between each two periods were not significant (Figure 2A).

In the I group, the median score for occlusal force before training was 330.3 N, and the scores after 3, 6, 9, 12 and 15-months of training were 298.0, 233.1, 183.9, 158.1 and 107.0 N, respectively. The Friedman–test results showed $p<0.01$ for the I group, but the differences between each two periods were not significant (Figure 2B).

Masticatory function

In the NI group, the median pre-training scores for masticatory function was 3, and the scores after 3, 6, 9, 12 and 15-months of training were 4, 4, 4, 4 and 5, respectively. The Friedman-test results showed $P<0.005$ and the score after 15-months of training was significantly higher than before training (Figure 3A).

In the I group, the median pre-training scores for masticatory function was 3, and the scores after 3, 6, 9, 12 and 15-month of training were 4, 4, 4, 3 and 3, respectively. The results of the Friedman-test showed no significant difference for the pre and post training masticatory function scores (Figure 3B).

Oral diadochokinesis

In the NI group, the median of ODK times before training was 3.9, and the times after 3, 6, 9, 12 and 15-month of training were 4.1, 4.4, 4.5, 4.6 and 5.2, respectively. The results of the Friedman-test showed a value of $P<0.0001$ for the NI group. The ODK times after 15 months of training were significantly higher than ODK times before training and the times 3 months after training (Figure 4A).

In the I group, the median of ODK times before training was 3.1, and the times after 3, 6, 9, 12 and 15-month of training were 3.6, 3.8, 4.5, 4.1 and 5.2, respectively. The results of the Friedman-test showed a value of $P<0.0001$ for I

group. The ODK times after 15 months of training were significantly higher than the ODK times before training, and the ODK times three and six-months after training (Figure 4B). In addition, there was a significant difference between the ODK times before training and the times of 9 and 12 months after training (Figure 4B).

Discussion

This study analyzed the association between cognitive and oral functions. The MMSE scores showed a correlation with age, the number of present teeth, masticatory function, and ODK. The results suggest that tooth loss leads to poor masticatory function, which may negatively affect brain function. Loss of teeth increases the risks for deterioration of cognitive function¹²⁾. Previous studies analyzed comparison values using odds ratios and reported that dementia was associated with the number of teeth, oral hygiene, and bite force^{17,18)}. However, in this study, we found a positive correlation between the number of teeth and occlusal force, but no correlation between MMSE scores and occlusal force. The reason for these differences could be attributed to the use of different analysis methods.

The MMSE scores were strongly related to age and ODK. One study found that a decrease in oral motor dexterity can be an early signal of MCI, so its detection might improve the prognosis of dementia¹⁹). We also hypothesized that oral motor skills may improve dementia and maintain cognitive function. A decrease in cognitive function may be due to age and the natural passage of time, but the results in our study found that the pronunciation function, not age alone, was strongly related to cognitive function. It is possible that age-related decrease in the functions of the motor area in the cerebral cortex and the dexterity of the tongue were improved by 15 months of tongue and lip motor training.

Tongue and lip motor training as an exercise that engages oral motor skills was offered continuously for 15 months and was well received by the subjects in the nursing home. The MMSE scores of the subjects in the I group after 15-months of training were significantly higher than their scores before the training and after 3-months of training. Moreover, all subjects in the I group improved in their cognitive function after 15 months of training. Tongue and lip motor training expands the dexterity of the tongue and lips, and the sense from these parts is transmitted to brain, which then increase the activities of the neurons and network in the brain. Thus, continuous training contributes to improving

cognitive function. However, we also found that the MMSE scores of subjects in the NI group were not always stable. This finding could be due to physical and mental conditions brought on by depressive symptoms²⁰). Therefore, it is necessary for old people to maintain a good physical state and a comfortable environment so as to maintain their brain functions. Overall, these results demonstrate that tongue and lip motor training induces a positive effect on the cognitive function of patients with dementia and poor cognition.

In both the I group and NI group, subjects' ODK scores after 15-months of training were significantly higher than their times before the training and after three months of training. Subjects' ODK times are used to evaluate oral motor skills. In Japan, "pa/ta/ka/ra" is used to create tongue movements to maintain swallowing function in the elderly²¹). Previous studies found that singing can enhance motor neurons associated with tongue and lip movements²²). The tongue and lip motor training increased the movements of the tongue muscle and the orbicularis oris muscle, which then improved subjects' pronunciation.

There are no significant differences between the occlusal force values of the two groups. The value of occlusal force shows a decreasing tendency in repeated measurement during training. The power of masticatory muscles may decrease

with age²³⁾, which induces the tendency to decrease occlusal force. This suggests that tongue and lip motor training cannot always strengthen masticatory muscles. On the other hand, the masticatory function of all subjects increased. However, when comparing each measurement, we found that they did not differ significantly from each other. These results demonstrate that masticatory function and occlusal force may be associated with the number of present teeth and the power of the masticatory muscle. Therefore, it is necessary for the elderly to maintain masticatory function to eat sufficient nutritious food¹²⁾. If not, they will need further training to enhance masticatory function.

Physical exercise such as aerobic exercise is recommended to prevent dementia as per clinical practice guidelines^{24,25)}. This is because physical activity protects against the loss of gray and white brain matter and reduces neurotoxic factors²⁶⁾. Audiovisual integrative training such as music therapy with digital devices can positively affect executive function and induce an improvement in memory, which can then increase MMSE scores²⁷⁾. Pleasant stimulation and physical activity activate the brain; stress promotes the pathogenesis of dementia, which is associated with decreased sociability and depression²⁸⁾. Therefore, emotion is the most important factor in the daily life of elderly people. As it is

relatively easy and affordable to participate in music therapy and tongue and lip motor training at home, the combined method could be effective for enhancing cognitive function in the elderly.

Many studies show that oral function is an important factor in maintaining cognitive function^{12,13,17,18)} and that intervention programs improve the cognitive function of patients with MCI^{2,10,19)}. Furthermore, our study found that advanced dementia, MD and MOD, were improved by 15 months of tongue and lip motor trainings. Our results also suggested that cognitive function may be improved by strengthening the muscle in the oral maxilla facial area by adding more teeth. This further suggests that cognition function in old people may be related to oral function, as measured by the frequency of pronunciations.

However, as there were just 100 subjects in this study, a small percentage of the elderly population, it will be necessary to verify these effects using many more subjects in a future study.

Conclusion

In this study, 15 months of tongue and lip motor training was found to be effective for improving cognitive and tongue and lip motor functions. Tongue and

lip motor training increased the MMSE scores of subjects with MCI and mild and moderate dementia, and the pronunciation frequency of all subjects. These results suggest that tongue and lip motor training can enhance the activity of the tongue and orbicularis oris muscle and enhance their dexterity, which can then improve cognitive function.

Figure legends

Figure 1. Comparison of MMSE scores between before and after tongue and lip motor training

A: non- impairment group B: impairment group

**P* < 0.05

Figure 2. Comparison of occlusal force between before and after tongue and lip motor training

A: non- impairment group B: impairment group

**P* < 0.05

Figure 3. Comparison of masticatory function between before and after tongue and lip motor training

A: non-impairment group B: impairment group

Figure 4. Comparison of ODK between before and after tongue and lip motor training

A: non-impairment group B: impairment group

* $P < 0.05$

Table 1. Age distribution

Table 2. Subject Characteristics

Mean \pm SD, MMSE: Mini-mental state examination, ODK: Oral diadochokinesis

Table 3. Correlation of Each Parameter

Values are presented as per the Spearman's rank-order correlation coefficient

** $P < 0.01$, * $P < 0.05$.

Table 4. Multiple Regression Analysis with MMSE scores as the Dependent

Variable

****** $P < 0.01$, ***** $P < 0.05$.

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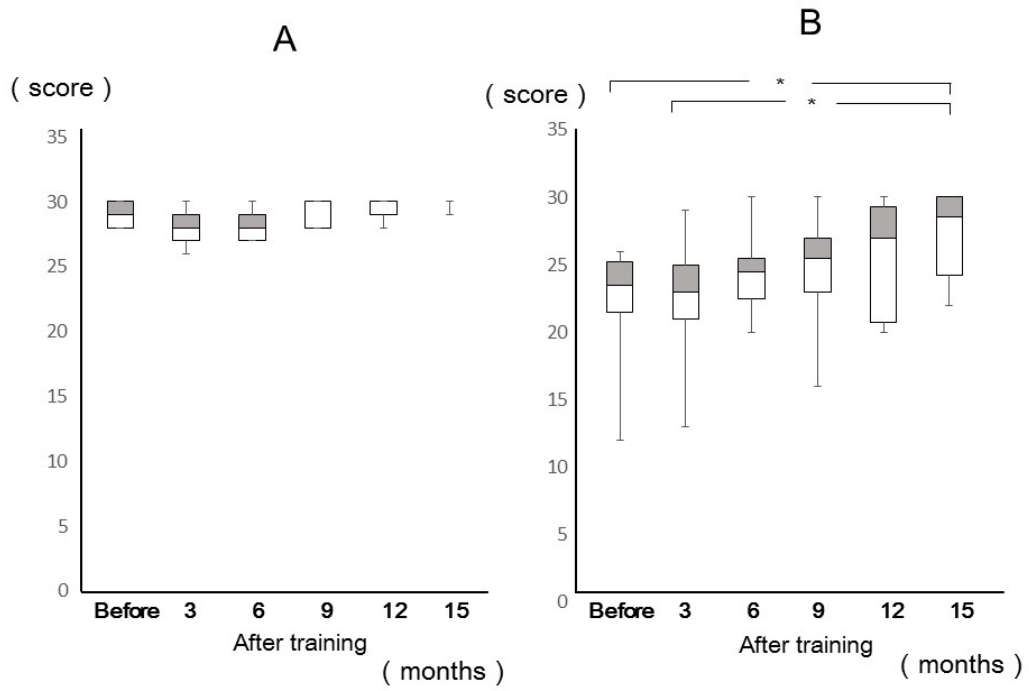
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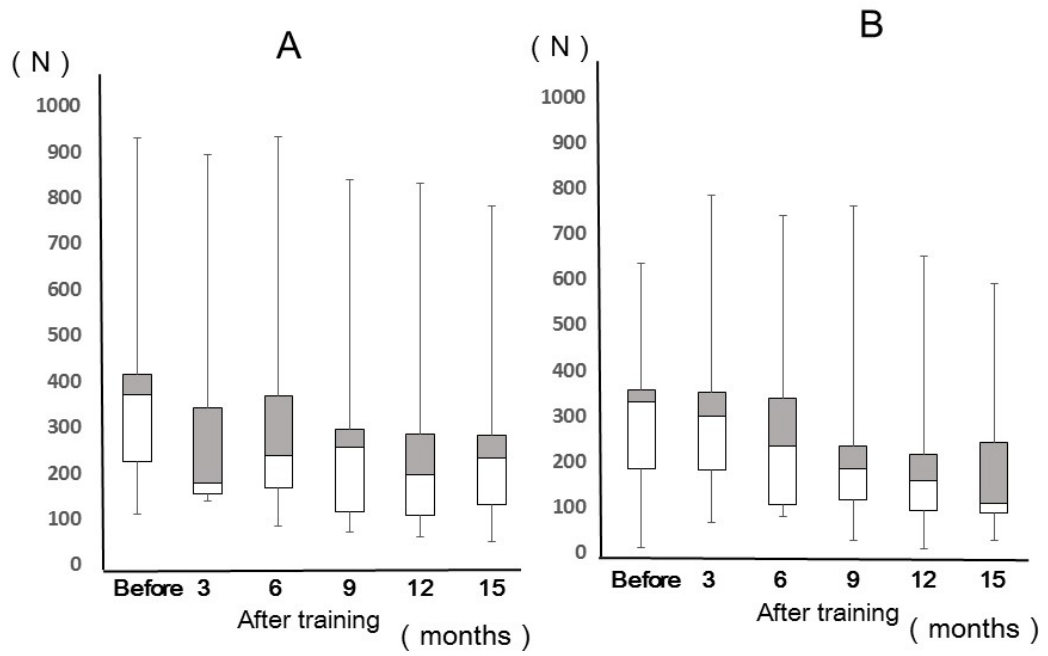


Fig. 2 Innami

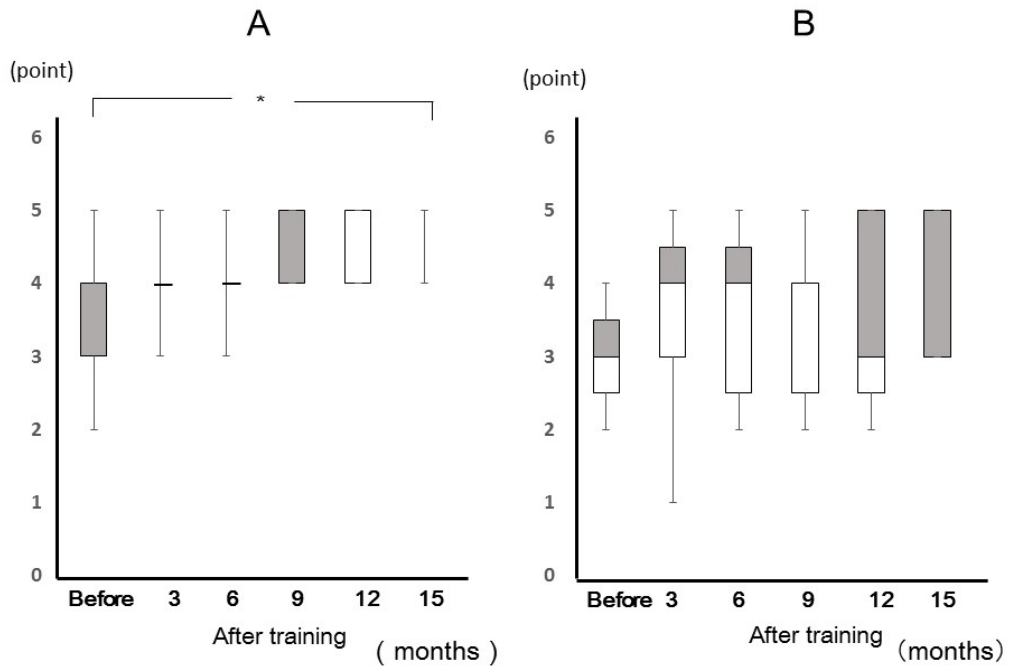
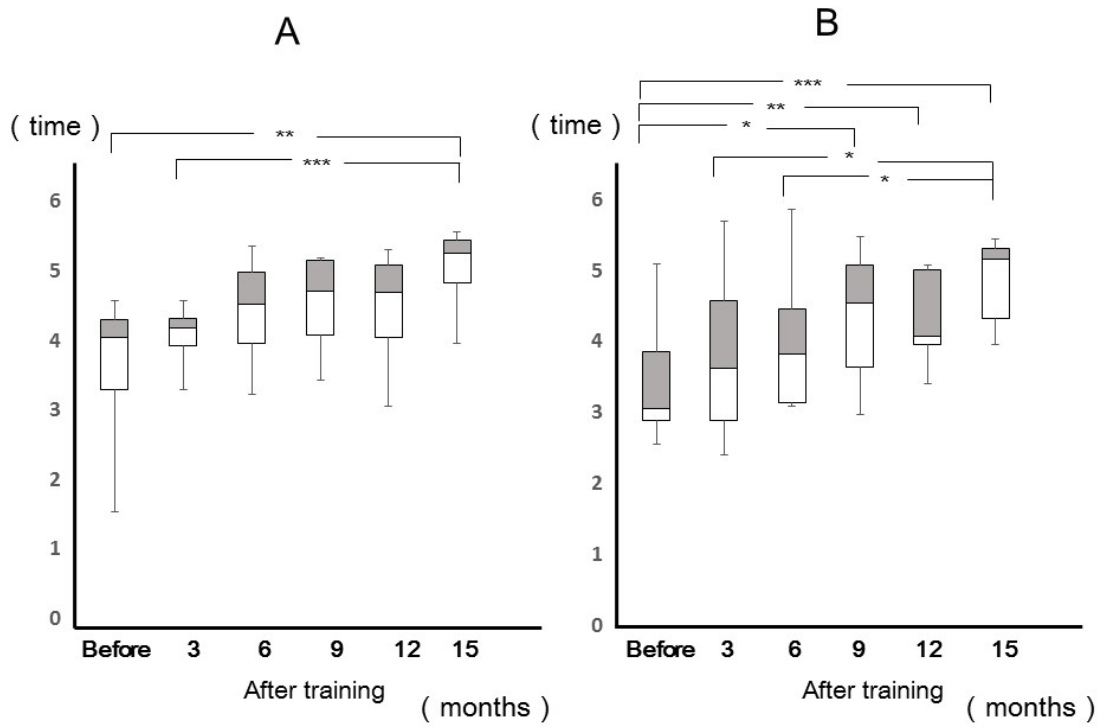


Fig. 3 Innami



Age	The number of people (n=100)
65 – 69	14
70 – 74	23
75 – 79	22
80 – 84	22
85 – 89	4
90 – 94	14
95 – 100	1

Table 1 Innami

Factor	Total (n=100)
Age (years old)	78.43 ± 7.72
Sex (men/women)	33 / 67
MMSE (score)	23.36 ± 5.97
Number of present teeth	16.30 ± 9.74
Occlusal force (N)	380.54 ± 293.58
Masticatory function (score)	3.33 ± 1.10
ODK (time/s)	4.13 ± 1.24

Table 2 Innami

Factor	MMSE	Age	Number of present teeth	Occlusal force	Masticatory function
MMSE					
Age	- 0.428**				
Number of present teeth	0.337**	-0.237*			
Occlusal force	0.163	-0.173	0.533**		
Masticatory function	0.426**	-0.367**	0.375**	0.422**	
ODK	0.436**	-0.280**	0.372**	0.330**	0.499**

Table 3 Innami

Factor	β	standard error	standardizing coefficient	t value	p value
Constant	31.018	6.72		4.62	0.00
Age	-0.204	0.073	-0.269	-2.79	0.006**
ODK	1.095	0.479	0.24	2.28	0.025*

Table 4 Innami