Hypothermia in the Treatment of Retinal Injury

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PUBLIC ABSTRACT

Objectives and Rationale: Eye injuries are very common among military personnel exposed to blasts in the battlefield. As a result of the blast, several biochemical reactions occur in the eye resulting in the destruction of key cellular components responsible for vision formation and transmission to the brain. Blocking or delaying these biochemical reactions may be a good strategy to prevent and/or delay eye damage and vision loss. Our previous experience with other models of eye injury, specifically studying damage produced by asphyxia at the time of birth, tells us that application of cold temperatures (hypothermia) to the eye results in an almost complete prevention of eye damage and consequent vision loss. Recent studies show that, although expression of most proteins gets reduced following temperature reduction, some of them react in the opposite way, constituting an interesting group of cold-inducible proteins that may be responsible for the beneficial effects of hypothermia. In this project, we plan to study the conditions needed to induce these proteins both in vitro (in cell lines) and in vivo (using an animal model of eye injury in rats) and establish the correlation between activating these proteins and preventing vision loss. In addition, we plan to screen a large collection of chemical compounds looking for those capable of stimulating the activity of the cold-induced proteins in order to generate new drugs able to generate the benefits of hypothermia in the absence of a cold source.

Ultimate Applicability and Potential Impact of the Research: Hypothermia has been shown to protect the brain and its derivatives (including the eye) from a variety of insults including trauma, lack of oxygen (which is called hypoxia or ischemia), and inflammation, among others. The discovery of cold-inducible proteins opens a door to the characterization of the molecular mechanisms underlying this process. In addition, the identification and characterization of new drugs capable of reaping the benefits of hypothermia in the absence of a cold source offers the possibility of treating traumatic lesions in remote areas where a cold source may not be available and to reach internal organs that may not be amenable to the topical application of cold devices.

Benefit for Service Members, Veterans, and/or Their Family Members: A recent study shows that between the years 2000 and 2010, more than 54,000 US troops experienced eye injury or vision loss in the battlefield. Furthermore, the incidence of ocular trauma increases progressively due to the use of new and more potent explosives in war theatres. The application of hypothermia, either through a cold source or our proposed new drugs, is an innovative, quick, and cheap remedy that could prevent or delay the blast effects on the eye. Although the actual percentage of vision loss prevention induced by hypothermia in the context of eye trauma will be studied during this project, our previous experiments on baby rats shows that hypothermia prevents almost 100% of the biochemical and morphological changes elicited by lack of oxygen during birth. Even a more modest effect will have impressive impact on the visual health of exposed service members and on the Department of Veterans Affairs’ budget.