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A New Mass Effect Research Rat Model to Explore the Occuping Effect on Secondary Brain Injuries after ICH

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Abstract: The mechanical response of brain tissue closely relates to cerebral blood flow and brain diseases. During intracerebral haemorrhage (ICH), a mass effect occurs during the initial bleeding. As the hematoma increases, the haematoma mass effect continues to squeeze the brain tissue mechanically, which can even lead to the formation of fatal cerebral hernia. However, fewer studies have focused on the brain damage mechanisms and treatment approaches associated with mass effects compared to the secondary brain injuries after ICH, which may be a result of the absence of acceptable animal models mimicking a mass effect. Thus, a thermo-sensitive poly (N-isopropylacrylamide) (PNIPAM) hydrogel was synthesized and injected into the rat brain to establish an ICH model for mass effect research. The PNIPAM hydrogel or autologous blood was injected to establish an ICH animal model, and the space-occupying volumes, brain tissue elasticity, brain oedema, neuronal cell death, iron deposition and behavioural recovery were evaluated. The lower critical solution temperature of PNIPAM hydrogel was 32°C, and the PNIPAM hydrogel had a rough surface with similar topography and pore structure to a blood clot. Furthermore, the ICH model animals who received an injection of PNIPAM and blood produced similar lesion volumes, elasticity changes and mechanically activated ion channel piezo-2 upregulation in brain tissue. Meanwhile, slight iron deposition, neuronal cell death and brain oedema were discovered in the PNIPAM hydrogel model compared to the blood model. In addition, the PNIPAM hydrogel showed good biocompatibility and stability *in vivo* via subcutaneous implantation. When the blood and PNIPAM were co-injection, the course of erythrocyte lysis and hemoglobin release accelerated significantly, and the iron deposition increased dramatically compared to the blood injection group. Our findings show that PNIPAM hydrogel cerebral infusion can form a mass effect similar to haematoma and minimize the interference of blood, and the haematoma mass effect has significant effect on erythrocyte lysis and metabolism. Therefore, the establishment of a mass effect ICH model is beneficial for understanding the mechanism of primary brain injury and the role of mass effects in secondary brain damage after ICH.

Keywords: Intracerebral haemorrhage; animal model; mass effect; PNIPAM; secondary brain injuries

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