Torsion-Induced Traumatic Optic Neuropathy (TITON): Animal Model for Diagnostics, Drug Delivery, and Therapeutics for Injuries to the Central Nervous System

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PUBLIC ABSTRACT

The cells of the optic nerve act like wires in a camera cable transmitting information from the retina to the brain. Even if the eye itself is uninjured in an accident, the optic nerve cells may be injured and die. Injuries to the optic nerve commonly result from automobile accidents, sports injuries, falls, explosions, and other scenarios arising in both civilian and combat settings. Depending on the severity of injury, the patient may suffer partial or total loss of vision depending on whether some or all of the nerve cells are injured. Diagnosing this injury remains a challenge due to inaccessibility, and small size, of the optic nerve. No treatment is currently available for such injuries.

Once an injury to the optic nerve occurs, the long nerve cells try to reconnect by growing extensions towards the site of injury. If the damage is very minor, the two sides of the nerve will reconnect and the cell will spontaneously regenerate. Unfortunately, and since nerves usually cannot reconnect, the two sides of the nerve retract and form a scar. Once this retraction begins, the cell goes through programmed cell death (apoptosis). Thus, the window of opportunity for treating optic nerve injuries is between the time of the accident and the beginning of nerve retraction -- within about 48 hours. Diagnosing the injury is difficult and usually requires magnetic resonance imaging (MRI) techniques, which are not available in a battlefield setting. Thus, even if a successful treatment were available, Soldiers injured in combat would not be diagnosed in time to receive treatment.

The proposed research focuses on the development of diagnostic tools and treatments for injuries to the optic nerve that may translate to injuries of other parts of the central nervous system. We will combine MRI and new molecular detection techniques to correlate the extent of injury with the presence of proteins in circulating blood, eventually developing a blood test for optic nerve injury that could be used for rapid, inexpensive diagnosis. Several drugs have shown promise in treating optic nerve injuries but have negative side effects due to systemic (e.g., intravenous) delivery. We will develop new, localized delivery techniques to overcome this shortcoming. We have also devised a new mechanism for mechanical enhancement of nerve regeneration in the central nervous system.

One of the most common mechanisms for this injury is a rapid rotation of the eye, which stresses the optic nerve. We have, therefore, developed a unique and novel robotic system that rapidly rotates the eye of rats to repeatably induce this injury. MRI and blood samples will be taken immediately following nerve injury. One of several treatments will then be applied locally to the site of injury via injection of appropriate therapeutic compounds behind the eye. The relative effects of each treatment will be quantified and compared to enhance current understanding of cell and tissue regeneration mechanism(s) of regeneration in the central nervous system.

Thus, even if the specific drugs chosen to be tested in this study do not achieve the desired outcome of successfully promoting nerve
regeneration, we will gain valuable insights into what the most important factors required to encourage this regeneration. By using a model of central nervous system injury, the outcomes of this study may also benefit Soldiers and civilians suffering from injuries to the brain and spinal cord.