Treatment Strategies

Nose-to-Brain Delivery of Therapeutic Agents against Blast-induced Traumatic Brain Injury (TBI)

Several neuroprotective compounds showing efficacy against neuronal injury in in vitro or ex vivo studies are limited for clinical applications due to their inability to cross the blood brain barrier (BBB). Non-invasive intranasal nose-to-brain delivery bypasses the BBB to rapidly deliver drugs to the central nervous system (CNS) along the olfactory and trigeminal neural pathways. Studies conducted in various laboratories have shown that drugs applied in this manner can be detected in the brain and CSF within five-10 minutes of application. Charged molecules, neuroactive peptides, and small proteins which cannot permeate the BBB can be rapidly delivered to the brain in minutes through the nasal route. The non-invasive intranasal administration doesn't require sterile conditions and hence can be self-administered in non-sterile environments such as on the battlefield. Since intranasally administered drugs avoid hepatic first-pass effect and subsequent dilution, it will be very cost effective. Using validated pre-clinical rodent models of single and repeated blast-induced TBI utilizing an advanced blast simulator (ABS), researchers at the Walter Reed Army Institute of Research (WRAIR) have demonstrated quantitative intranasal delivery to the brain of polar macromolecules otherwise excluded by the BBB and are evaluating the efficacy of these molecules as countermeasures to blast-induced neurotrauma following this novel route of administration. The intranasal brain delivery of drugs is being evaluated using the Precision Olfactory Delivery (POD) device from Impel NeuroPharma obtained using a Material Transfer Agreement. Preliminary data collected from this study showed that N-acetyl cysteine and N-acetyl tryptophan, two potential neuroprotective drugs which cannot easily penetrate the BBB, can be delivered to the brain in significant amounts using the POD in rats. By establishing an effective delivery route of efficacious agents to the injured brain that are otherwise excluded by the BBB, these experiments will expand the realm and provide valuable insights into intranasal brain delivery of therapeutic countermeasures for affected Service Members.