REGENERATION OF THE PAROTID GLAND IN THE RAT

A. G. Babaeva

Laboratory of Growth and Development (Head-Prof. L. D. Liozner) of the Institute of Experimental Biology (Dir.-Prof. L. N. Maiskii), AMN SSSR, Moscow

(Presented by Active Member AMN SSSR V. V. Parin)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 50, No. 10, pp. 113-118, October, 1960
Original article submitted October 12, 1959

There have been too few studies of the regenerative capacity of the salivary glands, and the data obtained by different authors are quite contradictory. It is thought that the submaxillary gland regenerates well [3, 5, 6, 7, 8], while the parotid gland has poor regenerative capacity [2, 4]. According to a widely held opinion, the recovery of either type of gland occurs through branching of the duct, with the formation of atypical, functionally imperfect glandular tissue. Some authors, taking a different view of the capacity of these glands to regenerate, have been guided solely by the size of the newly formed part of the gland. In the regenerated submaxillary gland this part occupies a greater area, according to available descriptions, than it does in the parotid gland. In the latter, the branching of the duct was so slight in experiments on dogs [4] and cats [2] that the authors questioned the capacity of the parotid to regenerate.

In a study of the parotid gland of the guinea pig [1] we found that the part of the gland formed as a result of atypical branching of the duct does in fact occupy a small area (at most 1/6) in relation to the area of the whole gland. We concluded, however, that the parotid possesses excellent regenerative capacity, since after removal of a large part of the gland its weight returns completely to normal, as a result of an increase in the size of the part that remains, which retains its normal structure for the most part. Thus, regeneration of the parotid gland of the guinea pig, like that of many other mammalian organs, comes about by regeneration hypertrophy – in this case, proliferation of the secretory cells of the acini over the entire organ, and not just near the site of injury. This proliferation ensures an increase in mass in a gland with normal structure, and this increase is the main mechanism by which the gland's weight is restored. Atypical branching of the duct is not of great importance in the regeneration of the organ as a whole. It might be supposed that the disagreement between our data on the mode and origin of salivary gland regeneration and the data of other authors depends on the fact that they adhered to classical concepts of the course of regeneration from the injured surface and paid most of their attention to that. Besides, other papers contain no quantitative account of the restoration of the mass of the organ, or of data on the dimensions of the region with atypical structure, which is evidently why the processes of regeneration hypertrophy escaped the authors' attention. But it is not impossible that the difference in results was caused by our use of a different species of animal from the one used by other authors, and by the fact that parotid rather than submaxillary regeneration was studied.

The present investigation was intended to show whether recovery by regeneration hypertrophy is peculiar to the salivary gland of guinea pigs or is a property of the salivary glands of other animals as well.

METHODS

As the object of this investigation, we used the parotid gland of the white rat, which is histologically a serous gland, like the parotid of the guinea pig, but is more compact and has a distinct connective tissue capsure. Two series of experiments were performed. In the first series we used 64 rats weighing from 60 to 100 g; in the second series we studied 14 adult rats weighing from 140 to 180 g. In all experiments, regeneration was studied after complete removal of the left parotid and extirpation of most of the right one. This arrangement was dictated by the need for obtaining results on rats that could be compared with the results of our experiments on guinea pigs. The importance of removing the contralateral gland is still not completely clear, since processes of compensatory hypertrophy do not occur in the salivary glands [7, 9, 10]. In the second series of experiments the animals were divided into two groups. In one group the capsule was sutured together after part of the gland was removed; in the other group only the

TABLE 1. Changes in Body Weight and Parotid Gland Weight in Rats with the Left Parotid Gland Removed (Supplementary Control)

No. of rat	Wt. of rat at start of expt. (g)	Weight of gland removed		Wt. of rat at end of expt. (g)	Weight of remaining gland		Weight gain (%)	
		absolute (mg)	relative (%)		absolute (mg)	relative (%)	rat	gland
1	62	32	0.516	174	80	0.459	180	150
2	67	40	0.597	166	73	0.439	147	82
3	78	39	0.500	163	70	0.429	108	72
4	86	38	0.441	218	99	0.454	153	160
5	93	41	0.440	209	74	0.354	124	80
6	100	41	0.410	194	69	0.355	194	168
Mean	81	38.5	0.484	187	77.5	0.415	134	102

muscle and skin were sutured. The animals in the first series were sacrificed two months after the operation; those in the second series, 1½ months after the operation. The glands were weighed, fixed in 10% formalin, and subjected to the usual histological treatment. Serial sections were stained with Gomori's stain and with hematoxylin and eosin.

RESULTS

First series. Young, rapidly growing rats were used in these experiments. In order to differentiate growth from regeneration, we sacrificed normal rats of the same age as those in the experiment at the beginning and the end of the experiment (there were seven rats in the initial control group, and 15 in the final one). Besides this, an additional control was set up to enable us to observe changes in body weight and gland weight in single animals. From the rats in this group we removed only the left parotid, leaving the other intact. This series was performed because of the published data, mentioned earlier, suggesting that processes of compensatory hypertrophy are absent from salivary glands.

According to the weight data from the initial and final controls, the difference in weight between the right and left parotid glands was insignificant; in the initial control it was not more than 4 mg, or 5%. Over a two-month period the body weight of the control rats increased by 97% on the average, and the weight of the parotid gland increased by 74%. This lag in the weight gain of the gland as compared to the body weight gain has the result that the relative weight of the organ has a tendency to decrease with age (from 0.474 to 0.427%). A similar pattern appeared in the supplementary control (Table 1): while the body weight increased 134% on the average, the weight of the gland increased by only 103%, resulting in a reduction of the relative weight from 0.484 to 0.415% during the two-month period. But the relative weight of glands in the rats of the supplementary control was no greater than that in the final control. This agrees with published data concerning the absence of pronounced compensatory hypertrophy in salivary glands. Data obtained on the control animals show that the animals' growth is accompanied by an increase in organ weight, during the two-month period, of roughly 74 – 103%. Since the weight of the glands in the experimental animals increased more during the same length of time, the difference must be attributed to restorative processes.

Analysis of the results obtained in the first series of experiments reveals that in individual rats the reaction to trauma was different, to judge from the change in the weight of the resected gland and the histological structure of these glands. On this basis the experimental rats can be divided into four groups.

In the rats of the first group (eight animals) the gland weight fell sharply during the experimental period The lumina of the acini of these glands were markedly enlarged as a result of flattening of the secretory epithelial cells. The nuclei of the epithelial cells were pycnotic. The gland had completely lost its specific form and had taken on the form of a system of excretory ducts, such as is characteristic for atrophying glands. The weight of the glands in rats of the second group (five animals) did not change during the experiment – that is, together with the weight of the removed portion it was approximately equal to the weight of the gland that had been removed intact. Degenerative changes were not so pronounced in these glands as in the previous group; the gland had not lost its specific form. In the animals of the third group (16 rats) the gland weight increased during the experiment, but this increase was either parallel with the gain in body weight or only a little greater. In the fourth group (Table 2) there were seven rats whose glands either weighed as much as those of the controls or else gained weight much faster than body weight increased in the experimental animals. It can be seen from Table 2 that with an average of 65%

TABLE 2. Changes in the Weight of theParotid Gland in Animals of the Fourth Group in the First Series

No. of rat	Wt. of rat at start of expt. (g)	Weight of glands removed (mg)		Wt. of rat at end of expt. (g)	Weight of regenerated gland	
		intact left gland	portion of right gland		absolute (mg)	relative (%)
1	71	43	25	181	56	0,309
2	92	40	28	270	95	0,351
3	92	36	25	187	67	0,358
4	98	34	29	171	55	0,321
5	99	40	30	205	43	0,209
6	111	53	26	269	95	0,359
7	112	53	32	201	55	0,273
Mean	96	42,7	27,8	212	66,5	0,311

TABLE 3. Changes in the Weight of the Parotid Gland in Animals of the First and Second Groups of the Second Series

No. of rat	Wt. of gland removed(mg)	Portion wt. of gland removed (mg)	Wt. of rat at end of expt. (g)	Wt. of regenerating gland	
				absolute (mg)	relative (%)
First group					
1	32	25	170	20	0,117
2	45	10	194	40	0,206
3	50	30	177	32	0,180
4	50	32	194	29	0,149
5	66	30	187	28	0,149
Mean	48,6	25,4	184	25,8	0,160
Second group					
1	34	21	204	57	0,279
2	43	20	169	57	0,337
3	—	—	195	45	0,230
4	46	24	192	44	0,228
5	62	26	195	40	0,205
Mean	46,2	22,7	191	48,6	0,255
Control					
				Right	Left	Right	Left
1	—	—	234	55	55	0,234	0,234
2	—	—	210	73	75	0,347	0,357
3	—	—	211	82	82	0,389	0,389
4	—	—	235	65	78	0,276	0,331
Mean	—	—	222	68,7	72,5	0,311	0,327

of the mass of the gland removed, the remainder grew 240% while the body weight increased only 120%, whereas in the control group, on the other hand, the gland gained weight somewhat more slowly than the body as a whole.

On the basis of these calculations, the presence of parotid gland regeneration cannot be questioned, although in several cases it cannot be considered complete, since complete restoration of its weight was not observed and the mean values of the absolute and relative weight are 80.1% and 72.8%, respectively, of the mean weight of glands of control animals at the end of the experiment. At histological examination it was found that in the glands of rats in the third group, which were mainly normal in structure, there were regions of marked vacuolization of the protoplasm of secretory epithelial cells.

In the fourth group of rats, the glandular tissue has little to distinguish it, with the stains used, from the glandular tissue of control rats; it retains the variations in the dimensions of nuclei in the secretory epithelium, in the size of the acini, and in the number of secretory cells constituting an acinus, that are characteristic of parotid glands in the rat. The regenerating gland differs from the normal in that it has a small connective-tissue scar, and in some cases (as in the third group) a very narrow strip of glandular tissue of atypical structure at the site of amputation. Even in those cases where such regions of atypical structure are present, they occupy an insignificant fraction of the area of the section (a few percent), so that they do not appear to play any major role in the increase in gland weight. This increase results from proliferation of the cells of the secretory epithelium (regeneration hypertrophy), as is indicated by the normal histological structure of the great bulk of the gland, the absence of atypical branching of the duct in several regenerated glands whose weight was close to that of the glands in control animals, and the large number of mitoses in the secretory cells (2.3 mitoses per thousand cells), which remained for as long as two months after the operation in some instances. In the control glands the number of mitoses did not exceed 0.6 per thousand cells.

Second series. The results of the first series of experiments showed that regeneration of the parotid gland of young rats can occur, but restoration occurred in only 19% of the cases, i. e., in a much smaller number of cases than with guinea pigs. We conjectured that the presence of a distinct connective tissue capsule in rats might have an effect on salivary gland regeneration. To test this hypothesis, we did not suture the capsule after the operation in some of the animals of the second series. In addition, in the second series we set out to determine whether regeneration of the parotid can occur in sexually mature rats growing more slowly than young rats. The results of these experiments are shown in Table 3. The difference between the two groups of animals was distinct. In the cases where the capsule was not sutured (second group), the increase in the weight of the resected gland $1\frac{1}{2}$ months after operation was greater. The increase in gland weight among animals in the first group was insignificant. The differences between the two groups of the second series were statistically significant ($P = 0.01$). As in the first series, in individual rats of the second group complete recovery of the entire traumatized organ occurred after removal of 50% of the gland; but the mean value of the relative weight was also somewhat below that for the control animals, being 82% of the latter. Upon histological examination of the regenerated glands, data were obtained that were similar to those described for the fourth group of rats in the first series. Thus, in rats, as in guinea pigs, regeneration of the parotid gland occurs by regeneration hypertrophy, but in contrast to guinea pigs, growth from the injured surface with the formation of atypical glandular tissue is much less marked.

SUMMARY

Parotid gland regeneration was studied in rats in which all of the left gland and part (50 – 60%) of the right had been removed. In young rats weighing 60 – 100 g, regeneration occurred in 19% of cases, as judged by the restoration of the weight of the organ. The weight of the glands did not always reach the initial level, however, and averaged 80% of the weight in control animals.

The number of cases with gland regeneration increased in adult rats when the capsule was left open after the operation. Histological investigation showed that regeneration does not occur by growth starting at the injured surface, but rather by the proliferation of the secretory epithelium (regenerative hypertrophy) of the acini over the whole organ.

LITERATURE CITED

1. A. G. Babaeva, Byull. Éksp. Biol. Med. 43, 3, 95 (1957).*
2. E. Sh. Gerlovin, Abstracts of Ukrainian Conference of Morphologists [in Russian] (Kharkov, 1956) Vol. 2, p. 51.
3. E. Sh. Gerlovin, Transactions of the Leningrad Sanitary Hygiene Medical Institute [in Russian] (1958) Vol. 42, p. 132.
4. V. M. Koropov, Materials on the Pathological Physiology of the Salivary Glands [in Russian] (Moscow, 1949).
5. W. Podwyssozki, Beitr. path. Anat. 2,19 (1887).
6. A. Carraro, Frankf. Z. Path. 3, 26 (1909).
7. B. B. Milstein, J. Exper. Path. 31, 664 (1950).
8. Ribbert, Arch. Entwicklungs Mechan. 6, 537 (1898).
9. E. H. Schäfer, and B. Moor, J. Physiol. 19, 13.†
10. H. Teir, Acta path. et microbiol. scandinav. 32, 337 (1953).

* Original Russian pagination. See C. B. translation.

† No year given in original - Publisher.