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A physiologically plausible spatiotemporal model of bold allows deconvolution of hemodynamic and neuron response components

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Abstract
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ORAL-17-01  
EFFICIENT DELIVERY OF siRNA TO NEURONS USING LAYERED DOUBLE HYDROXIDE NANOPARTICLES  
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Purpose: Small interfering RNAs (siRNAs) are capable of targeting and destroying specific mRNAs, making them particularly suited to the treatment of neurodegenerative conditions such as Huntington’s Disease. However, the delivery of unprotected siRNAs is ineffective due to their susceptibility to degradation by ubiquitous nucleases. Layered double hydroxide nanoparticles (LDHs) are now emerging as a potential drug delivery system as they exhibit low cytotoxicity and are highly biocompatible. This study aims to develop LDHs as an efficient and safe siRNA delivery system for the central nervous system.  

Methods: Initially, fluorescently tagged dsDNA-cy5-LDH complexes were injected into the lateral ventricles of C57BL/6 mice (n=3) to determine the extent of penetration. Effectiveness of gene targeting was then assessed by injection of siRNA siFP-LDH complexes into the ventricles of EGFP expressing mice (n=3). Coronal sections of C57BL/6 mice were processed for fluorescence analysis and EGFP levels were assessed by Western Blotting. Results: The fluorescence intensity observed in the brain of the dsDNA-cy5-LDH group was significantly higher than that injected with dsDNA-cy5 only (Student t-test, p<0.05%). The Western Blot results showed that the EGFP protein level in the siRNA-EGFP only group (Student t-test, p<0.05%). Conclusion: Our study demonstrated that intraventricular injection of dsDNA-loaded LDHs resulted in widespread distribution in the brain of the dsDNA-cy5-LDH group was lower than in the siRNA-EGFP only group (Student t-test, p<0.05%). The Western Blot results showed that the EGFP protein level in the siRNA-EGFP only group (Student t-test, p<0.05%).