Elucidation of Inflammation Processes Exacerbating Neuronal Cell Damage to the Retina and Brain Visual Centers as Quest for Therapeutic Drug Targets in Rat Model of Blast Overpressure Wave Exposure

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PUBLIC ABSTRACT

A frequent cause of traumatic eye injuries on the battlefield to soldiers is exposure of the face to bomb blast shock waves, which in severe cases results in non-penetrating eye damage that can lead to permanent loss of vision. Typically, these injuries involve serious damage to the retina, but can also include disruption of areas in the brain responsible for processing visual information. Despite the difficult lifelong disability that loss of vision represents, there are a limited number of animal studies in rodents that have assessed blast wave injuries to the visual system, and only one has tested potential drug therapies. Also, none have looked at the combined roles that the retina and brain play in shaping the outcome of visual system injuries. Thus, we feel there is an urgent medical need to advance the characterization in our lab of blast wave injuries to the visual system (retina and brain), such that the biological processes behind the injuries can be better understood to help identify candidate drug treatments. Inflammation plays a key role in aggravating the destruction of tissues following blast wave injuries and is carried out by the negative activities of immune cells (white blood cells), and thus this biological process is a highly promising drug target. The scope and timing, however, of the immune cell activities must be better understood to help narrow down the search. Our study will utilize a rat model of eye and brain injuries, as produced by exposure of the animals to simulated blast waves generated by a compressed air driven cannon (shock tube). Before blasting and continued thereafter, the rats will be placed on high saturated fat diets deficient in omega-3 polyunsaturated fatty acids, including docosahexaenoic acid (DHA), a nutritional state known to encourage inflammation. This will enhance our ability to detect inflammation processes and nerve cell death in the blast wave injured brain and retina. Conversely, some rats will be fed an omega-3 enriched diet by supplementing them with fish oil, an abundant source of DHA, which will look at the medicinal benefits of DHA toward blast injuries to the retina and brain. We will characterize the physical and functional damage to the eyes (retinas) and brain as judged by subjecting the live animals to retina electrical activity recordings (ERG test); a visual acuity task to discern a black and white bar pattern (optokinetics test); and then after euthanasia, by looking at the accumulation of inflammation inducing immune cells in the retina and brain as well as changes in the organ's physical appearance using advanced magnetic resonance imaging (MRI) techniques. Health of the removed eyes (retinas) and brains will also be judged by examining cut sections under a microscope after treating them with stains that highlight activated immune cells and dead nerve cells. We will also look at samples of brain, retina, and blood (plasma) for changes in levels of inflammation signaling molecules secreted by the immune cells. Overall, our mission is to provide scientific data that will lead to selection and animal testing of new drugs for blast-induced damage sustained to the visual system by members of the US Army.