

Denervation and Reinnervation of the Rat's Submaxillary Gland

It is well-known that section of the parasympathetic secretory nerves of salivary glands in cats and dogs causes a glandular atrophy and a supersensitivity to secretory agents¹. Further, the activity of the acetylcholine-synthetizing enzyme, choline acetyltransferase, decreases². In the present investigation the time course of events following parasympathetic denervation of the rat's submaxillary gland was studied by estimating the size of the gland, the sensitivity to sialagogue drugs and the activity of choline acetyltransferase from 1 day to 10 months after denervation.

Seventy female rats were used. A preganglionic parasympathetic denervation was achieved by section of the right chorda-lingual nerve using ether anaesthesia. The determinations on the submaxillary gland were done after 1, 2, 4, 8 and 16 days and each month up to 10. To study the sensitivity to secretory agents the rats were anaesthetized with chloralose (100 mg/kg) given i.v. after preliminary ether. The ducts of the submaxillary glands were cannulated on both sides using fine glass cannulae. A series of doses of the hydrochlorides of methacholine (0.02–2 μ g/kg) and adrenaline (0.1–2 μ g/kg) was given i.v. to determine the threshold doses. After the estimations the animals were killed and the submaxillary glands were carefully cleaned and weighed (wet weight). The activity of choline acetyltransferase was estimated according to a method described by HEBB³. The enzyme activity was calculated as μ g ACh/h/whole gland (total activity) and as μ g ACh/h/g acetone powder (concentration). All values of the denervated glands are expressed in % of those of the contralateral, normally innervated glands.

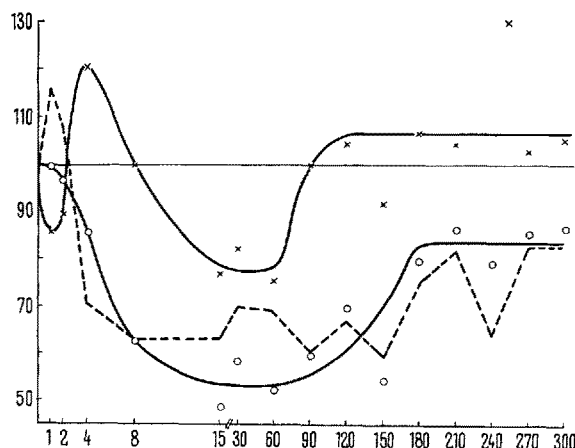
The weight of the denervated submaxillary gland was found to be increased by about 10% 1–2 days after denervation which agrees with previous findings³. From then on the usual denervation atrophy was obvious. Thus, the weight of the denervated gland was reduced to about 65% after 8 days. The size of the denervated glands was not further decreased, but after 5–6 months it was increased with time up to about 85% (Figure).

The sensitivity of the denervated glands to methacholine and adrenaline, noted as decrease in threshold dose, was slightly increased during the first days after denervation. The supersensitivity to secretory agents was most marked between 4 days and 1 month when the threshold dose of methacholine was decreased from about 0.5 to 0.1 μ g/kg and that of adrenaline from 1 to 0.2–0.5 μ g/kg. Later the supersensitivity was less marked though still after 10 months the denervated gland was slightly more sensitive than the contralateral one.

The total activity of choline acetyltransferase was found to decrease rapidly between 2 and 8 days after denervation. It was diminished to about 55% after 16 days. Between 2 and 6 months after denervation the total enzyme activity increased up to about 85%, later it was not further augmented. The enzyme concentration was first decreased and later increased during the first 4 days after denervation which is mainly due to opposite changes in the weight of the gland. Later the enzyme concentration was decreased to a level of about 80% which was reached 16 days after denervation. It was increased 2 months and later after denervation to about 100% (Figure).

Thus, it has been found that already during the first days after section of the parasympathetic secretory nerve to the rat's submaxillary gland a supersensitivity to secretory agents develops and the activity of choline

acetyltransferase starts to decrease. Later, e.g. 4 days after the operation, a glandular atrophy becomes obvious. The first sign of reinnervation of the gland is a less marked supersensitivity to sialagogue drugs which can be seen after about 2 months. At about the same time the activity of choline acetyltransferase starts to increase. On the other hand, the size of the glands increases much later, after about 6 months. In accordance with previous findings on other autonomically innervated organs⁴ it should be noted that the reinnervation of the rat's submaxillary gland after nerve section is not complete since the weight of the glands and the total activity of choline acetyltransferase does not return to 100%. In cats a complete reinnervation of the submaxillary gland has been noted after nerve crushing⁵.



The activity of choline acetyltransferase and the weight of the rat's submaxillary gland after preganglionic parasympathetic denervation. The enzyme activity and the weight of the denervated gland is expressed as a percentage of that of the contralateral gland. Abscissa: days after denervation; ordinate: % o—o total enzyme activity; x—x enzyme concentration; broken line indicates gland weight; each point represents the mean of 4–5 rats.

Zusammenfassung. Parasympathische chirurgische Denervierung der Submaxillarisdrüse der Ratte führt zu einer Sensibilisierung der Effektorzellen, einer reduzierten Gesamtaktivität der Cholin-Acetyltransferase innerhalb von 1–2 Tagen und zu einer Gewichtsabnahme der Drüsen innerhalb von 4 Tagen. Das erste Zeichen einer Reinnervation ist eine verminderte Sensibilisierung und eine gesteigerte Enzymaktivität nach etwa 2 Monaten; das Gewicht der denervierten Drüsen nimmt nach 5 Monaten zu. Die Reinnervation ist nach 10 Monaten noch nicht vollständig.

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¹ A. S. V. BURGEN and N. G. EMMELIN, *Physiology of the Salivary Glands* (Edward Arnold Ltd., 1961).

² I. NORDENFELT, *Q. Jl exp. Physiol.* 48, 67 (1963).

³ P. OHLIN and C. PEREC, *Q. Jl exp. Physiol.* 57, 196 (1966).

⁴ L. L. GUTH, *Physiol. Rev.* 36, 441 (1956).

⁵ I. NORDENFELT and C. PEREC, *Q. Jl exp. Physiol.* 52, 139 (1967).