THE FUNCTIONAL SIGNIFICANCE OF THE INNERVATION OF THE HUMAN UMBILICAL CORD

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The gelatinous tissue of the human umbilical cord is not only important to the fulfillment of the supporting-mechanical function. There are reports in the literature indicating that there are biologically active substances present in Wharton's jelly.

K. Ko [11] noticed that the biological action of the extract from the umbilical cord differed from the action of placental extracts. According to E. O. Ryabushko and M. M. Kholodenko [9], umbilicaline (the extract from the umbilical cord) in dilutions of 1:100-1:500 causes some intensification and frequency increase in the action of an isolated frog heart. K. M. Voloshina [3] found a sympathicotropic action of umbigen (water-alcohol extract from dried blood extracted from the umbilical vessels) on the anuclearized eyes of frogs. When umbigen was administered parenterally to rabbits, an increase in the sugar content of the blood was observed. N. S. Kharenko and R. I. Sharlai [10] reported on the content of definite amounts of dehydroadrenalin and acetylcholine in umbigen.

The purpose of this work was to compare the data regarding the content of biologically active substances in Wharton's jelly with the results of morphological study, particularly with the data on the innervation of the human umbilical cord gelatinous tissue.

EXPERIMENTAL METHODS AND RESULTS

Neurological and histological studies in recent years [1, 2, 4, 5, 6, 8] have examined in detail the innervation of the proximal portion of the human umbilical cord.

Using a supravital stain of methylene blue according to A. S. Dogiel and silver impregnation according to Kampos, we established that the penetration depth of single nerve fibers into the mature umbilical cord consisted of 12-20 cm from the umbilical ring. In Wharton's jelly, small ligneous endings and many primitive terminal apparatuses shaped like small loops and plates were found. The ligneous endings with the terminal plates did not contact the fibroblasts of Wharton's jelly, whereas the endings of the more primitive structures could be distributed both along the intercellular interstices and in the cytoplasm of the fibroblasts.

The delicate structure of the fibers innervating Wharton's jelly was completely heterogeneous. They all were nonmyelinated, but one could distinguish four varieties of these fibers. The first variety of fibers was flat and had a distinguishable neurofibrillar structure and a medium amount of neuroplasm. The second sort of fiber were axons, rich in neuroplasm and having bulges. The third kind of fiber was characterized by the formation and splitting off of neuroplasm drops in varying sizes. In accord with N. D. Zaitsev [4], we treated this process as an unusual neurosecretion. Finally, the fourth variety of fibers were axons in a state of destruction similar to wallerian degeneration. The axons with the signs of neurosecretion and degeneration were especially interesting.

In neurosecretion, spheroid, neuroplasmic protuberances could form. From a separate axon, or from one entering the body of a trunk, a neuroplasmic protuberance of 20 microns or more in diameter was formed. At first, this protuberance was connected with the axon engendering it, then the neuroplasmic stalk was resorbed and the substance of the spheroid protuberance gradually formed into an argentophilic drop, situated in the intercellular substance of Wharton's jelly. Then the drop was gradually resorbed into the gelatinous tissue.

As well as the large neuroplasmic protuberances which formed, many small drops could split off from the axon also, subsequently being resorbed into the interstitial substance of the umbilical cord gelatinous tissue (Fig. 1).

Fig. 1. Innervation of the gelatinous tissue of a mature human umbilical cord. The terminal branches of the axons are seen. Neurosecretion. Many small drops of neuroplasm secreted. Silver nitrate impregnation according to Kampos. Magnification 99. Immersion.

Many of the nerve fibers were in a process of physiological destruction similar to wallerian degeneration.

The neurosecretion and destruction processes of the nerve fibers increased during the second half of uterine development. In connection with this, it is interesting to note that, in studying the histogenesis of the gelatinous tissue of the human umbilical cord, M. Ya. Levina [7] found secretory processes occurring in the fibroblasts, and also destructive changes in the sedentary cells of Wharton's jelly, and these were also most sharply expressed during the second half of embryogenesis.

Since there were no nerve fibers discovered in the space 18-20 cm from the umbilical ring, we provisionally divided the umbilical cord of the human embryo into an innervated zone and a zone with no apparent innervation. Based on morphological observations, one can suggest that there is also a physiological difference between the proximal and distal sections of the umbilical cord. To prove this hypothesis, we studied the effect of extracts from the two sections of the umbilical cord on an isolated frog heart.

For the experiments, we used only the nonvascular portions of the umbilical cord, since the umbilical cord vessels are connected with the placenta, the extracts of which contain acetylcholine. The umbilical cord was cut into small pieces with scissors, ground into a pulp in a porcelain mortar, inundated with Ringer's solution in an amount of nine times its weight, carefully blended and extracted over a period of several hours. The pulp was then pressed through cloth filters. We considered the extracts obtained to be 10% solutions.

The activity of the extracts was tested on a frog heart, isolated according to Shtraub. More than 500 extracts from 48 umbilical cords of mature human embryos were tested. Physiological testing of the extracts was carried out with the appropriate morphological control.

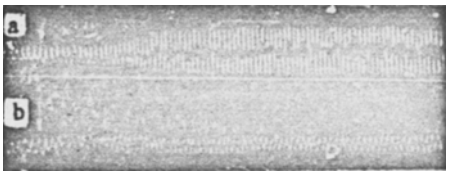

Fig. 2. Change in the action of an isolated frog heart during the action of the extract. a) extract from the proximal section of the umbilical cord; b) extract from the distal section. Dilution 1:100. The arrow shows the moment at which the extract was injected.

Figure 2, a, gives the recording of the action of the isolated frog heart exposed to the action of the extract from the proximal section of the umbilical cord. The kymogram shows the clear, positively inotropic effect. The rhythm of the heart action grew considerably faster. The extract took effect swiftly and the effect was observed in a series of experiments to last 10 minutes or longer (without washing by Ringer's solution). Thus, the use of the extract from the proximal portion of the umbilical cord caused an effect of a sympathomimetic character.

The extract from the distal portion of the same umbilical cord in the same dilution had only a slight effect on the isolated frog heart (Fig. 2, b).

The contraction amplitude even decreased slightly at first, and only afterwards returned to the initial level; the increase in the frequency of the cardiac contractions was considerably less than with the action of the extract from the proximal portion of the umbilical cord.

In some experiments, the extract from the distal potion of the umbilical cord caused only a gradual and very slight, as compared with the action of the extract from the proximal portion (Fig. 3, a), intensification of the cardiac contractions with a simultaneous slight frequency increase (Fig. 3, b).

Extracts from the middle portion of the umbilical cord caused a slighter adrenalin-like effect than extracts from the proximal portion, but a greater one than extracts from the distal portion. The rule was established for 1:100-1:5,000 dilutions of the extracts. Maximal efficiency of the extracts was observed with a dilution of from 1:100 to 1:200. Thus, the grade of sympathomimetic activity of the umbilical cord extracts decreased from the umbilical ring towards the placenta. Obviously, the problem is how the biologically active substances with the adrenalin-like action in the proximal section of the human umbilical cord are formed.

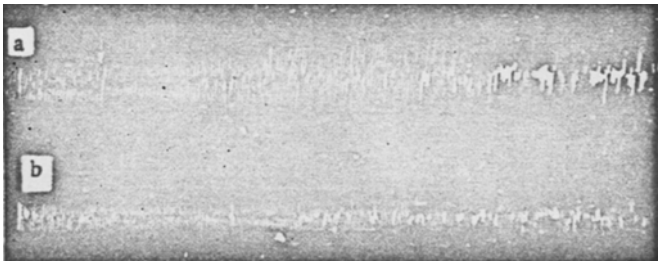

Fig. 3. Change in action of isolated frog heart due to the action of the extract.
a) extract from the proximal portion of the umbilical cord;
b) extract from the distal portion. Dilution 1:100. The arrow shows the moment at which the extract was injected.

In searching for the morphological expression of this formation process, we checked at the secretory-like phenomena – the formation of the neuroplasm drops which split off from the axons innervating Wharton's jelly, and the processes which M. Ya. Levina [7] described by which the gelatinous substance is formed.

In order to decide which of the above-mentioned morphological phenomena are most connected with the varying physiological action of the extracts from the different sections of the umbilical cord, we studied the question of the distribution of the secretion phenomena fibroblasts (according to M. Ya. Levina) in the proximal, middle and distal sections of the umbilical cord. No quantitative predominance of the secreting sedentary cells of Wharton's jelly in the proximal section, as compared with the distal, was found. When this fact is compared with the discovery of nerve fibers only in the first third of the umbilical cord, the hypothesis follows that the nerve fibers which innervate Wharton's jelly actively participate in the production of the biologically active substances with the adrenalin-like action.

It is possible that the formation of such substances is in some measure connected with the phenomena of mass drop-formation and destruction of the nerve fibers. Morphological data confirm this idea. In cases when a sharper sympathomimetic effect on the isolated frog heart was noted in the physiological experiments, silver impregnation showed a clearer expression of the neurosecretion and physiological nerve fiber destruction processes. Thus, it seems that the biological activity of the extracts from the proximal portion of the umbilical cord is also connected with the chromaffin paraganglia, which we recently discovered, localized in the region of the umbilical ring, along the path of the intra-abdominal part of the umbilical arteries and on the expanse of the first 5-6 cm of the umbilical cord. The problem of the paraganglia in the umbilical ring region will be treated in a special report.

Extracts prepared from the Wharton's jelly of the innervated portions of the umbilical cord show a positive chronotropic or inotropic action on the isolated frog heart. The extracts from the distal portions give a much weaker action. The descending morphological grade of umbilical innervation also corresponds to the descending sympathomimetic activity grade of the extracts from the different sections of the umbilical cord. A direct relation between the innervation of the umbilical cord and the biological activity of its extracts can be suggested.

SUMMARY

The morphological investigation of Wharton's jelly of the human umbilical cord led to the discovery of single nerve fibers in 12-20 cm from the umbilical ring. Many of the fibers which innervate the jelly tissue of the umbilical cord show signs of neurosecretion.

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