Effect of Transplantation of Embryonic Neural Tissue on the Dynamics of Brain Edema Following Experimental Craniocerebral Trauma

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INTRODUCTION

According to medical statistics, craniocerebral trauma (CCT) dominates among the traumatic damages causing disablement and death, especially among young and middle-aged population components. This is the reason for the great medical and social importance of investigations for new and improved approaches to treatment of acute CCT and its consequences. At present, CCT, regardless of its degree of its character and severity, is considered an integral pathological process, whose pathogenesis is to a great extent based on post-traumatic disturbance of metabolism in the damaged tissue [1].

Brain edema is one of the most dangerous complications following CCT [2]. According to modern concepts, two interconnected components should be distinguished in this process, the edema per se, i.e., the release of excessive water and electrolytes into the intercellular and perivascular medium, and swelling of cellular elements — a rise in the content of intracellular liquid. Both the edema per se and the swelling exert a significant (sometimes catastrophic) negative effect on numerous cellular functions, including functioning of the cell membrane channels [3].

It was shown in experimental studies and in clinical practice that such a clinical method as transplantation of embryonic neural tissue (ENT) can appear strongly effective if used to treat various types of pathology of the central nervous system, including damage to various brain structures [4-7], Parkinson's disease [8-11], diffuse brain impairments [12, 13], and infant cerebral paralysis [14]. Results confirming the possibility in principle of ENT transplantation into the damaged brain area were obtained. The positive influence of transplanted ENT on the recipient brain and functional integration of the transplant neurons and host brain were observed [15]. The possibility of positive influence of ENT transplants on metabolic processes, occurring...
both directly in the CCT area and in other, more remote recipient brain areas, was demonstrated [16]. Objective information about the degree of disturbance of the water-electrolyte equilibrium in the brain tissue following various pathological states, in particular CCT, can be obtained using the technique of impedancemetry [17].

The aim of our present study was to clarify the effect of ENT transplantation on the brain edema dynamics in the post-traumatic period following experimental heavy CCT.

METHODS

Three groups of female albino mongrel rats weighing 150 g were investigated (each group contained 35 animals). In group 1, the animals obtained dosed CCT without any subsequent interference. In group 2, the trauma was followed by surgical treatment of the damaged brain area. In group 3 animals, after trauma and surgical treatment of the damaged brain area with aspiration of smashed tissue, a block of ENT was grafted into the formed bed. Ten intact animals with the impedance measured in the left and right hemispheres were used as control. Clinical observations [1] showed that edema is most expressed from the 1st to the 7th day after the trauma and gradually decreased later. Taking this into account, the measurements were performed at the 1st, 3rd, 4th, 7th, 15th, 20th, and 30th post-traumatic days. In each of these periods, five animals were selected from each group, their impedance was measured, and then they were excluded from further experiment. This allowed us to avoid the errors caused by the long presence of electrodes in the tissue and their possible displacement relative to their initial position.

Heavy CCT was inflicted on the animals under standard conditions in the left parieto-temporal area using a graduated spring striker. The strength of a blow was calculated with the technique described earlier [18]. Surgical treatment of the damaged area included dissection of soft tissues, removal of small bone wreckage, formation of a trepanation orifice, removal of the intracranial hematoma, aspiration of the brain detritus, and hemostasis. After the operation had been performed, the bone fragment was put in its initial position, and soft tissues were sutured. We used for transplantation 1-2 mm² fragments of the sensorimotor cortex taken from 18-day-old rat embryos. The embryonic tissue was selected and picked up under standard conditions according to the technique described earlier [15].

The impedance was measured at the frequency of 10 kHz using an automated complex made in the Department of Experimental Neurosurgery KIRNS (Kiev Research Institute of Neurosurgery) and based on a high-precision AC bridge. The data were statistically treated. Errors of the measurements did not exceed 5%. Measuring electrodes were prepared from 0.2 mm nichrome wire; a 5-mm-long electrode had a 2-mm-long tip. Before measurements, the system was calibrated using 0.9% NaCl solution. A comparison electrode inserted subcutaneously was made from 1 mm platinum wire with a 25-mm-long working tip. The electrodes were sterilized in a formalin chamber and washed with the physiological solution before being used. Active electrodes were placed in the perifocal zone of the damaged brain area at the traumatized side and in the symmetrical site of the contralateral hemisphere. Surgical procedures were performed under i.p. anesthesia (sodium thiopental, 20 mg/kg).

RESULTS

The main results obtained in this study are illustrated in Fig. 1.

In intact animals, the mean impedance of the brain tissue was $1295.7 \pm 31.9$ Ω.

Let us consider in more detail the dynamics of impedance changes in the damaged hemisphere of all animal groups (Fig. 1). One day after the CCT, the impedance in this hemisphere of animals of the above three groups dropped by 30-37%, if compared with that in the intact group animals; the mean drop calculated for all groups was 34%. This result is indicative of a significant increase in the amount of intracellular liquid in the brain tissue, i.e., of the development of intensive edema. At the 3rd day, a rather sharp drop in the edema degree was observed in the animals of all groups: the impedance decreased, on the average, by 17%, if compared with that in the intact group. It should be emphasized that in this period the edema was expressed much less in the animals with surgical treatment of the damaged brain area than in the animals in which CCT was not followed by subsequent treatment. This allows us to suggest that post-traumatic surgical treatment is the most important factor promoting the edema involution at early stages of the post-traumatic period. Later on, edema in the brain tissue in animal groups 1 and 2 (with CCT only and with subsequent surgical treatment) decreased rather slowly, and the impedance exceeded 95% of the mean value for the intact group only by the 20th to 30th days. A noticeably different character of the edema involution was observed in group 3 (with ENT transplantation). By the 5th day, the impedance in this group differed from that in the intact group, on the average, by 12.1% (the difference in the group with surgical treatment was 14.0% only), while by the 7th day the impedance in group 3 reached 97.8% of the control one.