SYSTEMIC ADMINISTRATION OF A NOVEL AAV VARIANT RESULTS IN WIDESPREAD AND EFFICIENT GENE TRANSFER IN R6/2 MICE.

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Background: Therapeutic gene delivery to the central nervous system (CNS) remains a challenge in Huntington's disease research. The blood brain barrier restricts the delivery of therapeutic agents to various cell types in the CNS known to be involved in disease progression. Recombinant adeno-associated viral vectors (rAAVs) are frequently used for *in vivo* gene delivery in neurodegenerative research but can have poor or limited tropism in the CNS when delivered systemically. When injected directly into the CNS, AAVs are efficient at transducing a variety of cell types though with limited spread. Conversely, when naturally occurring AAVs are injected systematically they lead to widespread transgene expression but with low transduction efficiency.

Aims: The aim of this experiment was to utilise a novel AAV variant, ssAAV-PHP.B:CAG-GFP, to investigate and compare its transduction efficiency in brains of wild type (WT) and R6/2 mice.

Methods: Four week old WT and R6/2 mice were intravenously injected through the tail vein with 5×10^9 vg/g with ssAAV-CAG-NLS-GFP packaged into AAV-PHP.B. Three weeks later, the mice were perfused and the brains processed for immunohistochemistry. GFP expression was assessed using images captured by a laser scanning confocal microscope.

Results: We show that systemic delivery of this AAV variant results in widespread and efficient GFP expression in different cell types throughout the CNS in both WT and R6/2 mice. Currently, we are assessing the impact of age and disease stage upon transduction efficiency.

Conclusion: Our results demonstrate the potential for use of this AAV vector as an approach to knock-down or deliver genes of interest to the CNS.

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