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LYSOPHOSPHATIDIC ACID (LPA) MEDIATED VASOCONSTRICTION DEPENDS ON FATTY ACID CHAIN UNSATURATION AND CHANGES WITH AGE

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Our research group has recently reported that LPA1 receptor activation in the endothelium induces vasorelaxation, whereas in the vascular smooth muscle (VSM) it evokes cyclooxygenase 1 (COX1) activation with consequent thromboxane A2 (TXA2) release, which elicits vasoconstriction.

In this study, we aimed to compare the vasoactive effects of saturated and unsaturated LPA species on the vascular tone and to identify their signal transduction. Since vascular diseases are more common in the elderly, we also aimed to observe the age-related changes of the 18:2 LPA induced vasoconstriction.

In aortic segments isolated from young and middle-aged (8 and 32 weeks old, respectively) wild-type and knock-out (KO) mice the vasoactive effects of different LPA species were determined with wire myography. To compare the LPA induced signal transduction in the two age groups general contractility and TXA2 receptor sensitivity were tested by examining phenylephrine (PE) and U-46619 dose-response relationship, respectively. Expression profile of LPA1-3 receptors were demonstrated by qPCR in the VSM cells.

Saturated 14:0, 16:0 and 18:0 LPAs had no vasoconstrictor activity, and their vasorelaxant effect increased with the reduction of the fatty acid chain length. Highest vasorelaxant effect was mediated by the mono-unsaturated oleoil-LPA, whereas increase in the number of double bonds results in decreased vasorelaxing and increased vasoconstricting activity. Both relaxation and constriction disappeared in the LPA1-KO vessels. 18:2 LPA mediated vasoconstriction was increased in the aortae of the 32-week old mice. There was no difference between the two age groups neither in the expression of LPA1 receptor nor in the PE and U-46619 dose-response curves. 18:2 LPA mediated constriction was diminished in vessels of both the middle-aged and young COX1-KO animals.

In conclusion, polyunsaturated LPAs appear to have strong, age-dependent vasoconstrictor activity. This is particularly interesting in the case of endothelial injury and platelet activation where polyunsaturated LPAs can contribute to the progression of vasospasm and they may have an enhanced role in the cardiovascular diseases in the elderly.

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