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EFFECTS OF TISSUE NEUROTRANSPLANTATION ON SCELETAL MUSCLE TONE RESTORATION AFTER EXPERIMENTAL MECHANICAL INJURY OF THE CEREBELLUM

ABSTRACT

This work aimed to conduct a comparative study of the restorative effects of transplantation of fetal neural tissue (*FNT*), olfactory bulb tissue (*OBT*) and fetal kidney (*FK*) on the dynamics of muscle hypotonia after cerebellar hemisphere injury in the adult rats. Beam walking test (*BWT*) allowed detect at least three degrees of hypotonia which correspond to 2, 3, and 4 points. The authors selected animals with function index (*FI*) by *BWT* scale strictly lesser than 4 points on the 3rd day after injury. Moderate hypotonia was associated with *FI* 3 points, severe – 2 points, and mild-4 points. Major differences in the dynamics of the restorative process across study groups were detected at the first month of study: slow recovery of statics and coordination (control); fast recovery (during first 9 days, *FK*, *OBT* and *FNT* groups) that underwent changes by its slow increase during 9th-33rd day. Mild hypotonia in the control group showed itself by the end of the 1st month and on the 9th day in the *FK*, *OBT* and *FNT* groups. Normotony was observed on the 21st (group *FNT*) and 30th day (groups *FK* and *OBT*). These data suggest that neurotransplantation has a significant effect on muscle tone improvement after cerebellar injury, depending on the type of graft.

KEYWORDS: experimental cerebellar trauma, cerebellar hypotonia, fetal neural tissue transplantation, olfactory bulb, neuronal networks.

The nervous system is undoubtedly one of the most complex forms of tissue organization that is apparently linked with the realization of its various complex functions. In view of the complexity of the functional structure, the consequences of nervous system damage cannot be considered like any other body systems lesions: «destruction of of part of system – decrease in its functional activity». More often the result of the neural system damage is the change its functions: lesser realisation of one function along with excessive expressiveness of another. The classic example of this is the formation of excessive unconscious activity in the locomotor system against reduced or normal conscious activity. This can be illustrated of the example of a central paresis and its extreme manifestation spasticity as well as hyperkineses, epileptic seizures, etc. Another manifestation of this aspect of the neural pathology is the formation of various types of neuropathic pain syndromes.

For long time spasticity syndrome was beyond the focus of the researchers. Now the situation has changed significantly and the study of pathophysiological mechanisms of this ubicvitous fundamental presentation of the nervous system diseases is at the centre of researchers' attention. Primarily this concerns spinal cord injuries where spasticity syndrome is diagnosed in 60-78 % of patients [1]. Deconstruction of a great part of descending effects on the motor neurons and formation of spasticity syndrome is the leading feature of the pathogenesis of many acute cerebrovascular diseases (35% of cases), multiple sclerosis (85% of cases) and most forms of cerebral palsy [2-4].

In general, non-lethal lesions of the nervous system are the factor which determines its plastic reorganization and structure optimization in view of recovery of lost functions. The basic mechanism of such process is the plasticity of neuronal networks, the molecular mechanisms of which have been actively studied in recent time. Despite the possibility of plastic reconstruction of neuronal network of the survived part of nervous system, we find this mechanism very limited, leading in many cases to the formation of a stable pathological topology of neuronal networks – a substrate of the spasticity. Changes occur at proteome, transcriptome and, possibly, genome levels in the survived neurons [5].

Thus, formation of spasticity syndrome on spinal cord injury model incorporates persistent changes of the receptor apparatus of the motor neurons below injury, specifically glutamate, serotonin and noradrenaline receptors. In the two latter cases new types of receptors possess ability to auto activation of G-protein without binding with neurotransmitter [6-8]. One should not exclude a possibility of alteration of mediator type

interneurons, raise of the activity of the existing serotonergic interneurons or the appearance of new serotonin-synthesizing cells, leading ultimately to an increased serotonin production in the denervated segments of the spinal cord tissue. Such mechanism of spasticity syndrome development in spinal cord traumas and other kinds of pathology of the descending projective neurons plays a key role [8, 9].

Under physiological conditions, the sensitivity of motor neurons to serotonin released by synaptic endings of many descending fibers, determines the basic membrane depolarization without which none of other inputs to motor neurons can cause its stimulation and activation of contraction of the respective muscle fibers [10]. Sudden switching-off of such mechanism whereby excitability of motor neurons is maintained in spinal cord injury, according to most researchers, is the leading cause of spinal shock, while the deficient compensation in many cases leads to the formation of unregulated constant excessive stimulation of the motor neurons, an electrophysiological substrate of spasticity [10].

Nowadays most researches have been engaged in the study of the consequences of rapid exclusions of many descending serotonin- or noradrenergic projections to motor neurons. However, partial exclusion or decrease of activity of the serotonin and noradrenergic projections remains unclear. Such pathological conditions must be characterized by the presence of hypotonia syndrome. An example of the above is the cerebellum injury and ataxia formation, a component which is the hypotonia. The mechanisms of cerebellar hypotonia and its possible association with the emergence of hypermetria and the dynamic of muscle tone changes at cerebellum trauma are still to be elucidated. Surely, there several suggestions relative to possible link between cerebellum neurons and serotonin- and adrenergic neurons of the brain stem [11].

Every year about 10 million cases of head injury (HI) are registered in the world, cerebellar lesions are observed in 0.8% of them [12-15]. More often cerebellum injuries in HI are indirect, secondary and delayed [16-19]. At primary cerebellum injury and specifically at acute period one can detect the hypotonia, ataxia, dysmetria, cerebellar tremor, adiadochokinesis and vertigo [20].

Histopathologically, direct cerebellum injuries reflect the well-known processes of trauma development in the central nervous system (*CNS*) [21-23]. They are supplemented with specific dynamics of the neuronal death in the cerebellum, eg. Purkinje cells [24]. At the early period of cerebellar injury the neurons die due to direct mechanical damage, ischemia, non-specific inflammation, etc. A gradual diffuse elimination of cerebellar neurons, especially in the perifocal zone, occurs against lesion focus sanitation, remission of autoimmune neurodegenerative process, as well as manifestations of traumatic focus organization.

Neurodegenerative process in the cerebellum at injuring other parts of the brain is not detected in all *HI* cases. It is usually initiated during the first days after injury and lasts for 1 month. In this case diffuse neuronal death in the cerebellar cortex is detected with astrogliosis of granular and molecular layer. The degree of its manifestation correlates with *HI* severity [25-28]. The most likely reason for this type of degeneration of Purkinje cells is excitotoxicity, influence of activated microglia mediated via mechanical action of a traumatic factor [26, 27, 29, 30]. One of the reasons for degeneration of Purkinje cells in different types of *HI* is proposed to be the aksonotomy – a powerful pro-apoptotic factor [17, 31, 32]. However, many authors have doubts relative this hypothesis, since there are considerable evidences pointing to exceptional stability of the Purkinje cells in this type of lesion, having in mind low expression of their intracellular axons growth factor *GAP-43* (growth-associated protein 43) [16, 26, 27, 33, 34]. The genes triggering a cascade of neuron transformations after aksonotomy are activated only in the isolated Purkinje cells located near the lesion focus [35, 36]. This fact indicates the low Purkinje cells' ability to restore axons fully. After aksonotomy of this kind of the neurons, some regenerative changes are not seen for several weeks. Later there is an observation of a wide branching (sprouting) of the proximal stump of the damaged axons going on with the formation of a large number of thin terminals going back to the cerebellar cortex, which form heterotopic synapses with dendrites of granule cells [33].

Currently, there are few data about the effectiveness of restorative treatment of cerebellar lesions [25, 36, 37]. Tissue transplantation of the olfactory bulb from adult organism is believed to be a promising method of functional recovery of the *CNS* in clinic [38]. However, transplantation of fetal neural tissue has been more thoroughly studied [39-41]. When using each of the above methods, a positive functional effect has been achieved mainly by stimulating endogenous regenerative processes. The impact of neural transplantation on the formation of hypotonia has yet to be studied. Hence it was interesting for us to explore this aspect and several other topics relative tissue neuro- transplantation and neural function recovery.

MATERIALS AND METHODS

In our experiments we used adult female rats, 5.5 months old, weight 250-300 g, taken from the vivarium of A. P. Romodanov Institute of Neurosurgery NAMS of Ukraine. All manipulations were performed according to the bioethics principles. We formed 6 groups: 1) a group of «control-1» (*C-1*), in which animals were exposed to local dosed injury of left cerebellar hemisphere of medium severity (n = 30); 2) a group of «control 2» (*C-2*), which were exposed to a repeated mechanical removing of the necrotic masses (n = 21) on 7th day after applying local dosed injury of left cerebellar hemisphere 3) The *FNT* group, which on 7th day after applying a local dosed injury of left cerebellar hemisphere underwent a repeated surgery with mechanical cleansing of a cerebellum contusion seat by necrotic masses removing, and immediate transplantation into formed defect a fragment of allogeneic fetal neural tissue, 18 days of gestation (n = 20); 4) The *OBT* group, in which the animals on 7th day after applying a local dosed injury of left cerebellar hemisphere underwent a repeated cleaning surgery and immediate transplantation into formed cerebellar hemisphere tissue defect a fragment of allogeneic tissue of olfactory bulb (n = 21); 5) The *FK* group, in which the animals on 7th day after applying a local dosed injury of left cerebellar hemisphere underwent a repeated surgery with mechanical cleaning, and immediate transplantation into formed cerebellar hemisphere tissue defect a fragment of allogeneic tissue of fetal kidney (n = 20); 6) a group of intact animals (n = 13).

Surgical procedure was performed under general anesthesia administered by intraperitoneal injection of 15 mg/kg xylazine (*«Sedazin»*, *Biowet*, Poland) at the rate and 70 mg/kg ketamine (*«Calypsol»*, *A. Gedeon Richter*, Hungary). After removing the wool on the head and hindhead and skin desinfection with 5% iodine solution a longitudinal skin incision was performed on the external occipital crest, 3-4 mm to the left of the midline. Occipital and the left parietal bones were skeletonized. Trephine opening was performed on occipital bone scales, 3 mm from the left branch of lambdoid suture and 5-7 mm from the midline. The hole was expanded to the size of 5 mm; the dura mater was left intact. The animal was fixed abdomen down; the head was fixed with flat side clips. A device for injury modeling included a spring striker and a metal plate with registering tensoelectric elements, to which a rod with variable length, 3 mm in diameter, was perpendicularly [42]. The end of the rod was injected into trephine opening close to the dura mater. The plate was rigidly fixed on the object table with additional clips. Spring striker was fixed on the plate, and its striking pin led up to the projection of striking pin mount point on the opposite surface of the plate. Beat of a striker with strength 81.79 H passed through the rod to the dura mater and brain tissue. Simultaneously there happened a deformation of the plate with tensoelectric elements that was recorded using analog-to-digital converter in the form of tenso-graphic curve.

After modeling an injury, hemostasis and skin suturing were performed in aseptic condition. The animals were kept at ambient temperature of 30-33°C for 2-4 h, further in special cages for 3-6 mice each with an average temperature of 21-24 °C, under conditions of constant room ventilation.

Repeated surgery in *C-2*, *FNT*, *OBT* and *FK* groups was conducted on 7th day of the experiment. A cerebellum contusion zone was purified with necrotic masses removing. Transplantation of tissue fragments was performed in a bed formed in such way (*FNT*, *OBT* and *FK* groups). Olfactory bulb tissue was received from outbred line of white adult female rats 5.5 months old immediately, after killing them with an overdose of the drugs. In sterile conditions the material was purified from vessels and minced to pieces of 2×3 mm. Allogeneic fetal nervous tissue and fetal kidney tissue were obtained on 18th day of gestation, minced to pieces of 2×3 mm, which was kept in saline at 37 °C before transplantation.

State estimate of statics and coordinating of experimental animals was performed by beam walking test (*BWT*), according to the 7-point scale [43], which allows determine accurately the level of statics and coordinating function **(Table 1)**. The test was performed using the beam width of 2 cm and a length of 122 cm, set at an angle of 18 °C towards the movement. At the end of the beam a closed illuminated chamber with food was mounted. *BWT* was recorded with an analog camcorder *SONY CCD-TRV408E* (*Sony Co*., Japan). Before the experiment for 2 weeks the animals were being trained to fulfill the test properly. The animals, which after training course performed *BWT* with mistakes, were not included in the experiment.

During the experiment in all groups *BWT* was performed since 3rd day after first surgery that is explained by a prolonged renewal of animal's locomotor activity after recovering from anesthesia. Further testing of each animal was performed every three days. Testing of each animal included 3 attempts. All results were calculated as average mean and in the study differentiated as a function index (*FI*) of animals' statics and coordinating sphere. The maximum period of animal observation was 60 days.

To analyze in detail the data relative restorative process dynamics, we studied the dynamics of the *FI* increment (*ΔFI*). Since for the first 2 days after cerebellar injuries modelling due to complicated postoperative status of an animal, the determination of *FI* was not performed. The moment, when the decline of *FI* values after injury completed, remains unclear. The absolute value of *FI* decline within first 3 days of the experiment was much higher than the absolute values for *ΔFI* calculated for subsequent recovery process, which made it impossible for their detailed analysis. Therefore we conditionally accepted that during the third day of the experiment *ΔFI* was third of the value of *FI* decline within the first three days: *ΔFI* on the 3rd day = (7 – FI on the 3rd day) / 3.

In order to align small time variations of *ΔFI* and enlarge absolute values, during further period of the experiment this index was calculated as a change of *FI* for 6 days of experiment. $\Delta FI = FI_2 - FI_1$, where FI_1 is an indicator of motor activity, determined by BWT, at the beginning of selected 6-day observation period; FI_2 is an indicator of motor activity determined by *BWT* at the end of the selected 6-day observation period.

Statistical analysis was performed using *Matlab R2010B* software (*Mathworks*, USA). The statistical significance of the differences between mean values was determined using a Mann-Whitney U-test st. Approximation of the data was performed using a *MsExcel software* (*Microsoft*, USA). At the same time we used a polynomial approximation of the data with polynomial degree 6.

RESULTS AND DISCUSSION

Detailed analysis of *FI* dynamics in the experimental groups showed **(Fig. 1)** the lowest intensity and effectiveness of the restorative process in FK group, slightly higher in *C-1* and *C-2* groups, significantly higher in *OBT* group, and maximum in *FNT* group.

According to our previous study [44] the increase of *FI* in *C-1* group during the experiment was 2.1 points; in *C-2* group – 2 points, in *FK* group – 1.8 points, in *OBT* group – 2 points, in *FNT* group – 2.5 points. On the 60th day of the experiment the average *FI* in *FK* group was 5.4 ± 1.2 points; in *C-1* group – 5.7 ± 1 points; in *C-2* group – 6.2 ± 1.1 points; in *OBT* group – 6.3 ± 0.7 points, in *FNT* group – 6.6 ± 0.5 points.

In *FK* and *OBT* groups the recovery process had three-phase character in *C-1*, *C-2* and *FNT* groups – two-phase **(Fig. 2)**. The maximum intensity of the restorative process in FK and OBT groups was on 3-9th, 23-27th, and 45-57th days, in of *C-1*, *C-2* and *FNT* groups – on 21-27th and 45-57th days of the experiment, and at the same time they were characterized

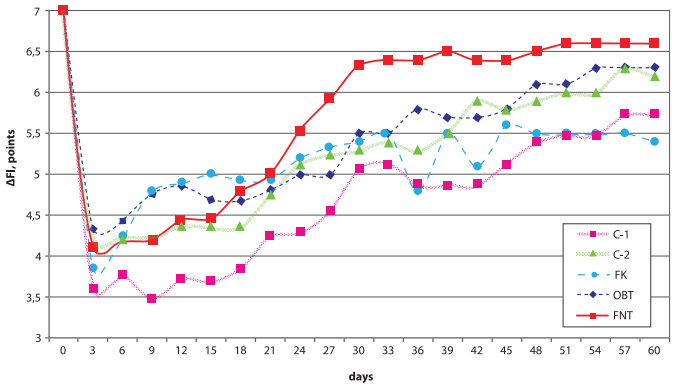

Fig. 1. Dynamics of statics and coordinating FI restore in animals up to 60 days of experiment.

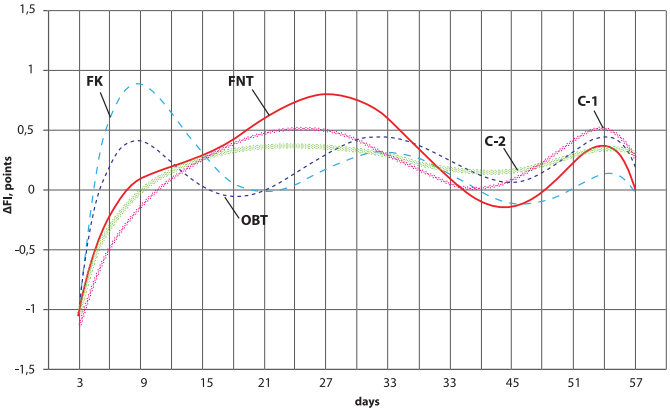

Fig. 2. Dynamics of 6-day FI increment (ΔFI) in the experimental groups, polynomial curves.

Table 1. Beam-walking test scale for estimate of statics and coordinating in rats

7 points	The rat crosses the beam and stumbles no more than twice.
6 points	The animal crosses the beam, but stumbles no more than 50 % its steps.
5 points	The animal crosses the beam and stumbles more than 50 % its steps.
4 points	The rat traverses the beam and at least once hindpaw slide down but the animal returns on the beam.
3 points	The animal traverses the beam on the abdomen.
2 points	The animal places the paws on the beam and maintains balance.
1 point	Falls off the beam immediately.

by different values. During the second week of the experiment the highest increment of *FI* was shown in *FK* and *OBT* groups; during 3-4th weeks – in *FNT* group; during the second month – in *OBT*, *C-1* and *C-2* groups.

The obtained data relative recovery process dynamic confirm the above results about Purkinje cells regeneration after aksonotomia. These cells are the main functional elements of the cerebellar cortex [33].

BWT test used by us allowed detect and assess not only complex disorder of static and coordinating sphere in trauma of the cerebellum, but it also allowed to assess one of the least studied expression of cerebellar pathology- hypotonia. With this test hypotonia was revealed in animals with the index of static and coordinating sphere function 2, 3 and sometimes 4 points. The symptom was seen in animals' disability to separate the body from the surface of the beam. We suggest that it is not only a specific defense reaction in response to a significant disorder in body equilibrium maintaining mechanisms (mostly – in animals with 2 points of *FI*), but also the decrease in muscle tone of extremities extensors (mostly in animals with 3 and 4 points of *FI*). Moreover, when studying the specific movements of legs at the moment of missing, we conclude that mistakes in walking may be linked not only with failure of accuracy of motor activity. These reactions animals perform after durable training. Their performance is less dependent on the current correction made by cerebellum. It is mostly an automated response. Mistakes of the animals are also connected with weakness of the muscles, especially hind limb adductors. Such kind of hypothetical assumptions do not allow associating less expressed hypotonia variants with *FI* above 4 points. For animals in which *FI* measured at 4 points, we found no homogeneity regarding the tone of the extensor muscles. During the study we observed both, full and partial (temporary, with low location of abdomen above the beam), maintaining of body weight during the animal movement from the beginning to the end of the test trajectory. Therefore we have selected only those animals, in which on the 3rd day after modeling an injury *FI* revealed at the level strictly less than 4 points (*FI* < 4). Condition of severe hypotonia was associated with 3 points of *FI*, significantly expressed – hypothetically from *FI* = 2 points, mild – with *FI* = 4 points. According to these criteria we realized sampling: *C-1* group – 15 animals, *C-2* – 6, *FK* – 6, *OBT* – 6, *FNT* – 7 animals.

Analysis of the *FI* change dynamics in the above-discussed experimental groups showed the significant difference from the detected peculiarities of function restoration in the study groups on the whole **(Fig. 3, 4)**.

In the *C-1* group the average *FI* on the 3rd day was 2.7, on 30th – 4.5, on the 60th – 5.3 points **(Fig. 3a, b)**; during the observation period *FI* doubled (increased by 2.6 points), and a significant increase of *FI* was observed both, in the first and the second month (1.8 and 0.8 points respectively). Within 33-42 days a significant regression of *FI* (from 4.7 to 4 points) was observed, later replaced by progress with the following slowdown. The rate of *FI* changes in the group reflected the following feature of the dynamics. There were shown 2 its maximums on 9-21th and 39-57th days of experiment **(Fig. 4 a)**. Animals from this group reached a level in 4 points to 27th day, 5 points (hypothetically an absence of functionally significant hypotonia) – only up to 48th day.

In *C-2* group on the third day an average *FI* was 3, on 30th – 4.2, on 60th – 5.6 points **(Fig. 3a, b)**. During the experiment *FI* almost doubled (increased by 2.6 points), the total increase of *FI* during the first and second month was almost equal (respectively 1.2 and 1.4 points). During the first 18 days *FI* unchanged (overall increase – 0 points), the steady, gradual increase of FI was pointed from 21st day to the end of the experiment. Rate of *FI* change during this period ranged within 0.5 points (6 days) and had a tendency to a gradual decrease **(Fig. 4 a)**. Level of 4 points sampling animals reached by 30th day, 5 points – by 42th day.

In *FK*, *OBT* and *FNT* groups *FI* dynamics significantly varied. In *FK* group on the 3rd day an average *FI* was 3 points, 30th – 5 points, 60th – 4.8 points **(Fig. 3, 4)** during experiment *FI* increased by 1.8 points; during the first month – 2 points; the second -vary at the range of 5 points with a downward trend. The most intense *FI* progress was observed during the first 9 days of the experiment **(Fig. 3a, b, 4 a)**. Within 9-27 days there was

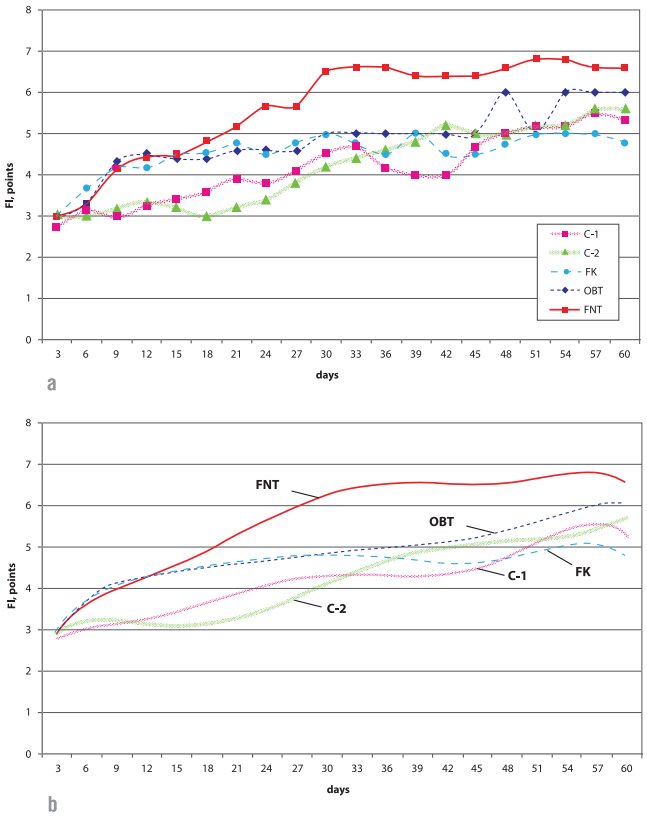

Fig. 3. Dynamics of statics and coordinating function restore in animals with severe cerebellar hypotonia (**a**); **b**) polynomial curves.

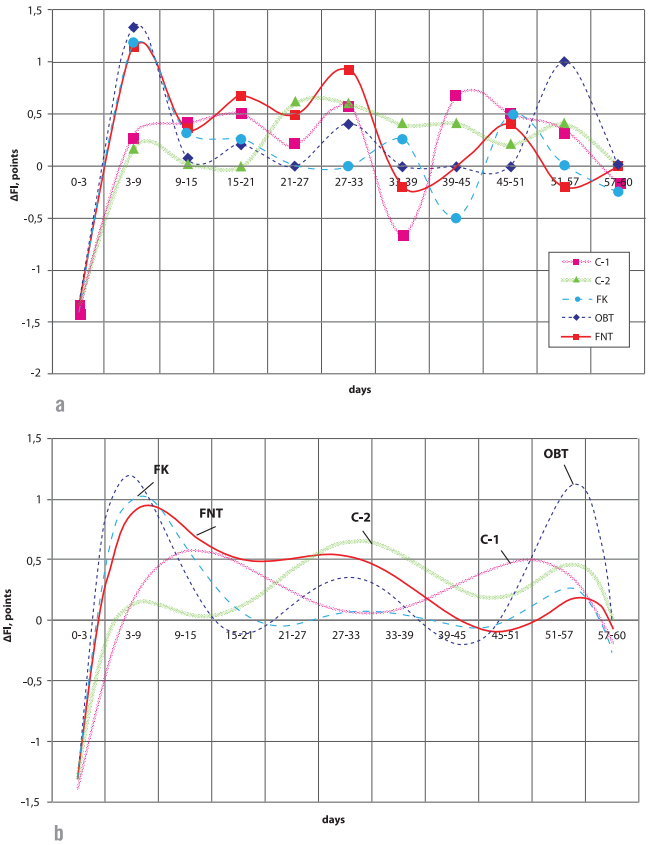

Fig. 4. Dynamics 6-day FI increment in animals with severe cerebellar hypotonia (**a**); **b**) polynomial curves.

less rapid increase of *FI* (*ΔFI* = 0.3 points / 6 days). 4 points of *FI* animals reached after 9 days, 5 points – 30 days.

Dynamics of *FI* in *OBT* group during the first month was similar to that in *FK* group **(Fig. 3, 4)**, but the phases of rapid (3-9 days) and slow (9-27 days) increase of *FI* were more strictly differentiated in time: within 9-15 days *FI* increase was hardly pointed out **(Fig. 4 a)**. It was impossible to perform a valid analysis of *FI* dynamics in *OBT* group during the second month of the experiment due to the insufficient number of animals of such observation period. *FI* in this group (as in *FK* group) reached 4 points on the 9th day of the experiment, 5 points – obviously after 30 days.

Dynamics of *FI* in *FTN* group during the first 15 days did not differ from *FK* and *OBT* groups **(Fig. 3a, b)**: on the 3rd day *FI* was 3 points, on 15th – 4.5 points. Phase of slightly restrained rapid increase was limited by 9th day of the experiment **(Fig. 3a, b, 4 a)**. In the future we registered a steady slow increase of *FI* till 33rd day with the increase *ΔFI* (0.36, 0.6, 0.93 points / 6 days). This phase was different from the phase of slow *FI* increment in *OBT* and *FK* groups by large values of *ΔFI*. Due to such dynamics on 30th day of observation *FI* was 6.5 points, significantly exceeding the equivalent figure in all other groups. During the second month there was observed a rapid stabilization of *FI* at 6.6 points until the end of the experiment **(Fig. 3a, b, 4 a)**. The animals of this group reached 4 points of *FI* after 9 days, 5 points – to 21st day. Animals with the most severe injuries showed another dynamics of recovery process. Unlike the general groups, we should distinguish at least three variants of the restorative process: the *C-1* and *C-2* groups, the *FK* and *OBT* groups, and *FNT* group. The main difference is in the restorative process during the first month of experiment. On this basis there should be distinguished *C-1* and *C-2* groups (slow course) and *FK*, *OBT* and *FNT* groups (fast course for 9 days, slow – for 9-33 days). During the second month of the experiment slow increase of *FI* was in *C-1* and *C-2* groups; in *FK* and *FNT* – stabilization. Leading position of *FNT* group is caused by significant activity of a recovery process component, limited in timeframe of 9-33 days, i.e. 2-4 weeks of posttraumatic period.

The most slowly restoration of muscular tone was in *C-1* group (continued for 7 weeks after an injury). In *C-2* group this process was slightly faster (for 6 weeks). 4 points of *FI*, i.e. a state of mild hypotonia, was observed in both groups at the end of the first month. In *FK*, *OBT* and *FNT* groups, mild hypotonia was detected after 9 days of the experiment; normotony (within *BWT*) – on 21st (*FNT* group) and 30th day (*OBT* and *FK* groups). Thus, neurotransplantation has a significant positive effect on muscular tone recovery after injury of the cerebellum.

According to the existing data [11], we may suggest that the cerebellar cortex sends efferent fibers to the vestibular nuclei (in the inferior cerebellar peduncle). Mediator specificity of these effects is not strictly determined. In addition, several nuclei of the cerebellum (especially fastigial nucleus, dentate nucleus, and interposed nuclei) pass the signals to vestibular nuclei, reticular nuclei of the brain stem, nucleus ruber and spinal cord. These projections may have immediate value in the formation of tonic effects on spinal cord motoneurons, primarily through the descending serotonergic (from seam nuclei of the reticular formation) and noradrenergic (from the nuclei of locus coeruleus) fibers provide a well-studied mechanism for maintaining excitability of motor neurons and tone of skeletal muscles at rest [10].

Considering the main volume of the cerebellar cortex projections form fibers of pear shaped neurons (*GABAergic*, i.e. inhibitory cells), and of cerebellar nuclei (mostly excitatory fibers), there raises the question of the possible mechanism of hypotonia, when cerebellar cortex is damaged. After all, when populations of pear-shaped neurons are damaged, the intensity of inhibitory effects on neurons of the cerebellar nuclei and vestibular nuclei should decrease. This detects an increase in the activity of these neurons and their hypothetical influence on the system of muscular tone maintaining. The answer should be sought in the architecture and mediator specifics of connections between the cortex of the cerebellum and vestibular nuclei, cerebellar nuclei and descending serotonin and adrenergic systems. Severe cerebellar injury, modeled by hitting on the surface of its cortex, is accompanied by the formation of necrotic foci and cerebral edema that goes far beyond the cerebellar cortex. This shows an involvement of the cerebellar nuclei neurons in the pathological process. In the case of dystonia, related to the pathology of the cerebellum, an extraction of the last leads to the disappearance of symptoms of this disease [45]. Hypotonia in slightly delayed period of the traumatic process may the reason of excessive activity of GABAergic neurons of pear cortex, which foci could easily be due to post-traumatic reconstruction of cerebellum neuronal network. However, the answers to these questions require further careful study of the phenomenon of cerebellar hypotonia.

CONCLUSIONS

TRANSPLANTATION OF FETAL NEURAL TISSUE OR OLFACTORY BULB TISSUE IMPROVES THE NEURAL FUNCTIONAL RECOVERY IN RATS; AND IS PROMISING IN CLINICAL APPLICATION ACCORDING CURRENT BIOETHICAL STANDARDS.

BASED ON OUR OWN FINDINGS AND OTHER AUTHORS' DATA, WE CAN SUGGEST THAT HIGH INTENSITY OF THE RECOVERY PROCESS OBSERVED WITHIN 2 WEEKS OF OUR EXPERIMENT IS TYPICAL FOR FETAL KIDNEY TRANSPLANT (*FK*) AND OLFACTORY BULB TISSUE (*OBT*) GROUPS. IN *FK* AND *OBT* GROUPS IT IS ASSOCIATED WITH ANGIOGENIC, AND IN THE OBT GROUP ALSO WITH NEUROPLASTIC IMPACT OF TRANSPLANTS ON THE CEREBELLUM TISSUE.

THE LOWEST RATE OF MUSCLE TONE RECOVERY IS CHARACTERISTIC FOR CONTROL GROUP. IN THE *FK*, *OBT* AND FETAL NEURAL TISSUE (*FNT*) GROUPS, ATTAINMENT OF MILD HYPOTONIA WAS REGISTERED ALREADY ON 9TH DAY AFTER THE BEGINNING OF THE EXPERIMENT; NORMOTONY ON 21ST DAY (FNT GROUP) AND ON 30TH DAY (OBT AND FK GROUPS).

THUS NEURAL TRANSPLANTATION HAS THE SIGNIFICANT POSITIVE EFFECT ON MUSCLE TONE RECOVERY AFTER CEREBELLUM INJURY THAT IS APPARENTLY LINKED WITH COMPENSATORY PLASTIC REARRANGEMENT OF THE NEURAL NETWORKS, SPECIFICALLY RELATIVE THEIR CONNECTIONS WITH BRAIN STEM CENTERS WHICH ARE RESPONSIBLE FOR THE MAINTENANCE OF THE SKELETAL MUSCLE TONE.

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