

## Methodology Article

# Dynamics of Brain-Specific Proteins and Melatonin Before and After Microwave Resonance Therapy in Patients with Aftereffects of Mild Brain Injury

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**Abstract:** The process of decompensation in the remote period of mild closed traumatic brain injury is due to the autosensitization to different structures of brain, and contributes to the enhancement of inflammatory processes, that in turn disrupts the activity of neurotransmitter mechanisms in the central nervous system. Methods: The study of brain-specific proteins (S-100, MBP, EP, 3G-9-D6, GFAP) and melatonin hormone in patients with long-term effects of mild closed traumatic brain injury, before and after microwave resonance therapy was undertaken. Results: The dynamic observation of 20 patients with aftereffects of mild closed traumatic brain injury showed that microwave resonance therapy (MRT) leads to normalization of hormone melatonin and cerebrospinal proteins' state in this group of patients. Conclusions: The study of brain-specific proteins and hormone melatonin contributes to the understanding of those biochemical processes that take place in this pathology. The microwave resonance therapy leads to the normalization of the functioning of neurohumoral cerebral mechanisms that have arisen in the remote period of traumatic brain injury. The application of microwave resonance therapy not only normalizes the state of the studied neurohumoral parameters, improves neuroplastic processes and protects the brain substance from damaging factors, but also restores the neurochemical organization of brain integration. The presented method of treatment restores the neurotransmitter mechanisms of the brain matter.

**Keywords:** Brain-Specific Proteins, Melatonin, Microwave Resonance Therapy, Aftereffects, Mild Traumatic Brain Injury

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## 1. Introduction

It is established that mild closed traumatic brain injury (CTBI) initiates the development of persistent dysfunction of nonspecific brain structures and the sustained post-traumatic and neurohumoral disorders, that further causes the formation of symptoms of neurological, psychovegetative and cognitive disorders [9, 10, 14, 19] which flow with the frequent periods of decompensation.

The pathologic integration that occurs in the nervous system in case of closed traumatic brain injury (CTBI) is a consequence of dysregulation pathology, and its long existence is possible due to neuroplasticity. The activity of the central nervous system (CNS), as the most important

integrative system of the organism that interacts with a constantly changing environment, is firmly connected with plasticity [18]. The development of adaptation mechanisms would be impossible without it. Any damage induces the flexible re-arrangements and the required reorganization of the corresponding divisions of the nervous system, that is why the pathologic plasticity should be categorized as the dysregulation pathology [4, 5].

Impairment of structural-functional organization of brain structures leads to the disruption of afferentation, and this, in turn, exacerbates vegetative disorders and forms a "vicious cycle". The functional inferiority of suprasegmental nonspecific brain structures is aggravated by the presence of allergic, paradoxical responses to drugs that intensifies the

dysregulation pathology of brain functional systems.

Thus, CTBI can be considered as a manifestation of pathological plasticity, violation of regional monitoring mechanisms and general integrative control of CNS, as a "failure of adaptation to the external conditions", as a "trigger factor of certain shifts", which impairs the normal course of physiological processes in the brain tissues [1, 8, 12, 14].

The main pathological mechanism of brain damage after cerebral trauma is a violation in the system of self-regulation of metabolic processes that determines the vital activity and functional activity of nerve cells. After CTBI another neurochemical organization of integrative interaction is forming, the distinction of which is the violation of neurohormones' excretion, including melatonin.

There was confirmed, by the applied and fundamental researches, the progressive pattern of changes in the CNS, which are arising in the acute period, determining the development of remote aftereffects of closed TBI [6, 10, 14].

The presence of autosensibilization to different brain structures in long-term mild CTBI is the evidence of violation of regulatory mechanisms, and TBI contributes to intensification of inflammatory reactions of autoimmune origin [10, 12, 13]. According to the data from literature [2, 11, 15], hypothalamus and suprachiasmatic nuclei damage during trauma contributes to the reducing of melatonin excretion by epiphysis, that in turn enhances the inflammatory reactions, disrupts the functions of neurally mediated mechanisms and activates apoptosis.

In the developed countries, there is an increased need for treatment methods that are not associated with the risk of occurrence of the side effects. This, however, does not mean refusal of official medicine, because, according to the recent survey, more than 70% of respondents would like to use drug-free methods as a supplement to the traditional treatment in order to avoid the possible adverse effects, and 38% of the population in the United States are under treatment with alternative methods. Drug therapy of CTBI's aftereffects is not an easy task, and frequent decompensation leads to the allergization of the organism, failure of regulatory processes and other disorders associated with the intake of medications [8].

The results of the researches conducted in recent years, dictate the necessity for consideration of the pathogenesis of many diseases of the nervous system (including craniocerebral trauma) and the recovery of impaired functions, taking into account the processes of neuroplasticity, in which a special role is given to melatonin, which belongs to physiologically active hormones, and which participates in the regulation of plasticity, ensuring the protection of brain cells from damage.

In a work of Kelso M. M. et al [15], it has been shown that melatonin has a high antioxidant activity. Along with this, it is able to normalize the function of the immune system, stimulating it by restoration of impaired antibody production and increasing the antiviral stability. Also, melatonin affects the regulation of carbohydrate and lipid metabolism, reduces the amount of cholesterol in the blood, reduces the intensity of

atherosclerosis, participates in hormonal regulation of blood pressure.

Melatonin is a multifunctional hormone, because its receptors are present in neurons of various formations of brain. The highest level of the hormone and density of melatonin receptors ( $MT_1$ ,  $MT_2$ ,  $MT_3$ ) is in the anterior hypothalamus (pre-optic, mediastinal area), followed by an intermediate brain, hippocampus, striatum and neocortex. Owing to these receptors, melatonin may affect those disorders that have arisen as a result of TBI. Another mechanism of regulatory influence of melatonin is in association of the epiphysis with the hypothalamic-pituitary-adrenocortical system, which plays a leading role in a response to external influences. With a background of a stressful situation, the epiphysis increases the secretion of melatonin, which suppresses the secretion of corticosteroids [3].

Above we have mentioned about the damage to the structures of the hypothalamus, the brain stem, and the mediastinal nuclei after CTBI. Since the neurons of these structures are characterized by sensitivity to melatonin, on the one hand, and on the other hand they participate in the regulation of a wake-sleep cycle, it is possible to assume that namely the change of melatonin secretion due to the TBI really are those pathogenetic mechanism which contributes to the formation of vegetative violations as an aftereffects of cerebral trauma [7, 11, 17].

## 2. Aim of the Work

Taking into account all of the above, the aim of this work was to study the dynamics of the brain-specific proteins and melatonin in patients with the aftereffects of mild traumatic brain injury before and after the microwave resonance therapy (MRT).

## 3. Methods

There were examined 20 patients with long-term aftereffects of closed TBI, at the ages from 25 to 43 years old, who were in inpatient treatment at the Institute's clinic. The duration of the injury was from 2 to 5 years. All patients have been medically treated with or without short-term positive effects. The control group consisted of 20 practically healthy people aged 27 to 40 years.

MRT was conducted using the generator G4-141, a source of millimeter emission, with a frequency band of 37.50 - 53.57 GHz and radiated power that did not exceed  $4 \text{ mV/cm}^2$  on the output of the waveguide. For each patient the individual, so-called resonance therapeutic frequency of exposure, was titrated, that caused the specific sensory responses, and using a fluoroplastic waveguide the researches were placing the source of emission to the targeted biologically active point ( $VB_{20}$ ;  $E_8$ ;  $TR_5$ ;  $F_2$ ;  $RP_6$ ;  $TR_{18}$ ;  $MC_7$ ). For each MRI session, only one biologically active point have been used. The session's duration was 20-30 minutes daily. The period of treatment consisted of 9-12 sessions.

To study the state of the dynamics of brain-specific proteins a

method of crossed immunoelectrophoresis have been used, that has high resolution and makes it possible to evaluate the fractional concentration of antigens under study. Autoantibodies (AAB) to proteins S-100; glial fibrillary acidic protein (GFAP), encephalogenic protein (EP); 3G-9-D6; myelin basic protein (MBP) were studied. Some proteins (S-100) are the specific biochemical markers for traumatic brain damage and play an important role in predicting of the disease.

Determination of melatonin indices in the patients' blood (pg/ml) was performed by method of immunoradiometric assay, using Gamma master analyzer and test system, Pharmacia LKB Biotechnology AB (Sweden), LDN Labor Diagnostica Nord GmbH (Germany).

The statistical analysis of the obtained data was conducted with the help of the program Statistica 6.0. The conclusion about the statistical significance of the obtained data was issued when the probability of error was equal to  $p < 0,05$ .

## 4. Discussion

**Table 1.** Content of AAB in serum of patients with aftereffects of mild TBI before and after the microwave resonance therapy.

Group	Content of autoantibodies (standard units) before:				
	S-100	MPM	EP	3G-9-D6	GFAP
Control (n=20)	0,115±0,020	2,516±0,250	0,688±0,100	0,872±0,090	1,266±0,130
Patients (n=20):					
before MRT	0,566±0,030	2,458±0,120	2,458±0,120	1,240±0,500	2,716±0,300
after MRT	0,117±0,020*	2,500±0,180*	2,500±0,180*	0,209±0,120*	1,238±0,300*

Note: \* -  $p < 0,05$

After MRT procedure the AAB content to proteins S-100, GFAP, and 3G-9-D6 decreased and was close to the control group indices, and the AAB content to the EP has increased, although before the treatment, this figure was three times higher than in the control group, this may indicate the prolonged neuroimmune processes against neurons and glia associated with damage to the brain blood-brain barrier in patients with CTBI. MRT reduces the activity of these reactions and balances the indicators of humoral regulation.

Prior to treatment in 14 (70±10%) ( $p < 0,01$ ) examined individuals the melatonin values were higher (24-32 pg/ml) than the control values of 8,0-20,0 pg/ml. In 2 (10±7%) patients, they were at the lower limit of normal, and in 4 (20±9%) patients they were lower (5,5-6,3 pg/ml) than the control values. After the treatment, the melatonin values within the normal range were in 13 (65±11%) patients ( $p < 0,05$ ), high levels were in 4 (20±9%) persons (21-23 pg/ml) (although they decreased but were not close to the control parameters), and in 3 patients (15±8%) they were lower than control values.

## 5. Conclusions

So, microwave resonance therapy leads to the normalization of the functioning of neurohumoral cerebral mechanisms that have arisen in the remote period of traumatic brain injury. Normalization of AAB in the serum and their balance in most of the examined patients under the influence of MRI improves the general condition of the patients and the

The evaluation and the effectiveness of results at MRT application in patients with aftereffects of mild TBI is given in the table.

Increase in levels of anti-cerebral antibodies and circulating immune complexes, as a rule, is one of the criteria for disease progression. The presence of neurospecific auto-antibodies in patients with aftereffects of CTBI confirms the process progression by launching the secondary autodestructive biochemical processes in the remote period (after 3-5 years) after the mild TBI, as well as the multidirectionality of autoimmune reactions to various neurospecific proteins, which may suggest the development of traumatic disease of brain. Thus, the content of autoantibodies to brain-specific proteins S-100, the main protein of myelin, encephalogenic protein, gliofibrillary-acidic protein, and 3G-9-D6 protein in patients with mild TBI significantly exceeded their concentration compared with the control group of donors, that had no CTBI in anamnesis.

current adaptogenic metabolic restructuring of the body.

Against this background, an increase in melatonin level was observed, which, on the one hand, is a manifestation of a compensatory reaction, and, on the other hand, is an attempt to normalize and inhibit the inflammatory autoimmune reactions that occur in the remote period of traumatic brain injury. In this case, the secondary mobilization of melatonin excretion by the pineal gland is considered as an auxiliary, protective phenomenon, aimed at those dysregulative disorders that occur in the remote period of closed traumatic brain injury. To slow down these autoimmune disorders the enhanced melatonin production occurs in the brain, which at the cellular level is able to provide complex neuroprotection aimed at limiting brain tissue damage and normalizing impaired neurotransmitter cerebral mechanisms.

Thus, it has been shown that the application of microwave resonance therapy not only normalizes the state of the studied neurohumoral parameters, improves neuroplastic processes and protects the brain substance from damaging factors, but also restores the neurochemical organization of brain integration, which takes place in the remote period of closed traumatic brain injury.

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