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No neurochemical evidence for brain injury caused by heading in soccer

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Background: The possible injurious effect to the brain of heading in soccer is a matter of discussion. 
Objective: To determine whether standardised headings in soccer are associated with increased levels of biochemical markers for neuronal injury in cerebrospinal fluid (CSF) and serum.

Methods: Twenty-three male amateur soccer players took part in a heading training session involving heading a ball kicked from a distance of 30 m at least 10 m forward. Ten players performed 10 and 13 players performed 20 approved headings. The players underwent lumbar puncture and serum sampling 7–10 days after the headings. The study also included 10 healthy male non-athletic control subjects. CSF was analysed for neurofilament light protein, total tau, glial fibrillary acidic protein, S-100B and albumin concentrations. Serum was analysed for S-100B and albumin.

Results: None of the biomarker levels were abnormal and there were no significant differences between any of the three groups, except for a slightly increased CSF S-100B concentration in controls compared with headers. Biomarker levels did not correlate with the number of headings performed.

Conclusion: Repeated low-severity head impacts due to heading in soccer are not associated with any neurochemical signs of injury to the brain.

SUBJECTS AND METHODS

Subjects and experimental setting
Twenty-three male amateur soccer players participated in a training session that involved heading a ball kicked from a distance of 30 m in front of the player. The players were required to head the ball from a standing position at least 10 m forward with an allowed deviation of 45° to each side (fig 1). The 30 m distance translates well to a regular corner kick. Ten players performed 10 and 13 players performed 20 approved headings. The total number of headings (approved and unapproved) ranged from 11 to 57. The ball used was an Adidas Teamgeist 2006 FIFA World Cup Official Match soccer ball fulfilling the FIFA approved standard of a weight between 420 and 445 g and a circumference of 68.5–69.5 cm. The ball was inflated to a pressure of 900 g/cm² (FIFA approved standard 600–1100 g/cm²).

Seven to 10 days after the training session the participants underwent lumbar puncture (LP) through the L3/L4 interspace for collection of CSF, and venous puncture for collection of serum. 

Abbreviations: CSF, cerebrospinal fluid; GFAP, glial fibrillary acidic protein; LP, lumbar puncture; NF-L, neurofilament light protein; T-tau, total tau.
The 7–10-day time point was chosen as the optimal point at which to detect a change in biomarker levels as a result of the headings on the basis of CSF biomarker kinetics in a study on stroke. CSF was collected in polypropylene tubes, aliquoted and stored at $-80^\circ$C pending analysis. The participants were examined physically and neurologically before the LP. All were healthy and none showed any signs of focal neurological injury. The study also included 10 healthy, male, age-matched, non-athletic control subjects who underwent LP and serum sampling but who did not participate in any activities involving head impacts. One control was excluded owing to marked blood contamination of the CSF. The study was approved by the ethics committee of Göteborg University, and written informed consent was obtained from all participants.

### Biochemical analyses

CSF T-tau concentration was determined by a sandwich ELISA (Innotest hTAU-Ag, Innogenetics, Gent, Belgium) specifically constructed to measure all tau isoforms irrespectively of phosphorylation status, as previously described. CSF concentrations of NF-L and GFAP were analysed using previously described ELISA methods. The detection limit of the NF-L ELISA was 125 ng/l. Serum and CSF levels of S-100B were determined by an electrochemoluminescence immunoassay using the Modular system and the S100 reagent kit (Roche Diagnostics). Albumin levels in CSF and serum were measured by immunonephelometry on a Beckman Image Immunochemistry system (Beckman Instruments, Fullerton, California, USA). The albumin ratio was calculated as CSF albumin (mg/l)/serum albumin (g/l). The coefficients of variation for all biochemical analyses were <10%.

### Statistics

The statistical calculations were performed using SYSTAT 11.0 (SYSTAT Software GmbH, Erkrath, Germany). The non-parametric Kruskal–Wallis test was used for comparisons between groups for quantitative variables. The Pearson correlation coefficient was used for analyses of correlation between biomarker levels and number of headings. A value of $p<0.05$ was considered significant.

### RESULTS

No significant differences were found between CSF or serum biomarker concentrations between soccer players who had performed 10 or 20 approved headings (table 1). Likewise, there were no significant differences between either of these two groups and the control group, except for a slightly increased CSF S-100B concentration in the control group compared with players with 10 and 20 approved headings ($p = 0.049$ and $p = 0.008$, respectively, table 1). There were no correlations between the number of approved headings or the total number of headings and any of the biomarker levels (table 2), and there were no intra-individual correlations between any of the biomarkers in any of the groups or in the whole material (data not shown).

### DISCUSSION

The current study is to our knowledge the first determined attempt to determine whether there is a direct injurious effect of heading on brain tissue as reflected by CSF levels of T-tau, NF-L, GFAP and S-100B, which are sensitive and specific markers for neuronal and astroglial injury. Further, we assessed brain-barrier function using the albumin ratio, and serum levels of S-100B, which may reflect injury to the brain. In contrast to our earlier finding for amateur boxing, where increased levels of T-tau, NF-L and GFAP that correlated with the number of received head punches were detected,
the results of this study suggest that standardised headings in soccer do not result in neuronal or astroglial injury. Notably, the CSF levels of these biomarkers are more likely to reflect damage to brain tissue in a sensitive and specific manner than the corresponding serum levels, which may be influenced by biomarker release from extracerebral tissues.9 10

The reason for the slightly increased S-100B levels in CSF from controls compared with soccer players is unknown, but it should be noted that they are well below the levels found in independent control populations that were used when establishing clinical reference values for this analyte in our laboratory (CSF S-100B <1.7 µg/l).

It is estimated that professional soccer players head the ball five to six times a game.24 Thus, the negative results in this study are unlikely to be because the number of headings performed by the participants was too low. Further, the distance of the ball flight of 30 m is similar to a regular corner performed by the participants was too low. Further, the study are unlikely to be because the number of headings in soccer may be influenced by biomarker release from extracerebral tissues.9 10

In conclusion, this study suggests that the head-to-ball contact in a controlled heading does not cause any acute neuronal or astroglial injury. In agreement with this view, the majority of head injuries in soccer seem to be caused by head-to-head contact with another player or goalpost collisions.24 Thus, efforts to prevent brain injury associated with heading may be focused on reducing the likelihood of head-to-head or head-to-goalpost contact and improving the technique so that uncontrolled head-to-ball contact is avoided.

ACKNOWLEDGEMENTS
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What is already known on this topic

• CSF biomarkers can detect acute subclinical brain injury caused by amateur boxing.

• There are limited data available on the possible injurious effects to the brain of repeated headings in soccer.

What this study adds

• Standardised headings in soccer are not associated with any biochemical signs of neuronal or astroglial injury.

• The biomechanical effect on the brain of heading in soccer seems quite different from that caused by head punches in boxing.

Table 2 Correlations between total number of headings and biomarker levels in the whole group of soccer players (n = 23)*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sample correlation coefficient</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin ratio</td>
<td>0.37</td>
<td>−0.047 to 0.68</td>
<td>0.080</td>
</tr>
<tr>
<td>T-tau</td>
<td>−0.004</td>
<td>−0.42 to 0.41</td>
<td>0.98</td>
</tr>
<tr>
<td>GFAP</td>
<td>−0.19</td>
<td>−0.56 to 0.24</td>
<td>0.38</td>
</tr>
<tr>
<td>S-100B in CSF</td>
<td>−0.019</td>
<td>−0.43 to 0.40</td>
<td>0.93</td>
</tr>
<tr>
<td>S-100B in serum</td>
<td>−0.35</td>
<td>−0.67 to 0.669</td>
<td>0.099</td>
</tr>
</tbody>
</table>

CSF, cerebrospinal fluid; GFAP, glial fibrillary acidic protein; T-tau, total tau.

*No correlation for neurofilament light protein (NF-L) is presented since the NF-L concentration was <125 ng/l in all samples.

REFERENCES

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