Methamphetamine's Influence on the Blood-Brain Barrier: Dissecting Changes in Microvascular Endothelial Cell Structure and Function

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Methamphetamine is known for its addictive potential and rapid impact on the central nervous system's dopaminergic pathways. Recent studies suggest it exacerbates stroke outcomes by increasing the permeability of endothelial cells, affecting the blood-brain barrier (BBB). This study investigates the specific mechanisms behind this effect. We propose that high concentrations of methamphetamine influence junctional proteins in endothelial cells by amplifying oxidative stress, thereby impacting cellular permeability. The study employed a multi-faceted approach. First, an Electrical Cell-Substrate Impedance Sensing (ECIS) machine assessed permeability changes in Mouse Brain Microvascular Endothelial Cells (MBMEC) upon meth exposure. Next, we measured superoxide levels in MBMECs using High-Performance Liquid Chromatography (HPLC) to evaluate the production of reactive oxygen species (ROS) induced by meth. Finally, Western Blot analyses for claudin-5, occludin, ß-catenin, and superoxide dismutase (SOD2) were conducted to investigate the drug's effects on oxidative stress and junctional proteins. The ECIS data indicated increased permeability in MBMECs at meth concentrations of 250μM and 500μM. Meth at 250μM concentration also significantly elevated superoxide levels and reduced SOD2 levels. A marked down regulation in the expression of occludin, claudin-5, and ß-catenin was also observed at both 250μM and 500μM concentrations ($p<0.01$). Methamphetamine decreases junctional protein levels in MBMECs in a concentration-dependent manner, partly due to increased oxidative stress. These findings elucidate the drug's detrimental impact on the BBB and its potential role in exacerbating stroke, highlighting the need for further research into protective and therapeutic interventions.

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