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Abstract.

Introduction: Selective degeneration of motoneurons is the pathological hallmark of amyotrophic lateral sclerosis (ALS). Does serotonin (5-HT) play a role in progression or development of disease is under the research.

Aim: The topic of the present paper is pressing as there is no data available regarding the spread of ALS. It is also noteworthy that previous studies have indicated that the pathogenesis of amyotrophic lateral sclerosis (ALS) is closely linked to 5-hydroxytryptamine (5-HT).

Materials and methods: The clinical research was conducted in Georgia. During the last five years, 60 patients from different parts of Georgia have been studied, searched, and examined by us. including from Samegrolo, Kartli, Adjara, Abkhazia, Guria, Kakheti regions. The Georgian Neurologists Corps participated and helped us in finding patients.

Brain MRI and electromyography were also performed. 60 patients with different forms of ALS participated in the study, including 34 (56.66%) men and 26 (43.33%) women. Their age ranges from 30 to 81 years. The study was conducted after obtaining the written consent of the patients, taking into account the ethical requirements for the study. we also compared the results of the serotonin level of patients with amyotrophic lateral sclerosis with a control group of 20 people (aged 18 to 50 years) who had no neurological disease in past medical history.

Results: Patients of the first group, with LMN damage, are observed with decreased amount of serotonin (61.3) %, compared to other pairs, followed by patients of the upper neuron and bulbar syndrome groups, the level of serotonin in the control group is quite high. Thus, the level of serotonin in the group of patients with bulbar events is higher than in the other groups.

Conclusions: Low serotonin requires further investigation. According to our research, the longer the anamnesis of amyotrophic lateral sclerosis patients is, the lower the level of serotonin is observed. It should also be taken into account that a low level of serotonin may be due to the presence of depression, which requires additional research.

We speculate that 5-HT could therefore be a potential therapeutic target for amyotrophic lateral sclerosis.

Key words. Serotonin, Amyotrophic lateral sclerosis (ALS), motoneuron, depression, Georgia.

Introduction.

Serotonin (5-HT) has been intimately linked with global regulation of motor behavior, local control of motoneuron excitability, functional recovery of spinal motoneurons as well as neuronal maturation and aging. Selective degeneration of motoneurons is the pathological hallmark of amyotrophic lateral sclerosis (ALS) [1-3]. Amyotrophic lateral sclerosis (ASL) is one of the heavy neurodegenerative diseases. It constitutes a progressive neuromuscular disease, first records of which have been made in medical literature in the first half of 19th century [4-10].

Contrary to the above, according to the WHO, epidemiology of the disease is based on 2016 meta-analysis results, which illustrate, that in north European countries, incidence of the disease varies at 1.92 (1.49-2.34), in southern European countries 2.22 (1.72-2.73) and in western European countries 2.35 (1.79-2.92). In USA, prevalence reaches 5.2 for 100,000 persons. Based on data as of 2014, 16 583 clinical cases were identifying in USA [11-16]. The incidence of amyotrophic lateral sclerosis is approximately two cases per 100,000 people per year. In addition, ALS has been observed to affect certain groups of people more, including football players and war veterans. However, the reasons for this phenomenon have not yet been established. Serotonin levels were determined in blood plasma, for which immunoenzymatically analysis was performed using ELISA method.

The pressing nature of the matter:

The topic of the present paper is pressing as there are no data available regarding the spread of ALS. It is also noteworthy, that previous studies have indicated that the pathogenesis of amyotrophic lateral sclerosis (ALS) is closely linked to 5-hydroxytryptamine (5-HT).

Recent studies have confirmed that serotonin stimulates the formation of new mitochondria in neurons, which leads to the synthesis of cellular ATP at the expense of reducing the demand for oxygen.

Purpose of the study.

The aim of the study was to analyze the clinical features of patients with ALS and their serotonin levels in the blood serum during and we also compared the results of the serotonin level of patients with amyotrophic lateral sclerosis with a control group of 20 people (aged 18 to 50 years) who had no neurological disease in their history.

Study design and Methods.

The clinical research was conducted in Georgia. During the last five years, 60 patients from different parts of Georgia have been studied, searched, and examined by us. including from Samegrolo, Kartli, Adjara, Abkhazia, Guria, Kakheti regions. The Georgian Neurologists Corps participated and helped us in finding patients.

Brain MRI and electromyography were also performed. 60 patients with different forms of ALS participated
in the study, including 34 (56.66%) men and 26 (43.33%) women. Their age ranges from 30 to 81 years. The study was conducted after obtaining the written consent of the patients, taking into account the ethical requirements for the study.

Brain MRI and electromyography were also performed. 60 patients with different forms of ALS participated in the study, including 34 (56.66%) men and 26 (43.33%) women. Their age ranges from 30 to 81 years. Patients were included in the study according to the El Escorial criteria (Brooks B.R. et al., 2000; Ludolph A. et al., 2015) [1–4]. The control group consisted of 20 practically healthy patients.

Pedigree analysis was also performed: a pedigree was compiled using standard symbols, which includes information on the health status of the proband’s relatives. As a result, relatives who are at risk of developing the disease or are carriers of the pathogenic allele have been identified. Such individuals were given appropriate genetic counseling and recommended for genetic testing. In addition, upon necessity, the risk of developing the disease for the next generation was calculated.

Statistical analysis performed with Statistical Package for Social Sciences SPSS 20.0. Baseline patient characteristics were reported using the mean (SD) for continuous variables according to their distribution. Student’s T-paired test and ANOVA analysis was used to compare the means for normally distributed continuous variables. p value <0.05 was considered to be significant.

Results.

5 (8.33%) patients had confirmed diabetes mellitus, and one (1.6%) patient had a family history of athetosis. 4 (6.66%) patients had to come into contact with poisonous chemicals. 2 (3.33%) patients have a history of brain trauma, 35 patients (58.33%) are tobacco users.

- 8 (30%) patients have a one-year anamnesis of confirmed ALS disease.
- Three years old - 34 (56.66%) patients.
- 5 (8.33%) patients have a history of 5 years.
- - 2 (3.33%) patients have a history of 10 years.

- One (1.66%) patient has an anamnesis of more than 10 years. The first group consisted of patients suffering from amyotrophic lateral sclerosis with initial symptoms, including muscle weakness, fasciculations, 36 (60%), they also had pronounced muscle atrophy and atony.

The second group consisted of patients whose ALS disease (23 patients (38.33%)) started with limitation of movement of one or both legs, decrease in range and strength of movement; increase of deep reflexes and expansion of the reflexogenic zone, pathological reflexes; increase of spasticity. The third group consisted of patients whose disease started with bulbar events. ALS was diagnosed in 24 (40%) patients with speech difficulties, the patient spoke "through the nose", had difficulty swallowing, speech disorders (dysarthria, anarthria), voice production disorders (dysphonia, aphonia). Disappearance of soft palate and throat reflexes, salivation, breathing disorders were soon added to the symptoms.

Discussion.

60 patients with different forms of ALS diagnosed with amyotrophic lateral sclerosis were examined by us in Georgia over the last five years, including 34 (56.66%) men and women - 26 (43.33%) of which the most patients were from 1955-1965 (55%) were born, 12 women (20%), 11 men (18.33%). 5 (8.33%) patients with ALS disease in the anamnesis of our research have confirmed diabetes mellitus, 1 (1.6%) patient has a family anamnesis of athetosis. 4 (6.66%) patients had contact with poisons and chemicals, 2 (3.33%) patients have a history of brain trauma, 35 (58.33%) patients are tobacco users.

Among our patients, the most patients with a history of long-term disease have three years - 34 (56.66%), while the history of confirmed ALS disease with one year - 18 (30%) patients. 5 (8.33%) patients have a history of 5 years; 2 (3.33%) patients have an anamnesis of 10 years, one (1.66%) patient has an anamnesis of more than 10 years.

Patients of the first group, with damage to the lower motoneuron, are observed with a decreased amount of serotonin (61.3 %). Patients of the second group, with damage to the upper motoneuron, have a low level of serotonin (24.1%, p < 0.05). Patients of the third group with bulbar complaints have a higher level of serotonin than patients of the first group and its level reaches 2.541±0.149 µmol/L (p < 0.01), while the level of serotonin in the healthy group is only low in 12.1% (p < 0.04). Patient diagnosed with ALS had higher depression levels compared to control group, results will be presented in another manuscript, studies have proven our findings that the prevalence of depression in ALS ranges from approximately 20% to 50%, which is notably higher than in the general population.

One proposed mechanism through which serotonin may exert its neuroprotective effects in ALS is by modulating neuroinflammation. Neuroinflammation, characterized by the activation of immune cells and release of inflammatory molecules in the central nervous system, plays a crucial role in the progression of ALS. Serotonin has been shown to inhibit the activation of microglia, the primary immune cells of the central nervous system, and reduce the production of pro-inflammatory cytokines, thereby attenuating neuroinflammation.
and protecting against neuronal damage in ALS. One study that investigated Potential Effects of Serotonin in the Cerebrum of SOD1 G93A Transgenic Mice, concluded that 5-HT (Serotonin) plays a protective role in ALS, likely by regulating neural stem cells in the subventricular zone that might be involved in neuron development in the piriform cortex. Serotonin may also promote neuroprotection by enhancing neuronal survival and function. Animal studies have demonstrated that serotonin can stimulate the production of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), which support the survival and growth of neurons. Furthermore, serotonin receptors are expressed on motor neurons, and activation of these receptors has been shown to promote neuronal survival and regeneration in experimental models of ALS.

**Conclusion.**

Patients of the first group, with lower motoneuron damage, are observed with decreased amount of serotonin (61.3) %, compared to other pairs, followed by patients of the upper neuron and bulbar syndrome groups, the level of serotonin in the control group is was higher.

Thus, the level of serotonin in the group of patients with bulbar events is higher than in the other groups, although both upper and lower motoneuron group patients are distinguished by the age of the disease. Low serotonin requires further investigation. According to our research, the longer the anamnesis of amyotrophic lateral sclerosis patients is, the lower the level of serotonin is observed. It should also be taken into account that a low level of serotonin may be due to the presence of depression, which requires additional research: 5-HT could therefore be a potential therapeutic target for amyotrophic lateral sclerosis. It's important to note that the role of serotonin in ALS is complex, and its effects may depend on various factors, including the stage of the disease and the specific neuronal populations involved. While some studies suggest a neuroprotective role for serotonin in ALS, others have reported conflicting findings or no significant effect. Further research is needed to fully elucidate the mechanisms underlying the potential protective effects of serotonin in ALS and to explore its therapeutic potential as a target for disease-modifying treatments.

**Conflict of interest:** Nothing to declare.

**Authors’ contribution:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, formal analysis-Nana Kvirkvelia, Maia Beridze, Mariam Kekenadze. Formal analysis, investigation, resources, data curation-Shorena Vashadze.

Redaction—Mariam Kekenadze.

**REFERENCES**

Тема актуальна, поскольку данных о распространении в Грузии про БАС нет. Также примечательно, что исследования показали, что патогенез бокового амиотрофического склероза (БАС) тесно связан с 5-гидрокситриптамином (5-НТ).

Целью исследования было проанализировать клинические особенности больных БАС и уровень серотонина в сыворотке крови у них.

Материалы и методы. Клинические исследования проводились в Грузии. За последние пять лет нами были изучены, обысканы и обследованы 60 пациентов из разных уголков Грузии. в том числе из Самегрело, Картли, Аджарии, Абхазии, Гурии, Кахетии. Корпус неврологов Грузии принял участие и помог нам в поиске пациентов. Также были проведены пациентам МРТ головного мозга и электромиография. В исследовании приняли участие 60 пациентов с различными формами БАС, из них 34 (56,66%) мужчин и 26 (43,33%) женщин. Их возраст колеблется от 30 до 81 года. Исследование проводилось после получения письменного согласия пациентов с учетом этических требований к исследованию. и сравнили результаты уровня серотонина у больных боковым амиотрофическим склерозом с контрольной группой из 20 человек (в возрасте от 18 до 50 лет), не имевших заболевания в анамнезе.

Результаты У пациентов первой группы с поражением нижних мотонейронов наблюдалось пониженное количество серотонина (61,3 %), по сравнению с другими парами, за ними следуют пациенты групп верхних нейронов и бульбарного синдрома, уровень серотонина в контрольной группе достаточно высок. Таким образом, уровень серотонина в группе больных с бульбарными явлениями выше, чем в остальных группах, хотя по возрасту заболевания различаются пациенты как верхней, так и нижней мотонейронной группы.

Выводы. Низкий уровень серотонина требует дальнейшего исследования. По данным наших исследований, чем длительнее анамнез больных боковым амиотрофическим склерозом, тем ниже наблюдается уровень серотонина. Также следует учитывать, что низкий уровень серотонина может быть следствием наличия депрессии, что требует дополнительных исследований.

Таким образом, 5-НТ может быть потенциальной терапевтической мишенью при боковом амиотрофическом склерозе.

КЛЮЧЕВЫЕ СЛОВА: Серотонин, Боковой амиотрофический склероз (АЛС), Мотонейрон Депрессия, Грузия.