



Experimental Design to Assess Blood Biomarkers in Concussed Collegiate Football Players: A Matched Cohort Study

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Introduction

The neurologic consequences of concussions in sports are well established. Accurate diagnoses of concussions are challenging and studies have looked at biomarkers to provide an objective measure in the diagnosis of concussion. We have designed and implemented a study of collegiate football players with the aim of exploring both novel and known biomarkers to identify a panel to accurately evaluate concussed athletes. This study also correlates biomarkers with concussive events, cognitive testing, and helmet accelerometer data.

Methods

We sampled 56 Louisiana State University football players. All players underwent a pre-season baseline blood draw, weekly blood draws and a post-season blood draw. Concussed players were matched to non-concussed controls and provided blood samples 2 hours and 18 hours following any on-field concussion. Physical exams and questionnaires were used to collect data on immediate changes related to injury. Helmet accelerometer data was retrospectively assessed and correlated with clinical and laboratory data. Blood samples were tested for concentrations of arachidonic acid and docosahexaenoic acid derivatives, as well as known concussion biomarkers such as S100B, t-tau, apolipoprotein A1 and GFAP.

Results

There were twelve total concussions suffered by players throughout the preseason & regular season. Of the concussed players, seven had previously sustained a concussion. Only one player still reported having post-concussive symptoms on his final questionnaire. Two of the players suffered concussions off the field (an MVC and an altercation), so timed & matched control draws were unavailable. There were universal increases over baseline in tau and all arachidonic acid derivatives immediately post game, in all players. In addition, all players had significant increases in all biomarkers when practices transitioned to "full pads," where contact was increased. The concussed players had larger increases over baseline in tau and 14-HDHA (an arachidonic acid derivative) when compared to the matched controls. This difference did not meet statistical significance, however. In addition, while there were only 12 clinical concussions, accelerometer data indicates many players had a large number of subconcussive hits. The offensive and defensive linemen had the largest amount of total hits. Further statistical analysis of the biomarkers, as well as the helmet accelerometer data is ongoing.

Conclusions

We suspect the increases over baseline for tau and the arachidonic acid derivatives did not reach statistical significance due to a small number of concussions. The arachidonic acid derivatives could be valuable new biomarkers for minor and major head trauma. These substances have been shown to have prognostic value in other brain injury models such as Alzheimer's and CVA. Their increases correlated with the known concussion biomarker, t-tau. Future studies will look to see if this is predictive of concussion recovery on a larger scale, as well as what role these substances may play in more severe head trauma. The design of this study gives a reproducible protocol for collecting samples from the collegiate athletic field to be studied in the laboratory and correlated with physical exam, cognitive testing, and impact data. We expect the present study will establish a multidisciplinary approach for the collection of a wide array of clinical and laboratory data, further increasing the accuracy with which concussions are diagnosed.

Learning Objectives

Readers should be able to 1) discuss the importance of accurate concussion diagnosis and 2) implement a multidisciplinary protocol for concussion diagnosis.

References

- Guskiewicz, K.M., et al., Cumulative effects associated with recurrent concussion in collegiate football players: the NCAA Concussion Study. JAMA, 2003. 290(19): p. 2549-55.
- Davis, G.A., et al., Contributions of neuroimaging, balance testing, electrophysiology and blood markers to the assessment of sport-related concussion. Br J Sports Med, 2009. 43 Suppl 1: p. i36-45.
- Bazan, N.G., et al., Docosahexaenoic acid signalolipidomics in nutrition: significance in aging, neuroinflammation, macular degeneration, Alzheimer's, and other neurodegenerative diseases. Annu Rev Nutr, 2011. 31: p. 321-51.
- Zhao, Y., et al., Docosahexaenoic acid-derived neuroprotectin D1 induces neuronal survival via secretase- and PPAR?-mediated mechanisms in Alzheimer's disease models. PLoS One, 2011. 6(1): p. e15816.
- Bazan, N.G., et al., Novel aspirin-triggered neuroprotectin D1 attenuates cerebral ischemic injury after experimental stroke. Exp Neurol, 2012. 236(1): p. 122-30.
- Jeter, C.B., et al., Biomarkers for the diagnosis and prognosis of mild traumatic brain injury/concussion. J Neurotrauma, 2013. 30(8): p. 657-70.