Impaired Cognitive Performance in Youth Athletes Exposed to Repetitive Head Impacts

Inga K. Koerte^{1,2} Elizabeth Nichols¹, Yorghos Tripodis³, Vivian Schultz^{1,2} Stefan Lehner⁴, Randy Igbinoba⁵, Alice Z. Chuang⁶, Michael Mayinger^{1,2}, Eliana M. Klier⁵, Marc Muehlmann⁷, David Kaufmann⁸, Christian Lepage², Florian Heinen⁹, Gerd Schulte-Körne¹, Ross Zafonte¹⁰, Martha E. Shenton^{2,11}, and Anne B. Sereno⁵

Abstract

Worldwide, more than 22 million children and adolescents are exposed to repetitive head impacts (RHI) in soccer. Evidence indicates cumulative effects on brain structure, but it is not known whether exposure to RHI affects cognitive improvement in adolescents. The aim of the study was to determine whether exposure to RHI while heading the ball in soccer affects improvement in cognitive performance in adolescents over time. The study group consisted of a convenience sample of 16 male soccer players (mean age 15.7 ± 0.7 years). A comparison cohort of 14 male non-contact sports athletes (mean age 14.9±1.1 years) was recruited from competitive athletic clubs and group-matched in age. Using the ProPoint and AntiPoint tasks, sensorimotor and cognitive functions were measured over both immediate (pre- vs. posttraining) as well as across multiple time points within a play season. The number and type of head impacts that occurred during the training were counted. The main outcome measure was the change in response time (RT) in the ProPoint and AntiPoint tasks. The immediate (pre- vs. post-training) and longer-term (across a play season) change in RT was analyzed, and the effect of the number and type of head impacts was tested. Thirty athletes with and without exposure to RHI demonstrated a decrease in RT in both tasks immediately after training. Over the play season, both groups showed improvement in sensorimotor function. While the control group also improved in cognitive performance, the soccer players did not, however. Further, the more long headers performed, the slower the improvement in RT over the season. Youth athletes experience an immediate cognitive improvement after training most likely because of physical exercise. Results of this study also suggest an association between exposure to specific RHI (long headers) and lack of improvement in cognitive performance in youth athletes over time.

Keywords: cognitive function; cognitive improvement; heading; repetitive head impact; soccer; sports-related brain trauma

Introduction

SOCCER IS THE MOST POPULAR and fastest growing sport in the world. Worldwide there are more than 260 million players, of whom 22 million are children and adolescents. Soccer players are exposed to repetitive head impacts (RHI) when heading the ball. On average, soccer players perform 6–12 headers per game and many

more during practice, resulting in thousands of headers over a player's career.¹ These RHI are often considered harmless because there are no immediate symptoms. Recent evidence suggests, however, that RHI, especially if they occur in close proximity in time, may lead to structural and functional brain alterations and clinical impairment even if there are no acute symptoms^{2–5} (for review, see Koerte and associates⁶). More severe effects are

¹Department of Child and Adolescent Psychiatry, Psychosomatic, and Psychotherapy, Ludwig-Maximilians-Universität, Munich, Germany. ²Psychiatry Neuroimaging Laboratory, Department of Psychiatry, Brigham and Women's Hospital, and Harvard Medical School, Boston,

Massachusetts.

³Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts.

⁴Department of Applied Sciences and Mechatronics, University of Applied Sciences, Munich, Germany.

⁵Department of Neurobiology and Anatomy, McGovern Medical School, University of Texas Health Science Center, Houston, Texas.

⁶Department of Ophthalmology and Visual Science, McGovern Medical School, University of Texas Health Science Center, Houston, Texas.

⁷Institute for Clinical Radiology, Ludwig-Maximilians-Universität, Munich, Germany.

⁸Department of Radiology, Charité, Berlin, Germany.

⁹Department of Pediatric Neurology, Dr. von Hauner Children's Hospital, Ludwig-Maximilians- Universität, Munich, Germany.

¹⁰Spaulding Rehabilitation Hospital, Massachusetts General Hospital, Brigham and Women's Hospital, Department of Physical Medicine and Rehabilitation, Harvard Medical School, Boston, Massachusetts.

¹¹VA Boston Healthcare System, Boston, Massachusetts.

expected when a child with insufficient neck strength attempts to head a ball.⁷

Exposure to RHI may potentially have negative consequences for brain development (for review, see Prins and Giza⁸). Despite evidence indicating cumulative effects, there are few studies investigating whether RHI lead to immediate and/or longer-term cognitive impairment in children and adolescents.^{9–11} No studies have determined whether or not exposure to RHI in childhood and adolescence is a determinant of impaired cognitive development, cognitive improvement, or learning.

Last year, the United States Soccer Federation announced a directive to ban headings for players under age 11. To date, however, there is no scientific evidence supporting a cutoff at age 11. In fact, Zhang and associates¹² found cognitive dysfunction after exposure to RHI in a small sample of teenage female soccer players tested immediately after training. Specifically, using a tablet-based application that measures reflexive and voluntary pointing responses, they demonstrated that heading the soccer ball during practice leads to increased response time (RT) compared with a control group, with increased slowing related to the number of hours played per week and number of years of soccer playing.¹²

There are, however, additional effects that need to be taken into account. For example, there is evidence of sensorimotor and cognitive benefits^{13–16} immediately after vigorous physical exercise. This improvement in cognitive performance is because of a number of mechanisms, including an increase in arousal response stimulating the reticular-activating system that regulates ascending tracts to the prefrontal cortex¹³ and increased levels of brain-derived neurotropic factor.^{15,17} In addition to the immediate effects after training, there may also be cumulative effects of physical exercise and exposure to RHI over time. Research suggests physical activity in children results in increased brain regional volume and connectivity as well as superior cognitive function and scholastic achievement. We are not aware of any study, however, that has examined whether or not exposure to RHI in childhood and adolescence is a determinant of impaired cognitive development.

The aim of this study was to measure cognitive function in adolescent high-performance athletes with and without exposure to RHI over both short-term (immediately before and after training) and longer-term (across a play season). We hypothesized that all athletes would show increased cognitive performance immediately after training because of the benefits of exercise.^{13–16} Over multiple testing sessions, however, we expected differences between athletes exposed to RHI and those without exposure to RHI.

Methods

Study design

This prospective, longitudinal, observational, comparison study recruited teenage (13–19 years) subjects from soccer and noncontact sport clubs in Germany between February and May 2015 (see Fig. 1). Participants were tested before (pre-training) and immediately, within 15 min, after training (post-training). Training consisted of a sport practice lesson that was of similar length and intensity between the groups. One pre- and one post-training session were obtained per day of testing, with one to 4 days of testing attained per week.

Participants

The ethics committee of the University of Munich as well as the University of Texas Health Science Center Committee for the Protection of Human Subjects approved the study, and written informed consent was obtained from each participant as well as their legal guardian if the participant's age was below 18 years. Inclusion criteria for the subjects in the soccer player cohort were participation in organized soccer training at least three times a week, being male, age 13-19 years, and right-handed. Subjects who had a history of diagnosed or suspected traumatic brain injury within the last year, neurological disorder, psychiatric illness, or learning disorder were excluded. The soccer player group consisted of 16 soccer players (mean age 15.7 ± 0.7 years).

A comparison cohort of 14 age-matched, right-handed, male athletes (mean age 14.9 ± 1.1 years), participating in either table tennis (n=9) or swimming (n=5), both non-contact sports, were recruited from competitive athletic clubs. Both table tennis and swimming are sports with equal intensity of physical activity level to soccer, as measured by maximum oxygen consumption, $^{18-21}$ but with very low risk for exposure to RHI. The comparison cohort exclusion criteria were: history of suspected or diagnosed concussion or other traumatic brain injury, participation in organized training in a contact sport, neurological disorder, psychiatric illness, or learning disorder.

Study protocol

All study participants were tested before and after training in their respective sport. The soccer players were exposed to RHI (mean 7.2 ± 6.1 , range 0–22) during the sport practice lesson on testing days. None of the athletes in the comparison group participated in any form of activity during training that could be considered a head impact. Depending on their presence on the testing day, soccer players were tested on a mean of 7.8 (standard deviation $[SD] \pm 2.6$, range 3-11) days, and controls were tested on a mean of 4.1 (SD ± 2.7 , range 1–8) days over the course of the spring season. The number of headers performed by each soccer player during training was counted and classified through observation by a trained research assistant. The type of head ball (long: e.g., goalkeeper kick or corner crosses of more than 30 m; short: e.g., players throwing the ball to each other in practice drills; high: e.g., goalkeeper punts (high velocity ball punt by the goalkeeper and commonly headed by a center midfielder) and any other type of head impact were noted.

Stimulus and tasks

The study was performed on iPad 2 tablets (Fig. 1), which have a 9.7 inch screen (diagonal) with a LED-backlit, capacitive display and pixel resolution of 1024-by-768. An application was installed on the iPad 2²² that contained two pointing tasks: ProPoint and AntiPoint (Fig. 1). The ProPoint task provides a measure of sensorimotor function. In the ProPoint task (Fig. 1A), the subject is asked to place and hold the index finger on a circle (diameter = 1.4 cm and viewing angle of 2.4 degrees, from a viewing distance of 33 cm) in the center of the iPad screen until a stimulus in the form of a white square appears in one of four possible locations surrounding the center circle (left, right, up, and down). The subject must then pick up his finger and tap on the white square as quickly as possible. The AntiPoint task (Fig. 1B) is identical to the ProPoint task with respect to visual stimuli and amplitude of pointing movements; however, the subject must instead quickly tap on the square that is opposite to the white stimulus square that appears on the screen. The AntiPoint task measures cognitive control and recruits the frontal lobe because the response requires the subject to inhibit a stimulus-directed hand-pointing movement and generate instead a willful or internally based ("opposite") hand-pointing response.23,24

Each subject completed at least 48 trials for each of the ProPoint and AntiPoint tasks. If the subject made an error (touched a location more than 3.3 degrees (1.9 cm) from the center of the correct location, calculated by the iPad), the trial was scored as an error and presented in random order again at the end of the task, up to a

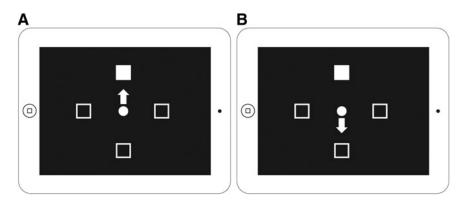


FIG. 1. Schematic of the two tasks displayed on iPad screen. (A) ProPoint task on the iPad with white arrow indicating direction of a correct response (toward the target square). (B) AntiPoint task on the iPad with white arrow indicating direction of a correct response (away from the target square).¹²

maximum of 60 total trials. Overall, participants performed an average of 49.7 trials (SD \pm 2.8). For each trial, the RT (the duration in msec from the onset of the stimulus to the time when the subject's finger taps on a goal location) and whether the response was correct or not (within 3.3 degrees of goal location) was recorded. Each testing session took about 2 min to complete.

There were three testing sessions from three participants in the soccer group in which participants performed the opposite task. Because these participants did not complete a single correct trial that could be used in our analyses of RT, these testing sessions (all post-training session, ProPoint task [n=1] and AntiPoint task [n=2]) were excluded from the data analysis. Further, there were six testing sessions (from four soccer players, pre-training [n=1] and post-training session [n=5]) in which the participants either initially performed the task incorrectly for a number of trials or switched in the middle of a task to performing the task incorrectly for a number of trials, but then corrected themselves and performed the correct task. Even including these set-shifting errors, subjects made few errors (mean 3.3% across all trials).

Analysis

Sample size calculation. The estimated SD for RT was approximately 23 msec for ProPoint and 38 msec for AntiPoint based on a previous study.¹² A sample size of 14 per group is sufficient to detect 25 msec and 40 msec differences between groups in RT for ProPoint and AntiPoint tasks, respectively, at a 5% significance level and 80% power.

Dependent measures. The key dependent variable recorded by the iPad during the testing sessions was RT, in msec, defined as the duration of time from the appearance of the target stimulus to the subject's touch response on the iPad touch screen. The RTs were adjusted by subtracting the externally measured (with photodiode, microphone, and storage oscilloscope; see Kirchgessner and coworkers²⁵) average delay of detecting a touch event on the capacitive device (73.88 msec). Only correct trials were used in the analysis of RT (see above). This removed 3.0% of trials and 3.6% of trials for ProPoint and AntiPoint task, respectively. Conditional means were calculated for each Task (ProPoint and AntiPoint), each session, and each participant.

In addition, individual RTs that were greater than 2.75 SDs away from the respective conditional mean were excluded, removing an additional 5.2% and 4.4% of trials for ProPoint and AntiPoint task, respectively.

Mixed model analyses. The conditional mean RTs, for each pointing task at each session, were compared across groups in a mixed effects model analysis in which the main fixed effect was group (soccer group vs. comparison group) with random effects for the intercept and slope of session to account for correlation between multiple sessions per subject. Within the soccer group, additional mixed effects models, with random intercepts and slopes, were estimated to assess the effect of numbers of each type of headers (long, short, and high) on RT by including an interaction term for the number of headers and sessions. We also evaluated the effect of all headers cumulatively over all sessions on the change of their RT by also including an interaction term. All mixed models were adjusted for fixed effects of age, group, and time since first session. A p value <0.05 was considered statistically significant.

Results

Data were first summarized and reported below as unadjusted means and standard deviations and used in figures (Fig. 2 and 3). All statistical effects and interactions reported below were adjusted for age, group, and time since first measurement.

RHI exposure

The mean age when organized soccer training started for the soccer participants was 5.1 (SD ± 0.8 , range 4–6) years. The athletes played in the following positions: forward (n=4), central midfielder (n=3), outside midfielder/defensive (n=6), central defensive (n=3), goalkeeper (n=0). The mean number of headers performed per training and athlete was 7.2 (SD ± 6.1 , range 0–22). Short headers were most frequently performed per training with a mean of 6.2 (SD ± 5.9 , range 0–22) headers, while the mean long headers was 0.9 (SD ± 1.2 , range 0–6) and the mean high headers was the most infrequent, 0.2 (SD ± 0.7 , range 0–4). Players' position in the field was associated with a difference in the number of long headers. Table 2 lists the mean and SD of long headers for each position in the field.

Pre-training performance

There were no significant differences in pre-training performance between the two study groups in both the ProPoint (t(334)=-1.23, p=0.22) and AntiPoint task (t(334)=-0.87, p=0.22)

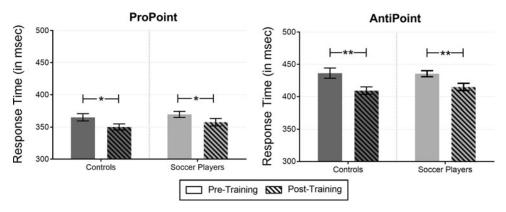


FIG. 2. Pre- versus post-training response time. Averaged data from all pre-training compared with all post-training unadjusted response times in msec for ProPoint (left) and AntiPoint (right) of controls and soccer players. The whiskers indicate the standard error of the mean. Statistical effects reported in the text were adjusted for age, group, and time since first measurement.

p=0.38). Figure 3 shows the mean unadjusted RTs for the pretraining session in the ProPoint and AntiPoint tasks.

Short-term effects (immediate post-training effects)

ProPoint: There was a significant decrease in the RT from pre- to post-training in both the soccer group (mean RT change = -11.3 (standard error [SE]=4.6) msec, t(674)=-2.45, p=0.0147) and the control group (mean RT change=-16.1 (SE=6.9) msec, t(674)=-2.34, p=0.0193).There were no significant effects of group or interaction with group (t(674)=0.57, p=0.57). AntiPoint: There was a statistically significant decrease in RT after the training session in both groups (soccer: mean RT change = -19.0 (SE=4.6) msec, t(674)=-4.1, p<0.0001 and controls: mean RT change = -28.5 (SE=6.8) msec, t(674)=-4.2, p<0.0001). There were no effects of group or interaction with group (t(674) 1.14, p=0.25). Figure 2 shows the mean unadjusted RTs before and after training for both the ProPoint and AntiPoint tasks.

Longer-term effects (across training sessions within a play season)

The mean changes in unadjusted RTs of the athletes in both groups over the course of the study on the ProPoint and AntiPoint iPad tasks are displayed in Figure 3. ProPoint: Both study groups showed a significant decrease in mean RT on the ProPoint task over the course of the study. The control group's adjusted mean RT, however, decreased per training session significantly more over the weeks compared with the soccer group's RT (estimate=5.96 (SE=1.21), t(650)=-4.93, p < 0.0001). AntiPoint: Controls showed significant improvement in their adjusted mean RT on the AntiPoint task over sessions, whereas soccer players showed no such improvement. As in ProPoint, the improvement in RT in the soccer players was significantly less per training session than that observed in the controls (estimate=-4.14 (SE=1.21), t(650)=-3.43, p=0.0006). These findings show that athletes in the control group experienced a significant improvement in sensorimotor function and cognitive performance; however, the soccer players only improved in sensorimotor function but not in cognitive performance.

Effects of headers performed during the training on immediate RT effects (improvement across pre- and post-training of the same day)

Within the soccer group, the total number of headers performed during the training was not correlated with the improvement in RT between pre-training and post-training assessment in either the ProPoint (estimate = -0.49, (SE = 0.5), t(217) = -0.99, p = 0.33) nor AntiPoint task (estimate = -0.07, (SE = 0.5), t(217) = -0.16, p = 0.87).

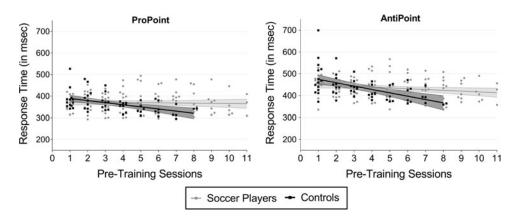


FIG. 3. Pre-training response time over time. Scatter plot and regression line with 95% confidence intervals of unadjusted response times in msec for ProPoint (left) and AntiPoint (right) of controls and soccer players over eight pre-training tests (controls) and 11 pre-training tests (soccer players). Statistical effects reported in the text were adjusted for age, group, and time since first measurement.

IMPAIRED COGNITION IN SOCCER PLAYERS

Table 1. I	Demographic	INFORMATION	OF PARTICIPANTS
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Variable	Soccer players $(n = 16)$	Controls $(n = 14)$
Age (years, mean ± SD [range])	15.7 (± 0.7) [15 to 17]	14.8 (± 1.1) [14 to 17]
History of mTBI (n, %)	5 (31%)	1 (7%)
Number of test days (mean ± SD [range])	7.8 (± 2.6) [3 to 11]	4.1 (± 2.7) [1 to 7]
Time period	04/2015-05/2015	02/2015-04/2015
Head impacts per session (number, mean (± SD) [range])	7.2 (± 2.8) [3 to 15]	n/a
Years of training (years, mean (± SD) [range])	$10.6 (\pm 1.1) [9 \text{ to } 13]$	8.8 (± 1.5) [8 to 11]
BMI (mean (± SD) [range])	21.1 (± 1.6) [18.7 to 23.8]	19.3 (± 0.6) [18.6 to 19.9]

SD, standard deviation; mTBI, mild traumatic brain injury; BMI, body mass index.

Effects of headers performed during the entire study on longer-term RT improvement

The total number of headers performed over all testing days had no statistically significant effect on the soccer player's rate of improvement in RT over the entire study. For both ProPoint and Anti-Point, however, there was a statistically significant relationship between the number of long headers performed and change in RT. The more long headers a player performed, the less his improvement in RT over the course of the study (ProPoint: slope = 0.37, (SE=0.11) per long header, t(451)=3.29, p=0.0011; for AntiPoint: slope = 0.26, (SE=0.11) per long header, t(451)=2.2, p=0.0285).

Discussion

Athletes with and without exposure to RHI demonstrate a decrease in RT immediately after training, indicating an improvement in sensorimotor and cognitive function likely because of the wellknown immediate benefits of physical exercise. Over the course of the entire study, both groups showed improvement in sensorimotor function. While the control group also improved in cognitive performance, the soccer players did not, however. Further, the more long headers a soccer player performed, the lower his improvement in RT over the course of the study. This suggests that cognitive performance can improve in youth athletes over time likely because of developmental changes in adolescence, but this benefit may be suppressed by the effects of exposure to specific RHI characteristics.

Immediate improvements

All athletes showed an improvement in their RT immediately after training. Soccer players who were exposed to RHI while performing on average seven headers during the training yielded similar results compared with the control group. These results are in line with the existing literature on the association of improvement in sensorimotor and cognitive performance after physical exercise^{13–17,26} and suggest that the effects of RHI will not be evident

TABLE 2. TYPE OF HEADER BY POSITION IN THE FIELD

	Ν	Long headers	
Position in the field		Mean	SD
Forward	110	4.05	1.92
Center midfield	91	9.73	5.02
Center defense	104	6.87	1.74
Outside midfield/defense	180	7.09	3.29

SD, standard deviation.

immediately after training. This is in line with previous publications reporting no immediate effects of heading the soccer ball.²⁷

Alternatively, it is possible that there are immediate cognitive deficits after RHI12 that are masked in the soccer players by other factors that improve performance. First, increased arousal with exercise could potentially mask immediate deficits from RHI. In addition, previous work has shown that well-trained athletes have greater adrenaline response to exercise²⁸ at the same absolute or relative intensity than untrained subjects.²⁹ This finding may account for differences between our study showing no immediate cognitive impairment in highly trained soccer players (i.e., greater adrenaline response) and a previous study showing small but significant cognitive slowing in less well-trained high school soccer players.¹² Second, it is possible that headers may produce an additional increase in arousal because of a visual looming effect (visual stimulus rapidly approaching the head).^{30,31} The visual looming effect is purported to activate fast intercortical connections and increase sensorimotor function³² and may even lead to an increase in cognitive function. Such effects, if present, could mask immediate negative effects from RHI.

Interestingly, only soccer players made the mistake of performing the task incorrectly, either initially starting with the other task or maintaining the wrong set throughout the entire task. This occurred almost exclusively in post-training assessment. This observation may also suggest immediate subtle deficits in soccer players in cognitive flexibility, another aspect of cognitive control, often measured by task or set shifting paradigms (e.g., ³³) and should be investigated further in future studies.

Longer-term slowing

The control group experienced a significant improvement in sensorimotor function and cognitive performance over a longer period; however, the soccer players only improved in sensorimotor function but not in cognitive performance. Further, within the soccer group, the total number of headers performed over all assessments had no effect on the soccer player's improvement. The more long headers a player performed, however, the slower his improvement in RT over the course of the study. These results suggest that cognitive performance in youth athletes improves over a play season, but this benefit can be suppressed or eliminated by RHI. In addition, specific characteristics of RHI (i.e., long headers with high velocity) might play a more important role than the total number of head impacts.

Study limitations

First, although the data were collected from players of various field positions, future studies are needed to elucidate the generalization of our findings across field positions, age spectrum, and playing levels. Second, there were a few athletes who only participated in a small number of assessments because of missed training days. Although our mixed effect regression models account for missing at random and unequal timing of dropout, conditional on group participation, future studies could examine changes across a longer period and may also consider including testing after a period without exposure to RHI to explore the effects of the intervals between successive practices and games on changes in RT. Third, the current study did not use a second observer, which would make it possible to calculate inter-rater reliability. Because of the distinct difference in distance between short and long headers, however, we are confident that the data is sufficiently reliable and robust. Future studies might consider the inclusion of multiple observers.

Finally, the differentiation between different types of headers was qualitative. Previous work suggests that there are several factors important in determining head impact severity: first, the velocity of a long header performed during a game. The highest-velocity ball a player might voluntarily head would be from a punt (approximately 70 km/h), drop kick (approximately 85 km/h), or goal kick (also approximately 85 km/h).³⁴ Second, the likelihood of sustaining a brain trauma is increased when the athlete is not anticipating to head the ball.³⁵ Finally, important other factors include rotational versus linear velocity, neck muscle strength, size/weight of ball, athlete's body mass, and heading technique. Future studies should include quantitative measures of head acceleration to further explore the effects of type and frequency of head impact exposure.

Conclusion

The immediate improvement in cognitive performance after training can be observed in both youth athletes with and without RHI and is most likely because of physical exercise. Over a longer period, however, results of this study also suggest an association between exposure to RHI while heading the ball in soccer and lack of improvement in cognitive performance. This indicates that, although cognitive performance improves in youth athletes over time, this benefit may be suppressed by the cumulative effects of RHI, especially those with high velocity. This slowing may have far reaching impact on the developmental trajectory and learning in general.

Acknowledgments

We thank all study participants. This study was in part supported by the Else Kröner-Fresenius-Stiftung, Germany (IK), the U.S. Department of State Fulbright Scholarship, 2014-2015 (EN), Mission Connect, a program of TIRR Foundation (AS), NIH P30-EY010608 (AC), a VA Merit Award (MES), and the German Academic Exchange Service PROMOS Award (VS).

Author Disclosure Statement

Co-author AS is named inventor in a pending patent application for a "Touch sensitive system and method for cognitive and behavioral testing and evaluation" (US 2014/0249447 A1). For the remaining authors, no competing financial interests exist.

References

 Matser, J.T., Kessels, A.G., Jordan, B.D., Lezak, M.D., and Troost, J. (1998). Chronic traumatic brain injury in professional soccer players. Neurology 51, 791–796.

- Koerte, I.K., Ertl-Wagner, B., Reiser, M., Zafonte, R., and Shenton, M.E. (2012). White matter integrity in the brains of professional soccer players without a symptomatic concussion. JAMA 308, 1859– 1861.
- Koerte, I.K., Lin, A.P., Muehlmann, M., Merugumala, S., Liao, H., Starr, T., Kaufmann, D., Mayinger, M., Steffinger, D., Fisch, B., Karch, S., Heinen, F., Ertl-Wagner, B., Reiser, M., Stern, R., Zafonte, R.D., and Shenton, M.E. (2015). Altered neurochemistry in former professional soccer players without a history of concussion. J. Neurotrauma 32, 1287–1293.
- Koerte, I.K., Mayinger, M., Muehlmann, M., Kaufmann, D., Lin, A.P., Steffinger, D., Fisch, B., Rauchmann, B.S., Immler, S., Karch, S., Heinen, F.R., Ertl-Wagner, B., Reiser, M., Stern, R.A., Zafonte, R., and Shenton, M.E. (2016). Cortical thinning in former professional soccer players. Brain Imaging Behav. 19, 792–798.
- Lipton, M.L., Kim, N., Zimmerman, M.E., Kim, M., Stewart, W.F., Branch, C.A., and Lipton, R.B. (2013). Soccer heading is associated with white matter microstructural and cognitive abnormalities. Radiology 268. 850–857.
- Koerte, I.K., Lin, A.P., Willems, A., Muehlmann, M., Hufschmidt, J., Coleman, M.J., Green, I., Liao, H., Tate, D.F., Wilde, E.A., Pasternak, O., Bouix, S., Rathi, Y., Bigler, E.D., Stern, R.A., and Shenton, M.E. (2015). A review of neuroimaging findings in repetitive brain trauma. Brain Pathol. 25, 318–349.
- Dezman, Z.D., Ledet, E.H., and Kerr, H.A. (2013). Neck strength imbalance correlates with increased head acceleration in soccer heading. Sports Health 5, 320–326.
- Prins, M.L., and Giza, C.C. (2012). Repeat traumatic brain injury in the developing brain. Int. J. Dev. Neurosci. 30, 185–190.
- Talavage, T.M., Nauman, E.A., Breedlove, E.L., Yoruk, U., Dye, A.E., Morigaki, K.E., Feuer, H., and Leverenz, L.J. (2014). Functionallydetected cognitive impairment in high school football players without clinically-diagnosed concussion. J. Neurotrauma 31, 327–338.
- Bazarian, J.J., Zhu, T., Blyth, B., Borrino, A., and Zhong, J. (2012). Subject-specific changes in brain white matter on diffusion tensor imaging after sports-related concussion. Magn. Reson. Imaging 30, 171–180.
- Tsushima, W.T., Geling, O., Arnold, M., and Oshiro, R. (2016). Are there subconcussive neuropsychological effects in youth sports? an exploratory study of high- and low-contact sports. Appl. Neuropsychol. Child 5, 149–155.
- Zhang, M.R., Red, S.D., Lin, A.H., Patel, S.S., and Sereno, A.B. (2013). Evidence of cognitive dysfunction after soccer playing with ball heading using a novel tablet-based approach. PLoS One 8, e57364.
- Byun, K., Hyodo, K., Suwabe, K., Ochi, G., Sakairi, Y., Kato, M., Dan, I., and Soya, H. (2014). Positive effect of acute mild exercise on executive function via arousal-related prefrontal activations: an fNIRS study. Neuroimage 98, 336–345.
- Hogervorst, E., Riedel, W., Jeukendrup, A., and Jolles, J. (1996). Cognitive performance after strenuous physical exercise. Percept. Mot. Skills 83, 479–488.
- Winter, B., Breitenstein, C., Mooren, F.C., Voelker, K., Fobker, M., Lechtermann, A., Krueger, K., Fromme, A., Korsukewitz, C., Floel, A., and Knecht, S. (2007). High impact running improves learning. Neurobiol. Learn. Mem. 87, 597–609.
- Budde, H., Voelcker-Rehage, C., Pietrabyk-Kendziorra, S., Ribeiro, P., and Tidow, G. (2008). Acute coordinative exercise improves attentional performance in adolescents. Neurosci. Lett. 441, 219–223.
- Ferris, L.T., Williams, J.S., and Shen, C.L. (2007). The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. Med. Sci. Sports Exerc. 39, 728–734.
- 18. Suchomel, A. (2010). A comparison of exercise intensity on different player levels in table tennis. Int. J. Table Tennis Sci. 6.
- Tonnessen, E., Hem, E., Leirstein, S., Haugen, T., and Seiler, S. (2013). Maximal aerobic power characteristics of male professional soccer players, 1989–2012. Int. J. Sports Physiol. Perform. 8, 323–329.
- Holmer, I., Lundin, A., and Eriksson, B.O. (1974). Maximum oxygen uptake during swimming and running by elite swimmers. J. Appl. Physiol. 36, 711–714.
- Billat, V., Faina, M., Sardella, F., Marini, C., Fanton, F., Lupo, S., Faccini, P., de Angelis, M., Koralsztein, J.P., and Dalmonte, A. (1996). A comparison of time to exhaustion at VO2 max in elite

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cyclists, kayak paddlers, swimmers and runners. Ergonomics 39, 267-277.

- Sereno, A.B., Patel, S.S., Shresthra, Y. and Red, S.D. Touch sensitive system and method for cognitive and behavioral testing and evaluation. United States patent application US 2014/0249447 A1.
- DeSouza, J.F., Menon, R.S., and Everling, S. (2003). Preparatory set associated with pro-saccades and anti-saccades in humans investigated with event-related FMRI. J. Neurophysiol. 89, 1016–1023.
- Funahashi, S., Chafee, M.V., and Goldman-Rakic, P.S. (1993). Prefrontal neuronal activity in rhesus monkeys performing a delayed antisaccade task. Nature 365, 753–756.
- Kirchgessner, M.A., Chuang, A.Z., Patel, S.S., and Sereno, A.B. (2015). Intact reflexive but deficient voluntary social orienting in autism spectrum disorder. Front. Neurosci. 9, 453.
- Kemppainen, J., Aalto, S., Fujimoto, T., Kalliokoski, K.K., Langsjo, J., Oikonen, V., Rinne, J., Nuutila, P., and Knuuti, J. (2005). High intensity exercise decreases global brain glucose uptake in humans. J. Physiol. 568, 323–332.
- Rieder, C., and Jansen, P. (2011). No neuropsychological consequence in male and female soccer players after a short heading training. Arch. Clin. Neuropsychol. 26, 583–591.
- Warren, J.B., Dalton, N., Turner, C., Clark, T.J., and Toseland, P.A. (1984). Adrenaline secretion during exercise. Clin. Sci. (Lond) 66, 87–90.
- Zouhal, H., Jacob, C., Delamarche, P., and Gratas-Delamarche, A. (2008). Catecholamines and the effects of exercise, training and gender. Sports Med. 38, 401–423.

- Maier, J.X., Chandrasekaran, C., and Ghazanfar, A.A. (2008). Integration of bimodal looming signals through neuronal coherence in the temporal lobe. Curr. Biol. 18, 963–968.
- Field, D.T. and Wann, J.P. (2005). Perceiving time to collision activates the sensorimotor cortex. Curr. Biol. 15, 453–458.
- Clery, J., Guipponi, O., Odouard, S., Wardak, C., and Ben Hamed, S. (2015). Impact prediction by looming visual stimuli enhances tactile detection. J. Neurosci. 35, 4179–4189.
- Pang, E.W. (2015). Different neural mechanisms underlie deficits in mental flexibility in post-traumatic stress disorder compared to mild traumatic brain injury. Front Psychiatry 6, 170.
- Kirkendall, D.T., and Garrett, W.E., Jr. (2001). Heading in soccer: integral skill or grounds for cognitive dysfunction? J. Athl. Train. 36, 328–333.
- Boden, B.P., Kirkendall, D.T., and Garrett, W.E., Jr. (1998). Concussion incidence in elite college soccer players. Am. J. Sports Med. 26, 238–241.

Address correspondence to: Inga K. Koerte, MD Psychiatry Neuroimaging Laboratory Brigham and Women's Hospital 1249 Boylston Street Boston, MA 02215

E-mail: ikoerte@bwh.harvard.edu