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Review Article

Functional Anatomy

**Phenomenon of Muscle Anti-aging after Dental Treatment
-Changes in Oral Function of Muscle Fiber Characteristics-**

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Short running title: Muscle anti-aging research

Table: 1 Fig.: 3

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Abstract

Oral function of the patient improves and muscle function becomes better after prosthetic treatment. Various phenomena during this process have now been clear through basic experiments. Weakened muscle tissue before dental treatment is induced by mechanical stress after the therapy and this stimulation results in expression of various genes. Then various cascades are switched on and muscle function recovers in accordance with mechanism of muscle hypertrophy. Thus involvement of the muscle stem cells, satellite cell and muscle side population (SP) cell has been come into knowledge for muscle hypertrophy. Again alterations in characteristics of muscle fibers associated with changes in function of oral field makes clear existence of remodeling of the muscle tissue, which carries the functional role. Based on results of these researches, dental treatment is proved to give rise to anti-aging for oral function.

Key words: Anti-aging – Muscle – Mechanical stress – Growth factor - Myosin heavy chain

INTRODUCTION

Oral function of the patient is improved after dental therapy such as prosthetic treatment and eating function changes into a good condition after passing of a constant time. During this period, it is thought that various alterations of muscle tissues of oral and pharyngeal regions happen to yield adequate function. When the time before dental treatment is selected as a starting point and the time several months after the treatment is chosen as a target, sufficient understanding of the alterations in the muscle tissue within this period is an essential subject for the therapy performer dentist. That is to say, various appropriate mechanical stresses after dental therapy start to influence weakened pre-treatment muscle tissue. Although various genes are expressed, and altered-mechanism is considered to happen in internal muscle tissue under the influence of mechanical stress, the research focusing this function in detail is nearly absent and most points in this field remain unknown.

Skeletal muscle hypertrophy upon training is well known for long time. However mechanism for this phenomenon has not been completely clarified. When it was considered at individual level, the hypertrophy is a result of functional involvement of various factors such as hormones and growth factors, and thus it cannot be explained with a simple mechanism. On the other hand, direction of the basic research on this subject should be focused on the mechanism of regulation of gene expression at the cellular level upon loading of mechanical stress. Regarding with changes in the muscle tissue upon loading of adequate force on oropharyngeal muscles after dental treatment, identification of the basic phenomenon is recently rushed.

Thus in this review, I will introduce about the recent information regarding with induction of muscle hypertrophy and various alterations in the body as a result of

the sport. In this respect, I would emphasize that the differentiation onset of the muscle stem cell play an important role for the phenomenon of muscle hypertrophy. And the muscle shows not only hypertrophy but also starts to function properly after reconstructing the muscle fiber characteristics. Then I will mention about the recent information on how the muscle tissue influences the characteristics of muscle fiber upon alterations of oral function.

Stem cell of skeletal muscle

Tissue stem cell produces differentially advanced progenitor cell while maintaining of its self-renewal ability, and takes charge of the tissue regeneration and repair. And it has been known that plasticity of differentiation as a characteristic of stem cell has also seen in the muscle stem cell.¹⁾

In medial side of the skeletal muscle fiber, satellite cell exists. The satellite cell is stem cell of the muscle. So far as a role of the satellite cell, repair of the damaged muscle tissue has been considered. It has already been shown that skeletal muscle specific transcription factor MyoD is expressed by the satellite cells upon induction of muscle damage, and then mitosis begins.²⁾ And the satellite cell that started mitosis has been known as muscle progenitor cell (myoblast). Then the muscle progenitor cell will return to the satellite cell with a state of paused mitosis when the muscle repair is not needed. This is called as ability of self-renewal.

Mechanical stress and early response gene

Muscle hypertrophy is considered as a rationale adaptation to meet strong mechanical stress. Therefore, mechanical stress is most important within early inductive factors. In fact, when cultured myoblasts were exposed to mechanical stretching, the growth is promoted.^{3,4)}

In the muscle fiber and other various cells, structures, which transmit the mechanical stress inside and outside of the cell, have been known to exist. That is to say, either in the muscle fiber or in the satellite cell, transmission of mechanical stress is imagined to occur through two pathways after interaction with integrins on the cell membrane, (1) either direct communication of the cytoskeleton-nucleoskeleton, or (2) chemical transmission by activation of tyrosine kinases. When this kind of signal transduction is activated, early response genes such as c-fos and c-jun are normally expressed within a short time. Each of c-fos and c-jun produces their protein (Fos/Jun) and dimer of these proteins (Fos/Jun or Jun/Jun) forms the transcription factor AP-1 (activator protein-1).

AP-1 is thought to be involved in proliferation and growth of various cells, including an important role for muscle hypertrophy. When mouse hindlimb muscle is exposed to induction of isometric training, c-fos expression reaches to a peak level one hour after the stimulation and the expression amount increases parallel to the induction impulse. Consequently, it is suggested that AP-1 expression is involved in the process of change from mechanical stress to chemical signal.⁵⁾

Changes in oral function and characteristics of muscle fiber

Skeletal muscle fibers are multinucleate myocytes formed by the fusion of myoblasts with the growth of individuals. Fusion of myoblasts occurs simultaneously with muscle differentiation. In addition, in matured in vivo muscle tissue, intermittent muscle differentiation adapting to functional changes also occurs. Therefore, compared with other in vivo tissues, muscle tissue is one of high plasticity. In the oral region, various functional changes occur after weaning. However, changes in muscle fiber characteristics and the functional roles of muscle tissue during this process have been unclear.

Cytobiological methods recently developed have facilitated the establishment of objective parameters for the evaluation of muscle fiber characteristics and muscle function during development. Myosin is an important protein that accounts for the overwhelming majority of proteins that make up muscle fibers. Of the various types of myosin, the myosin heavy chain (MyHC) is known to be most closely concerned with muscle functions.⁶⁻¹⁶⁾ It has become clear in recent years that there are different isoforms of MyHC, such as MyHC-fast (MyHC-2a, 2b and 2d) and MyHC-slow (MyHC-1). It has also been suggested that composition ratios of these isoforms determine muscle contraction properties (Table 1).¹⁷⁾ Therefore, I summarized our studies that evaluated alterations in muscle tissue characteristics in terms of changes in the composition of muscle contraction protein after weaning as a local functional changes occurring in the oral region.

In addition, at present, our basic experiments for the reactivation of muscle function using some experimental systems are underway. Muscle hypertrophy is important in the reactivation of muscle function (Figure 1). Muscle protein synthesis should be promoted as compared to their degradation, and muscle tissue should acquire new contraction proteins during this process, changing muscle fiber characteristics into those allowing the exertion of force. One of the means to induce muscle hypertrophy is the transmission of mechanical loads to muscle fibers. Therefore, we evaluated not only skeletal muscle hypertrophy (increase) but also changes in muscle fiber characteristics and the acquisition of muscle function after transmission of information by mechanical loading on myoblasts.

Changes of the Muscle Fiber Characteristics before and after Weaning

MyHC-2b isoforms were observed in the superficial layer after weaning. However, MyHC-2a isoforms with slower contraction speeds were not apparent. By contrast,

in the deep layer, MyHC-2a isoforms as well as MyHC-2b isoforms were present, however, there were fewer MyHC-2b isoforms in the deep layer than in the superficial layer (Figure 2). Therefore, we conclude that complicated masticatory movement is achieved by the presence of various muscle bundles within the masseter, each carrying out different roles.^{13, 14)} Similar phenomenon was also reported in mouse temporal muscle²⁰⁾ and tongue muscle (Figure 2).^{21, 22)}

The results of these studies demonstrate that weaning, and the associated changes in eating movements, has a marked impact on not only the masticatory muscle, but also the tongue, which is closely involved with eating activity. It was also observed that weaning brings about a change in MyHC isoform composition, and alterations in MyHC isoforms are thought to be adaptations to the variations in muscle movements²³⁾. In addition, we introduced the results of studies in which mechanical stress was reported to increase the number of muscle fibers as well as to change muscle fiber characteristics^{3,4)}.

Conclusions

In the current review based on the recent information, following alterations were considered to occur in oropharyngeal muscle tissue upon acquiring of appropriate functions after application of dental treatment. First of all, muscle protein synthesis in the existing muscle fiber exceeds muscle protein inhibition. Next, muscle stem cells including satellite cell and muscle SP (side population) cell start to differentiate upon stimulation of various signals such as growth factor (Figure 1). This process is supported by the appearance of differentiation with muscle specific transcription factor expression (Figure 3). Then these new myoblasts reciprocally agglutinate and change from muscle stem cell to muscle fiber. These phenomena occur in a constant time after dental treatment in accordance with mechanism of

muscle hypertrophy. Finally, characteristics of muscle fiber are constructed in consistent with its designated function. The point in which characteristic of muscle fiber is reconstructed is considered to be final target (B) for the dental treatment.

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Legends to figures

Figure 1. Extracellular signals involved in muscle growth/differentiation.

Mechanical stimulation is the most important in muscle growth/differentiation, not only directly acting on cells but also being involved in secretion of endocrine factors, growth factors, and neurological factors. Furthermore, associated with this phenomenon, expression of growth factor IGF1 as well as muscle specific transcription factor MyoD is known.

Figure 2. Characteristics of mouse head and neck muscle groups related with mastication meet with big alterations after weaning. Thus a shift to the higher distribution ratio of MyHC-2b, which is fastest protein for muscle contraction speed, occurs. Then antero-posterior rapid cycle of characteristic mouse mastication becomes possible. Similar to this phenomenon, characteristics of muscle fibers also change in human in accordance with functional alteration of the muscle.

Figure 3. Stem cell of skeletal muscle. The cells existing medial side of skeletal muscle fibers such as satellite cells and muscle SP cells start mitosis upon stimulation of mechanical stress and muscle damage. (Modified from “Understanding Regenerative Medicine”, Asakura Atsushi, P94, Yodosha)

Designation	Nomenclature	Distribution
Embryonic	MyHCemb	Myobubes, intrafusal fibers, regenerating fibers
Neonatal	MyHCneo	Neonatal muscles, masseter, intrafusal fibers
Fast-twitch	MyHCeom	Super-fast fibers in extraocular muscles
Fast-twitch	MyHC-2m	Super-fast fibers in muscles derived from the first branchial arch
Fast-twitch	MyHC-2b	} Fast-type isoforms in digastric muscle of mice contraction speed: 2b>2d>2a
Fast-twitch	MyHC-2d	
Fast-twitch	MyHC-2a	
Slow-twitch	MyHC-1	Type I fibres

Souce: Brueckner JK *et al.* J Muscle Res Cell Motil 1996; 17: 279-312.

Table 1. Myosin heavy chain isoforms identified in skeltal muscle

Fig. 1

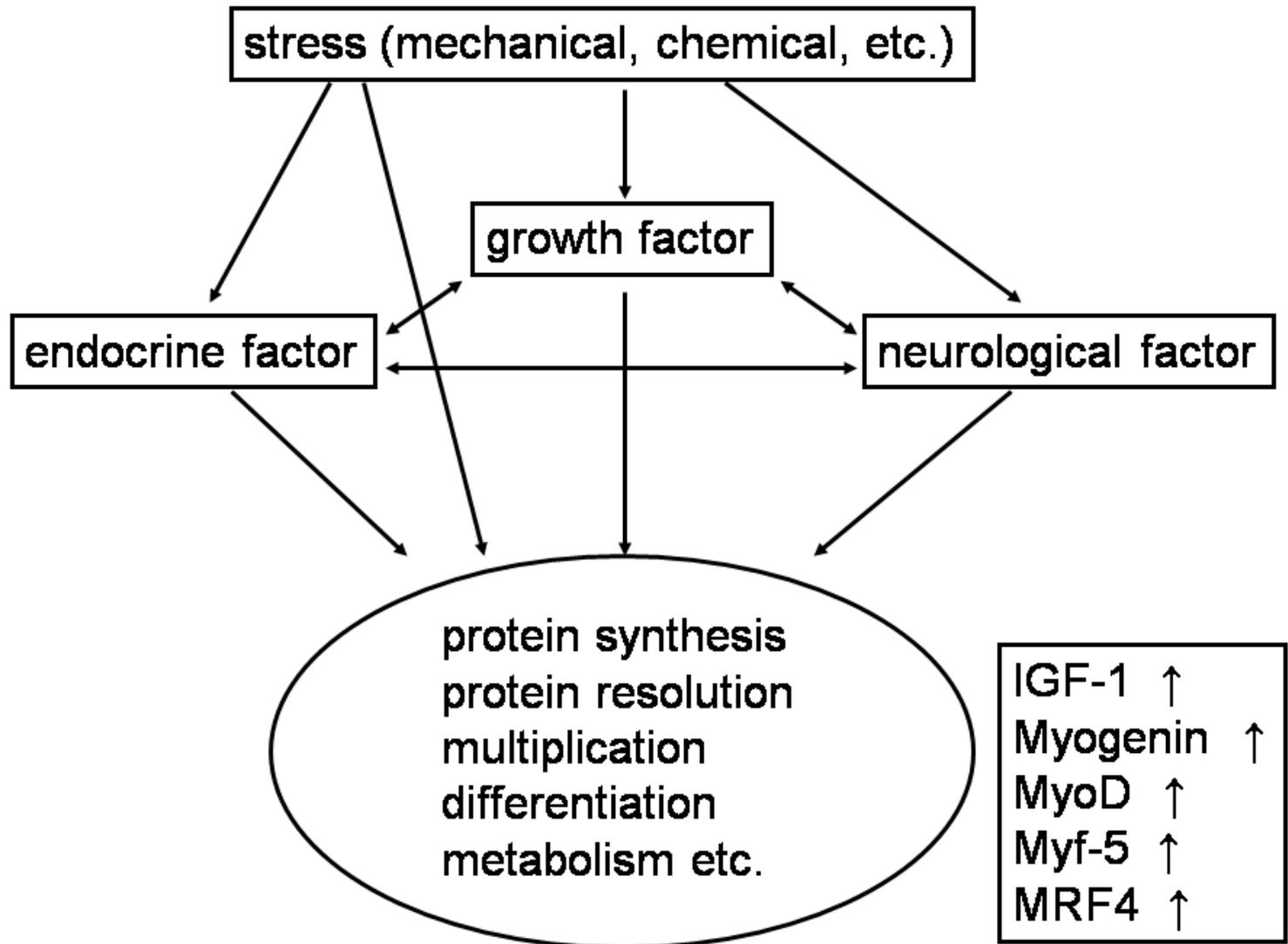


Fig. 2

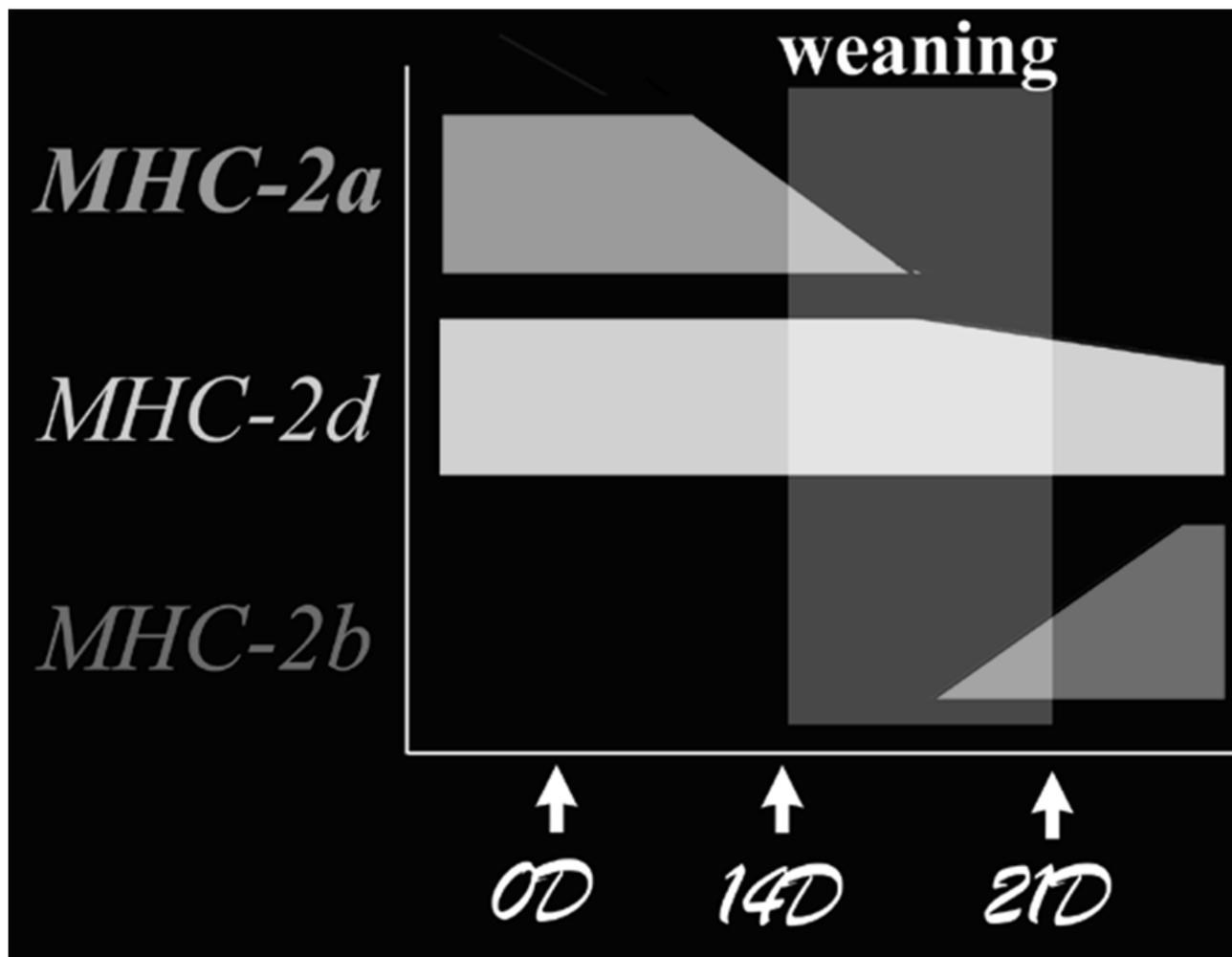


Fig. 3
Activation of satellite cell for regeneration of muscle function.

