Biomechanical correlates of symptomatic and asymptomatic neurophysiological impairment in high school football

Evan L. Breedlove a, Meghan Robinson b, Thomas M. Talavage b,c, Katherine E. Morigaki d, Umit Yoruk c, Kyle O’Keefe a, Jeff King c, Larry J. Leverenz d, Jeffrey W. Gilger e, Eric A. Nauman a,b,f,

a School of Mechanical Engineering, Purdue University, 585 Purdue Mall, West Lafayette, IN 47907-2088, United States
b Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN 47907, United States
c School of Electrical and Computer Engineering, Purdue University, West Lafayette, IN 47907, United States
d Department of Health and Kinesiology, Purdue University, West Lafayette, IN 47907, United States
e Department of Psychological Sciences, University of California, Merced, CA 95343, United States
f Department of Basic Medical Sciences, Purdue University, West Lafayette, IN 47907, United States

A R T I C L E   I N F O

Article history:
Accepted 29 January 2012

Keywords:
Traumatic brain injury
Athletic telemetry
Functional magnetic resonance imaging
Subconcussive neurotrauma

A B S T R A C T

Concussion is a growing public health issue in the United States, and chronic traumatic encephalopathy (CTE) is the chief long-term concern linked to repeated concussions. Recently, attention has shifted toward subconcussive blows and the role they may play in the development of CTE. We recruited a cohort of high school football players for two seasons of observation. Acceleration sensors were placed in the helmets, and all contact activity was monitored. Pre-season computer-based neuropsychological tests and functional magnetic resonance imaging (fMRI) tests were also obtained in order to assess cognitive and neurophysiological health. In-season follow-up scans were then obtained both from individuals who had sustained a clinically-diagnosed concussion and those who had not. These changes were then related through stepwise regression to history of blows recorded throughout the football season up to the date of the scan. In addition to those subjects who had sustained a concussion, a substantial portion of our cohort who did not sustain concussions showed significant neurophysiological changes. Stepwise regression indicated significant relationships between the number of blows sustained by a subject and the ensuing neurophysiological change. Our findings reinforce the hypothesis that the effects of repetitive blows to the head are cumulative and that repeated exposure to subconcussive blows is connected to pathologically altered neurophysiology.

© 2012 Elsevier Ltd. All rights reserved.

1. Introduction

An estimated 3.8 million sports-related traumatic brain injuries (TBIs) occur in the United States every year (Langlois et al., 2006), many of which are concussions (Gessel et al., 2007). Repeated concussions have been linked to early-onset Alzheimer’s disease (Guskiewicz et al., 2005), depression (McCrory et al., 2009), dementia (Guskiewicz et al., 2005), and chronic traumatic encephalopathy (McKee et al., 2009). Currently the medical cost of TBI in the United States is approximately $60 billion per year without considering the increase in TBI associated with recent military conflicts. Yet despite the prevalence of concussions and the serious long-term consequences, the link between the injury biomechanics and the ensuing pathophysiology remains poorly characterized (Goldsmith and Monson, 2005; McCrory et al., 2001).

Talavage et al. (2010) recently reported observation of neurophysiological changes in high school football players without observable symptoms of concussion. The reported finding of degraded neurological performance in the absence of classical symptoms of concussion is consistent with prior observation of chronic traumatic encephalopathy (CTE) in the absence of history of concussion in three ex-NFL players, as reported in (Field Hearing: Legal Issues Football Head Injuries, 2010; Omalu et al., 2005, 2010). More recent discussion in the neuropathology community has implicated repetitive sub-concussive events as a significant source of accrued damage (Field Hearing: Legal Issues Football Head Injuries, 2010; McKee et al., 2009).

With the challenges of neural injury detection and the potential consequences if TBI goes unrecognized, it is critical that...
scientists, engineers, and medical professionals develop a better understanding of the mechanical events that lead to neuropsychological changes, how those events may accumulate over time, and how this accumulation affects healing processes. Toward this goal, neuropsychological changes and the biomechanical history of a cohort of high school football athletes were tracked for two seasons using instrumented helmets, functional magnetic resonance imaging (fMRI), and computer-based neuropsychological testing. This study expands upon our previous work (Talavage et al., 2010) by examining how the head collision histories of the athletes correlate with the observed changes in their neuropsychology, with the hypothesis being that the number and location of blows is directly correlated to the neuropsychological changes exhibited by the athlete.

2. Methods

All research methods were approved by an Institutional Review Board prior to the initiation of the study. Parental consent and participant assent were obtained from all subjects. The study is still ongoing, and the data reported here represents the aggregate data from two football seasons (2009 and 2010) (Talavage et al., 2010). In brief, the study consists of a cohort of high school football athletes for whom a neuropsychological and neuropsychological baseline was established in the pre-season. They were monitored throughout the season using a telemetry system embedded in their helmets. At least two players without a diagnosed concussion were recruited for follow-up neurophysiological and neuropsychological testing each week during the season. One was selected from the top 50% of players according to number of blows sustained in that week of play. The other was selected from the bottom 50%. Players with a diagnosed concussion were also recruited for follow-up testing (for additional details see the Appendix). Additional details of the neuropsychological testing, fMRI procedures, and statistical analyses are available (Supplementary material).

2.1. Subjects

Twenty four male high school football players between the ages of 15 and 18 (mean=17.0) were enrolled in the study for season 1, and 21 of the 24 participated throughout the entire season (Talavage et al., 2010). Twenty-eight male subjects between the ages of 14 and 18 (mean=16.8) were enrolled in the study for season 2, including 14 subjects from season 1 (Supplementary Table 1), and 25 of the 28 participated throughout the entire season. A self-reported history of concussion was obtained by a certified Athletic Trainer. No players were excluded from the study on the basis of previous concussions.

2.2. Helmet Telemetry

The Head Impact Telemetry (HITeM) System (Simbex; Lebanon, NH) was installed in subject helmets to monitor head impacts at every contact practice and game throughout both seasons. Each subject’s helmet was outfitted with a sensor array comprising six uniaxial accelerometers, from which the location of blows and the head center-of-gravity linear acceleration were estimated (Crisco et al., 2004) (Table 1). A researcher was present at each practice, home game, and away game to ensure proper function of all sensors at all times.

2.3. Definition of injury groups

All subjects were classified according to “clinically-observed impairment” (COI)—brain-injury induced changes that were detected by a clinician, such as concussion—and “functionally-observed impairment” (FOI)—changes that were detected using neuropsychological testing and fMRI (Talavage et al., 2010). Using this system, an individual with a diagnosed concussion is COI+/FOI+ (all of the individuals diagnosed with a concussion demonstrated functional impairment). Individuals with no diagnosed concussion and no functional impairment were COI-/FOI-. Individuals were defined as being COI-/FOI+ if they had no observable signs of concussion but nevertheless showed a statistically significant reduction in at least one of their visual composite score or verbal composite score categories for ImPACT (Talavage et al., 2010). The COI−/FOI− and COI−/FOI+ groups are collectively referred to as the COI−/FOI× group. Because FOI designations depend only on ImPACT scores, these designations are insensitive to the variability in fMRI.

3. Results

There was no significant difference in the median peak linear acceleration for any of the three groups (Kruskal–Wallis, $\chi^2=1.28$, $p > 0.52$, Fig. 1 and Table 2); however, a significant difference in the median total number of blows was found (Kruskal–Wallis, $\chi^2=6.1$, $p < 0.05$, Table 2). Subsequent pairwise tests indicated that the COI−/FOI× group sustained more blows than the COI−/FOI− group (Tukey–Kramer, $p < 0.05$).

The number of side blows sustained by each of the groups (Fig. 2) was significantly different (Kruskal–Wallis, $\chi^2=6.29$, $p < 0.04$), and pairwise tests indicated the COI−/FOI× group sustained significantly more side blows than the COI+/FOI+ group (Tukey–Kramer, $p < 0.05$). Scatterplots displaying a two-dimensional projection of recorded impact location and peak linear acceleration illustrated that the members of the COI−/FOI× group sustained a majority of their blows to the top-front region of the helmet, especially those above 80 G (Fig. 3).

Of the 116 regions of interest (ROIs), 33 ROIs yielded significant regressions ($p < 2 \times 10^{-10}$) relating changes in fMRI to the blows sustained by the COI−/FOI× group (Table 3, Fig. A). Of the 116 ROIs, 39 ROIs yielded significant regressions ($p < 5 \times 10^{-22}$) relating changes in fMRI to the blows sustained by the COI−/FOI× group (25 non-cerebellar ROIs, Table 4; 14 cerebellar ROIs, Table 5, Fig. A).

The spatial distributions of the ROIs in the COI−/FOI× and COI−/FOI× groups for which a significant regression was obtained indicate distinct regions of correlation (Fig. 4(A and B)). While some overlap exists in the frontal, cerebellar, and basal ganglia regions, the COI−/FOI× group exhibited a concentration of correlations in the upper parietal and occipital regions.
corresponding to visual processing (Fig. 4(g), Fig. 4(i) slice 2); in contrast, the COI+/FOI+ group exhibited an additional concentration of correlations in the temporal and lower parietal regions, corresponding to language processing (Fig. 4(I) slice 4).

4. Discussion

The purpose of this study was to characterize the magnitude, location, and number of blows sustained by athletes participating in high school football and to establish correlations between these blows and ensuing changes in neurophysiology. According to Talavage et al. (2010), three distinct impairment groups are observable among high school football athletes: those with clinically observed impairment and functional impairment as measured by fMRI and neuropsychological testing (COI+/FOI+), those with no outward symptoms and no functional impairment (COI−/FOI−), and those with no outward symptoms but substantial functional impairment (COI−/FOI+). This work extended that study with the incorporation of a second season of data, also classifying subjects into one of the three impairment groups, and identified the biomechanical characteristics that correspond with their classification. Having obtained data for 23 subjects over the course of two seasons, we found significant regressions for the COI−/FOI− and COI+/FOI+ groups consistent with progressive neurophysiological changes with accumulated blows to the head. These findings are consistent with our season 1 results (Talavage et al., 2010) and support the hypothesis of cumulative subconcussive damage (Field Hearing: Legal Issues Football Head Injuries, 2010; McKee et al., 2009).

The majority of previous concussion research has emphasized the magnitude and duration of individual blows (Goldsmith, 2001; Goldsmith and Monson, 2005). While identifying the characteristics of the specific blow that caused concussion was beyond the scope of the present work, it was found that the distributions of all blows sustained by COI+/FOI+, COI−/FOI+, and COI−/FOI− were not significantly different (Fig. 1; Table 2). This is consistent with the findings of Guskiewicz et al. (2007) that the magnitude of a blow in football was neither correlated with the probability of concussion nor the severity.

The primary difference between the groups was the number of blows sustained and their distribution (Table 3, Fig. 2). Talavage et al. (2010) had previously reported that the number of top-front blows between 20 G and 80 G sustained by the COI−/FOI+ group was a significant biomechanical differentiator. Consideration of subsets of blows according to magnitude was beyond the scope of this study; therefore, it is likely that the COI−/FOI+ population reported here also received more top-front hits than the other impairment groups if the blows are restricted to the 20 G–80 G magnitude range. In fact, the scatterplots showing both the location and magnitude of recorded impacts for characteristic blows between 20 G and 80 G are significantly different (Fig. 1; Table 2). This is consistent with the findings of Guskiewicz et al. (2007) that the magnitude of a blow in football was neither correlated with the probability of concussion nor the severity.

Neurophysiological changes were measured using fMRI. Such measurements paired with working memory tasks, such as the N-back task, have been reported to be sensitive to the effects of neurotrauma (Chen et al., 2008) and accumulated subconcussive blows (Talavage et al., 2010). While substantial spurious inter-subject variability is possible in a general fMRI experiment, the experimental design and post-processing procedures employed here specifically controlled for these factors. For instance, several studies have shown the N-back task to be generally insensitive to drug use, except in cases of overt intoxication (Gundersen et al., 2008a;
Gundersen et al., 2008b; Murphy et al., 2006). The remaining factors, such as diet and sleep, certainly affect the resulting effect size (Gonzalez-Castillo and Talavage, 2011); however, the subtracted global contrast average is believed to largely account for these effects. In particular, the global contrast average did not exhibit any significant correlations with the regression variables \((p < 0.1)\), indicating that the global contrast average only captures session-specific variation unrelated to cumulative neurotrauma. Furthermore, while substantial inter-subject variability may exist in the raw value of the \(t\)-statistic in any given scanning session, this study focuses on the changes in \(t\)-statistic between the pre-season scan and an in-season scan. Given the good repeatability of the N-back task in non-athletes (Gradin et al., 2010), substantial inter-subject variability in the change from pre-season values is not expected, except for that variability arising from blows to the head during football gameplay. Therefore, the relative insensitivity of the N-back task to outside factors and the use of pre-season data to obtain changes in fMRI allowed us to connect neurophysiological changes to biomechanical insults sustained during football-related activity.

The models relating the left and right middle frontal gyrus (MFG; Tables 3 and 4) are of particular interest because neuropsychological tests have indicated that changes in MFG activation are related to measureable decreases in verbal and visual working memory that have been documented in concussed individuals (Hoskison et al., 2009). Disruption and/or degradation of gray-matter tissue in the MFG has also been documented in boxers who have sustained repeated blows to the head (Chappell et al., 2006). Finally, the MFG has been identified as a region where strains are particularly large for impacts in the sagittal plane (Bayly et al., 2005), which corresponds with the dependence of the models on PW_TF.

Significant models were also found for both the COI–/FOI+ and COI+/FOI+ groups relating history of blows to structures of the basal ganglia and limbic circuits, such as the putamen, caudate nucleus, globus pallidus, cingulate cortex, hippocampus, and parahippocampal gyri (Tables 2 and 3). Neurodegeneration in these ROIs has been documented in cases of CTE and is believed to be the cause of emotional and behavioral disorders that are commonly reported in patients diagnosed postmortem with CTE (Mckee et al., 2009; Omalu et al., 2005, 2006). These ROIs show correspondence with both cumulative and previous week hits sustained to the top-front and side of the head and have been identified as high-risk regions for neurotrauma (Bayly et al., 2005; Ommaya et al., 1971; Sabet et al., 2008).

Several models were also identified for cerebellar ROIs with both the COI–/FOI+ and COI+/FOI+ groups (Tables 2 and 4). Moderate to severe levels of cerebellar neurodegeneration have been reported on autopsy of persons with CTE (Mckee et al., 2009).
and disruption and/or degradation of the cerebellar tissue has been documented in boxers who have sustained repeated blows to the head (Chappell et al., 2006).

While the correlation of individual ROIs to a history of blows is informative, a full interpretation of any given regression is difficult. To the knowledge of the authors, this is the first time the number of blows a player has sustained has been related to changes in neurophysiology; therefore, individual ROIs are only implied that the changes in COI+/FOI+ and COI−/FOI− individuals arise from distinct biomechanical processes.

More strikingly, both the COI+/FOI+ map and the COI−/FOI− map bear substantial resemblance to the strain patterns documented for sagittal motion by Bayly et al. (2005). There is further similarity with the pattern of lesions found on autopsy of fatal traumatic brain injury (Gurdjian, 1976). It has long been believed that tissue strain is the fundamental biomechanical process that engages pathophysiological sequelae (Goldsmith, 2001). Our findings support this hypothesis. Moreover, they indicate that the effects of strain linger in the tissue, so that the effect of cumulative blows on tissue health is akin to mechanical fatigue. However, the dependence of regression models for some ROIs on previous week blows instead of cumulative blows suggests that the cumulative effect is in competition with some sort of healing. The rate of damage accumulation and the relative rate of healing are critical components in understanding concussion and ultimately the link to progressive degenerative neuropathy.

The biomechanical correlates presented here do not present a complete picture of the insults sustained by our subjects and warrant future work. In particular, the HIT System does not measure angular accelerations (Rowson et al., 2009) and only estimates linear accelerations and direction (Crisco et al., 2004). Angular accelerations are of particular concern in the biomechanics of concussion. Holbourn (1943) originally hypothesized that rotational strain fields could be at least as large as linear strains, which Ommaya et al. (1968) later verified, showing that injury

<table>
<thead>
<tr>
<th>ROI</th>
<th>R²</th>
<th>Variables (X1:X2)</th>
<th>β₀</th>
<th>β₁</th>
<th>β₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcarine fissure, L</td>
<td>0.13</td>
<td>C_TF</td>
<td>-0.346</td>
<td>0.341</td>
<td></td>
</tr>
<tr>
<td>Calcarine fissure, R</td>
<td>0.18</td>
<td>C_TF</td>
<td>-0.371</td>
<td>0.421</td>
<td></td>
</tr>
<tr>
<td>Caudate nucleus, R°</td>
<td>0.17</td>
<td>PW_F</td>
<td>-0.523</td>
<td>0.133</td>
<td></td>
</tr>
<tr>
<td>Cuneus, L</td>
<td>0.22</td>
<td>C_TF</td>
<td>-0.526</td>
<td>0.579°</td>
<td></td>
</tr>
<tr>
<td>Cuneus, R</td>
<td>0.23</td>
<td>C_F</td>
<td>-0.608</td>
<td>0.542°</td>
<td></td>
</tr>
<tr>
<td>Declive, R°</td>
<td>0.31</td>
<td>C_F; C_B</td>
<td>-0.342</td>
<td>0.518°</td>
<td></td>
</tr>
<tr>
<td>Frontal operculum, inf. L</td>
<td>0.18</td>
<td>C_F</td>
<td>0.674</td>
<td>0.517</td>
<td></td>
</tr>
<tr>
<td>Frontal operculum, inf. R</td>
<td>0.19</td>
<td>PW_B</td>
<td>0.199</td>
<td>-0.540°</td>
<td></td>
</tr>
<tr>
<td>Globus pallidus, L°</td>
<td>0.14</td>
<td>PW_B</td>
<td>0.295</td>
<td>0.303</td>
<td></td>
</tr>
<tr>
<td>Hippocampus, L°</td>
<td>0.14</td>
<td>C_S</td>
<td>0.574</td>
<td>-0.339</td>
<td></td>
</tr>
<tr>
<td>Inf. occipital gyrus, R</td>
<td>0.18</td>
<td>C_S</td>
<td>-0.498</td>
<td>0.517</td>
<td></td>
</tr>
<tr>
<td>Inf. parietal gyrus, R</td>
<td>0.20</td>
<td>PW_B</td>
<td>1.091</td>
<td>-0.763°</td>
<td></td>
</tr>
<tr>
<td>Inf. temporal gyrus, R</td>
<td>0.13</td>
<td>C_S</td>
<td>0.312</td>
<td>-0.244</td>
<td></td>
</tr>
<tr>
<td>Lingual gyrus, R</td>
<td>0.15</td>
<td>C_F</td>
<td>-0.379</td>
<td>0.321</td>
<td></td>
</tr>
<tr>
<td>Lingula II, L°</td>
<td>0.40</td>
<td>PW_S; PW_B</td>
<td>0.011</td>
<td>-1.218°</td>
<td></td>
</tr>
<tr>
<td>Mid. frontal gyrus, L°</td>
<td>0.22</td>
<td>PW_TF</td>
<td>0.216</td>
<td>-0.369</td>
<td></td>
</tr>
<tr>
<td>Mid. frontal gyrus, R°</td>
<td>0.18</td>
<td>PW_TF</td>
<td>0.060</td>
<td>-0.442°</td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal gyrus, sup. R°</td>
<td>0.14</td>
<td>C_F</td>
<td>0.352</td>
<td>0.283</td>
<td></td>
</tr>
<tr>
<td>Paracentral lobule, L</td>
<td>0.20</td>
<td>PW_TF</td>
<td>0.089</td>
<td>0.397°</td>
<td></td>
</tr>
<tr>
<td>Paracentral lobule, R</td>
<td>0.45</td>
<td>PW_TF; PW_B</td>
<td>0.145</td>
<td>0.877°</td>
<td></td>
</tr>
<tr>
<td>Pars triangularis, L</td>
<td>0.23</td>
<td>C_F</td>
<td>0.497</td>
<td>-0.451°</td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus, L</td>
<td>0.16</td>
<td>C_S</td>
<td>-0.288</td>
<td>0.391</td>
<td></td>
</tr>
<tr>
<td>Precuneus, L</td>
<td>0.22</td>
<td>PW_TF</td>
<td>-0.329</td>
<td>0.407°</td>
<td></td>
</tr>
<tr>
<td>Precuneus, R</td>
<td>0.15</td>
<td>PW_S</td>
<td>-0.403</td>
<td>0.327</td>
<td></td>
</tr>
<tr>
<td>Rectus, R</td>
<td>0.12</td>
<td>C_F</td>
<td>0.709</td>
<td>-0.354</td>
<td></td>
</tr>
<tr>
<td>Rolandic operculum, L</td>
<td>0.15</td>
<td>C_B</td>
<td>-0.273</td>
<td>0.489</td>
<td></td>
</tr>
<tr>
<td>Sup. frontal gyrus, lateral R°</td>
<td>0.16</td>
<td>PW_TF</td>
<td>0.138</td>
<td>-0.328</td>
<td></td>
</tr>
<tr>
<td>Sup. occipital gyrus, L</td>
<td>0.14</td>
<td>C_TF</td>
<td>-0.124</td>
<td>0.405</td>
<td></td>
</tr>
<tr>
<td>Sup. occipital gyrus, R</td>
<td>0.12</td>
<td>C_B</td>
<td>-0.381</td>
<td>0.394</td>
<td></td>
</tr>
<tr>
<td>Suppl. motor area, L</td>
<td>0.14</td>
<td>PW_F</td>
<td>0.436</td>
<td>-0.246</td>
<td></td>
</tr>
<tr>
<td>Supramarginal gyrus, L</td>
<td>0.25</td>
<td>PW_B</td>
<td>-0.686</td>
<td>0.576°</td>
<td></td>
</tr>
<tr>
<td>Vermis IX°</td>
<td>0.13</td>
<td>C_B</td>
<td>0.460</td>
<td>-0.331</td>
<td></td>
</tr>
<tr>
<td>Vermis VI°</td>
<td>0.13</td>
<td>PW_TF</td>
<td>0.089</td>
<td>-0.447°</td>
<td></td>
</tr>
</tbody>
</table>

* p < 0.01.
° McKee et al. (2009).
°° McKee et al. (2010).
thresholds double when head rotation is disallowed. Sabet et al. (2008) have also shown that rotational accelerations generate substantial strain fields, which are believed to result in more severe injury. The inability of the HIT System to reliably determine the angular accelerations, and consequently the inability to relate angular accelerations to our fMRI findings, is a regrettable deficit in the present work. Considerable progress is certainly warranted in the field of sports telemetry technology if biomechanics researchers are to formulate a more complete picture of what happens in football gameplay.

Table 4
Results of stepwise regressions relating changes in the average t-statistic in non-cerebellar ROIs for the COI+/FOI+ group to their respective history of blows to the head throughout the season and in the week preceding scanning. The slopes ($\beta_1$) and intercept ($\beta_0$) relate to the general regression model (1) and correspond to the respective model variables ($X_n$) reported below. All slopes are significant at the $\alpha = 0.05$ level except where noted. ROIs in which CTE-related neurodegeneration has been reported are indicated by superscripts identifying the relevant literature.

<table>
<thead>
<tr>
<th>ROI</th>
<th>$R^2$</th>
<th>Variables ($X_1$-$X_2$)</th>
<th>$\beta_0$</th>
<th>$\beta_1$</th>
<th>$\beta_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cingulate gyrus, ant. 1a</td>
<td>0.59</td>
<td>PW_B</td>
<td>0.964</td>
<td>-0.558</td>
<td></td>
</tr>
<tr>
<td>Cingulate gyrus, post. 2b</td>
<td>0.83</td>
<td>C_F</td>
<td>-0.969</td>
<td>0.540a</td>
<td></td>
</tr>
<tr>
<td>Frontal operculum, inf. 3a</td>
<td>0.73</td>
<td>C_F</td>
<td>1.815</td>
<td>-0.575</td>
<td></td>
</tr>
<tr>
<td>Frontal operculum, inf. 4a</td>
<td>0.95</td>
<td>PW_TF; PW_B</td>
<td>-0.034</td>
<td>-0.527a</td>
<td>0.890a</td>
</tr>
<tr>
<td>Fusiform gyrus, R</td>
<td>0.73</td>
<td>C_F</td>
<td>-1.332</td>
<td>0.593</td>
<td></td>
</tr>
<tr>
<td>Globus pallidus, L4b</td>
<td>0.90</td>
<td>PW_S</td>
<td>1.088</td>
<td>-0.386a</td>
<td></td>
</tr>
<tr>
<td>Globus pallidus, R4b</td>
<td>0.63</td>
<td>PW_B</td>
<td>0.194</td>
<td>-0.451</td>
<td></td>
</tr>
<tr>
<td>Inf. parietal gyrus, R</td>
<td>0.84</td>
<td>PW_S</td>
<td>-1.181</td>
<td>0.714a</td>
<td></td>
</tr>
<tr>
<td>Insula, R</td>
<td>0.82</td>
<td>PW_B</td>
<td>0.943</td>
<td>-0.539a</td>
<td></td>
</tr>
<tr>
<td>Lingual gyrus, L</td>
<td>0.62</td>
<td>PW_F</td>
<td>-0.472</td>
<td>0.397</td>
<td></td>
</tr>
<tr>
<td>Med. frontal gyrus, L5a</td>
<td>0.61</td>
<td>PW_TF</td>
<td>0.702</td>
<td>-0.606</td>
<td></td>
</tr>
<tr>
<td>Med. frontal gyrus, R5a</td>
<td>0.61</td>
<td>PW_S</td>
<td>0.983</td>
<td>0.610</td>
<td></td>
</tr>
<tr>
<td>Med. temporal pole, R</td>
<td>0.59</td>
<td>PW_TF</td>
<td>-1.475</td>
<td>0.648</td>
<td></td>
</tr>
<tr>
<td>Olfactory bulb, R</td>
<td>0.59</td>
<td>PW_B</td>
<td>1.163</td>
<td>-0.599</td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal gyrus, inf. 3a</td>
<td>0.96</td>
<td>C_S; PW_B</td>
<td>0.544</td>
<td>0.510a</td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal gyrus, mid. 3a</td>
<td>0.58</td>
<td>PW_TF</td>
<td>1.465</td>
<td>-0.729</td>
<td></td>
</tr>
<tr>
<td>Parahippocampal gyrus, R3a</td>
<td>0.58</td>
<td>C_F</td>
<td>0.914</td>
<td>-0.597</td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus, L</td>
<td>0.93</td>
<td>C_TF; PW_B</td>
<td>-0.804</td>
<td>0.271</td>
<td>-0.174</td>
</tr>
<tr>
<td>Postcentral gyrus, R</td>
<td>0.93</td>
<td>C_F; PW_B</td>
<td>-0.210</td>
<td>-0.359</td>
<td>0.589a</td>
</tr>
<tr>
<td>Putamen, L5a</td>
<td>0.64</td>
<td>C_S</td>
<td>1.192</td>
<td>-0.896</td>
<td></td>
</tr>
<tr>
<td>Putamen, R5a</td>
<td>0.77</td>
<td>C_B</td>
<td>1.761</td>
<td>-0.836a</td>
<td></td>
</tr>
<tr>
<td>Sup. parietal gyrus, L</td>
<td>0.70</td>
<td>PW_F</td>
<td>0.723</td>
<td>-0.917</td>
<td></td>
</tr>
<tr>
<td>Sup. parietal gyrus, R</td>
<td>0.59</td>
<td>PW_TF</td>
<td>0.689</td>
<td>-0.514</td>
<td></td>
</tr>
<tr>
<td>Sup. temporal pole, L</td>
<td>0.76</td>
<td>C_S</td>
<td>0.648</td>
<td>-0.786</td>
<td></td>
</tr>
<tr>
<td>Sup. temporal pole, R</td>
<td>0.60</td>
<td>C_B</td>
<td>0.422</td>
<td>-0.372</td>
<td></td>
</tr>
</tbody>
</table>

* $p < 0.01$.

* McKee et al. (2009).

* McKee et al. (2010).
It should also be noted that these regressions do not indicate the precise functional relationship between head collision history and ensuing neurophysiological changes. The exploratory nature of these regressions can only indicate likely connections between biomechanics and neurophysiology. Functional relationships should be based on a more complete theory for the biomechanical basis of neurotrauma; however, these regressions help to direct future research and the development of such a theory.

It should be noted that the effect of healing and recovery is not readily apparent in this study. The neurophysiological changes observed may not persist for a sufficiently long period of time to be connected to any later-life neurodegeneration, and this hypothesized recovery process should be more thoroughly explored. Nevertheless, the descriptive power of cumulative blow regressors suggests that the effects of blows may persist for a much longer period than previously believed. During this time, individuals may be in a vulnerable state, so that the blow that results in symptoms is the “straw that broke the camel’s back.” If this concern is valid, a particular blow may cause a “physiological bifurcation” that places the brain in a distinct pathophysiological regime, much in the way that minor injuries precondition an eventual catastrophic tear in musculoskeletal soft tissues. Certainly, if concussion were a purely asymptomatic (COI+ /FOI+) changes in neurophysiology arise from distinct biomechanical events and represent distinct changes in neurophysiology. Further work will elucidate why these two groups exhibit distinct pathophysiologicals and how these differences relate to the possible development of acute neurological injury and long-term neurodegeneration, such as CTE.

Conflict of interest statement

The authors declare that they have no financial interest in this study or its outcomes.

Acknowledgments

This work was supported by grants from the Indiana State Department of Health Spinal Cord and Brain Injury Research Fund, General Electric Healthcare, and through the National Science Foundation and National Defense Science and Engineering Graduate Fellowships. The authors thank Jeff Clevenger for his assistance in collecting helmet telemetry data and coordinating weekly battery changes. Finally, the authors thank Dr. Gregory G. Tamer, Jr., and Dr. Ruwan D. Ranaweera for their assistance with data collection.
Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jbiomech.2012.01.034.

References