Effects of Acute and Chronic Alcohol Consumption on the Blood-Brain Barrier

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The most abused chemical, alcohol, has been linked to dementia and ischemic stroke, in which blood-brain barrier (BBB) dysfunction is a common characteristic. The goal was to investigate if and how alcohol induces BBB dysfunction. In in vivo studies, adult male C57BL/6J mice were given 0.7 or 2.8 g/kg ethanol once or once a day for two months. Sodium fluorescein (NaFl) extravasation and expression of endothelial junctional proteins, autotaxin, and lipid phosphate phosphatase-3 (LPP3) in the cerebral cortex were measured before and after a 90-minute ischemic stroke. In in vitro studies, C57BL/6J mouse brain microvascular endothelial cells (MBMVECs) were exposed to 10 or 50 mM ethanol once or once a day for two weeks. Morphology of endothelial junctional proteins, transendothelial electrical resistance (TER), mitochondrial superoxide production (MSP) and oxygen consumption rate (OCR) were evaluated before and after a 3-hour oxygen-glucose deprivation (OGD). 2.8 g/kg ethanol was found to have significantly increased baseline and post-ischemic NaFl extravasation, downregulated endothelial junctional proteins and LPP3, and upregulated autotaxin. Moreover, 50 mM ethanol induced a discontinuous junctional protein alignment, significantly decreased TER and baseline and post-OGD OCR, and increased baseline and post-OGD MSP. In contrast, 0.7 g/kg ethanol attenuated post-ischemic NaFl extravasation and 10 mM ethanol alleviated post-OGD MSP and improved post-OGD OCR. Thus, heavy alcohol consumption may cause BBB dysfunction by promoting mitochondrial oxidative stress and dysfunction and activating lysophosphatidic acid (LPA) signaling, whereas light alcohol consumption may protect against post-ischemic BBB dysfunction by diminishing mitochondrial oxidative stress and dysfunction.