Focal delivery of AAV2/1-transgenes into the rat brain by localized ultrasound-induced BBB Opening

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Background

Blood brain barrier (BBB) is one of the major components of central nervous system (CNS) which prevents all kinds of external molecules to infest CNS.¹ However this protection also prevents gene and targeted drug delivery to CNS. The tight junctions of BBB pose as an impermeable wall for components to penetrate within the BBB.² Recently an upcoming approach of utilizing Ultrasound with ultrasound contrast components is of interest to researchers as it allows the penetration of these components without damaging neuronal cell. Using the above technique till now antibodies or plasmid DNA has been successfully delivered into rodents.³

Study Design

The vector plasmid encoding for AAV2 terminal repeat elements and the transgene nlsLacZ (nuclear localization signal; β -galactosidase) driven by a CMV promoter was created. For opening of BBB 500 KHZ transducer was used. It was positioned stereotactically over the wistar rat and one hemisphere was isolated. Transducer was run by wave form generator and amplifier. To validate BBB opening the rat had to undergo MRI scan of brain. Gulo-dinum a chemical which do not pass the

intact BBB in histochemical sections was found to be located in transfected cells of CNS. Immunohistochemistry and RTPCR quantification were done to analyse the transfection of vector plasmid into the rat brain.

Implications

Authors describe the targeted delivery of AAV into BBB by ultrasound. It opens up new paths and possibilities to treat disorders linked to CNS. However further studies on animal models are required to validate the technique having immense potential in clinical therapy.

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Reference

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