Секция «Нейрофизиология и физиология ВНД»

Stimulation of EPOR/CD131 in ethanol-exposed rats results in changed expression of neural regeneration-, autophagy, apoptosis- and neuroinflammation-related genes

Научный руководитель – Дейкин Алексей Васильевич

Yusuf Maryam Wuraola

Student (specialist)

Белгородский государственный национальный исследовательский университет, Белгород, Россия

E-mail: maryamwuraola@gmail.com

Due to the intricacy of ethanol pharmacodynamics, the neurobiological basis of ethanol-induced neurodegeneration is still poorly understood. Nonetheless, long-term effects of known pathogenic factors that cause neuronal damage, such as oxidative stress, neuroinflammation and glutamate excitotoxicity, result in the activation of proapoptotic cascades and a decrease in neurotrophin synthesis. Some of the defense mechanisms targeted at responding to the neurotoxic effects of ethanol include autophagy activation and apoptosis inhibition; thus, pharmacolog regulation of apoptosis and autophagy may have potential therapeutic benefits in alcohol-induced neurodegeneration. Erythropoietin, an endogenous regulator of erythropoiesis (EPO) possesses both the properties of an apoptosis inhibitor and an autophagy activator [zubareva, 2016]. These properties are mediated by the EPOR/CD131 receptor agonist, which has been linked to tissue protection, anti-inflammatory, and antioxidant effects, even in nerve tissue damage [Zhong, 2020].

Aim: To analyze the expression patterns of genes associated with autophagy, apoptosis, neuroregeneration and neuroinflammation in ethanol-induced neurodegeneration.

Materials and methods: The study included 48 male wistar rats, (age 20 weeks, weight; 270-300g) grouped into 4 according to ethanol sensitivity. 1) Ethanol; 2) Ethanol + PHBSP; 3) Ethanol + EPO; and 4) Control.

To simulate ethanol-induced neurodegeneration, Rats were given 5%, 10%, 20% ethanol in this specific order in the span of 20 weeks. PHBSP and recombinant erythropoietin were administered at doses of 5μg/kg and 10μg/kg subcutaneously twice a week. Ethanol and control groups received apyrogenic water in an equivalent volume. Quantitative PCR was carried out to analyze the expression of autophagy, neuroinflammation and apoptosis genes in the rats.

Results: The qPCR analysis showed increase in the expression of *Atg7*, *Becn1* and *LC31* genes, associated with autophagy, which is consistent with results from other studies [Li, 2018]. Furthermore, this study revealed that EPO and PHBSP significantly attenuated the expression of *Il1b*, *Tnf* and *Ccl2* proinflammatory genes, reduced proapoptotic gene expression and restored the impaired expression of the *Bdnf* and *Ngf* neurotrophic factor genes.

Conclusion: Results confirm the significant roles of therapeutic regulation of apoptosis and autophagy in ethanol-induced neurodegeneration.

References

1) E. V. Zubareva, S. V. Nadezhdin, Y. E. Burda, et al., Pleiotropic effects of erythropoietin. Research Results in Pharmacol., 5(1), 53 – 66 (2019); doi: 10.3897 / rrpharmacology.5.33457.

2) L. Zhong, H. Zhang, Z. F. Ding, et al., Erythropoietin-induced autophagy.. improves neurological function. Mol. Neurobiol., 57(10), 3993 – 4006 (2020); doi: 10.1007 / s12035-020-01997-0.

3) Q. Li, Y. Han, J. Du, et al., Life Sci., 1 194, 15 – 25 (2018); doi: 10.1016 / j.lfs.2017.12.014.

Illustrations

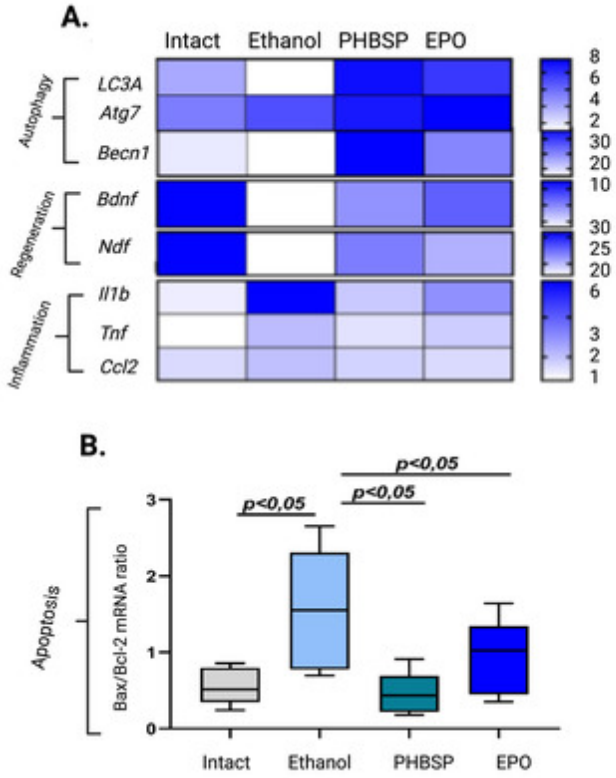

Fig.A Analysis of the expression of autophagy, regeneration and inflammation genes

Fig.B Analysis of the expression of apoptosis gene

Рис. 1. Analysis of the expression of autophagy, regeneration and inflammation genes