Neurohistological Study of the Development of Experimental Epileptogenic Cortical Cobalt-Gelatine Foci in Rats and their Correlation with the Onset of Epileptic Electrical Activity

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Summary. In 77 adult male rats a standard cortical epileptic focus was produced by means of a cobalt-gelatine rod. In 22 male rats the brain cortex was injured by a rod of standard size in which the cobalt powder was substituted by glass powder. The animals were examined electrophysiologically after 2, 4, 6, 8, 10, 14, 21 days, thereafter killed and examined neurohistologically. In animals with the cobalt-gelatine rod there developed on the 6th day an obvious epileptic pathological electrophysiological activity both in the area of the experimental region (primary focus) and on the contralateral side (mirror focus). In animals with the glass-gelatine rod no epileptic pathological electrophysiological activity could be proved. Neurohistologically the cobalt-gelatine focus was characterized by three zones: 1. the zone showing coagulation necrosis; 2. the zone characterized by oedema until the 6th day after operation, later by a glio-mesenchymal, pio-cerebral scar; 3. the transitory zone where the ganglion cells show vacuolization, tigrolysis, “acute” and “severe” changes and dissipation at all time intervals examined after operation; from the 14th day insular changes could also be observed. In correlating the morphological with the neurophysiological dynamics coincidence was found between the time of the occurrence of the glio-mesenchymal, pico-cerebral scar and the onset of the pathological electrical epileptiform activity.


Key-Words: Experimental Epilepsy—Cortical Cobalt-Gelatine Focus—Glass-Gelatine Rod—Neurophysiological—Neuropathological Correlations.

A standard epileptogenic focus in the rat’s brain was produced by means of a cobalt-gelatine rod introduced into the brain tissue according to our method described in one of our previous papers (FISCHER et al., 1967). This method was chosen because it enables one to follow satisfactorily the development of both the morphological and the electrophysiological features of the cortical focus in the rat.
The development of the epileptic activity is subacute and also the morphological focus develops gradually, so that its study presents no special difficulties. Since the results are standard, this technique also enables the correlation of the morphological and functional findings. Such correlation is the purpose of our present study.

**Material and Methods**

99 male rats of our own breeding (weight about 200 g) were used for the experiment, of which 22 served as controls. In both groups (77 experimental animals and 22 control animals) the skull was opened under chloralose anaesthesia and sterile conditions, over the left hemisphere immediately anterior to the coronary suture. The trepanation hole was 4 mm in diameter. The exposed dura mater was gently torn in the middle and a cobalt-gelatine rod of size 0.75 x 0.75 x 1.5 mm was introduced into the cortex. The preparation of the rod was described in another paper (Fischer et al., 1967). The trephine hole was then covered by a plastic disc of corresponding size. In the control group the cobalt-gelatine rod was replaced by a glass-gelatine rod, prepared by simply using glass powder instead of cobalt powder. Animals of both groups were then examined electrophysiologically 2, 4, 6, 8, 10, 14 and 21 days after operation.

After the electroencephalogram has been recorded the animals were killed and the brains were examined neurohistologically. The same procedure was always used for the electrophysiologically examination: the animals was anaesthetized by ether, respiration was kept up by means of the intratracheal tube with the aid of an air pump, 2 mg/kg tubocurarin was administered intraperitoneally. The external soft tissues were then removed from the calvaria and the cortical surface was exposed. 35–45 minutes after introduction of the artificial respiration the electroencephalogram was recorded simultaneously from two points in the head: one point just behind the lesion (primary focus), the other point on the symmetrical site of the undamaged hemisphere (mirror focus). Cotton wick electrodes and a double-beam cathod ray oscillograph were used.

The animals were then killed by decapitation, their brains were carefully removed and fixed in neutral formalin or in Hortega-formalin. The injured areas were examined in serial sections stained according to Nissl, by the ordinary haematoxylin-eosin method, and by special techniques after Bodian, Malík, Globus, Penfield, Hortega and Cajal; some were stained for lipids and myelin sheaths.

**Results**

I. Neurohistological Examination

a) Cobalt-Gelatine Animals

2 days after operation the pia mater just above the lesion is only partially preserved. Laterally from the site of puncture the red blood cells are partly dissipated, partly well preserved. Histiocytic cells are activated; occasionally we find inflammatory round cells, occasionally leucocytes. Toward the periphery the findings in the leptomeninges are normal. In the cerebral tissue we find the rod mass (Fig. 1) characterized by clustered cobalt powder granules; between these clumps we see a gelatine network, in which there are scattered free islets, sometimes filled with red blood corpuscles. The rod is surrounded by a very narrow rim of crusted tissue still containing undamaged red blood corpuscles. From the rod toward periphery we observe three zones. In the first zone, about 1 mm thick, the tissue is necrotic. The second zone (about 1/4–1/2 mm thick) is the zone of severe oedema. This zone is surrounded by the third zone (approx. 1 mm thick). We call this third zone the transitory zone. Here the oedema is not so marked and the findings gradually become normal toward the periphery. Under a high-power objective, the first zone is characterized by the disappearance of the ganglion cells. Those, which can still be seen, show coagulation necrosis.