Impaired endothelium-dependent vasodilator responses of retinal blood vessels in adult rats with a history of retinopathy of prematurity

Asami Mori[1], Ayuki Nakano[1], Daiki Sumida[1], Rho Kondo[1], Daiki Asano[1], Akane Morita[1], Kenji Sakamoto[1,2], Tsutomu Nakahara[1]

[1]Dept. Mol. Pharmacol., Kitasato Univ. Sch. Pharm. Sci., [2]Lab. Med. Pharmacol., Fac Pharma-Sci. Teikyo Univ.

Retinopathy of prematurity (ROP) is the leading cause of childhood blindness. We reported that short-term interruption of retinal vascular development with blockade of vascular endothelial growth factor (VEGF) signaling pathway in neonatal rats induces ROP-like retinal blood vessels, such as aggressive angiogenesis and tortuous arteries. Using this ROP model rat, we examined whether a history of ROP affects retinal vasodilator responses in adulthood. ROP was induced in rats by the subcutaneous injection of the VEGF receptor tyrosine kinase inhibitor KRN633 on postnatal day (P) 7 and P8. Tortuous arteries were observed in retinas of P56 KRN633-treated (ROP) rats. Retinal vasodilator responses to endothelium-dependent vasodilators (acetylcholine and GSK1016790A [an activator of TRPV4 channels]) were smaller in P56 ROP rats than age-matched control rats. No diminishment of acetylcholine-induced retinal vasodilator response was observed in P56 ROP rats treated with L-NAME, an inhibitor of NO synthase. Retinal vasodilator responses to NOR3, an NO donor, and salbutamol, a β_2 receptor agonist, were unaltered. These results suggest that the production and release of NO in retinal blood vessels are impaired in adult rats with a history of ROP. A history of ROP may increase the risk of the onset of retinal vascular diseases in adulthood.