Systemic effects of the peripheral disturbance of the trigeminal system: Influences of the occlusal destruction in dogs

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Systemic effects of the peripheral disturbance of the trigeminal system: Influences of the occlusal destruction in dogs

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Abstract: Although there is an increasing amount of information pertaining to intracranial pathways of the trigeminal nerve, its clinical significance still remains unclear in many ways. I assumed that dental disorders including malocclusion would lead to the disturbance of the central nervous system via the trigeminal nerve. Based on this belief, this study was conducted to find out systemic effects of the occlusal destruction by grinding teeth unilaterally in dogs. As the result, abnormal involuntary movement and symptoms of autonomic failure were observed.

These experimental results indicate that the trigeminal nuclear complex contains not only the functions of the sensory relay in the face and the control of chewing movement, but it is likely that it modulates motor, especially postural control and autonomic system. It is believed that the dental aspects, especially occlusion, play an important role for the proper functioning of the trigeminal system.

Key words: Trigeminal system, Occlusal destruction, Postural control, Involuntary movement, Autonomic failure.

Introduction

Trigeminal pathways to the basal ganglia[1)2)3)], the parabrachial nucleus[3)4)5)], the cerebellum[6)7)8)9)], the vestibular nuclei[10)11)], the brain stem reticular formation[10)11)12)13)] and superior colliculus[9)14)15)] have been reported in recent years. Their function and clinical significance, however, have not been clarified in many respects.

Mandibular dysfunction leads to an increased incidence of those diseases that are thought to be attributed to improper posture and autonomic failure[16)]. It has been pointed out that orofacial dyskinesia is improved dramatically by the adjustment of the denture occlusion[17)18)]. These findings suggest that various disorders may result from the disturbance of the peripheral trigeminal inputs, which may be caused by malocclusion.

Few experiments have been made so far to study chronic systemic effects of malocclusion. In this study, I examined experimentally long-term systemic effects of dental disorders involving malocclusion in beagle dogs. Specifically, dogs' teeth were

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destroyed unilaterally by grinding artificially. This dental procedure led to the reduction of dental dimensions, which resulted in the mandibular displacement with the difference in length between right and left jaw-closing muscles. I regarded this mainly as chronic changes of the trigeminal proprioceptive inputs. Important findings for the following one year on systemic effects of the disturbance of the peripheral trigeminal inputs will be reported.

Materials and Methods

Three female beagle dogs born in June, 1986 were used in this experiment. These dogs had been specially raised for safety tests by Fujisawa Pharmaceutical Co. Ltd. with known genetic predispositions and charactristics. For this reasons, no control was set up. The experiment was initiated, when the terminal molars erupted at the age of eight months. The dogs were raised in cages where temperature and humidity were kept constant at Fujisawa experimental service center.

The dogs' teeth were destroyed unilaterally on the first day of experiment. This was accomplished by grinding both upper and lower teeth on the right side with a diamond bur (made by Shofu, No. 3) under anesthesia with 30 mg/kg of pentobarbital to reduce the dental dimension by about 3 mm in the terminal molar region (Fig. 1). These pulps were exposed in some areas.

These dogs were fed soft diet (Dogmeal with milk) for a week after the treatment. Ordinary meal consisted of a daily amount of 300 g of solid food (Labodiet) during an experimental period of one year.

Observations were made of not only food intake, body weight and stool, but also external appearance including movement and posture. General hematological examination were made on a monthly basis.

Experimental Results

1. Changes in intraoral and occlusal condition

The mandibular midline always shifted to the right about a half a lower tooth one week after the occlusal destruction (Fig. 2). An extraoral fistula was formed in the right maxillary area five months after the treatment in Case No. 1 (Fig. 3).

2. Symptoms of autonomic failure

There were no changes in general hematological finding before and one year after the occlusal destruction in all cases. Fig. 4 shows changes in body weight of each dogs. All the dogs left one third of the meal uneaten for about two months following the occlusal destruction, but they ate all the given amount subsequently. All the dogs lost weight for up to two weeks after the occlusal destruction. However, they gained their weights to about 7-8 kg in ten to twenty weeks and maintained the level thereafter.

The observation of stool samples during the experimental period revealed no particular abnormalities.

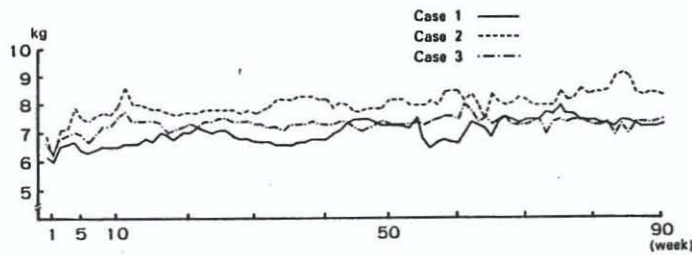

Fig. 4. Body weight changes of the dogs with the occlusal destruction for one year.

Loss of the hair luster was observed in all cases a few months after the occlusal destruction, which remained unchanged with no improvement throughout the exerimental period. Severe hair loss was observed in Case No. 1 ten months after the occlusal destruction (Fig. 5).

Salivation was observed in all cases for about two weeks after the occlusal destruction. Lacrimation began to appear three months after the occlusal destruction and remained throughout the experimental period in all cases. This lacrimation was observed on both side at first, which remained on the right side in Case No. 1 and Case No. 2 (Fig. 6) but in Case No. 3 on the left side.

The dog of Case No. 2 showed the symptom of lacrimation on the right side, which was accompanied by persisted reddish nodule in the left eye throughout the experimental period (Fig. 7).

3. Effects on the motor system

Resting tremor was observed in Case No. 1 severely, a slight one in Case No. 3 for a few months, starting in Case No. 1 three months after and in Case No. 3 six months after the occlusal destruction. Up and down movement twice per second was observed mainly in the left hind leg. These movement was no longer observed clearly after four months.

All the dogs showed the muscle weakness in the left hind leg. Case No. 1 and No. 3 began to show adduction of the left hind leg with pelvic distortion a few months after the occlusal destruction (Fig. 8,9). Case No. 1 and No. 3 walk lame like scoliosis. These states did not improve after half a year. The adduction of the left hind leg caused the pelvis to rotate, resulting in unnatural horizontal sitting position (Fig. 10). In contrast, increased tendon reflex was observed in the right hind leg in Case No. 1 and No. 3, persisting throughout the experimental period after lameness. With adduction of the left hind leg, the dogs moved in such a manner to protect the left leg. When forces were applied to the left hind leg, Case No. 1 show little resistance against the forces. Consequently, the dog was unable to walk straight and walked slanting the body (Fig. 9).

Discussion

Few reports suggest that toothache and other forms of dental disorders may cause

specific clinical symptoms, except temporomandibular joint arthrosis, which seems to be closely related with malocclusion. I conducted experimental occlusal destructions in dogs to study the influence exerted by such malocclusions that cause chronic changes in length of the masticatory muscles. As the result of this experiment, the mandible was displaced to occlude. Weight loss, lacrimation, salivation, hair loss, etc. were observed as autonomic symptoms, while tremor, lameness and improper posture were observed as motor dysfunctions. There were mandibular displacement and two possible systemic influences in this experiment.

1. Oral condition of the occlusal destruction

The grinding of tooth structure for the occlusal destruction stimulated the pulpal tissues directly, causing severe pain during meals. The act of eating seemed to be restricted until pulpal protection was completed with the formation of secondary dentin. It is believed that pain disappears after the destruction of pulpal tissues, but that prior to the pulpal destruction, excessive nociceptive stimuli from trigeminal extroceptors are inputted mainly into the trigeminal spinal nucleus via the semilunar ganglion. In this experiment, this process seemed to have continued for approximately one month after the start of the experiment.

The mandible was displaced to the ipsilateral side one week after the unilateral occlusal destruction, which resulted in the difference in length of the masticatory muscles, especially jaw-closing muscles. Consequently, occlusion is defined as appropriate contact between upper and lower teeth on both side. That is to say, dental conditions involving occulsion made an great influence on the trigeminal proprioceptive informations such as the muscle spindle afferents of jaw-closing muscles and the mechanoreceptor afferents of periodontal ligaments.

The muscle contraction for mastication is activated by a centrally-formed reflex mechanism having a rhythmical pattern[19)20)]. In spite of the unilateral occlusal destruction, occlusion is completed with the mandible shifting. Therefore, γ-based outputs of the masticatory system and the whole motor system should also modified. It seems that the experimental unilateral occlusal destruction did produce the chronic laterality in the trigeminal proprioception, resulting in abnormal movement and posture.

2. Systemic influences of the occlusal destruction

No noteworthy changes were observed in general hematological examinations seen in a state of autonomic failure.

Body weight decreased for about two weeks following the occlusal destruction, as shown by the body weight curve (Fig. 4). This was followed by an increasing tendency for four months, but the experimental dogs weighted about 2 kg less than usual in this condition[21)]. The observed weight loss seemed to be a direct result of abnormal inputs other than pain sensation. Inputs from the temporomandibular joint are conveyed to the trigeminal spinal nucleus[22)23)]. It is connected with the parabrachial nucleus and the amygdala[3)5)]. In this experiment, subsequent temporomandibular joint dysfunction may have caused the dysfunction of the amygdala which is closely associated with the autonomic function including ingestion, resulting in weight loss, lacrimation, salivation and hair loss.

The largest changes produced by the unilateral occlusal destruction in dogs were tremor, lameness and improper posture. The fact that the tremor was transient may have been an influence of the other nociceptive sensation such as the temporomandibular joint pain. Abnormal motor dysfunctions such as resting tremor, lameness with pelvic distortion were observed. The lateralities of muscle tone and tendon reflex were also observed. The information from mechanoreceptors and muscle spindles in the areas innervated by the trigeminal nerve is inputted into the striatum and substantia nigra[1)2)24)]. These trigeminal proprioceptions are well known to reach the trigeminal mesencephalic nucleus. A possibility of autonomic and somatic effectors in the spinal cord being modified by the spinal trigeminal nucleus has also been raised from anatomical viewpoint[25)]. Therefore, the occlusal destruction would induced systemic motor dysfunctions. The trigeminal nuclear complex have a close relation to motor function including postural control, so that these trigeminal nuclei have connections with the basal ganglia[1)2)3)], the cerebellum[6)7)8)9)], the vestibular nuclei[10)11)], the brain stem reticular formation[10)11)12)13)] and superior colliculus[9)14)15)].

These sympotoms and abnomal phenomena seen in this experiment may have resulted from the disturbance of the peripheral trigeminal inputs caused by the occlusal destruction. A close connection has been proven to exist between the trigeminal spinal nucleus and the amygdala via the parabrachial nucleus[3)5)]. The trigeminal mesencephalic nucleus is also connected with the striatum[26)]. The amygdala is considered to be closely associated with autonomic function, while the striatum is thought to have an influence on involuntary movement. For these reasons, I believe that the occlusal destruction in this study have resulted in autonomic symptoms as well as motor and postural abnomalities. The observed individual differences in symptoms and phenomena may be a result of varying conditions of the occlusal destruction including the situations of the temporomandibular joint.

These experimental results suggest that the systemic effects of the trigeminal input disturbance are too important to be neglected. Especially, the systemic influences of dental disorders involving malocclusion must be reexamined.

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References

1) Lidsky, T. I., T. Labuszewski, M. J. Avitable & J. H. Robinson (1978) The effects of stimulation of trigeminal sensory afferents upon caudate units in cats. Brain Res. Bull. 4, 9-14.

2) Labuszewski, T. & T. I. Lidsky (1979) Basal ganglia influences on brain stem trigeminal neurons. Exp. Neurol. 65, 471-477.

3) Shneider, J. S. (1986) Interactions between the basal ganglia, the pontine parabrachial region, and the trigeminal system in cat. Neur-

oscience **19**, 411-425.
4) Cechetto, D. F., D. G. Standaert & C. S. Saper (1985) Spinal and trigeminal dorsal horn projections to the parabrachial nucleus in the rat. J. Comp. Neurol. **240**, 153-160.
5) Ma, W. & M. Peschanski (1988) Spinal and trigeminal projections to the parabrachial nucleus in the rat: Electron-microscpic evidence of a spino-ponto-amygdalian somatosensory pathway. Somatosens. Res. **5**, 247-257.
6) Ikeda, M. (1979) Projections from the spinal and the principal sensory nuclei of the trigeminal nerve to the cerebellar cortex in the cat, as studied by retrograde transport of horseradish peroxidase. J. Comp. Neurol. **184**, 567-586.
7) Somana, R., N. Kotchabhakdi & F. Walberg (1980) Cerebellar afferents from the trigeminal sensory nuclei in the cat. Exp. Brain Res. **38**, 57-64.
8) Matsushita, M., M. Ikeda & N. Okado (1982) The cells of origin of the trigeminothalamic, trigeminospinal and trigeminocerebellar projectins in the cat. Neuroscience. **7**, 1439-1454.
9) Steindler, D. A. (1985) Trigeminocerebellar, trigeminotectal, and trigeminothalamic projections: A double retrograde axonal tracing study in the mouse. J. Comp. Neurol. **237**, 155-175.
10) Lovick, T. A. & J. H. Wolstencroft (1983) Projections from brain stem nuclei to the spinal trigeminal nucleus in the cat. Neuroscience. **9**, 411-420.
11) Walberg, F., E. Dietrichs & T. Nordby (1985) On the projections from the vestibular and perihypoglossal nuclei to the spinal trigeminal and lateral reticular nuclei in the cat. Brain Res. **333**, 123-130.
12) Walberg, F., E. Dietrichs & T. Nordby (1984) The medullary projection from the mesencephalic trigeminal nucleus. An experimental study with comments on the intrinsic trigeminal connections. Exp. Brain Res. **56**, 377-383.
13) Rokx, J. T. M., P. J. W. Jüch & J. D. van Willigen (1986) Arrangement and connections of mesencephalic trigeminal neurons in the rat. Acta Anat. **127**, 7-15.
14) Edwards, S. B., C. L. Ginsburgh, C. K. Henkel & B. E. Stein (1979) Sources of subcortical projections to the superior colliculus in the cat. J. Comp. Neurol. **184**, 309-330.
15) McHaffie, J. G., K. Ogasawara & B. E. Stein (1986) Trigeminotectal and other trigeminofugal projections in neonatal kittens: An anatomical demonstration with horseradish peroxidase and tritiated leucine. J. Comp. Neurol. **249**, 411-427.
16) Berry, D. C. (1969) Mandibular dysfunction pain and chronic minor illness. Br. Dent. J. **127**, 170-175.
17) Sutcher, H. D., R. B. Underwood, R. A. Beatty & O. Sugar (1971) Orofacial dyskinesia: A dental dimension. JAMA. **216**, 1459-1463.
18) Schneider, J. S., S. G. Diamond & C. H. Markham (1986) Deficits in orofacial sensorimotor function in Parkinson's disease. Ann. Neurol. **19**, 275-282.
19) Dellow, P. G. & J. P. Lund (1971) Evidence for central timing of rhythmical mastication. J. Physiol. **215**, 1-13.
20) Nakamura, Y., Y. Kubo, S. Nozaki & M. Takatori (1976) Cortically induced masticatory rhythm and its modification by tonic peripheral inputs in immobilized cats. Bull. Tokyo Med. Dent. Univ. **23**, 101-107.
21) Itoh, N., T. Furukawa, K. Iwanami, J. Tanimoto, A. Nakaoka, M. Uematsu, Y. Hirako, H. Sakamoto, T. Fujii & A. Tenshou (1986) Toxicity study of cefixime (Ist report): Acute, subacute and chronic studies (in Japanese). The Clinial Report, **20**, 137-168.
22) Romfh, J. H., N. F. Capra & G. B. Gatipon (1979) Trigeminal nerve and temporomandibular joint of the cat: A horseradish peroxidase study. Exp. Neurol. **65**, 99-106.
23) Capra, N. F. (1987) Localization and central projectins of primary afferent neurons that innervate the temporomandibular joint in cats. Somatosens. Res. **4**, 201-213.
24) Harper, J. A., T. Labuszewski & T. I. Lidsky (1979) Substantia nigra unit responses to trigeminal sensory stimulation. Exp. Neurol. **65**, 462-470.
25) Ruggiero, D. A., C. A. Ross & D. J. Reis (1981) Projections from the spinal trigeminal nucleus to the entire length of the spinal cord in the rat. Brain Res. **225**, 225-233.
26) Herdman, P. R. (1980) Rostral projections of the trigeminal mesencephalic nucleus. Anat. Rec. **196**, 77A.

＜和文抄録＞

三叉神経系の末梢における障害が全身に及ぼす効果について

——犬における咬合破壊の影響——

住　岡　輝　明

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三叉神経の脳内経路は解剖学的に解明が進んでいるが，その機能及び臨床的意義については不明な点が多い．咬合異常を含む歯科的障害が，三叉神経を介して中枢神経系に混乱を生じていると考え，安全試験用のビーグル犬において，片側の歯を，人為的に削合することにより咬合を破壊し，三叉神経の末梢における咬合の人力の異常が，全身に与える影響について検索した．その結果，一時的な振戦，骨盤の歪みをともなった跛行や膝蓋腱反射の左右差などの異常な不随意運動および，痩せ，脱毛，流涎，流涙といった自律神経失調症状が認められた．この実験から，三叉神経核複合体の機能は，顔面の感覚の中継や咀嚼機能だけではなく，姿勢制御を含む運動や自律神経機能を調整している可能性が示唆された．そして，三叉神経系が正常に機能するためには，歯科的要因，特に咬合の重要性が認められた．

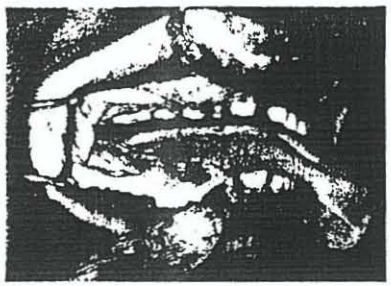

Fig. 1.

Fig. 2.

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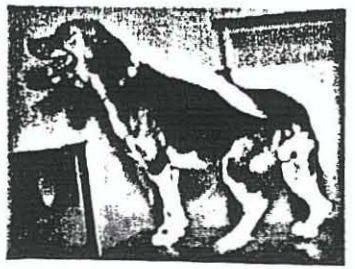

Fig. 9.

Fig. 10.

Fig. 1. The occlusal destruction by grinding teeth unilaterally.

Fig. 2. The mandibular midline shift to the right about a half a lower tooth observed in all cases after the occlusal destruction. Case of No. 1 dog is shown.

Fig. 3. An extraoral fistula in the maxillary area in Case No. 1.

Fig. 5. Loss of hair luster and hair loss observed in all cases. An example of Case No. 1 is shown.

Fig. 6. Abnormal lacrimation on the right eye observed in Case No. 1 and No. 2. Case No. 1 is shown.

Fig. 7. Abnormal lacrimation on the right eye and reddish nodule in the left eye in Case No. 2.

Fig. 8. The adduction of the left hind leg with pelvic distortion observed in Case No. 1 and Case No. 3. The case of No. 1 dog is shown.

Fig. 9. Walking lameness with pelvic distortion in Case No. 1 and No. 3. The case of No. 3 dog is shown.

Fig. 10. Unnatural horizontal sitting in Case No. 1 and No. 3. The case of No. 1 dog is shown.