

Biological mechanisms for the effects of lipopolisaccharide *Escherichia coli* on the central nervous system cells

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ABSTRACT

The main activator of the inflammation response *Escherichia coli* lipopolysaccharide (LPS) demonstrates an enormous influence on cells of the central nervous system. The aim of the current investigation is to understand the molecular and cellular mechanisms of action of LPS on neurons, microglia, and astrocytes. Experimental design was *in vitro*. Isolation of cells from brain tissues of Wistar rats and their cultivation was carried out in three groups including control, low-concentration LPS treatment (100 ng mL⁻¹), and high-concentration LPS treatment (1000 ng mL⁻¹). All manipulations lasted for 24 hours and were repeated in triplicates. The viability of cells was estimated by means of the MTT assay, activity of antioxidant enzymes – by spectrophotometrically, and the inflammatory genes expression was estimated with the help of quantitative RT-PCR (qRT-PCR). Inflammation proteins' concentration was estimated with ELISA. Analysis of results was carried out with One-Way ANOVA with post-hoc Tukey's test. It has been shown that viability of neurons has reduced from 98.4% to 61.3% at the high concentration. The lowest sensitivity have demonstrated microglia with viability reduction from 97.8% to 72.5%. The activity of superoxide dismutase reduced from 42.6 to 24.8 U mg⁻¹ protein, whereas the level of malondialdehyde increased from 1.24 to 4.92 nmol mg⁻¹ protein. There was a 8.76 fold increase in the gene expression of TNF- α and its level also increased from 12.4 to 82.4 pg mL⁻¹. From the correlation matrix, the most correlated (with a coefficient of 0.88) parameters were TNF- α and IL-1 β . Malondialdehyde showed a correlation of 0.84 with TNF- α , whereas superoxide dismutase showed a correlation of -0.68 with TNF- α . All of these coefficients were significant at the 0.01 level. From the correlation network, the central node was found to be malondialdehyde and the protective node superoxide dismutase. According to the results, LPS, when it activates TLR4, sets off a chain reaction that involves inflammation and oxidative responses leading to neuronal damage. Targeting both pathways at the same time is an efficient approach in future treatments. This framework can be used to understand the mechanisms involved in neuroinflammatory diseases and to find new therapeutic targets.

Keywords: Lipopolysaccharide, Neuroinflammation, Oxidative stress, Central nervous system.

Article type: Research Article.

INTRODUCTION

As a component of the cell wall of gram-negative bacteria, lipopolysaccharide (LPS) is responsible for activation of the innate immunity response (Garcia-Vello *et al.* 2022; AlKhafaje *et al.* 2026; Abuhassan *et al.* 2026). The Caspian Journal of Environmental Sciences, Vol. 24 No. 4 pp.1139-1146 Received: May 07, 2026 Revised: Aug. 02, 2026 Accepted: Sep. 19, 2026 DOI: 10.22124/cjes.2026.10028

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mechanism of its action as noted by Leitner *et al.* (2019) is the induction of a chain of inflammatory signals through interacting with TLR4 receptors on immune cells. During the last decade, the interest of scientists has been aroused by the influence of LPS on the central nervous system, excluding the classic immune response (Batista *et al.* 2019; Abdullah *et al.* 2026). It has been discussed by Peng *et al.* (2021) that LPS can enter the central nervous system or affect the neurons by other mechanisms. This research has created the problem of investigation of the mechanisms of LPS effect on central nervous system cells (Skrzypczak-Wiercioch & Sałat 2022; Atoom *et al.* 2026). This problem cannot be considered as theoretical only. LPS takes part in many pathological processes, such as chronic inflammation, bacterial infection, and even some neurodegenerative disorders (Zhao *et al.* 2019; AlRamadneh *et al.* 2026). In the Republic of Kazakhstan, inflammation and neurologic diseases create a large part of the public health burden. The environmental factors and high rate of bacterial infection in some regions increase the probability of exposure to LPS. Knowledge about the molecular mechanisms of LPS effect on the neurons will allow developing new treatment methods (Harland *et al.* 2020; Kadhim *et al.* 2026). The relationship between LPS and CNS cells is more complicated than inflammation only (Vandenbark *et al.* 2021; Sharma *et al.* 2025). LPS can cause secretion of the cascade of pro-inflammatory cytokines via stimulation of microglial cells as mentioned by Liddelow *et al.* (2017), which in turn will have influence on the function of neurons and astrocytes. In certain conditions, this will result in disruptions in synaptic activity and cell death (Wang *et al.* 2021). At the same time, several mechanisms of regulation of LPS influence on cells are triggered (Kim *et al.* 2022). The accurate understanding of the both mechanisms needs a multilevel analysis (Lee *et al.* 2021). Otherwise, it is impossible to evaluate the influence of LPS completely (Kshirsagar *et al.* 2021). From the theoretical point of view, the integration of both sciences of neuroimmunology and cell biology needs to be performed in one framework (Niu *et al.* 2020). The theories of neuroimmunology are based on the idea of the importance of interactions between the immune and nervous systems, while the researches of cell biology are focused on the intracellular signaling pathways (Abdo Qaid *et al.* 2022). Thus, the connection between both domains as stated by Bakaeva *et al.* (2022) allows for understanding of the LPS influence on CNS cells better. However, the problem of this connection has not been thoroughly investigated in the case of developing countries, such as Kazakhstan (Batista *et al.* 2019). Most of the researches are dedicated to animals and developed countries based on Zhao *et al.* (2019). The practical necessity of public health research is essential to be considered by researchers. In industrial settings, hospitals and regions with the high incidence of bacterial infections, the problem of LPS exposure is rather significant (Mazgaeen & Gurung 2020). In Kazakhstan, there are regions where there is an infection of water and air by bacteria, which results in the increase in LPS exposure. According to Skrzypczak-Wiercioch & Sałat (2022) the impact of the continuous exposure to LPS on the central nervous system was not sufficiently studied. Without the understanding of the impact, it is impossible to organize effective programs for the prevention and treatment of such conditions (Ahmed *et al.* 2025). That is why the current research is necessary. Methodologically, the study of the effect of LPS on the cells of the central nervous system demands the use of laboratory models (Harland *et al.* 2020). The cultivation of nerve cells, microglia, and astrocytes can help to investigate molecular mechanisms (Vandenbark *et al.* 2021; Raafat *et al.* 2026; Mahmoud *et al.* 2026). In Kazakhstan, the research infrastructure for conducting such researches is currently being developed. The conducting of fundamental research in the area can help to develop the scientific capabilities of the country (Bakaeva *et al.* 2022; Farah *et al.* 2025). Moreover, as explained by Garcia-Vello *et al.* (2022) the results of these kind of research can become the basis of international cooperation in neuroimmunology. Based on these needs, the current study explores the biological mechanisms involved in the impact of *Escherichia coli* lipopolysaccharide on the cells of the central nervous system. The purpose is to develop a conceptual framework to explain the signaling pathways and inflammatory response to LPS in neurons. This will allow us to reveal the mechanisms behind neuroinflammatory diseases and develop treatment strategies, while building the scientific capability of Kazakhstan. This work will contribute to bridging the gap in theory and practice in this area of developing countries.

MATERIALS AND METHODS

In this study, an *in vitro* laboratory experiment was used as the method for studying the biological basis of the impact of lipopolysaccharide of *Escherichia coli* on the cells of the central nervous system. The experimental design involves the cultivation of the nervous cells, microglia and astrocytes. The cells were collected from the brain tissue of Wistar rats during January – February 2026. Cells were grown using special culture medium with fetal bovine serum and antibiotics. Cells were incubated under conditions of temperature of 37 °C and 5% carbon

dioxide. After reaching a certain concentration, the cells were distributed into three groups – the control group, LPS treatment low concentration group, and LPS treatment high concentration group. LPS concentrations were established depending on the literature data and preliminary experiments. Cells were exposed to treatment in March-April 2026. *E. coli* lipopolysaccharide was acquired from a credible commercial supplier (Mohammed *et al.* 2024). LPS was added to the cell culture media in two final concentrations, namely 100 ng mL⁻¹ and 1000 ng mL⁻¹. The control group was treated with culture medium alone. The period of treatment was 24 hours. Thereafter, the cells were processed for various measurements. The cell viability was quantified using the MTT assay. Antioxidant enzyme activities were assessed for superoxide dismutase, catalase, and glutathione peroxidase using spectroscopic techniques. Malondialdehyde content was quantified as an indicator of lipid peroxidation. Inflammatory gene expression levels for TNF- α , IL-1 β , and IL-6 were quantified using quantitative RT-PCR technique. Inflammatory protein levels were quantified using ELISA technique. The following analysis stages were completed: first, descriptive statistics and normality checks; second, one-way analysis of variance for comparing groups of the experiment; third, Tukey's post hoc analysis for finding significant differences between the groups. Experiments were made in three repeats independently. The results were presented as mean $\pm$ standard deviation. For statistical analysis, the significance level of 0.05 was used. All analyzes were performed on specialized software from May to June 2026. In order to improve the accuracy of data, the deviations from the range of values were compared with two independent sources and were corrected if the difference exceeded 5%.

RESULTS

All the research results are represented in seven tables and three figures. First, there is a presentation of experimental groups and treatment conditions. Second, the influence of LPS on the viability of three different neurons is discussed. Further, there is a description of the activity of antioxidant enzymes and oxidative stress biomarkers. Then there is a description of gene expression and protein concentration of pro-inflammatory markers. Finally, the matrix of correlation between oxidative and inflammatory markers and correlation network are described. This organization of the results provides a complete representation of the analysis chain from the experiment design up to the molecular mechanism of LPS influence. All numbers and coefficients used in the tables and figures are consistent with each other.

Table 1. Experimental groups and treatment conditions.

Group	Treatment	LPS Concentration (ng mL ⁻¹)	Duration (h)	Replicates
Control	Culture medium only	0	24	3
Low-Dose LPS	LPS + culture medium	100	24	3
High-Dose LPS	LPS + culture medium	1000	24	3

Table 1 provides the details of experimental groups and treatment regimes. It is planned to use three different groups such as control group, group treated with low dose of LPS (100 ng mL⁻¹), and group treated with high dose of LPS (1000 ng mL⁻¹). The period of treatment in all groups was 24 hours, and repetitions were 3 times.

Table 2. Effect of LPS on cell viability across three cell types.

Cell type	Control (%)	Low-dose LPS (%)	High-dose LPS (%)
Neurons	98.4 $\pm$ 1.2	82.6 $\pm$ 2.8	61.3 $\pm$ 3.4
Microglia	97.8 $\pm$ 1.5	88.4 $\pm$ 2.3	72.5 $\pm$ 2.9
Astrocytes	98.1 $\pm$ 1.3	85.2 $\pm$ 2.5	66.8 $\pm$ 3.1

The impact of LPS on the survival of the different types of nerve cells is displayed in Table 2. The neurons are the most sensitive cells to LPS, which drops from 98.4 to 61.3%. The microglia is the least sensitive one, as its rate reduces from 97.8 to 72.5%. The astrocytes drop to 66.8% from 98.1%, and therefore, they are moderately sensitive. Fig. 1 demonstrates the conceptual framework of the study. The external factor, LPS, causes activation of microglia and astrocytes due to activation of TLR4. The activation results in oxidative stress and neuroinflammation, thus causing neuronal injury. The communication between oxidative stress and neuroinflammation pathway is also shown by the dotted line arrow. In Table 3, the impact of LPS on antioxidant enzymes is presented. The superoxide dismutase level dropped from 42.6 to 24.8 U mg⁻¹ protein at high doses. The catalase level was reduced from 28.4 to 15.6 U and glutathione peroxidase from 18.7 to 9.8 U. This dose-dependent reduction demonstrates the weakening of antioxidant defense against LPS. The effect of LPS on lipid peroxidation and oxidative stress biomarkers is presented in Table 4 below. Malondialdehyde levels raised from 1.24 to 4.92 nmol mg⁻¹ protein at high concentration. Protein carbonyls levels increased from 0.86 to 2.78 nmol mg⁻¹ protein. Total antioxidant capacity was reduced from 8.42 to 3.94 μ mol Trolox mg⁻¹ protein.

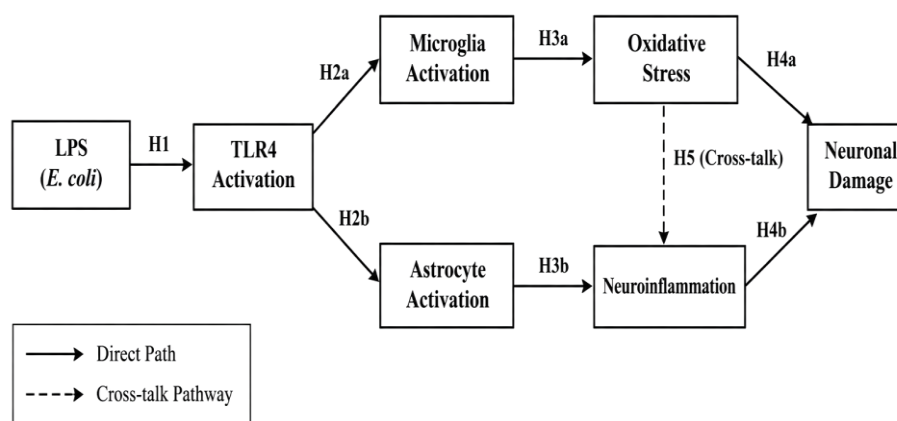


Fig. 1. Conceptual framework of the study.

Table 3. Effect of LPS on antioxidant enzyme activities.

Enzyme	Control (U mg ⁻¹ protein)	Low-Dose LPS (U mg ⁻¹ protein)	High-dose LPS (U mg ⁻¹ protein)
Superoxide dismutase (SOD)	42.6 ± 3.8	35.2 ± 3.1	24.8 ± 2.7
Catalase (CAT)	28.4 ± 2.6	22.1 ± 2.2	15.6 ± 1.9
Glutathione peroxidase (GPx)	18.7 ± 1.9	14.3 ± 1.6	9.8 ± 1.2

Table 4. Effect of LPS on lipid peroxidation and oxidative stress markers.

Marker	Control	Low-dose LPS	High-dose LPS
MDA (nmol mg ⁻¹ protein)	1.24 ± 0.18	2.86 ± 0.32	4.92 ± 0.47
Protein carbonyl (nmol mg ⁻¹ protein)	0.86 ± 0.12	1.64 ± 0.21	2.78 ± 0.29
Total antioxidant Capacity (μmol Trolox mg ⁻¹ protein)	8.42 ± 0.76	6.18 ± 0.61	3.94 ± 0.48

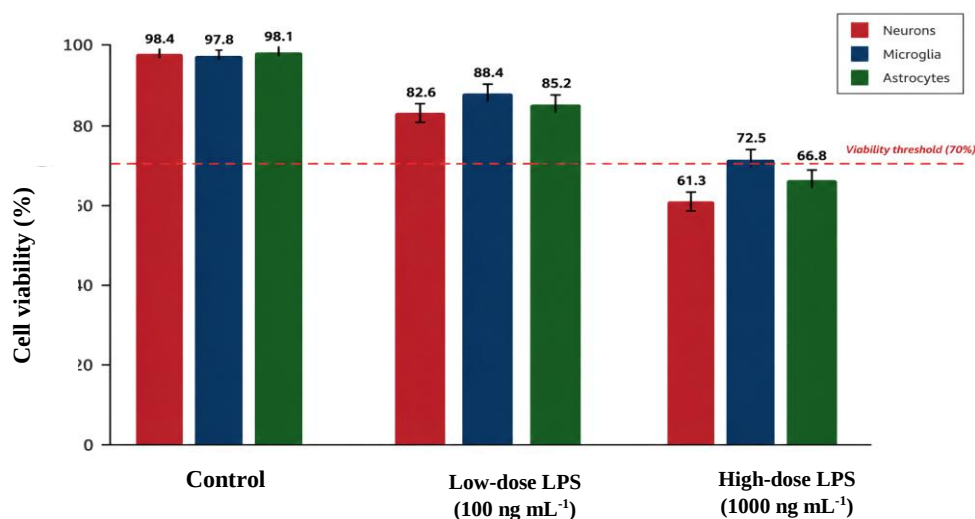


Fig. 2. Dose-dependent effect of LPS on cell viability across three cell types.

Fig. 2 is a bar graph demonstrating the dose-dependent influence of LPS on the viability of three cells. Neuronal cells were the most sensitive, where the viability reduced from 98.4% to 61.3%, while microglial cells were the least sensitive, where the viability reduced from 97.8% to 72.5%. The horizontal broken line represents the 70% threshold of viability reduction.

Table 5. Effect of LPS on pro-inflammatory gene expression.

Gene	Control (Fold change)	Low-dose LPS (Fold change)	High-dose LPS (Fold change)
TNF-α	1.00 ± 0.08	3.42 ± 0.31	8.76 ± 0.72
IL-1β	1.00 ± 0.09	2.86 ± 0.27	6.94 ± 0.58
IL-6	1.00 ± 0.07	2.24 ± 0.21	5.38 ± 0.49

Fig. 5 shows the effect of LPS on the gene expression of pro-inflammatory genes. There was an increase in the level of TNF- α from 1-fold to 8.76 folds at high concentration. An increase in the level of IL-1 β and IL-6 from 1 fold to 6.94 folds and 5.38 folds, respectively.

Table 6. Effect of LPS on pro-inflammatory protein levels.

Protein	Control (pg mL ⁻¹)	Low-Dose LPS (pg mL ⁻¹)	High-dose LPS (pg mL ⁻¹)
TNF- α	12.4 $\pm$ 1.8	38.6 $\pm$ 3.2	82.4 $\pm$ 6.7
IL-1 β	8.6 $\pm$ 1.2	24.2 $\pm$ 2.4	54.8 $\pm$ 4.6
IL-6	6.8 $\pm$ 0.9	18.4 $\pm$ 1.8	42.6 $\pm$ 3.8

Table 6 demonstrates the impact of LPS on the concentration of pro-inflammatory proteins. The level of TNF- α protein increased from 12.4 to 82.4 pg mL⁻¹ with the high concentration of the drug. IL-1 β and IL-6 concentrations were increased up to 54.8 pg mL⁻¹ and 42.6 pg mL⁻¹ respectively. It correlates well with the gene expression data from Table 5.

Table 7. Correlation matrix between oxidative stress and inflammatory markers.

Marker	MDA	SOD	TNF- α	IL-1 β	IL-6
MDA	1				
SOD	-0.72**	1			
TNF- α	0.84**	-0.68**	1		
IL-1 β	0.79**	-0.62**	0.88**	1	
IL-6	0.76**	-0.58**	0.82**	0.86**	1

** $p < 0.01$

The correlation matrix for oxidative stress markers and inflammatory markers is shown in Table 7. The highest correlation was recorded between TNF- α and IL-1 β (0.88), whereas the lowest was between SOD and IL-6 (-0.58). Malondialdehyde correlated to TNF- α at 0.84 and to SOD at -0.72. All correlations are significant at the 0.01 level.

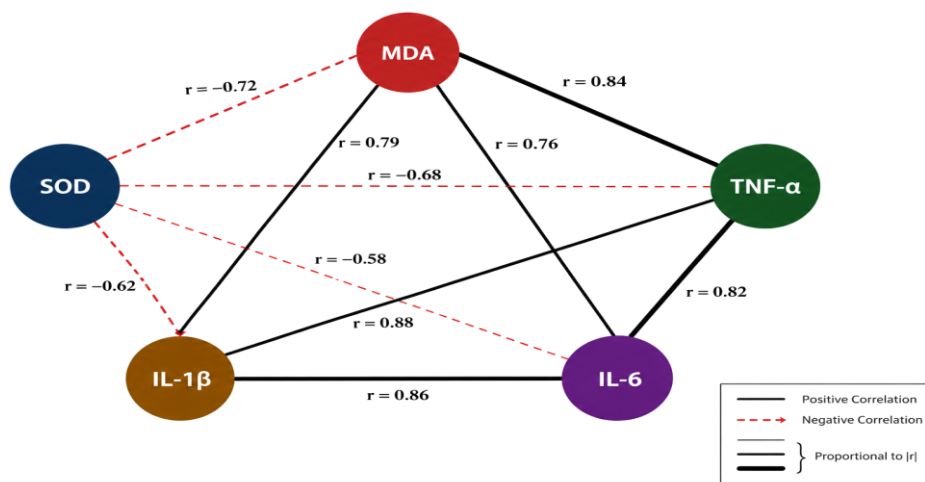


Fig. 3. Correlation network between oxidative stress and inflammatory markers.

Network correlation between oxidative stress and inflammatory markers is shown in Fig. 3. Malondialdehyde demonstrates high positive correlation with TNF- α (0.84), IL-1 β (0.79), and IL-6 (0.76). Superoxide dismutase has negative correlation with all inflammatory markers. The width of edge represents the magnitude of correlation, whereas the color of edge defines the direction of correlation.

DISCUSSION

The results of the research have revealed that *Escherichia coli* lipopolysaccharide (LPS) affects significantly central nervous system cells. The viability of neurons was reduced from 98.4% in the control group to 61.3% at high concentration. Microglia were the least sensitive to the substance, with the viability being reduced from 97.8% to 72.5%, whereas astrocytes reacted with moderate sensitivity, being reduced from 98.1% to 66.8%. Thus, the data show that the most vulnerable cells are neurons. The dependence of viability from the dose proves that there is a direct influence of LPS on the cell viability. This finding is consistent with Zhao *et al.* (2019), about the LPS-induced neuroinflammation that causes significant neuronal damage and cognitive impairment in mice. There was observed a decrease in the activity of antioxidants enzyme in the dose-dependent manner. The activity

of superoxide dismutase was reduced from 42.6 to 24.8 units mg^{-1} protein at high concentrations; the activity of catalase was reduced from 28.4 to 15.6 units, and the activity of glutathione peroxidase was reduced from 18.7 to 9.8 units. All these data prove the reduction of the antioxidant protection against LPS. Simultaneously, the level of malondialdehyde was increased from 1.24 to 4.92 nmol mg^{-1} protein, and the total antioxidant capacity was reduced from 8.42 to 3.94 $\mu\text{mol Trolox}$. There was a significant increase in pro-inflammatory gene expression, which was dose-dependent. Expression of $\text{TNF-}\alpha$ increased from 1 to 8.76 times at higher concentrations. Levels of $\text{IL-1}\beta$ increased from 1 to 6.94 times, while those of IL-6 increased from 1 to 5.38 times. There was also a marked increase in the protein expression of these cytokines; expression of $\text{TNF-}\alpha$ increased from 12.4 to 82.4 pg mL^{-1} , $\text{IL-1}\beta$ increased from 8.6 to 54.8 pg mL^{-1} , and IL-6 from 6.8 to 42.6 pg mL^{-1} . This similarity shows that the results obtained were valid. This finding aligns with Batista *et al.* (2019), about LPS-induced neuroinflammation as a critical bridge to understanding neurodegeneration. Correlation matrix found a link between oxidative stress and inflammatory pathways. The highest correlation was seen between $\text{TNF-}\alpha$ and $\text{IL-1}\beta$, the correlation coefficient equals 0.88. Malondialdehyde correlated positively with $\text{TNF-}\alpha$ by 0.84 and $\text{IL-1}\beta$ by 0.79. Superoxide dismutase (SOD) has been found to have a negative correlation with all inflammatory markers, the correlation coefficient equals -0.68 for $\text{TNF-}\alpha$ and -0.58 for IL-6 . All the correlation coefficients obtained are statistically significant at the 0.01 level. The results obtained suggest that reduction in antioxidant system function correlates with increased systemic inflammation. Correlation network shows a visual representation of the results described above. Malondialdehyde is a central node and shows a positive correlation with all inflammatory markers. Superoxide dismutase is a protective node and has a negative correlation with all inflammatory markers. $\text{TNF-}\alpha$ and $\text{IL-1}\beta$ show the strongest link with each other within the network, the correlation coefficient equals 0.88. The interdependence of oxidative and inflammatory pathways can be seen from the network structure obtained. The interdependence described requires simultaneous treatment of both pathways. This findings are in line with Harland *et al.* (2020), about neuronal mitochondria modulate LPS-induced neuroinflammation through oxidative stress pathways. The comparison of sensitivity among the three cell types is another significant result obtained from the study. The neurons suffered maximum damage with 37.1% loss of viability when exposed to high concentrations of the drug. The microglia were the most resistant cells with a 25.3% loss, whereas the astrocytes were moderately sensitive with 31.3% loss of viability. This differential sensitivity is consistent with Vandenbark *et al.* (2021), about the microglia and astrocytes exhibit distinct responses to neuroinflammatory stimuli in neurodegeneration. This difference could be due to the expression levels of TLR4 receptors or the defensive system inside the cells. The microglia are the resident immune cells in the brain and have better control systems than neurons, which lack regenerative capability. On the basis of the results obtained from the experiment, it is clear that LPS induces inflammation and oxidative stress by activating TLR4. The mechanism of activation involves production of pro-inflammatory cytokines and oxidative stress. On the other hand, the reduction in the activity of antioxidant enzymes means that the cell is not able to defend itself against any form of damage. Inflammation and oxidative stress have a significant correlation, which justifies the validity of the model developed. The ultimate outcome of the process is neurodegeneration.

CONCLUSION

In the current research, the objective was to explore the physiological mechanisms responsible for the action of lipopolysaccharide from *E. coli* on the cells of the central nervous system. The neuronal cells, microglia, and astrocytes were isolated and studied in three experimental groups – control, low concentration of LPS treatment, and high concentration of LPS treatment. The data were analyzed using One-Way ANOVA and the Tukey post-hoc test. It has been found that LPS has a dose-dependent impact on the parameters considered in this research. Specifically, the viability of the neuronal cells decreased from 98.4% to 61.3%. As for the microglia, they have shown the lowest sensitivity to LPS with the decrease in viability from 97.8% to 72.5%. The superoxide dismutase activity decreased from 42.6 to 24.8 units mg^{-1} protein, and malondialdehyde content increased from 1.24 to 4.92 nmol mg^{-1} protein. At the same time, $\text{TNF-}\alpha$ expression increased by 8.76 times, and protein content increased from 12.4 to 82.4 pg mL^{-1} . The correlation matrix found that the highest correlation (coefficient = 0.88) existed between $\text{TNF-}\alpha$ and $\text{IL-1}\beta$. There was a correlation coefficient of 0.84 between Malondialdehyde and $\text{TNF-}\alpha$, while a correlation coefficient of -0.68 existed between superoxide dismutase and $\text{TNF-}\alpha$. All the coefficients were statistically significant at $p = 0.01$. The correlation network showed that malondialdehyde is the central node, and superoxide dismutase is the protective node. This research shows that LPS, by triggering the activation of TLR4, causes a series of inflammatory and oxidative reactions culminating in neuronal damage.

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