Effects of Selective Denervation and Nerve Growth Factor on Activity-Mediated Growth of Rat Parotid Gland (43404)

CHARLOTTE A. SCHNEYER,*[,1] MICHAEL G. HUMPHREYS-BEHER,[†] AND H. DAVID HALL[‡]

Department of Physiology and Biophysics, University of Alabama at Birmingham, Birmingham, Alabama 35294; Department of Oral Biology,[†] University of Florida, Gainesville, Florida 32610; and Department of Oral Surgery,[‡] Vanderbilt University School of Medicine, Nashville, Tennessee 37232*

Abstract. **A dietary change from all liquid to solid food is followed by an average increase of 200% in [^{3}H]thymidine uptake into the parotid gland of rat. However, removal of either the parasympathetic (Px) or the sympathetic (Sx) innervation to the parotid gland prior to the dietary change resulted in a partial inhibition of the increase; values for the parasympathectomized gland were 51% of those of the innervated gland, and values of the sympathectomized parotid gland were 42% of those of the innervated gland. Removal of both autonomic nerves caused a complete inhibition. Initiation of nerve growth factor (NGF) injection (1 μg/kg body wt, two times daily for the 2 days of chow refeeding) at the time of chow refeeding had no effect on completely or partially denervated glands, and thymidine values for the denervated parotid gland of rats given NGF did not differ statistically from those of rats not given NGF. With parasympathectomy, sympathectomy, and complete denervation, weight of parotid gland was decreased from that of innervated glands, and administration of NGF had no effect on the denervation-induced decreases. The data show that both branches of the innervation to parotid gland must be intact to ensure a maximal increase in thymidine uptake with the dietary change from liquid to solid food. The level of the enzyme, β1–4 galactosyltransferase, involved in proliferation, also depended on the presence of intact nerves. Enzyme activity of innervated parotid gland showed an average increase of 200% with chow refeeding of rats previously on liquid diet, but with Px, the average increase was 51% of that of the innervated parotid, and with Sx, it was 41%. NGF administration did not cause any change in levels of this enzyme in any Px or PxSx parotid gland and only a small change in Sx parotid; it did increase levels of this enzyme in parotid of rats without submandibular-sublingual glands.** [P.S.E.B.M. 1992, Vol 200]

β1–4 Galactosyltransferase is a constituent of the plasma membrane that has a prominent role in mediation of cell growth (1). A marked increase in levels of this enzyme is found following the increased acinar cell proliferation of parotid gland that occurs after chronic exposure of rats to the β-agonist isoproterenol (2). A marked increase in proliferation and cell surface levels of this enzyme are also induced in rat parotid gland when autonomically mediated activity of the gland is increased by a dietary change from all liquid to solid food (3–5). The increase in thymidine uptake that follows the dietary change appears to be regulated by activation of both autonomic nerves to the gland, since, in the absence of both nerves, thymidine uptake is not increased with dietary change (6). The effect of removal of both autonomic nerves on enzyme levels has not been examined, nor has the specific role of each branch of the innervation in mediation of either thymidine or enzyme changes been examined. This is of relevance, since only β-adrenoceptors were previously implicated in mediation of the enzyme increases (2). The specific influence of each branch of the innervation in regulation of enzyme as well as thymidine levels was examined by the use of selective denervation. Furthermore, since ablation of submandibular glands also prevents thymidine uptake in parotid gland when the diet is changed from liquid to solid food (6), the

[1] To whom requests for reprints should be addressed at Laboratory of Exocrine Physiology, University of Alabama at Birmingham, UAB Station, Box 301, Birmingham, AL 35294.

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effects of submandibular gland ablation on enzyme levels were also examined. In addition, nerve growth factor (NGF) was administered to animals without submandibular glands, since this growth factor is produced by the submandibular gland and has been implicated as a co-activator, with neurotransmitters, of hyperplasia (4, 6). It was also administered to rats with denervated parotid gland, since levels of NGF may be critically reduced under these circumstances. By these comparisons, the co-activity of autonomic receptors and NGF in mediation of hyperplasia and the involvement of β1–4 galactosyltransferase in these events were disclosed.

Materials and Methods

Long-Evans rats, 27–84 days of age, were used in these experiments. Animals were maintained on Purina solid lab chow and water *ad libitum*. The experimental animals were maintained on a liquid diet (S.M.A. (infant formula); Wyeth Laboratories, Inc., Philadelphia, PA) for 5 days before surgical procedures that involved removal of a single superior cervical ganglion (Sx) or a single auriculotemporal nerve (Px), or both (PxSx), or removal of both submandibular-sublingual glands (partial sialoadenectomy), or removal of submandibular-sublingual glands and either a superior cervical ganglion (Des-Sx), or an auriculotemporal nerve (Des-Px) under ether anesthesia. Several litters of the same age were used for a given experiment and were size- and sex-matched. At least three rats from a given litter of eight (reduced to this litter size at birth) were used for a given experimental procedure; all experimental animals and controls were sacrificed at one time. (Sham-operated animals were randomly done and were included, without separate designation, in the control groups, since values did not differ from unoperated controls.) Animals on liquid diet and partially sialoadenectomized, or completely denervated (PxSx), or selectively denervated (Px or Sx), or selectively denervated and partially sialoadenectomized, were maintained on liquid diet for 5 days prior to refeeding with solid chow for 2 days (with the exception of a group that remained on liquid diet throughout). On the morning of the third day after reintroduction of solid chow, [^{3}H]thymidine (in a dose of 50 μCi/100 g rat) was injected intraperitoneally into all rats. Five hours later parotid glands were removed under sodium pentobarbital anesthesia (50 mg/kg body wt, ip), weighed rapidly on a torsion balance, and placed in Tris-HCl buffer for monitoring of [^{3}H]thymidine incorporation. Samples (100 μl) of tissue (homogenized at 4°C) were removed for precipitation with trichloroacetic acid on glass fiber filters, followed by the addition of scintillation cocktail for measuring [^{3}H]thymidine incorporation. Part of the sample was removed for a protein assay. Glands from untreated animals were used to determine basal rates of synthesis. Gland homogenates were prepared by centrifugation at 250*g* for 10 min (4°C) to remove connective tissue. Protein concentrations were determined by a modification of the Lowry protein assay using bovine serum albumin as standard (7). Values for [^{3}H]thymidine uptake in parotid gland are related to total protein rather than DNA.

Total membrane fractions were prepared at 4°C by homogenization of intact parotid tissue from treated and control animals in 10 mmol/liter of Tris/HCl buffer (pH 8.0), with a tissue homogenizer and Dounce apparatus. A low speed centrifugation at 500*g* was then performed to remove connective tissue as well as unlysed cells. The resulting slurry was then centrifuged at 100,000*g* for 1 hr to recover total membrane. The activity of β1–4 galactosyltransferase and sialyltransferase was measured as described previously by Humphreys-Beher *et al.* (2). Student's *t* test was used for statistical analysis of the data.

Results

The data in Table I show the effects of selective denervation on [^{3}H]thymidine incorporation of parotid gland in rats refed with solid chow after a period of maintenance on liquid diet only. There was a 2- to 3-fold increase in [^{3}H]thymidine uptake of parotid gland when values of innervated parotid gland of rats on liquid diet were compared with those of animals refed solid chow for 2 days following maintenance on liquid diet. When the parasympathetic nerve to the parotid gland of rats on liquid diet was severed prior to reintroduction of solid food, values of the denervated parotid of chow-refed animals were, on an average, 51% of those of the innervated parotid of chow-refed animals. The removal of the sympathetic postganglionic pathway effected a generally similar change and values were, on an average, 42% of those of innervated parotid gland. Removal of both pathways prevented any statistically significant ($P > 0.01$) changes from values of parotid of rats on liquid diet. In a single group of rats examined (49 days of age), Sx combined with submandibular gland ablation caused a maximal decrease in thymidine uptake (legend to Table I) when rats were refed chow and values for Liq Des Sx Ref chow were not statistically different from those of Liq Des Ref chow; both exhibited complete inhibition of the usual activity-induced thymidine increase (Table I).

NGF was administered to rats with denervated parotid glands in a deliberately high dosage to compensate for any decrease in serum levels of NGF that might be induced with unilateral sympathectomy. Unilateral Sx (alone or in conjunction with parasympathectomy) results in unilateral denervation of both submandibular and parotid glands. Since release of NGF from the submandibular gland, a major site of synthesis and

Table I. Nerve Growth Factor Effects on Dietary-Induced Changes in Thymidine Uptake into Parotid Gland after Complete or Partial Denervation, or Submandibular-Sublingual Gland Ablation[a]

Age (days)	Thymidine uptake into parotid gland (cpm/mg/protein)						
	Con	Liquid	Liq Ref	Liq Px Ref	Liq Sx Ref	Liq PxSx Ref	Liq Des Ref
36	422 ± 27 (11)	417 ± 45 (11)	1321 ± 155 (14)	747 ± 41 (9)	750 ± 89 (8)	519 ± 71 (3)	
44	312 ± 57 (4)	354 ± 39 (6)	1293 ± 126 (5)	578 ± 89 (4)	611 ± 57 (4)	514 ± 77 (5)	358 ± 88 (4)
					N689 ± 21 (4)	N543 ± 60 (4)	
45	282 ± 21 (5)	361 ± 38 (5)	1091 ± 91 (5)	758 ± 77 (4)	648 ± 22 (5)	523 ± 46 (5)	568 ± 75 (5)
					N687 ± 32 (5)		N1174 ± 129 (4)
47	358 ± 39 (4)	429 ± 55 (5)	1240 ± 101 (6)	509 ± 48 (5)	515 ± 53 (3)	358 ± 83 (4)	
	N421 ± 21 (3)		N1245 ± 92 (4)	N760 ± 190 (4)	N661 ± 57 (3)	N368 ± 40 (5)	
49	187 ± 33 (4)	148 ± 10 (4)	1512 ± 91 (3)		248 ± 31 (3)		143 ± 30 (4)
58	1172 ± 106 (5)	971 ± 59 (5)	2382 ± 168 (9)	1742 ± 181 (5)	1272 ± 88 (5)	1189 ± 72 (3)	
	N1645 ± 101 (4)	N1140 ± 80 (5)	N2368 ± 549 (5)	N1570 ± 196 (5)	N1177 ± 99 (5)		
84	230 ± 45 (4)	247 ± 12 (6)	1022 ± 356 (3)	231 ± 93 (3)	173 ± 41 (3)	174 ± 21 (3)	

[a] Values are means ± SE. Numbers in parentheses equal number of rats. [^{3}H]Thymidine values for parotid gland of rats with conditions described: Con, control, rats maintained exclusively on chow diet; liquid, rats maintained exclusively on liquid diet; Liq Ref, rats maintained for 5 days on liquid diet, followed by solid chow for 2 days. In all instances the prefix N indicates that NGF was administered; unilateral removal of auriculotemporal nerve (Px) of rats maintained on liquid diet for 5 days prior to reintroduction of solid chow for 2 days = Liq Px Ref (without NGF) and Liq Px Ref NGF (injection of NGF at 1 μg/kg body wt) two times daily for 2 days; unilateral removal of a superior cervical ganglion (Sx) of rats maintained on liquid diet for 5 days prior to reintroduction of solid chow for 2 days = Liq Sx Ref (without NGF) and Liq Sx Ref NGF (with NGF) (dosage as above); unilateral removal of a superior cervical ganglion and auriculotemporal nerve (PxSx) of rats maintained on liquid diet for 5 days prior to reintroduction of solid chow for 2 days = Liq PxSx Ref (without NGF) and Liq PxSx Ref NGF (with NGF) (dosage as above); liquid NGF, rats maintained for 5 days on liquid diet and then given NGF (dosage as above) for additional 2 days. The 49-day-old group includes these additional data: Liq Des Sx Ref, 149 ± 7 (3); Liq Des Px Ref, 228 ± 41 (3). In these animals, submandibular-sublingual glands, as well as indicated innervation, were removed, as described above. Con and liquid values are not statistically different from each other, or from Liq Des Ref or Liq PxSx Ref ($P > 0.01$). Values of Liq Des Ref NGF differ statistically from the non-NGF-treated group of same condition ($P < 0.01$). Values of Liq PxSx Ref NGF, Liq Px Ref NGF, and Liq Sx Ref NGF do not differ statistically ($P > 0.01$) from non-NGF-treated group of same condition; partial sialoadenectomy (submandibular-sublingual glands removed) (Des) of rats maintained on liquid diet for 5 days prior to reintroduction of solid chow = Liq Des Ref (without NGF) and Liq Des Ref NGF (with NGF) (dosage as above).

storage of NGF (8–10), depends on sympathetic stimulation (11), NGF would not be expected to be released from the sympathectomized submandibular gland, and thus serum levels (9) would be decreased by 50%. Although Px of parotid would not result in a reduction in serum levels of NGF in rats with intact submandibular glands, in order to make valid comparisons, NGF in the same high dose was administered to rats with parasympathectomized parotid.

Administration of NGF did not affect thymidine uptake in either parasympathectomized or sympathectomized parotid gland, and values for [^{3}H]thymidine uptake of denervated (either Px or Sx) parotid of rats given NGF during the period of chow refeeding showed no statistically significant difference ($P > 0.01$) from those of denervated parotid of rats not given NGF during the period of chow refeeding (Table I).

The administration of NGF did not cause any increase in [^{3}H]thymidine uptake in the completely denervated parotid gland, and values with NGF did not differ statistically from those of rats not given NGF (Table I). On the other hand, administration of NGF to partially desalivated rats during the period of chow refeeding reversed the inhibitory effects of sialoadenectomy on thymidine uptake into parotid gland. The parotid of partially sialoadenectomized rats refed with chow and given NGF during this period of refeeding showed an average increase of 254% when a comparison was made with intact liquid-fed rats (Table I). In contrast to these effects, administration of NGF to chow controls caused an average increase of 92% (Table I), and did not cause any statistically significant ($P > 0.01$) increase in thymidine uptake (Table I) of parotid gland of rats maintained on liquid diet exclusively.

In all of the age groups examined, weight of parotid gland of rats maintained on liquid diet was decreased by an average of 58% when a comparison was made with parotid of control rats (maintained on chow only) (Table II). When solid food was reintroduced to rats on liquid diet, gland size increased to, or nearly to, control levels within 2 days after refeeding (Table II), and values, on an average, were 90% of control values. However, if the parasympathetic nerve was severed prior to the dietary change from liquid to solid food, the return to control levels was inhibited; values for weight of the Px-parotid of chow-refed rats did not differ statistically ($P > 0.01$) from those of the animals maintained only on liquid diet (except for the 84-day-old group). The effects of Sx were similar, and values for Sx-parotid of chow-refed rats were not statistically different ($P > 0.01$) from those of rats fed liquid diet, again except for the 84-day-old group. Complete denervation prevented the return to control levels with chow refeeding (Table II); on the other hand, partial desalivation did not change weight of the parotid gland (either with submandibular gland ablation alone, or when

Table II. Nerve Growth Factor Effects on Dietary-Induced Changes in Gland Weight of Parotid Gland after Complete or Partial Denervation, or Submandibular-Sublingual Gland Ablation[a]

Age (days)	Parotid gland weight (mg)						
	Con	Liquid	Liq Ref	Liq Px Ref	Liq Sx Ref	Liq PxSx Ref	Liq Des Ref
36	153 ± 5	64 ± 4	144 ± 12	72 ± 7	85 ± 9	59 ± 9	
44	189 ± 9	80 ± 3	128 ± 7	75 ± 14	84 ± 10	78 ± 12	
					N81 ± 3		
45	166 ± 6	73 ± 6	152 ± 6	99 ± 37	106 ± 14		167 ± 19
					N105 ± 10		N164 ± 12
47	173 ± 9	73 ± 6	122 ± 9	93 ± 5	102 ± 12	91 ± 16	169 ± 20
			N147 ± 8			N81 ± 8	N171 ± 16
49	197 ± 13	77 ± 3	162 ± 10				195 ± 14
58	170 ± 15	100 ± 7	189 ± 3	123 ± 14	111 ± 12	89 ± 4	
	N162 ± 10	N76 ± 7		N118 ± 13	N120 ± 4	N82 ± 4	
84	183 ± 9	84 ± 5	197 ± 3	127 ± 15	160 ± 16	93 ± 9	

[a] Values are means ± SE. Number of rats indicated in Table I. Gland weight of parotid gland of rats with conditions as described in Table I. Gland weights of parotid for following: values for Con and liquid differ statistically from each other ($P < 0.01$); values for liquid differ statistically from those of Liq Ref and Liq Des Ref ($P < 0.01$); values for Liq PxSx Ref differ significantly from Liq Ref ($P < 0.01$) but not from liquid ($P > 0.01$). Values for NGF-treated rats for either Liq Des Ref ($P > 0.01$) or Liq PxSx Ref do not differ from non-NGF in each group. The 49-year-old groups include these additional data: Liq Des Sx Ref, 166 ± 11 (4); Liq Des Px Ref, 121 ± 19 (3). All designations are as in Table I.

combined with Sx), and with chow refeeding, weight of the parotid of such animals was not statistically different from that of controls (Table II).

NGF had no effect on size of the denervated parotid gland (Px, Sx, or PxSx) when administered during chow refeeding and values for weight of parotid gland with NGF administration were similar to those without NGF (Table II).

The data in Table III and Ref. 4 show values for β1–4 galactosyltransferase activity in total membrane preparations from parotid gland of rats refed with solid chow for 2 days after a prior period of maintenance on liquid diet only. When compared with values of parotid of rats maintained exclusively on either solid chow or liquid food, there was more than a 3-fold increase in β1–4 galactosyltransferase activity. If the submandibular-sublingual glands were removed prior to reintroduction of solid food, β1–4 galactosyltransferase activity was, on an average, 1.7 times greater than that of parotid of animals maintained exclusively on liquid or solid food. When both the parasympathetic and sympathetic nerves to parotid were removed prior to the dietary substitution, values for β1–4 galactosyltransferase activity of denervated parotid were, on an average, 1.3 times those of control rats; administration of NGF (with chow refeeding) to rats with completely denervated parotid did not result in any increase from the levels seen in the completely denervated parotid gland of rats not given NGF. However, administration of NGF to partially desalivated rats during the period of refeeding caused an increase in β1–4 galactosyltransferase activity of parotid; values were very similar to those

Table III. Total Membrane β1-4 Galactosyltransferase Specific Activity of Selectively Denervated Parotid Gland of Rats on Liquid Followed by Chow Diet[a]

Condition	β1-4 Galactosyltransferase specific activity (nmol/hr/mg protein)			
	47 days old	58 days old	64 days old	71 days old
Control	0.035 ± 0.004	0.057 ± 0.008	0.025 ± 0.002	0.038 ± 0.09
Liquid	0.037 ± 0.004[b]	0.049 ± 0.009[b]	0.030 ± 0.004[b]	0.027 ± 0.001[b]
Liq Ref	0.113 ± 0.005	0.179 ± 0.005	0.069 ± 0.004	0.093 ± 0.003
Liq Px Ref	0.072 ± 0.003	0.067 ± 0.003		
Liq Px Ref NGF	0.087 ± 0.003	0.057 ± 0.003[b]		
Liq Sx Ref	0.058 ± 0.003	0.055 ± 0.004[b]		
Liq Sx Ref NGF		0.081 ± 0.009		
Liq PxSx Ref	0.053 ± 0.003[b]	0.061 ± 0.006[b]	0.027 ± 0.003[b]	0.062 ± 0.004
Liq PxSx Ref NGF	0.058 ± 0.004	0.058 ± 0.003[b]	0.035 ± 0.005[b]	0.058 ± 0.003
Liq Des Ref	0.078 ± 0.003	0.065 ± 0.004[b]	0.045 ± 0.003	0.065 ± 0.004
Liq Des Ref NGF	0.110 ± 0.004	0.108 ± 0.003	0.109 ± 0.009	0.108 ± 0.004

[a] Values are means ± SE. Designations are as in Tables I and II.
[b] Indicates value does not differ statistically from control ($P > 0.01$). Values with NGF and without, for each condition indicated, do not differ statistically from each other, except for Sx Ref and Sx Ref NGF (58 days).

of innervated parotid gland of intact rats following chow refeeding, with the increase in each case nearly 3-fold.

However, when only the parasympathetic innervation to parotid gland was removed prior to chow refeeding, there was partial inhibition of the increases in β1–4 galactosyltransferase activity normally observed in innervated parotid with chow refeeding, and values of the denervated parotid were 37–51% of those of the innervated parotid of chow-refed rats. Administration of NGF during the 2-day period of chow refeeding did not reverse the effects of parasympathetic denervation, and values for denervated parotid of animals given NGF did not differ statistically ($P > 0.01$) from those of animals not given NGF. In the single group of rats with sympathectomized parotid and injected with NGF, there was a modest increase of 47% from values of parotid of rats not given NGF. The levels of sialyltransferase did not differ significantly from control values for any of the experimental groups (data not shown).

Discussion

Present data as well as our earlier work show that the increase in autonomically mediated glandular activity that follows the change from liquid to solid food (3, 5) is also accompanied by marked increases in parotid levels of β1–4 galactosyltransferase (2, 4), an enzyme implicated as a mediator of growth in a variety of normal (12–14) and malignant cells (14, 15). Increased thymidine uptake into DNA of parotid gland also follows the change in enzyme levels, but if the autonomic nerves to the parotid gland are removed prior to reintroduction of solid food, increase in thymidine uptake does not occur (6), and, as present data show, β1–4 galactosyltransferase did not increase as expected. In fact, values for enzyme levels of the completely denervated parotid differed little or not at all from those of controls.

Present data also show that a marked reduction in parotid levels of the enzyme, and in thymidine uptake, occurred when either the parasympathetic or sympathetic innervation to parotid gland was severed prior to the dietary change. Moreover, the effects of parasympathetic and sympathetic denervation were generally similar. Thus, with the change from liquid to solid food, the average increase in thymidine uptake of the parasympathectomized parotid gland was 51% of that of innervated parotid of chow-refed rats, and that of the sympathectomized parotid was 42% of that of innervated parotid of chow-refed rats. Thus, a substantial inhibition was induced by either kind of denervation.

The reductions in enzyme levels induced by denervation generally paralleled the thymidine decreases. Thus, enzyme levels for parasympathectomized parotid gland of rats refed with chow were 37–64% (average, 51%) of those observed in the fully innervated gland, and values for the sympathectomized parotid gland were 31–51% (average, 41%) of those observed in the fully innervated parotid gland. While a maximal decrease in thymidine uptake and enzyme levels was induced only when both nerves were absent, removal of only one branch (and it could be either parasympathetic or sympathetic) resulted in enzyme levels that were not much higher than those observed with complete denervation. Thus, a maximal inhibition of the proliferative response occurs only with complete denervation, but absence of only a single branch causes a substantial inhibition.

While earlier work, as well as present data, showed that the parasympathetic innervation to parotid gland has an important role in regulation of activity-induced hyperplasia (3), the present work provides the first data showing an important role of this branch of the innervation in regulation of levels of β1–4 galactosyltransferase. The fact that the sympathetic innervation has an important role is not unexpected, since our earlier work showed a marked increase in levels of this enzyme following the chronic administration of the β-adrenergic agonist isoproterenol (4).

Although the innervation has an important role in regulation of the enzyme and thymidine changes associated with increased glandular activity, the submandibular glands have an equally important role. Without them, the increases do not occur, even in the presence of intact nerves to the parotid gland. Since NGF administration reversed the inhibitory effects of submandibular gland ablation, it is concluded that submandibular glands normally provide NGF (10, 16). However, localization of NGF to the granular tubules of the submandibular gland has only been demonstrated for mouse (8–10), but because exogenous NGF reverses the inhibitory effects caused by submandibular gland ablation in rat, we infer that rat submandibular gland also provides the NGF (16, 17) found to be essential for mediation of autonomically mediated mitogenesis of parotid gland.

In the absence of one or both autonomic nerves to parotid gland, however, NGF administration had little or no effect on enzyme levels or thymidine uptake of parotid gland. However, the necessity of providing exogenous NGF to animals with intact submandibular glands can be questioned. This was done to compensate for a probable 50% deficit in serum levels of NGF that was caused by unilateral Sx. The release of NGF from its storage sites (8) in submandibular gland is reported to be induced by cyclocytidine (11), which probably involves stimulation of the sympathetic nerve. Removal of a superior cervical ganglion causes sympathectomy of the submandibular, as well as the parotid gland. Without its sympathetic innervation, the submandibular gland is incapable of contributing its usual share of NGF. By providing an excess of NGF, any deficit

caused by Sx is overcome; thus, the inhibitory effects of denervation can then only be attributed to a lack of neurotransmitters at appropriate parotid sites and not to a lack of NGF. This conclusion is strengthened by the data that show that injected NGF does not have its usual salutary effect on thymidine and enzyme levels of parotid of partially sialoadenectomized animals if an autonomic nerve to the parotid is absent. Thus, while NGF (administered during chow refeeding) normally increases enzyme and thymidine of neurally intact parotid of the sialoadenectomized rats to levels normally observed in intact rats with chow refeeding, it has no effect on parotid of sialoadenectomized rats if either nerve is absent. Thus, if even one autonomic branch is absent, injected NGF does not reverse the inhibitory effect of submandibular gland ablation.

It may be concluded, therefore, that without the presence of neurotransmitters, growth factors have no major influence in regulation of the enzyme changes in parotid gland that lead to hyperplasia, or the hyperplasia itself. Co-activation of autonomic receptors with growth factors is the prerequisite for the enzyme increase and for hyperplasia in salivary glands.

On the other hand, only neurotransmitters are required for the hypertrophic response. The increase in gland and acinar size with chow refeeding are maximal even when the submandibular glands are absent. However, the response is less than maximal when either branch of the innervation is absent; the deprivation of the cholinergic neurotransmitter causes a more marked reduction in gland size than that caused by absence of the adrenergic neurotransmitter (3), and, thus, the parasympathetic innervation has the principal role in regulation of size. The galactosyltransferase has no role in mediation of hypertrophy, since gland size is not reduced with partial desalivation, but levels of the enzyme are maximally reduced.

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