

Methods: Wild-type and knock-out (KO), young (8 weeks) and aged (32 weeks) murine aortae segments were isolated, vasoregulator effects of different LPA species were tested with myography. To examine general contractility and TXA2 receptor sensitivity we used phenylephrine (PE) and U-46619 dose-effect relationship, respectively. Assessment of mRNA expression was performed by qPCR.

Results: Saturated LPAs had no vasoconstrictor activity, but their vasorelaxant effect increased with fatty acid chain length reduction. In contrast, unsaturated LPAs evoked strong vasoconstriction in parallel with fatty acid chain unsaturation, while their vasorelaxant effect decreased with the degree of unsaturation. Both vasorelaxation and vasoconstriction disappeared in LPA1-KO vessels. 18:2 LPA mediated vasoconstriction was increased in the aortae of the 32-week population. There was no difference between the two age groups neither in the expression of LPA1 receptor nor in the PE and U-46619 dose-effect curves. The aged COX1-KO vessels shown no response to 18:2 LPA, as well as the young ones.

Conclusions: In conclusion, polyunsaturated LPAs, mainly increased in cardiovascular diseases, appear to have strong, age-dependent vasoconstrictor activity.

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E/6 ROLE OF AUTO-ANTIBODIES AGAINST THE NICOTINIC ACETYLCHOLINE RECEPTORS IN NEUROLOGICAL AND PSYCHIATRIC DISEASES

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Aims: Autoimmune diseases affect 6-7% of the world population. The potential relation between autoantibodies (AA) and neurological disorders was confirmed in connection with anti-NMDA-receptor encephalitis syndrome, where AA-s target NMDA receptors in the brain. According to our hypothesis AA-s against nicotinic acetylcholine receptors (nAChRs) have a central role in the development of neuroinflammation and in pathologies affecting brain structures.

Methods: In the first phase of our experiments we tested 165 monoclonal AA samples produced by B-lymphocytes isolated from the liquor of patients with NMDA-R encephalitis syndrome using indirect ELISA method. The antigens used in these experiments were the extracellular domains of the $\alpha 2$, $\alpha 7$ and $\alpha 4\beta 2$ subunits of the nAChR. Next tested the functional activity of the samples found positive for $\alpha 7$ in *Xenopus Laevis* oocytes expressing $\alpha 7$ -nAChR using whole-cell clamp technique.

Results: Of these, 29 were positive in the ELISA testing in the following distribution: 9 for [$\alpha 7$], 8 for [$\alpha 4\beta 2$], 1 for [$\alpha 2$], 6 for [$\alpha 4\beta 2+\alpha 2$], 1 for [$\alpha 4\beta 2+\alpha 7$], 2 for [$\alpha 2+\alpha 7$], 2 for [$\alpha 2+\alpha 7+\alpha 4\beta 2$]. In 5 cases of the whole-cell clamp experiments current generated by the activation of these receptors was reduced by more than 50% in the presence of the AAs, suggesting an inhibition of intracellular Ca^{2+} levels.

Conclusions: Based on our results we can conclude that a large number of patients with anti-NMDA-receptor encephalitis syndrome had nAChR-specific and functionally active AA producing cell in their central nervous system. This observation opens new perspective in understanding diseases affecting the central nervous system and suggest new therapeutic strategies against autoimmune diseases.