S47-6 The analysis of mechanisms underlying blood-brain barrier dysfunction using a novel *in vitro* BBB model

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Blood-brain barrier (BBB) is a physical barrier formed by tight junctions (TJs) between brain microvessel endothelial cells (BMECs), and serves to maintain the homeostasis of the brain microenvironment. In addition, it has been demonstrated that direct and indirect crosstalk between BMECs and other CNS cells, such as astrocytes and neurons, is important for the integrity of BBB. However, the cellular and molecular mechanisms underlying such a crosstalk are still poorly understood. In this study, we examined alterations in barrier function after neuronal injury using a novel *in vitro* BBB model composed of rat primary BMECs, astrocytes and neurons. The barrier function was evaluated by transendothelial electrical resistance (TEER) and permeability of dextran. NMDA treatment, which causes severe neuronal injury, decreased TEER and increased permeability of FITC-dextran after 48 h of exposure to NMDA. Immunoblot and immunohistochemical analyses revealed that these functional changes were accompanied by reduced membrane localization of TJ proteins, such as occludin and claudin-5. These results suggest that neuronal injury causes the BBB dysfunction by alterations in the subcellular localization of TJ proteins. The present results suggest the usefulness of our novel *in vitro* BBB model to investigate the neuronal injury-induced BBB dysfunction and possibly to examine the mechanism for invasion of inflammatory cells into the damaged brain parenchyma.