Endovascular perforation murine model of Subarachnoid Hemorrhage

An applicable Murine Model of Subarachnoid Hemorrhage should have the characteristics of low mortality rate, limited surgical manipulation, and adaptation, which permits reproducibility and standardization.

In theory, endovascular perforation replicates the trauma experienced by the brain upon ruptured aneurysm. Pathophysiological events observed in SAH patients during intracranial aneurysm rebleeding are also replicated by EVP model. For these reasons the EVP model is considered the closest representation of human SAH and is commonly employed to study early brain injury [1) 2) 3)].

Sehba presented a brief review of historical development of the EVP model and details the technique used to create SAH and considerations necessary to overcome technical challenges [4)].

An intensive discussion of how to improve the techniques and refine the procedure has taken place in the last decade. Du et al. described the experiences with a murine model of SAH. They aimed to standardize and optimize the procedures to establish a relatively stable animal model for SAH research [5)].

A total of 159 dynamic and static gait parameters from the endovascular perforation murine model for simulating clinical human SAH were determined using the CatWalk system. Eighty gait parameters and the mRNA expression levels of 35 of the 88 SAH-associated genes were differentially regulated in the diseased models. Totals of 42 and 38 gait parameters correlated with the 35 SAH-associated genes positively and negatively with Pearson's correlation coefficients of > 0.7 and < -0.7, respectively. p-SP1453 expression in the motor cortex in SAH animal models displays a significant correlation with a subset of gait parameters associated with muscular strength and coordination of limb movements. Our data highlights a strong correlation between gait variability and SAH-associated gene expression. p-SP1453 expression could act as a biomarker to monitor SAH pathological development and a therapeutic target for SAH [6)].

Schüller et al. in a published a standardized mouse model of subarachnoid hemorrhage (SAH). Bleeding is induced by endovascular Circle of Willis perforation (CWp) and proven by intracranial pressure (ICP) monitoring. Thereby a homogenous blood distribution in subarachnoid spaces surrounding the arterial circulation and cerebellar fissures is achieved. Animal physiology is maintained by intubation, mechanical ventilation, and continuous on-line monitoring of various physiological and cardiovascular parameters: body temperature, systemic blood pressure, heart rate, and hemoglobin saturation. Thereby the cerebral perfusion pressure can be tightly monitored resulting in a less variable volume of extravasated blood. This allows a better standardization of endovascular filament perforation in mice and makes the whole model highly reproducible. Thus it is readily available for pharmacological and pathophysiological studies in wild type and genetically altered mice [7)].

References

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