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Histological aspect of the effects of soft food on major salivary glands

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ABSTRACT : The modern Japanese population favors soft foods, which do not demand extensive mastication. However, daily intake of soft foods is considered to have unfavorable influences on the mind and body. This is especially within the oral maxillofacial region. Consequently, many studies using experimental animals, feed a liquid or powdered diet and indicate that soft foods negatively affect the jaw bones, masseter muscle, and temporomandibular joint. Furthermore, since a report by Hall and Schneyer in 1964, the effects of soft foods on salivary glands have been under investigation. Soft food intake induces atrophic alteration to the parotid glands in adult animals. In these glands, shrinkage, suppression of proliferation, and apoptotic deletion of acinar cells were observed. In growing animals fed soft foods, parotid gland growth is inhibited through the suppression of an increase of acinar cell size and of acinar cell proliferation, but not through apoptosis. These findings support that unfavorable effects on parotid glands are induced by the intake of soft food regardless of growing or mature phases. However, different observations exist between these two phases. Despite accumulated knowledge on parotid glands, the debate whether soft food affects submandibular and sublingual glands remains controversial. It is the case that many studies agree soft food unfavorably affects parotid glands to a greater extent than submandibular and sublingual glands. This article reviews the histological effects of soft food on major salivary glands and introduces recent data from our research group.

Key Words : soft food, major salivary glands, atrophy, cell proliferation, apoptosis

Introduction

Over several decades, a majority of the Japanese population has frequently relied on ready-to-eat meals, many of which are processed and frozen. This trend has therefore increased the consumption of soft foods that do not require extensive mastication¹⁻³⁾. According to Yanagisawa *et al.*⁴⁾, about 60 percent of the foods eaten daily in Japan are soft. There are now concerns that such a dietary habit might negatively influence health of the mind and body, especially within the oral maxillofacial regions. To investigate this problem, an experimental model of feeding soft foods to animals is

widely used. Based on findings from these studies, a smaller maxilla and mandible⁵⁻⁷⁾, low mineral apposition in the jaw bones⁸⁾, reduction of remodeling of jaw bones⁹⁾, atrophy of the masseter muscle, alterations in the composition of the muscle fiber types¹⁰⁻¹³⁾, low growth of the temporomandibular joint^{14, 15)}, and alterations in collagens and chondrocytes in the temporomandibular joint cartilage¹⁶⁾ are reported.

Salivary glands are important exocrine glands to maintain health of the oral cavity. Therefore previous investigators have reported on cell morphology and function of the salivary glands. In 1964, Hall and Schneyer¹⁷⁾ first reported the effects of soft food on

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salivary glands. In their investigation, three to five-month-old rats were given a liquid diet for 14 days, and three major salivary glands were examined. Weight of the parotid glands was remarkably reduced (39-52%), and those of the submandibular and sublingual glands were lightly decreased (14-32%). Although the duct cells were histologically unchanged, shrinkage of the acinar cells was observed in all three major salivary glands¹⁷⁾. This report has attracted a lot of interest in salivary gland research, and ensured that the effects of soft food on salivary glands are studied further.

This review describes the histological findings on major salivary glands accumulated by previous investigators in addition to describing our own current research with discussion on the effects of soft food on major salivary glands.

1. Effects of soft food on parotid glands

According to previous reports, parotid gland weight is decreased in animals fed a soft diet. In these atrophic parotid glands, decreases in the diameter and individual area of the acinar cells were demonstrated by histomorphometric analysis^{18, 19)}, suggesting that predominantly shrinkage of acinar cells causes parotid gland atrophy. Using electron microscopy, it has also been reported that degenerate²⁰⁾ and necrotic²¹⁾ acinar cells are observed in the atrophic parotid glands, and that the gland DNA content is reduced²²⁾. Taking these data into consideration, atrophy of parotid glands in experimental animals fed soft diets might be induced not only by shrinkage of acinar cells but also by decreased acinar cell number.

It is difficult to directly count the total number of acinar cells in the parotid glands. We therefore investigated acinar cell proliferation and apoptosis during atrophy of parotid glands in rats fed a liquid diet to determine changes in acinar cell number. Reportedly, apoptosis often plays an important role in removal of acinar cells during atrophy of salivary glands induced by several pathological conditions²³⁻²⁸⁾. In our investigation²⁹⁾, rats in the experimental group were fed a liquid diet and compared to pellet-fed control rats. The parotid glands were examined using histological analysis, immunohistochemistry for 5-bromo-2'-deoxyuridine (BrdU) and cleaved-caspase-3 (Casp-3) as makers of cell proliferation and apoptosis, respectively, and transmission electron microscopy (TEM). In the experimental parotid

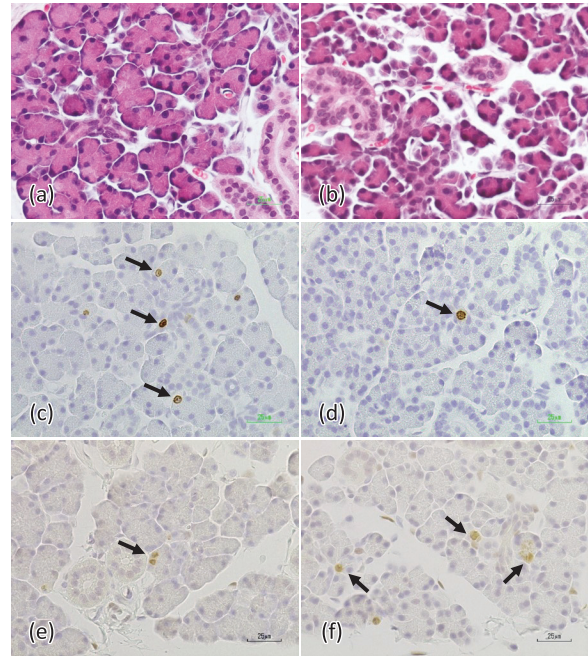


Fig. 1 Mature parotid glands of rats fed a pellet diet (control) (a, c, e) and a liquid diet (experimental) (b, d, f); HE on day 21 (a, b), BrdU on day 14 (c, d), Casp-3 on day 7 (e, f), Scale bars=25µm.

Acinar cells in experimental parotid glands (b) are smaller than in control glands (a). There are more BrdU-positive acinar cells (arrows) in control glands (c) than in experimental glands (d). More Casp-3-positive acinar cells (arrows) are identified in experimental glands (f) than in control glands (e).

glands, acinar cells were reduced in size (Fig. 1a, b) and numbers of BrdU-positive acinar cells were decreased (Fig. 1c, d) as the parotid gland weight was reduced. Furthermore, there were more Casp-3-positive acinar cells in the experimental parotid glands than in the control glands (Fig. 1e, f), and acinar cells with a typical appearance of apoptosis were often identified by TEM. Our findings showed that acinar cell number decreased with lower proliferative activity and increased apoptosis in the parotid glands of rats fed a liquid diet. Therefore, it could be considered that decreased acinar cell number, as well as decreased acinar cell size, participate in atrophy of parotid glands of liquid-fed rats²⁹⁾.

It is well known that children particularly tend to prefer soft foods to hard foods^{30, 31)}, and the influence of this dietary habit on growth of the oral maxillofacial regions is a clinical concern^{32, 33)}. We therefore used infant rats that immediately after weaning were fed a liquid diet for 8 weeks to clarify the effects of this on parotid gland growth³⁴⁾. Parotid gland weight of the pellet-fed rats increased considerably, while that of the liquid-fed rats increased only marginally. In the pellet-fed rats,

acinar cells were initially small (Fig. 2a), but grew larger over time (Fig. 2b). However, acinar cell size remained almost unchanged in the liquid-fed rats over time (Fig. 2c). In both groups, BrdU-positive acinar cell numbers were high at the beginning of the experiment (Fig. 2d), but decreased over time. However, numbers in the liquid-fed rats were decreased to a greater extent than in the pellet-fed rats (Fig. 2e, f). Casp-3-positive acinar cells were rarely identified in both groups. These observations in our study demonstrate that liquid diet feeding inhibits growth of parotid glands in growing rats through suppression of growth in size and proliferation of acinar cells, but not through apoptosis³⁴.

It can be concluded from this section that unfavorable effects on parotid glands are induced by intake of soft food regardless of growing or mature phases. In the next section, we describe the effects of soft food on two other major salivary glands.

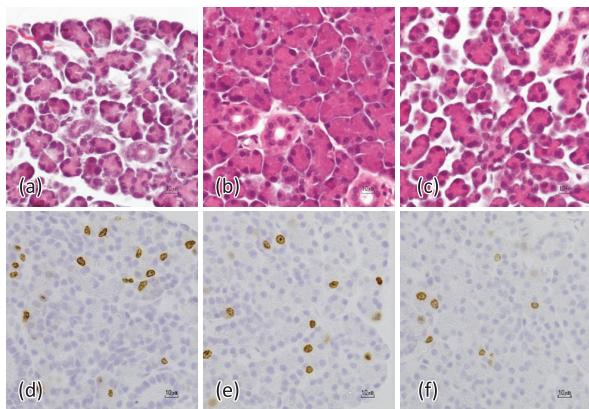


Fig. 2 Growing parotid glands of rats fed a pellet diet (control) (a, b, d, e) and a liquid diet (experimental) (c, f); HE at week 0 (a) and week 4 (b, c), BrdU at week 0 (d) and week 1 (e, f), Scale bars=10μm.

Acinar cells are small at the start of experimentation (a), but become larger in the control gland over time (b). Acinar cells are unchanged in the experimental glands over time (c). BrdU-positive acinar cells are common in control glands (d, e), but are fewer in experimental glands (f).

2. Effects of soft food on submandibular and sublingual glands

Despite accumulated knowledge concerning the effects of soft diet on parotid glands, fewer reports have investigated these effects on submandibular and sublingual glands³⁵⁻⁴⁰. Although many studies report that soft food does not induce atrophy in the submandibular glands³⁵⁻³⁸, but other studies contradict this^{39, 40}. Similarly,

Mansson et al.³⁶ and Kurahashi and Inomata³⁸ report that sublingual glands become atrophied by soft food feeding, however this effect was not observed in other studies^{19, 35, 37}. Consequently, whether soft food affects submandibular and sublingual glands remains highly controversial.

We therefore examined these glands using the same experimental model⁴¹. In the mature submandibular and sublingual glands, there was no difference in gland weight, acinar cell size (Fig. 3), proliferative activity of the acinar cells, occurrence of acinar cell apoptosis, and ultrastructure between the pellet-fed and liquid-fed rats, indicating that the liquid diet does not affect these two mature glands⁴¹. The salivary glands in growing rats fed a liquid diet were also examined⁴². Although the liquid diet had no effect on the growing submandibular glands (Fig. 4a-c), acinar cells smaller in size and with lower proliferative activity were observed in the growing sublingual glands from the liquid-fed rats compared with the pellet-fed rats at 8 weeks (Fig. 4d-f). Despite these changes in the sublingual glands, sublingual gland weight was comparable between liquid-fed and pellet-fed rats throughout the growth period. It is possible that these effects might be too weak to affect sublingual gland weight enough to be detected numerically. Regardless of this, our results showed that growing sublingual glands were influenced very slightly by the liquid diet⁴².

As described above, differences in results exist between studies, including our own. This may be due to the subtle differences in experimental conditions employed in each study, such as the nature of the

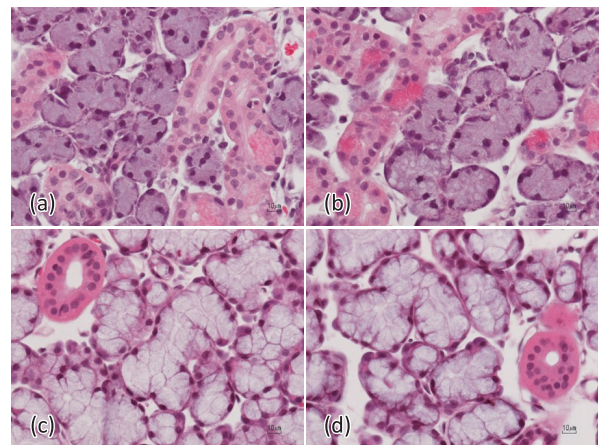


Fig. 3 Histology (HE) of mature submandibular (a, b) and sublingual glands (c, d) of rats fed a pellet diet (control) (a, c) and a liquid diet (experimental) (b, d) on day 7; Scale bars=10μm.

The morphology of acinar cells in control glands (a, c) is similar to that in experimental glands (b, d).

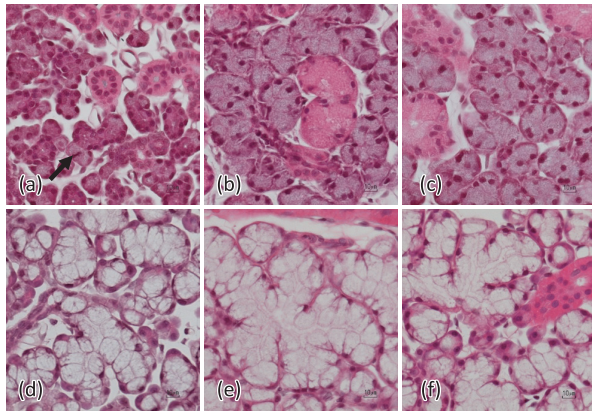


Fig. 4 Growing submandibular (a, b, c) and sublingual glands (d, e, f) of rats fed a pellet diet (control) (a, b, d, e) and a liquid diet (experimental) (c, f); HE at week 0 (a, d) and week 8 (b, c, e, f). Scale bars=10 μ m.

Small acinar cells are observed in submandibular (a) and sublingual glands (d) at the start of experimentation. Mitotic figure of an acinar cell (arrow) is shown. Acinar cell morphology in control submandibular glands (b) is similar to that in experimental glands (c) throughout the feeding period. Acinar cells in experimental sublingual glands (f) are a little smaller than in control glands (e) at week 8.

soft food (liquid or powdered diet, ratio of mixture of powdered diet and water) and length of the experimental period. Therefore, further studies are necessary to clarify these exact reasons.

Concluding remarks

Although controversy exists on the effects of soft diet on major salivary glands, we can conclude that soft food unfavorably affects parotid glands to a greater extent than submandibular and sublingual glands. Based on the major highlights of this review, it is clear that diet and mastication are necessary to maintain healthy salivary glands and promote salivary gland growth. We would therefore emphasize that dental scientists and clinical dentists should appeal to the general public on the importance of dietary habit and mastication.

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References

- 1) Maki K, Nishioka T, Morimoto A, Naito M, Kimura M : A study on the measurement of occlusal force and masticatory efficiency in school age Japanese children. *Int J Paediatr Dent* 11 : 281-285, 2001.
- 2) Yamanaka R, Akther R, Furuta M, Koyama R, Tomofuji T, Ekuni D, Tamaki N, Azuma T, Yamamoto T, Kishimoto T : Relation of dietary preference to bite force and occlusal contact area in Japanese children. *J Oral Rehabil* 36 : 584-591, 2009.
- 3) Sugimoto K, Shimahara M, Kono K : Effects of dietary consistency on the growth and development of the jaw in growing rats. *Bull Osaka Med Coll* 43 : 37-47, 1997.
- 4) Yanagisawa Y, Tamura A, Akasaka M, Teramoto Y : A study on the physical properties of food and ingestion functions. The 1st report: On objective method of measurement of physical properties of foods, and classification of foods. *Jpn J Ped Dent* 23 : 962-983, 1985.
- 5) Watt DG, Williams CHM : The effects of the physical consistency of food on the growth and development of the mandible and the maxilla of the rat. *Am J Orthod* 37 : 895-928, 1951.
- 6) Ito G, Mitani S, Kim JH : Effect of soft diets on craniofacial growth in mice. *Anat Anz* 165 : 151-166, 1988.
- 7) Enomoto A, Watahiki J, Yamaguchi T, Irie T, Tachikawa T, Maki Y : Effects of mastication on mandibular growth evaluated by microcomputed tomography. *Eur J Orthod* 32 : 66-70, 2010.
- 8) Yamada K, Kimmel DB : The effect of dietary consistency on bone mass and turnover in the growing rat mandible. *Arch Oral Biol* 36 : 129-138, 1991.
- 9) Tanaka E, Sano R, Kawai N, Langenbach GEJ, Brugman P, Tanne K, Eijden TMGJ : Effect of food consistency on the degree of mineralization in the rat mandible. *Ann Biomed Eng* 35 : 1617-1621, 2007.
- 10) Maeda N, Kawasaki T, Osawa K, Yamamoto Y, Sumida H, Masuda T, Kumegawa M : Effects of long-term intake a fine-grained diet on the mouse masseter muscle. *Acta Anat* 128 : 326-333, 1987.
- 11) Kiliaridis S, Engstrom C, Thilander B : Histochemical analysis of masticatory muscle in the growing rat after prolonged alteration in the consistency of the diet. *Arch Oral Biol* 33 : 187-193, 1988.

- 12) Miehe B, Franghanel J, Kubein-Meesenburg D, Nagerl H, Schwestka-Polly R : Masticatory musculature under altered occlusal relationships -a model study with experimental animals-. *Ann Anat* 181: 37-40, 1999.
- 13) Kitagawa Y, Mitera K, Ogasawara T, Nojyo Y, Miyauchi K, Sano K: Alterations in enzyme histochemical characteristics of the masseter muscle caused by long-term soft diet in growing rabbits. *Oral Dis* 10 : 271-276, 2004.
- 14) Kiliaridis S, Thilander B, Kjellberg H, Topouzelis N, Zafiriadis A : Effect of low masticatory function on condylar growth: A morphometric study in the rat. *Am J Orthod Dentofacial Orthop* 116 : 121-125, 1999.
- 15) Kato T, Takahashi S, Domon T : Effects of a liquid diet on the temporomandibular joint of growing rats. *Med Princ Pract* 24 : 257-262, 2015.
- 16) Uekita H, Takahashi S, Domon T, Yamaguchi T : Changes in collagens and chondrocytes in the temporomandibular joint cartilage in growing rats fed a liquid diet. *Ann Anat* 202 : 78-87, 2015.
- 17) Hall HD, Schneyer CA : Salivary gland atrophy in rat induced by liquid diet. *Proc Soc Exp Biol Med* 117 : 789-793, 1964.
- 18) Scott J, Berry MR, Gunn DL, Woods K : The effects of a liquid diet on initial and sustained, stimulated parotid salivary secretion and on parotid structure in the rat. *Arch oral Biol* 35 : 509-514, 1990.
- 19) Scott J, Gunn DL : A comparative quantitative histological investigation of atrophic changes in the major salivary glands of liquid-fed rats. *Arch Oral Biol* 36 : 855-857, 1991.
- 20) Hand AR, Ho B : Liquid-diet-induced alterations of rat parotid acinar cells studied by electron microscopy and enzyme cytochemistry. *Arch Oral Biol* 26 : 369-380, 1981.
- 21) Wilborn WH, Schneyer CA : Ultrastructural changes of rat parotid glands induced by a diet of liquid Metrecal. *Z Zellforsch* 103 : 1-11, 1970.
- 22) Johnson DA : Effect of a liquid diet on the protein composition of rat parotid saliva. *J Nutr* 112 : 175-181, 1982.
- 23) Walker NI, Gobe GC : Cell death and cell proliferation during atrophy of the rat parotid gland induced by duct obstruction. *J Pathol* 153 : 333-344, 1987.
- 24) Chisholm DM, Adi MM, Ervine IM, Ogden GR : Cell deletion by apoptosis during regression of rat parotid sialadenitis. *Virchows Arch* 427 : 181-186, 1995.
- 25) Chisholm DM, Adi MM : Cell proliferation and apoptosis in isoprenaline-induced sialosis in the rat submandibular glands. *Int J Exp Pathol* 76 : 263-269, 1995.
- 26) Scott J, Liu P, Smith PM : Morphological and functional characteristics of acinar atrophy and recovery in the duct-ligated parotid gland of the rat. *J Dent Res* 78 : 1711-1719, 1999.
- 27) Takahashi S, Nakamura S, Suzuki R, Islam N, Domon T, Yamamoto T, Wakita M : Apoptosis and mitosis of parenchymal cells in the duct-ligated rat submandibular gland. *Tissue Cell* 32 : 457-463, 2000.
- 28) Takahashi S, Shinzato K, Nakamura S, Domon T, Yamamoto T, Wakita M : The roles of apoptosis and mitosis in atrophy of the rat sublingual gland. *Tissue Cell* 34 : 297-304, 2002.
- 29) Takahashi S, Uekita H, Kato T, Yuge F, Ushijima N, Inoue K, Domon T : Involvement of apoptosis and proliferation of acinar cells in atrophy of rat parotid glands induced by liquid diet. *J Mol Histol* 43 : 761-766, 2012.
- 30) Takahashi N, Naya K, Masumori M, Nakano J, Ohama A, Hirata J, Akasaka M : On a survey on nutrition of infants in the Tokyo metropolitan area. -Part I : On caries dentitions, anomalies of occlusion and ways of eating-. *Jpn J Ped Dent* 27 : 708-715, 1989.
- 31) Ichiishi K, Kitamura M, Masumori M, Kikuti M, Dohi M, Akasaka M : Recent situation concerning dental disease and nutritive condition of young children. *Jpn J Ped Dent* 35 : 821-828, 1997.
- 32) Ohira A, Ono Y, Yano N, Takagi Y : The effect of chewing exercise in preschool children on maximum bite force and masticatory performance. *Int J Paediatr Dent* 22 : 146-153, 2012.
- 33) Tsuchiya M, Nijima-Yaoita F, Yoneda H, Chiba K, Tsuchiya S, Hagiwara Y, Sasaki K, Sugawara S, Endo Y, Tan-no K, Watanabe M : Long-term feeding on powdered food causes hyperglycemia and signs of systemic illness in mice. *Life Sci* 103 : 8-14, 2014.
- 34) Takahashi S, Uekita H, Kato T, Inoue K, Domon T : Growth of rat parotid glands is inhibited by liquid diet feeding. *Tissue Cell* 47 : 336-341, 2015.
- 35) Eksrom J : Choline acetyltransferase and secretory responses of the rat's salivary glands after liquid diet. *Q J Exp Physiol* 58 : 171-179, 1973.
- 36) Mansson B, Ekman R, Hakanson R, Ekstrom J : Neuropeptides and disuse of the rat parotid gland.

- Exp Physiol 75 : 597-599, 1990.
- 37) Nakamura K : Effects of short-term bulk or liquid diet feeding on the neurotransmitters in the salivary glands and various sialogogue-induced salivation in mice. Jpn J Oral Biol 39 : 655-664, 1997.
 - 38) Kurahashi M, Inomata K : Effects of dietary consistency and water content on parotid amylase secretion and gastric starch digestion in rats. Arch Oral Biol 44 : 1013-1019, 1999.
 - 39) Kim JH : The effects of a solid or liquidified diet on the submandibular glands of mice with age. J Jpn Orthod Soc 49 : 73-86, 1990.
 - 40) Kuntsal L, Firat D, Sirin Y : Prevention of liquid-diet-induced damages on submandibular glands by selenium supplementation in rats. Tohoku J Exp Med 201 : 191-199, 2003.
 - 41) Takahashi S, Uekita H, Kato T, Yuge F, Ushijima N, Inoue K, Domon T : Immunohistochemical and ultrastructural investigation of acinar cells in submandibular and sublingual glands of rats fed a liquid diet. Tissue Cell 46 : 136-143, 2014.
 - 42) Takahashi S, Uekita H, Taniwaki H, Domon T : Acinar cell response to liquid diet during rat's growth period differs in submandibular and sublingual glands from that in parotid glands. Tissue Cell 49 : 275-284, 2017.