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博 士 論 文

Effects of changes in sensory receptor sensitivity around the anterior teeth on motor learning

（前歯部における感覚受容器感度の変化が

食物摂取時の課題遂行能力と運動学習に及ぼす影響）

令和２年３月申請

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Abstract

Objective To investigate; if alteration of different orofacial afferent inputs would have different effects on the performance of a complex biting task; and if repeated performance of the task would enhance the performance, so-called motor learning, despite alteration of sensory inputs. **Methods** Fifty-four healthy subjects (27 ± 5.8 years) participated in a single experimental session. The subjects were randomly divided into three different groups based on the intervention, such as control group (Control, no anaesthesia, N = 18), topical-mucosal anaesthesia group (Topical, topical anaesthesia on lips and intraoral mucosa, N = 18), and injection intra-mucosal anaesthesia group (Injection, infiltration anaesthesia in buccal side of alveolar mucosa of the area of upper and lower incisors, N = 18). The subjects in each group were asked to perform in total of seven sessions (Baseline and Set1 to 6) of a complex biting task (hold, split and retrieve a sunflower seed from its shell without crushing the seed, 10 trials, each session). In Topical and Injection, the interventions were performed immediately after Baseline. For Topical, the intervention was repeated immediately after Set3 as well in order to maintain the intervention effects. The task performance was estimated by a five-point grading system. The duration of the task was also estimated using the jaw-tracking device (Handmade, Umea University, Sweden). **Results** The interventions (Topical and Injection) had significant effects of decreased performance scores ($P = 0.042$ and 0.032, respectively) and increase of total duration of the task ($P = 0.023$ and < 0.001, respectively). However, in all groups, they had significant training effects on

both increased performance scores ($P < 0.001$) as well as the decreased total duration of the task ($P < 0.001$). **Conclusion** Alteration of different orofacial afferent inputs had decreased the effect of performance ability during complex biting. However, the repeated performance of the task had enhanced the performance ability. It is suggestive that motor learning would occur even if the sensory input has changed, possibly indicating motor task optimization.

Introduction

Sensorimotor learning is a term commonly used to capture a variety of neural changes taking place during the acquisition of a new motor skill or during the adaptation of movements to changed circumstances such as changes in the environment. Recent research has emphasized the importance of motor adaptation due to external perturbations [1; 2]. The underlying mechanisms are considered to be related to the re-calibration of internal forward models, which predict the sensory consequences of the motor action. It is suggested that during the adaptation process, these internal forward models are re-calibrated based on a sensory prediction error, which is the difference between the internal forward model prediction and the actual sensory outcome. Therefore, skilled motor performance relies on accurate prediction of both of one's own body and the tools one interacts with.

Sensorimotor learning or adaptation due to perturbations has received little attention in the orofacial area until recently. The orofacial area undergoes dramatic changes during the growth and transition from deciduous dentition to

permanent dentition and later from loss of teeth and subsequent oral rehabilitation procedures. During these changes in the orofacial area, it could be important to pay special emphasis on skill acquisition and adaptation to these changes in order to optimize oral rehabilitation procedures. It has previously been shown that short-term training of a complex biting task increases the ability to perform the task accurately [3]. The effect of sudden deprivation of sensory inputs on simple biting and chewing tasks have been recently reported. However, the effect of perturbations caused by local anesthesia of the teeth on a complex yet natural behavioral biting task have not been studied. Therefore, the aim of the present study was to investigate the effect of alteration of different orofacial afferent inputs on the performance of a complex yet natural biting task.

Materials and Methods

Subjects

Fifty-four healthy subjects (23 males, 31 females) in the age range between 18 – 45 years (mean age ± SD = 27.2 ± 5.8 years) participated in this study. They were university students and local civilians recruited by advertisements on social networking sites and web pages (http://www.studentkaninen.se). All subjects were in good general health with normal healthy dentition but without any history of periodontal disease. The subjects exhibited a normal occlusion without any gross malocclusion, and without any overjet / overbite or open bite/deep bite of the anterior teeth. The subjects were also free from any previous/on-going endodontic, prosthetic, or orthodontic treatment of the anterior teeth. A temporomandibular disorder (TMD) screener questionnaire

ruled out the presence of any TMD or associated symptoms prior to the participation [21]. The subjects also reported that they were not taking any kind of medicine and were not allergic to nuts or seeds. The study was approved by the Regional Ethical Review Board, Stockholm in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

The subjects were randomly assigned to one of the three groups, such as the control group (Control, no anaesthesia, mean age 27 ± 5.3 years old, five males, and 13 females), the topical-mucosal anesthesia group (Topical, mean age 25 ± 4.9 years old, 10 males, and eight females), and the injection intra-mucosal anesthesia group (Injection, mean age 29.5 ± 6.5 years old, eight males, and 10 females). The randomization was done using computer-generated codes.

Study Design

The subjects sat on a comfortable office chair and were asked to perform one series of intraoral fine-motor behavioral task (Baseline). After that, the intervention (see Local Anesthesia) was made and the experimental tasks were performed for six times (Set1, 2, 3, 4, 5, and 6). Especially in Topical, the intervention was repeated immediately after the fourth session (Set3) in order to maintain the intervention effect (See Fig.1). The success rates of behavioral task were made after each session and jaw-movements during the tasks were traced using the jaw-tracking device.

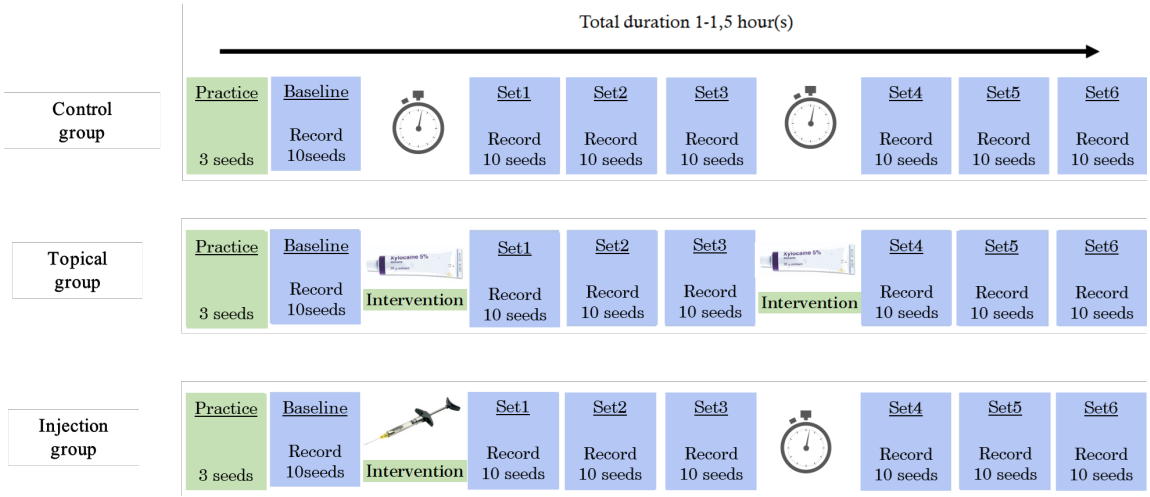

Fig.1

Behavioral Task

The behavioral task in the current study is based on the tradition in the Far-east to split sunflower seeds (Gua Zi) (Fig.2) between the front teeth to remove the outer un-eatable shell, spit out the shell, and, eat by chewing the seed and swallow. In this case, the subjects were asked to split between the front teeth and to separate the inner seed from the outer shell without breaking it. The subjects perform seven series of ten trials of intraoral refinement motion tasks. The behavioral task was demonstrated by the examiner and the participants were allowed three practice trials before the start of the experiment. The participants were given a break of about 3–5 min after each series. Thus, in a single experimental session, the participants in total performed 60 repetitions of

the behavioral task, after the intervention was made.

Fig.2

Local Anesthesia

In the topical anesthesia group, the oral mucosa was anesthetized by the intraoral application of a topical local anesthetic gel (Xylocaine 5%). The gel has a persistence of 20-30 minutes. In general, a contact time of 5 minutes is required to reach the full effectiveness of the gel [4]. Approximately 3-4 grams of the gel was spread all over the mouth of the participants, including the palate, gums, buccal, labial vestibule, and the tongue, by the finger of the examiner. After 5 minutes of holding the cream in their mouth, they could rinse with water. The intervention was made for the second time between the recordings of the third series and the fourth series because the anesthesia will not last long enough to block the afferent inputs from the oral mechanoreceptors the entire experiment otherwise.

In the remaining interventions (i.e., injection anesthesia group), injections of local anesthesia (30 mg/ml prilocaine hydrochloride + 0,54 µg/ml felypressin) were made with a 27-gauge needle. Injection anesthesia was achieved by locally infiltrating approximately 0.9 ml of local anesthetic solution into the buccal groove around the root apical area of the central incisors upper and

lower left and right central incisors respectively. The control group had no intervention, but there was a break of 5 minutes between baseline and set 1, and between the third series and the fourth series. Participants were asked to use anesthetized teeth when performing a behavioural task. The participants also reported the effect of anesthesia in the subject-based reports before the first series, the fourth series and after the sixth series of the behavioural tasks were performed.

In all groups, the anesthetic effect was confirmed by lack of response to tapping and touching of the teeth, lips and adjoining gingival.

Jaw Movements during the Task

The participants were seated in an office chair, in an upright position without any head support, and their jaw movements recorded while performing the behavioral task as described in detail previously [5, 6, 7, 8]. In brief, the movement of the lower jaw in relation to the upper was assessed in three-dimensions employing a small gold-plated magnet (10 × 5 × 10 mm; Neodymium Iron Boron, N42) attached to the labial surface on under the lower lip with Stomahesive® pasta. The position of this magnet was tracked with the help of eight sensors (four on each side; accuracy: 0.1 mm; bandwidth: DC – 100 Hz) attached to a lightweight wooden the frame (220-gram; Umeå University, Physiology Section, IMB, Umeå, Sweden) resting on the bridge of the nose like a pair of spectacles and anchored to the head with adjustable straps. (see, Fig.3-A)

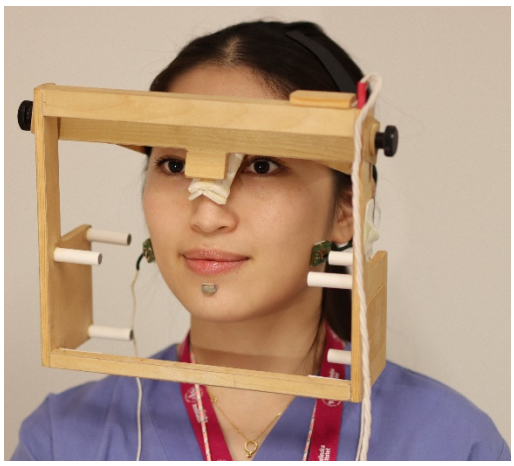

Fig.3-A

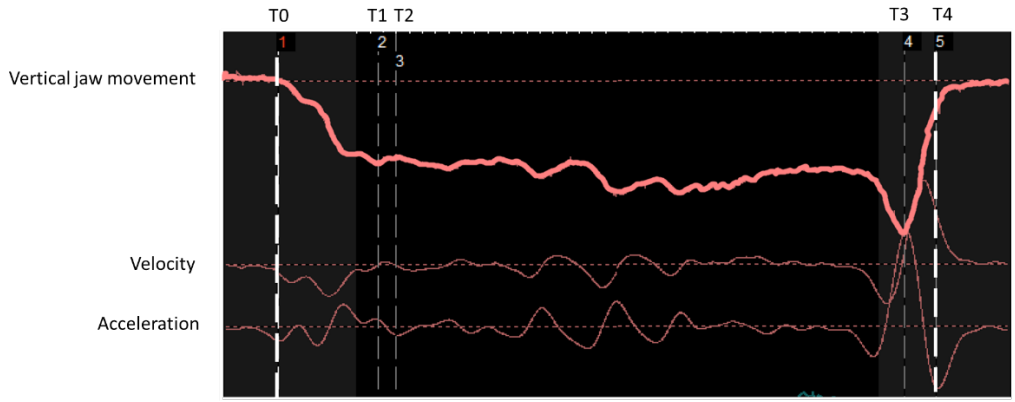

Fig.3-B

Data analysis

Five-point grading system

The Performance score of the task was assessed by rating the outcomes (the content of the cups) with a five-point grading system [9] (see, Fig.4). Score 5 is the perfect score and stands for a successful split and score 1 to 4 stands for (partially) unsuccessful splits, where score 1 means not being able to split the

seed at all (see Appendix). This system has a high inter- and intra-rater reliability of 0.979 (Cohen's kappa value) $p<0.001$ [9].

Performance scores	Description	Illustration
Score 1	Intact seed **or** seed is still in the shell.	
Score 2	Only seed shell or empty cup	
Score 3	The seed has been **split** in one or more pieces with or without the remnants of the seed shell spit in the cup	
Score 4	The whole seed and part of the seed shell in the cup	
Score 5	Only whole seed without any remnants of the seed shell in the cup	

Fig.4 Success Rate of Behavioral Tasks; This table referred to Behavioral learning and skill acquisition during a natural yet novel biting task.

Duration of the task

Data regarding the vertical and lateral movements of the lower jaw measurements we analyzed using customized software (WinSc/WinZoom v1.52; Umeå University, Physiology Section, IMB, Umeå, Sweden). The velocity

(mm/s) and acceleration (mm/s^2) of jaw movement were acquired through the software by symmetrical numerical time differentiation of the position and velocity. The start of the jaw opening phase (T0) is defined as the peak negative acceleration. Peak negative acceleration defines the end of this jaw-closing phase (T4). The total time taken to perform the task is the time interval taken from the beginning of the jaw opening phase to the end of the jaw-closing phase (T0-T4). In Fig.3-B an example of positioning the markers is illustrated [3].

Statistical analysis

Performance of the task

The data of the biting task performance was analyzed with a two-way analysis of variance model (ANOVA) with repeated measures. Before using ANOVA, the average score of each set (6 sets with 10 trials) and the relative changes to the average score of the baseline (1 set with 10 trials) were calculated for each subject. The two factors in the ANOVA were sets (6 levels; set1 - set 6) and groups (3 levels; Control, Topical, Injection). The Post Hoc analyses were done with the LSD test. Considered statistically significant is a P-value lower than 0.05. The statistical significance level was set at $p < 0.05$ and the study was analyzed with TIBCO Statistica™ version 13.3.

Duration of the task

The data of the jaw tracker was analyzed with a two-way analysis of variance model (ANOVA) with repeated measures. Before using ANOVA, the average time of each set (6 sets with 10 trials) and the relative changes to the average time of the baseline (1 set with 10 trials) were calculated for each subject. The two factors in the ANOVA were sets (6 levels; set1 - set 6) and groups (3 levels; Control, Topical, Injection). The Post Hoc analyses were done with the LSD test. Considered statistically significant is a P-value lower than 0.05. The statistical significance level was set at $p < 0.05$ and the study was analyzed with TIBCO Statistica™ version 13.3.

Results

Performance Scores

The results of the repeated measures ANOVA showed no significant main effect of groups (P=0.354). However, there was a significant main effect of series (P<0.001) and a significant interaction between groups and series (P<0.001).

Post hoc analysis of the interaction between groups and series showed significantly lower performance scores in the topical anaesthesia group than the control group during the first series (P=0.042). Further, the injection anaesthesia group also showed significantly lower performance scores during the first series than the control group (P=0.032, Fig.5-A).

Post-hoc analysis of sets showed a significantly higher performance score of the task in second to sixth series than compared to the first series (P<0.005). Post hoc analysis of the interaction showed higher performance score in the topical anaesthesia group during second to third series (P<0.001) and fifth to sixth series (P<0.002) than the first series. Further, the injection anaesthesia group showed significantly higher performance score during the third to sixth series than the first series (P<0.003, Fig.5-B).

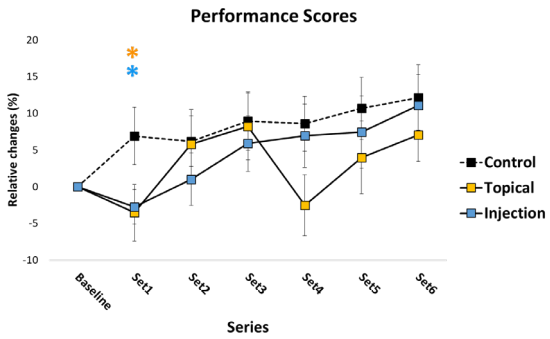

Fig.5-A

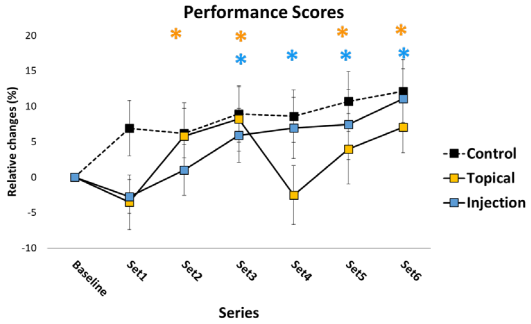

Fig5-B

Total duration

The results of the repeated measures ANOVA showed a significant main effect of groups (P=0.048) and series (P<0.001) and a significant interaction between groups and series (P=0.037).

Post hoc analysis of the interaction between groups and series showed significantly longer total duration in the topical anaesthesia group than the control group during the first series (P < 0.023). Further, the injection anaesthesia group showed significantly longer total duration during the first to third series than the control group(P < 0.001, Fig.5-C).

Post-hoc analysis of sets showed a significantly shorter duration of the task in second to sixth sets than compared to the first set (P<0.001). Post hoc analysis of the interaction showed longer total duration scores in the control

group on the sixth series (P = 0.04) than the first series. Further, the topical anaesthesia group during the second to sixth series (P < 0.042) than the first series. Further, the injection anaesthesia group showed significantly longer total duration during the second to sixth series than the first series (P < 0.001) (Fig.5-D).

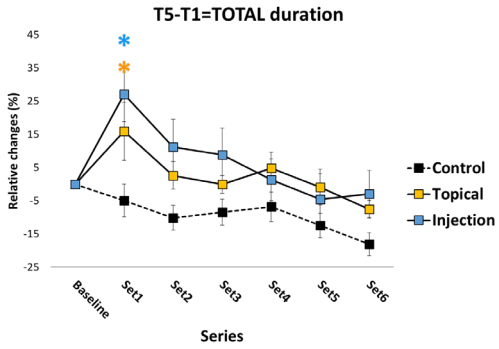

Fig.5-C

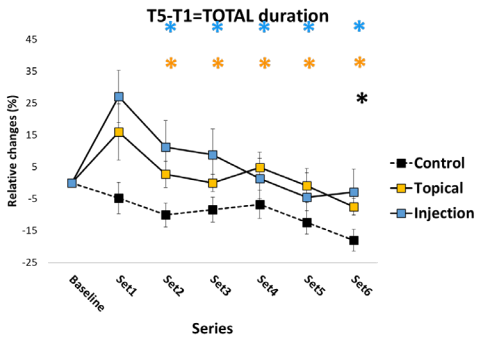

Fig5-D

Discussion

Empirical observations suggest an impressive oral dexterity orchestrated by the fast and efficient coordination of lip, tongue and jaw muscles in skilled individuals.

The previous study [9] has revealed a learning ability in the precision of performance while accomplishing a complex biting task using sunflower seeds. The present study assessed oral motor performance and behavioral adaptation after the alteration of different orofacial afferent inputs, during a complex biting task. There is substantial evidence from previous studies confirming that the cortical expression of body parts is continually adjusted in response to behavioral learning and skill acquisition. Please see [10, 11] for reviews. In the case of peripheral input damage or changes, either by afferent block (animal model) or local anesthesia, there is a reorganization of the central nervous system, which can be a useful model for studying short-term plasticity changes [11]. Furthermore, repeated movements are necessary to adapt to the changed motor movements. Therefore, in this study, we decided to change the peripheral orofacial sensory input (due to local anesthesia) and further investigate the motor learning of jaw movement by repeated complex biting tasks.

A Complex biting tasks

Functional magnetic resonance imaging studies related to finger tapping tasks have shown activation of additional cortical areas [12] and a greater increase in cerebral blood flow [13] during the performance of complex tasks as compared to simple tasks. Animal studies on intracortical macrostimulation of the motor cortex have shown a larger expansion and larger representation of motor cortex

areas due to an increase in the complexity of the motor skill task [14]. Therefore, the complexity of a motor task is an important determinant of motor learning and motor performance [15,16, 16]. Increasing the complexity of a novel motor task increases the cognitive effort and thereby enhances the cortical plasticity during training [17]. Previous studies on oral motor control have reported no robust effect of training on the performance of a simple biting task in healthy participants [19]. However, short-term training of a more complex and demanding task involving biting a spherical, sugar-coated chocolate candy into two equal halves resulted in an increase in accuracy of the task performance and decrease in the total duration of the task, after the training [20] with signs of cortical plasticity in the corticomotor pathways relevant to the masseter muscle [18]. Subsequently, a more demanding and specific precision task was introduced: the complex, natural biting task using sunflower seeds. This task could have more impact on oral fine motor skills [9]. Reported is short-term training of the complex behavioral biting task resulted in improved performance scores in the naive group and an indication of optimized jaw movements in terms of reduced duration of the task. Therefore, the complex biting task was thought to be useful for validating motor learning by changing the input of different afferent receptor sensations in this experiment.

Effects of changing orofacial afferent inputs

In the present study, we have compared the perturbation of the performance score and the duration of the task under the influence of local anesthesia (Topical and Injection) to a reference group. In order to obtain more precise results, we have analyzed the data by Relative changes relative to the baseline. Relative changes allow converting scores from different data sets into scores

that can be accurately compared to each other. The results of this study showed that set 1 performance scores and total duration immediately after anesthesia intervention were significantly worse in both the anesthesia groups. Furthermore, the Injection group was worse than the Topical group in the total duration. This suggests that changing different orofacial afferent inputs has different effects on the performance of complex biting behavior.

Motor learning

Motor learning reflects a relatively permanent change in a person's capability to perform a motor skill [21]. Variability has been established as a signature of skilled or rather unskilled motor performance [22]. The process of behavioral learning requires an update of motor commands through several exposures to motor errors. The motor errors are refined by forwarding models by a gradual decrease in prediction errors [23].

In a recent study, Short-term training of the complex behavioral biting task using sunflower seeds resulted in improved performance scores and an indication of optimized jaw movements in terms of reduced duration of the task in novices and experts [9].

It has been suggested that reduced sensory feedback does not inhibit but rather hinders or perturbs motor learning [24]. Transcranial magnetic stimulation studies in humans have shown neuroplastic changes in the face motor cortex following interruption of sensory inputs induced by local

anesthesia of orofacial tissues [24, 25]. As stated, the sensorimotor regulation during masticatory movements depends on the information from a variety of sense organs to regulate masticatory movements by the central nervous system [27]. By virtue of their location in the ligaments anchoring the tooth to the alveolar bone, the PMRs play a central role in encoding relevant aspects of forces acting on the dentition [26]. Therefore, they are likely to contribute tremendously to the generation and regulation of masticatory forces in various oral manipulative tasks.

The results in this study showed significant performance improvements in both the performance score and total duration in all three groups compared to the set immediately after anesthesia intervention (set 1). All groups showed a learning ability; the performance got better after repeating the task several times. Even after altering sensory inputs from the orofacial mechanoreceptors, the participants were able to learn and improve their oral fine motor skills.

Conclusion

The results of the study indicate that alteration of different orofacial afferent inputs had decreased the effect of performance ability during a complex biting task. However, the short-term repeated training had enhanced the performance ability. It is suggestive that motor learning would occur even if the sensory input has changed, possibly indicating motor task optimization. Previous studies have widely demonstrated the benefits of tissue response, occlusal function, biomechanics, and prosthetic repair and rehabilitation

procedures [28]. More recently, however, basic issues such as neural changes that occur when the stomatognathic system changes (eg, tooth loss, oral pain) and the neural processes underlying the oral rehabilitation process have attracted attention. [28]. Even if neural changes that occur when the stomatognathic system is altered, rehabilitation with repeated task actions may have an effect on improving feeding behavior. Further study is needed to determine whether short-term repeated training is effective for owners of prostheses such as implants, dentures, and bridges.

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