Evidence of Altered Brain Chemistry After Repetitive Subconcussive Head Impacts

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TARGET AUDIENCE: Clinicians and researchers in that study mild traumatic brain injury and/or sports medicine.

BACKGROUND: Soccer is played by more than 250 million people worldwide. It is thus the most popular sport in the world, although hits to the head and concussions are quite common, less is known about the long-term consequences of repeatedly heading the ball in soccer that result in g forces of up to 60g[1]. Repeatedly heading the ball places soccer players at high risk for repetitive subconcussive head impacts (RSHI). As soccer players perform, on average, 6-12 headings per game, a player's career likely involves the accumulation of thousands of headings[2]. Previous findings demonstrate alterations in the brain's white matter microstructure in professional soccer players even in the absence of concussive brain trauma[3]. Magnetic resonance spectroscopy (MRS) which measures brain chemistry may provide greater pathophysiological insight into these structural changes. Therefore the aim of our study is to examine RSHI in a professional soccer players by comparing with professional athletes in non-contact sports and the association with neurocognitive performance and number of headers.

METHODS: 11 former professional soccer players (mean age 52.0 ± 6.8 years) who had played at least one play season of professional soccer (1st, 2nd, or 3rd Bundesliga) and were still active at a recreational level. A comparison cohort of 11 athletes (mean age 49.8 ± 6.0 years), participating in non-contact sports, were recruited from competitive athletic clubs and matched regarding age-, handedness, and gender. The local ethics committee approved the study and written informed consent was obtained from each participant. A semi-structured interview was performed to acquire detailed information about training habits and life-style, including number of headings performed per week during the last year prior to the study, and position in the field. All study participants underwent a brief neurocognitive (TMTA/B, ROCF) and balance examination (BESS) by an examiner who was blinded to the athlete's sport.

Magnetic resonance spectroscopy (MRS) was acquired using single voxel point-resolved spectroscopy (PRESS; TE = 30 ms, TR = 2000 ms, voxel size = 20x20x20 mm3, 128 averages) in the posterior cingulate gyrus. Each voxel underwent automated optimization including 3D shimming, transmit gain, frequency adjustment, and water suppression. Magnetic field homogeneity was optimized for the selected spectroscopy volume of interest by manual shimming to a linewidth of less than 14 Hz. An unsuppressed water spectrum was then acquired using the same parameters except no water suppression and 16 averages. Spectra were then post-processed using LCmodel to measure N-acetyl aspartate (NAA), creatine (Cr), choline (Cho), glutamate (Glu), glutathione (GSH), and myo-inositol (mI). To account for subject-to-subject variability in coil loading, the unsuppressed water signal for each subject was measured and accounted for and ratios to Cr. An independent sample t-test was performed to evaluate differences between the age-matched groups. Correlations were conducted using Spearman rank correlation.

RESULTS: Significant biochemical differences were found between the two groups ($p<0.05$), as shown in Figure 1. Higher ratios of Cho/Cr were measured in the soccer players (0.21 + 0.03) than in their athlete controls (0.18 + 0.02; p = 0.009). mI/Cr levels were also found to be increased in the soccer players (0.9 + 0.03) compared to athlete controls (0.84 + 0.07; p = 0.02). There were no significant differences in Glu, GSH, or Cr measures between the two groups. Neurochemical levels of all soccer players were correlated with the number of headings performed per week during the last year, as well as a lifetime estimate of headings. A significant positive correlation was found between mI/Cr and number of headings performed per week during the last year, as well as lifetime estimate of headings (Figure 2 top). GSH/Cr levels were significantly correlated with lifetime estimate of headings but not with number of headings performed per week during the last year (Figure 2 bottom). In addition, test results of TMT B correlated with GSH/Cr+PCr.

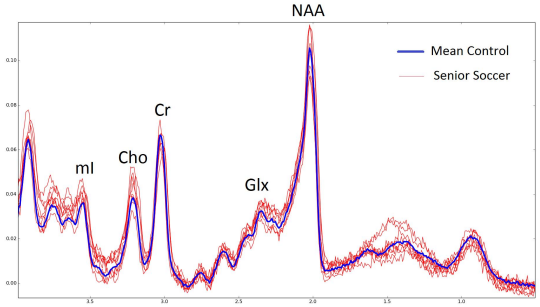

Figure 1. Stackplot of MRS spectra. All control spectra were averaged together, Fourier transformed and displayed in blue. Each individual senior soccer player spectrum is shown in red.

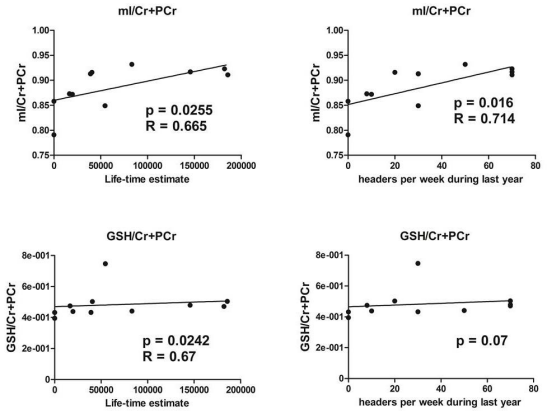

Figure 2. Correlation between myo-inositol (mI) and glutathione (GSH) and estimated exposure to RSHI.

DISCUSSION: Increased choline results from membrane disruption that may be secondary to demyelination or to diffuse axonal injury, although some studies have suggested its role in astrocytosis[4] and neuroinflammation[5] in studies of acute head injury. Further, mI, found primarily in astrocytes and microglia, functions as an osmolyte and is thought to increase as a result of glial proliferation due to reactive astrocytosis and microglial activation[6]. The relationship between increased MRS markers for neuroinflammation and concussive head injury has been previously reported in older ice hockey and American football players[7]. However, our study focused on former professional soccer players without a history of a diagnosed concussion, thus demonstrating, for the first time, that such changes are extant in athletes subjected to repetitive subconcussive impacts. It is especially noteworthy that GSH/Cr levels were significantly correlated with exposure to subconcussive brain trauma. GSH is an anti-oxidant that removes or reduces damaging reactive oxygen species such as free radicals and peroxides and is therefore directly involved in oxidative stress and neuroinflammation.

CONCLUSION: Results of this study indicate a possible association between RSHI from heading the ball in soccer, and neuroinflammation, in former professional soccer players, compared with athletic controls. Future studies, including longitudinal analyses, are needed to clarify the time course underlying changes in neurochemistry, as well as in the association of these changes with neurocognitive, motor functioning, and quality of life.

REFERENCES: 1.Naunheim RS et al. 2003; 2.Rutherford A et al. 2009; 3.Koerte IK et al. 2012; 4. Garnett MR et al.2004; 5. Brooks WM et al. 2000; 6.Kierans AS et al. 2014 7. Tremblay S et al. 2013