G52 Brain Tissue Responses After Traumatic Brain Injury in Animal Models

Kazuhiko Kibayashi, MD, Ken-ichiro Nakao, MS, and Ryo Shimada, PhD, Department of Legal Medicine, School of Medicine, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo, 162- 8666, JAPAN*

After attending this presentation, attendees will more clearly understand the types of animal models of traumatic brain injury (TBI), the significance of experimental studies of TBI and the mechanisms of brain damage after TBI.

This presentation will impact the forensic science community in aiding the understanding of the mechanisms of brain damage after closed and open head injuries. These studies also show the sequential changes occurring in the brain after TBI: changes that should be useful for estimating the time after trauma in cases of head injury.

TBI can be caused both directly, by immediate mechanical disruption of brain tissue, and indirectly, by delayed injury mechanisms that include intracranial hemorrhage, brain edema, and hypoxic/ischemic damage. Whereas human TBI is a highly complex multifactorial disorder, animal models of TBI are able to focus on various specific factors involved in TBI and so have helped develop a better understanding of pathophysiology after brain injury, including changes in cellular and molecular pathways. The commonly used models that replicate human closed head injuries are fluid percussion, controlled cortical impact, weight drop and freeze injury models. Utilizing these models allows us to produce a controlled range of severity of brain injury.

The magnitude- and time-dependent changes after TBI in a rat fluid percussion model was studied. The focus was on synaptophysin (SYP), a molecular marker of synapse. SYP immunoreactivity increased in both the cortex and subcortical white matter with increasing magnitude of injury and time after trauma. Increased SYP immunoreactivity was accompanied with neuronal degeneration and glial cell proliferation. The amount of SYP remained unchanged in brains after trauma. These findings indicated that after trauma, SYP accumulates at injured sites of neurons without any change in SYP content. The increased SYP immunoreactivity in the cerebral cortex following traumatic injury reflects an inhibition of synaptic vesicle transportation and synaptic dysfunction, thus providing a histological substrate for brain dysfunction.

In cases of open head injuries, a foreign body may remain in the brain for a period of time after the trauma. A animal model incorporating a foreign body in the brain was developed. The time-dependent brain changes caused by a foreign body was studied. A lead or a glass ball was used as the foreign body and was implanted in the cerebral cortex of rats. Brains were analyzed at various times between twelve hours and four weeks after implantation. Results from brains with a lead ball were compared with those with a glass one. The number of macrophages increased significantly with increasing time after implantation of a lead ball. Multinucleated giant cells appeared at three weeks in brains with a lead ball. The immunoreactivity of metallothionein, a metal binding protein, increased significantly in astrocytes and endothelial cells with increasing time after implantation of a lead ball. Moreover, apoptotic cells were identified at two weeks, but had mostly disappeared at four weeks after implantation of a lead ball. Apoptotic cells were not observed in brains with a glass ball. This study showed that lead leached from a lead ball induces macrophage infiltration, metallothionein expression and apoptosis in the brain.

Forensic Neuropathology, Head Injury, Experimental Model

 ** Presenting Author*