

An animal model of sport related concussive brain injury

Akademisk avhandling

som för avläggande av medicine doktorsexamen
vid Sahlgrenska akademien vid Göteborgs universitet
Kommer att offentligen försvaras i hörsal Arvid Carlsson,
Academicum, Medicinargatan 3
torsdagen den 23 oktober 2008 kl 9.00

av

Hayde Bolouri

Fakultetsopponent:
Docent Niklas Marklund
Akademiska sjukhuset, Uppsala

Avhandlingen baseras på följande delarbeten:

- I. David C. Viano, Anders Hamberger, Hayde Bolouri, Annette Säljö.
Concussion in Professional Football: Animal Model of Brain Injury – Part 15
Submitted for publication in Neurosurgery
- II. Anders Hamberger, David C. Viano, Annette Säljö, Hayde Bolouri. Concussion in the
NFL: Morphology of brain injuries in the NFL concussion model – Part 16
Accepted of Neurosurgery for publication
- III. Hayde Bolouri, Anders Hamberger, David C. Viano and Annette Säljö. Concussions in
the NFL: Cognitive impairment following repeat head impacts – Part 18
Submitted for publication in Neurosurgery



UNIVERSITY OF GOTHENBURG
Institute of Biomedicine

An animal model of sport related concussive brain injury

Hayde Bolouri

Institute of Biomedicine, University of Gothenburg, Sweden

ABSTRACT

A new animal model for concussion of the type seen in professional football was developed, since current animal models did not simulate these conditions. The model is characterized by a high velocity-low mass impact to the head of a freely moving object. Structural damages and functional effects of the model have been investigated.

Paper I describes the rat model. A pneumatically driven projectile impacted the temporal region of the head. A 50 g projectile matches the concussions in football players scaled to the rat. Exposures were also performed with a 100 g impactor. The pressure accelerated the projectile to velocities of 7.4 m/s, 9.3 m/s and 11.2 m/s. The head was protected with a padded aluminum helmet. A small accelerometer was attached on the opposite side of the head, inline with the impact, for recording the acceleration of the head. Rats were exposed to a single or repeated (3, with 6 hour intervals) impacts and were sacrificed 1, 4 or 10 days later. Peak head acceleration, ΔV , duration and energy transfer were determined. Brains were perfused and surface injuries identified. Skull fractures were never found. Impact velocity and head ΔV and acceleration were within 1% and 3% of the target.

In **paper II**, neuronal injury was assessed with immunohistochemistry for NF-200, the heaviest neurofilament subunit, and GFAP, an intermediate filament protein in astrocytes. Hemorrhages were visualized with unspecific peroxidase. NF-200 immunoreactivity was accumulated in neuronal perikarya and was reduced in the axons 10 days after impact. Reactive astrocytes were found in the midline regions of the cerebral cortex and periventricularly. Erythrocyte-loaded blood capillaries indicated brain edema in regions of the cerebral cortex, brain stem and cerebellum. A single impact at 7.4 and 9.3 m/s with the 50 g projectile resulted in minimal neuronal injury and astrocytosis. Repeated impacts with the 100 g projectile at 11.2 m/s and 9.3 m/s led to injury bilaterally in the cerebral cortex, subcortical white matter, hippocampus CA1, corpus callosum and the striatum. The pattern of injury is suggestive of Diffuse Neuronal Injury (DAI).

In **paper III**, cognitive function and exploratory behavior were investigated following repeated head impacts. Rats were trained daily for 6 days in the Morris Water Maze. The time of latency to find a hidden platform was reduced from 50 secs on day 1 to 15 secs on day 6. They were then exposed with the 50 g or the 100 g projectile at 9.3 or 11.2 m/s. Spontaneous exploratory activity was assessed with the open field test 2-4 days and 1 and 2 weeks after impacts with the 50 g projectile at 9.3 and 11.2 m/s. The results showed that rats exposed at 11.2 m/s (x3) with the 50 g projectile or 9.3 m/s (x3) and 11.2 m/s (x2) with the 100 g projectile had a significantly increased time of latency to the platform, while those exposed with the 50 g at 9.3 m/s did not differ from the controls. Rats impacted with 50 g (x3) at 9.3 or 11.2 m/s showed a significant decrease in spontaneous exploratory activity.

In conclusion, the model fulfilled the conditions of concussion in the freely moving animal, without preparatory surgery, still with good reproducibility. Some aspects of the neuropathology and functional effects were investigated and both showed dose-response effects. The functional changes were cognitive deficits and reduced exploratory activity.

Key words: Animal model, football, concussion, brain injury, neuropathology, cognitive function.