Acta Scientific Neurology (ISSN: 2582-1121)

Volume 4 Issue 5 May 2021

Research Article

Changers of Neurons of Central Nervous System and Immune Organs After Initiation of Demyelination and Remyelination with Interferon Beta-1a

Nataliia O Melnyk*

National O.O. Bogomolets Medical University, Kyiv, Ukraine

***Corresponding Author:** Nataliia O Melnyk, National O.O. Bogomolets Medical University, Kyiv, Ukraine.

Received: March 02, 2021

Published: April 10, 2021

Abstract

After initiation of experimental model of demyelination and remyelination, was investigate morphological changers of neurons and myelinated nerve fibers in organs of central nervous system (CNS) and organ of immune system - thymus.

In its experimental work was use model of demyelination - EAE (experimental allergic encephalomyelitis) in rats, and was study changers of neurons in cortex of cerebrum, cerebellum and spinal cord on 21 days and 39 days after initiation EAE. Histological sections of the brain and spinal cord was stain by toluidine blue and cresyl violet, we observed the percentage of neurons with unmodified, moderate and severe structural changes. In organs of CNS we studied of demyelination process in nervous fibers. In investigations of nervous fibers was use methods of electron microscopy and morphometry. On early period EAE we observed demyelination process of nervous fibers, after influence of Rebif® (interferon beta-1a) by 2 weeks, we observed of remyelination.

In late period of EAE after influence of Rebif® (interferon beta-1a) the percentage of normal neurons in the brain and spinal cord was increased, the amounts of neurons with severe and destructive changes were reduce and myelinated nerve fibers was regenerate.

Reactive changers in thymus was include - formation of small nodules in cortical part of lobules, decrease amount of lymphocytes in cortex of lobules in early period initiation EAE.

In its article was form some main rules of correlations between structural changes of neurons in CNS and organ of immune system - thymus.

Keywords: Demyelination; Experimental Allergic Encephalomyelitis; Multiple Sclerosis; Thymus

Introduction

Multiple sclerosis is one of the most spreading demyelinating disease of the central nervous system (CNS).

Damage of neurons may contribute to the changes of their functioning and the formation of such neurological symptoms of multiple sclerosis as disturbances of memory, emotions, intellect, vegetative disorders, etc.

Although multiple sclerosis generally occurs at younger years, today it can be registered after the age of 45 years. In older age this disease has mostly infectious and toxic nature, progressive character and more severe clinical symptoms [1].

Risk factors

- **Age:** MS can occur at any age, but most commonly affects people between the ages of 15 and 60.

- **Sex:** Women are about twice as likely as men are to develop MS.
- **Family history:** If one of your parents or siblings has had MS, you are at higher risk of developing the disease.
- **Certain infections:** A variety of viruses have been linked to MS, including Epstein-Barr, the virus that causes infectious mononucleosis.
- **Race:** White people, particularly those of Northern European descent, are at highest risk of developing MS. People of Asian, African or Native American descent have the lowest risk.
- **Climate:** MS is far more common in countries with temperate climates, including Canada, the northern United States, New Zealand, southeastern Australia and Europe.
- **Certain autoimmune diseases:** You have a slightly higher risk of developing MS if you have thyroid disease, type 1 diabetes or inflammatory bowel disease.
- **Smoking:** Smokers who experience an initial event of symptoms that may signal MS are more likely than nonsmokers to develop a second event that confirms relapsing-remitting MS.

Experimental autoimmune encephalomyelitis (EAE) - as a model for multiple sclerosis (MS) - based on activation Th1 and Th17. Th1 lymphocytes was produce IFN-γ and Th17 - IL-17 producing T lymphocytes. They are primed outside the CNS by dendritic cells, then cross the blood-brain barrier and encounter CNS antigen-presenting cells. They produce inflammatory products and cytokines that damage the myelin and axons [2].

The most effective drugs for treatment of demyelinating diseases are recombinant β-interferons ("Rebif", "Betaferon") [3]. In order to find effective methods of treatment of the pathological process - demyelination, it may be important to study influence to CNS and immune organ - thymus, of recombinant β-interferon-1a in different doses.

Objectives of the Study

- To observe differences of reactive changes of neurons of the CNS after initiation of demyelination process (initiation of EAE in rats).
- To investigate remyelination in condition of EAE and under the influence of recombinant β-interferon-1a (of "Rebìf").

The basis of the experimental work is - to investigate the changes of the neurons of the big hemispheres, the cerebellum and the lumbar spinal cord and immune organ (thymus).

The experimental groups of rats after initiation of EAE (experimental autoimmune encephalomyelitis)

Initiation was provide by method of group of authors from Institute of neurosurgery of Ukraine [4], EAE was induced using complete Freund's adjuvant.

Experimental animal groups (see table 1)

- The rats after initiation of EAE (control group) - 34 animals (organs for investigation was take - cerebrum, cerebellum, lumbar part of spinal cord was take after 21 and 39 days).
- Rats that received injections of recombinant β-interferon-1a (of "Rebìf"), subcutaneously in dose 0,55 μg every second day starting from the 14-th day after initiation of EAE during the following 15 days. Total dose was 4,4 μg (34 animals in this group).

	Clinical symptoms was absent - 0+	Decrease of tonus of tail - 1+	Weakness or light paraplegia of 2 legs - 2+	Severe paraplegia of 2 or all legs - 3+
Rats after 21 days of initiation of EAE	15%	14%	14%	57%
Rats after 39 days of initiation of EAE	29%	14%	57%	0%
Rats after 39 days of initiation of EAE and injection of recombinant **β**-interferon-1a (of "Rebìf")	88%	12%	0%	0%

Table 1: Different types of neurological symptoms in rats with EAE and after injection of recombinant β-interferon-1a (of "Rebìf").

All investigations was formed by European convention for the protection of vertebrate animals used for experimental and other scientific purposes (Council of European, Strasbourg, 1986).

Morphological studies organs of CNS

For morphological studies of the structures of the CNS (cortex, cerebellum, spinal cord) in rats used staining histological sections cresyl violet and toluidine blue (by Nissl) and electron microscopy.

Cresyl violet to determine the changes in myelin sheets of nerve fibers.

Toluidine blue selectively binds to membrane structures, allowing visualizing neuronal nucleus and cytoplasm.

Changes of structure of neurons in CNS was observe on histological specimens and was divide on different destructive forms:

- Moderate changes in neurons are those reactive to damage and characterized by displacement of the nucleolus to nuclear membrane, and by increase in the size of the nucleus. Cytoplasm of neurons become hypochrome, Nissl substance was not define.
- Severe changes of neurons are destructive and characterized by a decrease in the size of the nucleus, with change of its shape, the nucleolus was not visible. Size of cell bodies of neurons was considerably reduce and they are hyperchrome (Figure 1).

Figure 1: Moderate and severe changes of neurons in CNS after initiation of EAE in rats. A - moderate changers of neurons, histological specimen after staining toluidine blue, oc.10, ob.40; B - moderate changers of neuron, photo form electron microscopy; C - severe changers of neurons histological specimen after staining cresil violet, oc.10, ob.40; D - severe changers of neuron, photo form electron microscopy.

The study of the neurons in the cerebrum, cerebellum and lumbar spinal cord was able to determine the varying degrees of damage to cell bodies of neurons. Most profound pathological changes are observed in the Purkinje cerebellum cells, which determine the largest percentage of perikarions of these cells with severe changes in comparison with the state of neurons in other CNS regions. In rats at an early term, the study observed the highest percentage of Purkinje cerebellum cells with severe changes after the injection of the "Rebif" in doses of 0.55 micrograms daily for 4 days and 1.1 micrograms daily for 3 days.

The largest percentage of neurons with moderate changes after influence of the "Rebif" is observed as part of the cerebrum.

After the injection of "Rebif", the renewal processes are defined in all regions of the CNS, which were investigated, the greatest number of neurons without changers is observed in cerebrum (See table 2).

	Neurons without changers	Neurons with moderate changes	Neurons with severe changes	
Rats after 21 days of initiation of EAE	1,92%	88,46%	9,62%	In cerebrum
	11,94%	65,72%	18,30%	In cerebellum
	9,50%	80,90%	9,60%	In spinal cord
Rats after 39 days of initiation of EAE	10,65%	85,23%	4,72%	In cerebrum
	15,10%	69,52%	15,40%	In cerebellum
	16,63%	82,30%	1,09%	In spinal cord
Rats after 39 days of initiation of EAE and injection of recombinant **β**-interferon-1a	79,52%	20,48%	0,00%	In cerebrum
	71,83%	16,90%	11,27%	In cerebellum
	67,09%	32,91%	0,00%	In spinal cord

Table 2: Amount of neurons in organs of CNS in experimental groups of rats.

Influence of interferon beta-1a on immune organs after initiation of demyelination and remyelination

The basis of investigation of immune organ (thymus) after initiation EAE and provide interferon beta-1a - recognize morphological changers and specifically reactions in population of lymphocytes in its organs in demyelinate and remyelinate conditions.

After 21 days of initiation EAE in rats, we observed changers in structure of thymus:

- Disorders of hemodynamics can be observed in the cortex of lobules - dilation of small vessels.

- After 21 days, the area of the cortex decrease and the area of medulla was increase, in the lobules of thymus in rats with EAE.
- The number of lymphocytes is increased compared in cortex and in medulla of thymus.

Changers of thymus, after 39 days of initiation EAE in rats, based on some characteristics:

- The area of the cortex was decrease.
- In the cortex was observe "nodules " appear with a cluster of large lymphocytes (Figure 2).
- The amount number of lymphoid cells was increase appositive of intact rats.

Figure 2: In the cortex of lobule of thymus was observe "nodules " (1) appear with a cluster of large lymphocytes. Histological specimens after staining of hematoxylin and eosin, oc.10, ob.40.

Conclusion

Neurons with moderate changes predominate in CNS of rats with experimental EAE. **β**-interferon-1a induces remyelinisation after 2 weeks of treatment rats with experimental EAE. In the early term of the investigation, there is an increase in area of medulla, and in the cortex, there are determined accumulation of undifferentiated cells, which resemble nodules. In periods of 21 and 39 days after the initiation of EAE, number of small lymphocytes was decrease, but amount of large and medium lymphocytes was increase, its fact can provide differentiation process in thymus. Interferon beta-1a was activate process differentiation of lymphocytes in thymus on early period EAE in rats.

Bibliography

1. Ismailov MG., *et al.* "Multiple sclerosis and debut in the elderly". *Advances in Current Natural Sciences* 6 (2014): 122-123.

2. Cris S Constantinescu., *et al.* "Experimental autoimmune encephalomyelitis (EAE) as a model for multiple sclerosis (MS)". *British Journal of Pharmacology* 164.4 (2011): 1079-1106.

3. Melendez-Torres GJ., *et al.* "Clinical effectiveness and cost-effectiveness of beta-interferon and glatiramer acetate for treating multiple sclerosis: systematic review and economic evaluation". *Health Technol Assess* 21.52 (2017): 1-352.

4. Lisianyi MI., *et al.* "Modelling of experimental allergic encephalomyelitis for rats and his correction by the cells of allogenic cerebrum". *Physiology Journal* 47.5 (2001): 37-41.