Changes in Serum Proteins due to Lesion or Resection of the Olfactory Bulbs of the Rat

The effects produced by lesion, excision or stimulation of the olfactory bulbs on various functions in different animals have been studied assiduously during the last few years, particular interest being placed on the sexual function[1-7]. Papers have also been published on the influences of the above-named operations on water metabolism[8], sleeping habits[9], body growth and weight of organs[10], as well as in relation to the presence of osmosensitive elements in the olfactory bulbs[11,12].

The present work deals with the modifications which we have found in the serum proteins of rats with lesioned or excised olfactory bulbs.

Material and methods. 118 white rats of both sexes were used, weighing from 160–220 g each, bred in our institute on balanced food with a sufficient supply of proteins (minimum 17.5%).

The concentration of total serum proteins was determined by the biuret method, electrophoresis being used for that of the different subfractions. Tail sectioning provided the blood which was left to clot before isolating the serum by centrifugation.

The female subjects were divided into 2 main groups. The first (75 animals) was subdivided into 6 lots according to the following characteristics: a) bilateral lesion of olfactory bulbs; b) bilateral excision of olfactory bulbs; c) trepanation of skull; d) section of olfactory nerves; e) lesion in cerebral cortex, and f) unilateral excision of olfactory bulbs. Serum protein determinations were made in all these subjects 15 days before and 25 days after surgical intervention.

The second group (18 animals) was subdivided into 2 lots: a) normal intact animals used as controls (11 subjects), and b) bilateral excision of olfactory bulbs (7 subjects). Both lots were subjected to weekly serum protein determinations for 56 days, the control subjects being used to eliminate any possibility that the changes in serum proteins might be due to the repeated hemorrhages.

A group of 25 male rats was subdivided into 2 lots with a) trepanation of skull (10 subjects) and b) excision of both olfactory bulbs (15 subjects). The serum proteins were determined in both lots 15 days before and 25 days after surgery.

All the operations were performed under ether anesthesia. A modification of the WHITTEN method[7] was used to excise the olfactory bulbs. Any animal presenting signs of post-operative infection was discarded. A macroscopic analysis of the surgical lesions of randomly selected subjects was made with the aid of a magnifying glass.

A hematocrit determination and weight control were also carried out in intact female rats as well as in those deprived of olfactory bulbs in order to investigate whether the serum protein changes could have been caused by hemodilution or by variations in the nutritional state of the subjects. The analysis of variance[13] and the Student's t-test were used to effect a statistical study.

Results. Table I shows the values of pre- and post-operative serum protein concentrations (25 days after surgery) in the 6 lots of animals corresponding to the first group of female subjects.

A study of the pre-operative values in these lots by the variance analysis indicated that no significant differences existed in any of the fractions under study. On the other hand, a comparison of lots a) and bilateral lesion and bilateral excision of the bulbs b) with the 4 lots showed significant post-operative decreases in total proteins ($P < 0.001$), albumin ($P < 0.001$), α-globulin ($P < 0.05$) and β-globulin ($P < 0.01$), while the same comparison showed no differences in γ-globulin.

[1] H. M. BRUCE and D. M. V. PARROTT, Science *131*, 1526 (1960).
[2] R. DAVID, G. THIERY, M. BONVALLET and P. DELL, C. r. Séanc. Soc. Biol. *146*, 670 (1952).
[3] B. T. DONOVAN and P. C. KOPRIVA, Endocrinology *77*, 213 (1965).
[4] H. FRANCK, C. r. Séanc. Soc. Biol. *160*, 863 (1966).
[5] L. HEMER and K. LARSSON, Physiol. Behav. *2*, 207 (1967).
[6] CH. H. SAWYER, Am. J. Physiol. *180*, 37 (1955).
[7] W. K. WHITTEN, J. Endocrin. *14*, 160 (1956).
[8] V. NOVAKOVA and H. DLOUHA, Nature, Lond. *186*, 638 (1960)
[9] O. L. VACAREZZA and J. M. AFFANNI, Rvta. Soc. argent. Biol. *42*, 106 (1966).
[10] S. GIAMMANCO, V. LA GRUTTA, V. TESSITORE and C. DI BERNARDO, Boll. Soc. ital. Biol. sper. *44*, 1802 (1968).
[11] H. FERREYRA MOYANO and CH. M. BROOKS, Fedn. Proc. Fedn. Am. Soc. exp. Biol. *27*, 320 (1968).
[12] J. W. SUNDSTEN and CH. H. SAWYER, Proc. Soc. exp. Biol. Med. *101*, 524 (1959).
[13] H. C. BATSON, *An Introduction to Statistics in the Medical Sciences* (Burgess Publishing Co., Minneapolis, Minnesota 1956).

Table I. Effects of lesion and excision of the olfactory bulbs, skull trepanation, olfactory nerve section and cortical lesion on serum proteins

	No. of animals	Total proteins	Albumin	Globulins alpha	beta	gamma
Bilateral section of olfactory bulbs	8	(5.94 ± 0.14)[a] 5.58 ± 0.15	(3.13 ± 0.13) 2.94 ± 0.11	(0.99 ± 0.06) 0.89 ± 0.05	(0.79 ± 0.09) 0.72 ± 0.06	(1.04 ± 0.06) 1.02 ± 0.04
Bilateral excision of olfactory bulbs	24	(5.93 ± 0.19) 5.54 ± 0.24	(3.18 ± 0.13) 2.95 ± 0.14	(0.96 ± 0.06) 0.87 ± 0.06	(0.75 ± 0.08) 0.67 ± 0.08	(1.05 ± 0.06) 1.06 ± 0.08
Skull trespanation	12	(5.88 ± 0.12) 5.81 ± 0.19	(3.14 ± 0.10) 3.12 ± 0.11	(0.95 ± 0.03) 0.93 ± 0.03	(0.76 ± 0.09) 0.74 ± 0.09	(1.03 ± 0.05) 1.02 ± 0.07
Olfactory nerve section	11	(5.88 ± 0.23) 5.85 ± 0.29	(3.13 ± 0.13) 3.12 ± 0.12	(0.94 ± 0.09) 0.94 ± 0.10	(0.75 ± 0.09) 0.74 ± 0.10	(1.06 ± 0.08) 1.05 ± 0.07
Cerebral cortex lesion	10	(5.93 ± 0.14) 5.93 ± 0.19	(3.20 ± 0.12) 3.19 ± 0.11	(0.96 ± 0.05) 0.97 ± 0.07	(0.72 ± 0.06) 0.71 ± 0.06	(1.06 ± 0.06) 1.05 ± 0.08
Unilateral excision of bulbs	10	(5.82 ± 0.30) 5.78 ± 0.35	(3.12 ± 0.19) 3.11 ± 0.17	(0.92 ± 0.21) 0.91 ± 0.08	(0.76 ± 0.22) 0.73 ± 0.26	(1.04 ± 0.10) 1.04 ± 0.06

[a] Mean ± S.D. values are expressed in g/100 ml of serum. In every group the values in parentheses refer to preoperative values.

Table II. Evolution of total serum proteins and fractions in normal rats and in those deprived of olfactory bulbs

Days	7	14	21	28	35	42	49	56
Total proteins	(99.7 ± 0.32) 98.5 ± 0.32 $P < 0.02$	(98.4 ± 0.28) 97.0 ± 0.48 $P < 0.05$	(98.0 ± 0.26) 94.2 ± 0.59 $P < 0.001$	(97.2 ± 0.40) 90.4 ± 1.06 $P < 0.001$	(97.3 ± 0.36) 90.7 ± 0.71 $P < 0.001$	(96.6 ± 0.38) 90.9 ± 0.53 $P < 0.001$	(95.9 ± 0.37) 91.9 ± 0.91 $P < 0.001$	(95.3 ± 0.45) 92.3 ± 0.79 $P < 0.01$
Albumin	(99.5 ± 0.28) 99.3 ± 0.55	(99.0 ± 0.34) 98.8 ± 0.25	(98.8 ± 0.28) 95.2 ± 0.53 $P < 0.001$	(98.7 ± 0.36) 92.3 ± 1.24 $P < 0.001$	(98.3 ± 0.36) 92.3 ± 1.27 $P < 0.001$	(97.6 ± 0.40) 92.5 ± 1.15 $P < 0.001$	(97.4 ± 0.45) 94.1 ± 2.16	(97.0 ± 0.51) 95.7 ± 1.89
alpha	(98.8 ± 0.77) 98.2 ± 0.65	(96.3 ± 0.87) 93.9 ± 2.24	(96.7 ± 0.90) 89.8 ± 2.74 $P < 0.05$	(95.8 ± 0.86) 83.9 ± 1.43 $P < 0.001$	(95.9 ± 0.79) 84.4 ± 1.45 $P < 0.001$	(94.0 ± 0.87) 85.5 ± 1.90 $P < 0.001$	(92.9 ± 1.03) 84.2 ± 1.37 $P < 0.001$	(93.3 ± 1.30) 83.9 ± 0.95 $P < 0.001$
beta	(99.9 ± 1.41) 97.3 ± 0.75	(96.2 ± 0.96) 93.7 ± 2.25	(95.4 ± 0.83) 87.3 ± 1.58 $P < 0.001$	(95.9 ± 1.36) 84.1 ± 2.34 $P < 0.001$	(97.5 ± 2.18) 86.8 ± 2.49 $P < 0.01$	(97.4 ± 2.02) 87.0 ± 2.93 $P < 0.01$	(96.0 ± 2.47) 88.6 ± 3.49	(94.4 ± 1.69) 90.0 ± 3.48
gamma	(100.1 ± 1.09) 97.9 ± 0.53	(99.0 ± 1.14) 96.6 ± 1.27	(96.6 ± 1.06) 97.2 ± 1.46	(96.3 ± 1.22) 96.4 ± 0.85	(96.1 ± 0.82) 94.0 ± 1.51	(95.7 ± 0.79) 93.9 ± 1.46	(94.9 ± 1.16) 94.4 ± 1.13	(95.1 ± 1.23) 93.3 ± 1.48

Values represent % changes from their initial levels. Mean ± S.E.M.; the figures in parentheses refer to the values observed in normal rats (controls). The *t*-test was used to compare control and problem values. *P* is indicated when the differences were significant.

Table III

Days	Variations in body weight (%)	
	Normal	Deprived of olfactory bulbs
7	103.3 ± 1.09	100.5 ± 1.89
14	104.8 ± 1.78	101.0 ± 1.18
21	105.8 ± 1.51	105.7 ± 1.49
28	110.4 ± 1.23	109.3 ± 2.30

Mean ± S.E.M. of the weight expressed in % of change from the initial weight.

A comparison of serum protein levels in subjects with bilateral section of the bulbs (lot a) and others with bilateral excision of the same organ (lot b) showed no significative post-operative differences in any of the fractions studied. Nor were any differences observed in the other 4 groups under study (lots c, d, e and f).

The 2 lots of male subjects showed no differences in the pre-operative results, while the post-operative values were similar to those obtained in the females: total proteins ($P < 0.01$), albumin ($P < 0.01$), α-globulin ($P < 0.01$), β-globulin ($P < 0.05$) and again no differences in γ-globulin.

Table II shows the weekly variations in serum proteins and their fractions in 2 lots of animals, one a control group and the other deprived of olfactory bulbs. The latter showed a marked fall in albumin and α- and β-globulin compared with those of the controls, evidenced 21 days after surgical intervention. The albumin and β-globulin showed a tendency to return to normal control levels, presenting no significant differences from the 49th day on. The α-globulin, however, maintained its difference throughout the whole period of observation (56 days).

The total proteins showed a significant decrease after the 7th day and continued so to the very end (56 days), whereas the γ-globulin remained similar to that of the controls at all times.

On the 25th day after surgery, the hematocrit of a lot of 7 rats deprived of olfactory bulbs was compared with that of 8 intact subjects, no differences being observed between them (mean ± S.E.M.: operated animals 41.6 ± 1.13; controls 41.8 ± 0.74).

The results of Table III indicate that there were no variations in weight between intact subjects and those without olfactory bulbs.

Discussion. The changes observed in serum proteins were present only when the lesion or excision of the bulbs was bilateral. The lack of variations in the 4 control groups indicates that these changes were not caused by a lack of olfactory stimulation, nor by surgical manipulation, nor even by a non-specific effect through impairment of the nervous system.

The normality of the hematocrit and the results of Table III reject hemodilution and weight variations as possible causes of the changes. Certain operative injuries[14] can decrease the albumin, although temporarily, since it is normal within 15 days, which allows us to discard operative injury as a cause of the phenomenon.

TESSITORE et al.[15] found that bilateral excision of the olfactory bulbs is followed by histomorphological and functional modifications of the hypothalamic-hypophysial system. This gives rise to the query whether the effect obtained could have been due to repercussions from the excision of the olfactory bulbs on other parts of the nervous system.

Resumen. La sección y extirpación bilateral de los bulbos olfactorios, en ratas de ambos sexos, producen disminución de las proteínas séricas totales, albumina y globulinas α y β, sin modificaciones de la globulina γ. Esa disminución se hace significativa 21 días después de las operaciones.

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[14] O. W. NEUHAUS, H. F. BALEGNO and A. M. CHANDLER, Proc. Soc. exp. Biol. Med. *107*, 960 (1961).

[15] V. TESSITORE, S. GIAMMANCO and V. LA GRUTTA, Boll. Soc. ital. Biol. sper. *44*, 1804 (1968).