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F. LEMBECK

ASPECTS CONCERNING THE OCCURRENCE AND DISTRIBUTION OF SUBSTANCE P IN THE BRAIN

With regard to the occurrence of SP in the brain the following questions are of interest:

(a) Which cells of the brain contain SP?

(b) Which part of the cell contains SP?

(c) At what time of the embryonic development does SP already occur in the brain or in the intestine?

(a) Since about 90 per cent of the cerebral tissue consists of glia, it is impossible to say whether a substance found in a brain extract originates from nervous or glia cells. We tried to approach this question by determining the SP activity in brain tumors (Grabner and Lembeck, 1960). These tumors either consist of entirely immature, that is, undifferentiated nervous tissue or they develop from the glia at any stage of its development; the critical point, however, is that they never arise from mature nerve cells. A total of 20 brain tumors of different origin were extracted, but none of the extracts contained measurable amounts of SP when tested on the isolated guinea pig ileum under atropine and neoantergan. Two of the extracts were active in producing slow and highly atypical contractions which were not regarded as being due to SP. Since our material included samples from all the classes of the commonly occuring brain tumors we would like to conclude from these results that SP does not occur in the glia and, therefore, must come from nervous tissue. There is, however, one possibility to restrict our conclusion: all tumor tissue is, to a variable degree, immature and possibly could not have the same synthetic power to produce all the substances that occur in normal tissue. Some additional support for the location of SP in nervous elements is derived from the finding that the retina which is relatively poor in glia cells contains high amounts of SP (Dunér, Euler and Pernow, 1954). Further, there is an increase of SP in the proximal, and a decrease in the distal part after some days in a severed nerve (Andrews and Holton, 1958).

(b) Differential centrifugation of brain homogenates showed that the highest amount of SP is located in the »mitochondrial fraction« (Lembeck and Holasek, 1960; Zetler, 1961). This observation has been

extended by Gaddum (1961), who separated the mitochondrial fraction over sucrose layers and found the highest amount of SP in a granular fraction different from the mitochondria.

(c) The occurrence of SP during embryonic development was studied in collaboration with Dr. Petschke. We found, that in the brain stem of bovine fetus, SP occurs already at an early stage of development. In a brain weighing only 1.1 g which was therefore not separated into brain stem and fore brain already 21.5 U./g SP have been found. The brain stem at any time of the development already contained amounts of 21.5—65.6 U./g which are comparable to those found in the developed bovine brain. On the other hand, the fore brain was almost free of measurable amounts of SP during the whole period of embryonic development. The gut contained increasing amounts of SP during the second half of the embryonic development. It is tempting to correlate these results with respect to function: the brain stem gains its function quite early in the fetal life and is active during the development of the embryo. Concomitantly SP occurs early in that part of the brain. The cortex, on the other hand, which remains immature and quiet up to birth and some time thereafter is practically free of SP during this period. This correlation points toward the possibility of a physiological function of SP for the activity of the central nervous system.

Summary

Investigations on brain tumors indicate that SP is located in nervous elements and not in the glia.

The intracellular localisation of SP is highest in a granular fraction of brain homogenates.

During embryonic development SP was found already very early in the brain stem, in the cortex however not before birth.

POGLEDI NA PRISUTNOST I DISTRIBUCIJU SP U MOZGU

Istraživanja u vezi s moždanim tumorima pokazuju da se SP nalazi u nervnim elementima, a ne u gliji.

Intracelularna lokalizacija SP je najveća u granularnoj frakciji moždanih homogenata.

U toku embrionalnog razvoja SP se već vrlo rano nalazi u moždanom deblu; u kori se, međutim, ne pojavljuje prije poroda.

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