Video Article

An Investigation of the Effects of Sports-related Concussion in Youth Using Functional Magnetic Resonance Imaging and the Head Impact Telemetry System

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Abstract

One of the most commonly reported injuries in children who participate in sports is concussion or mild traumatic brain injury (mTBI)[1]. Children and youth involved in organized sports such as competitive hockey are nearly six times more likely to suffer a severe concussion compared to children involved in other leisure physical activities[2]. While the most common cognitive sequelae of mTBI appear similar for children and adults, the recovery profile and breadth of consequences in children remains largely unknown[2], as does the influence of pre-injury characteristics (e.g. gender) and injury details (e.g. magnitude and direction of impact) on long-term outcomes. Competitive sports, such as hockey, allow the rare opportunity to utilize a pre-post design to obtain pre-injury data before concussion occurs on youth characteristics and functioning and to relate this to outcome following injury. Our primary goals are to refine pediatric concussion diagnosis and management based on research evidence that is specific to children and youth. To do this we use new, multi-modal and integrative approaches that will:

1.Evaluate the immediate effects of head trauma in youth
2.Monitor the resolution of post-concussion symptoms (PCS) and cognitive performance during recovery
3.Utilize new methods to verify brain injury and recovery

To achieve our goals, we have implemented the Head Impact Telemetry (HIT) System. (Simbex; Lebanon, NH, USA). This system equips commercially available Easton S9 hockey helmets (Easton-Bell Sports; Van Nuys, CA, USA) with single-axis accelerometers designed to measure real-time head accelerations during contact sport participation [3-5]. By using telemetric technology, the magnitude of acceleration and location of all head impacts during sport participation can be objectively detected and recorded. We also use functional magnetic resonance imaging (fMRI) to localize and assess changes in neural activity specifically in the medial temporal and frontal lobes during the performance of cognitive tasks, since those are the cerebral regions most sensitive to concussive head injury [6]. Finally, we are acquiring structural imaging data sensitive to damage in brain white matter.

Video Link

The video component of this article can be found at https://www.jove.com/video/2226/

Protocol

1. Obtaining Pre-injury Neuropsychological Baseline Profile on Subject

1. Prior to subject arriving for testing, ensure all equipment is functioning properly and ready for testing and that the room is free from unnecessary distractions.
2. After reviewing parental and subject consent, measure and record subject's height, weight and head circumference.
3. Administer balance assessment while subject is standing on force plate in the following order of conditions: A1 - on force plate, eyes open; A2 - on force plate, eyes closed; A3 - on force plate while wearing the visual conflict dome.
4. Place AirexBalance-pad on top of force plate and repeat administration of balance assessment conditions (A1-A3) having the subject stand on top of the AirexBalance-pad and force plate combined.

5. Measure and record hand grip strength and administer the grooved pegboard test for both the left and right hands.
6. Administer the jump test on the jump mat, first from a squat position then the counter-movement, completing 3 trials for each position.
7. Conduct leg maximal voluntary contraction test using the force plate and strength bar.
8. Administer neuropsychological test battery in the following order according to Assessment Manual Instructions: Post-concussion Symptom Scale-Revised; Child Mood Checklist Self-Report; Waterloo Handedness Questionnaire; Rey Complex Figure Test: Copy Trial; Verbal Fluency Test; Rey Complex Figure Test: Immediate Recall Trial; Verbal Working Memory Task; Rey Auditory Verbal Learning Test; Rey Complex Figure Test: Delayed Recall Trial; Rey Complex Figure Test: Recognition Trial; Stroop Color and Word Test; Symbol Digits Modalities Test; Children's Color Trails Test; Visual Working Memory Task; Rey Auditory Verbal Learning Test: Delayed Recall; Rey Auditory Verbal Learning Test: Recognition Trial; Children's Paced Auditory Serial Attention Task (see Figure 1 for an illustration of the Verbal and Visual Working Memory tasks).
9. Score neuropsychological tests following the corresponding test manual instructions where appropriate.
10. Enter all test scores into database.

2. Acquiring Structural and Functional MRI Baseline Images on Subject

1. Prior to the testing session, conduct an MRI screening interview via telephone to ensure participant can safely undergo an MRI.
2. Upon arriving for their test session, review consent/assent form with the subject and their parent(s), repeat the MRI screening, provide a thorough orientation and overview of the MRI machine and experiment in an age-appropriate manner. Ask if the subject has any questions.
3. Have subject remove all metal jewelry, accessories and objects from pockets.
4. Demonstrate how subject is to respond to stimuli presented during the working memory task through the use of Lumitouch paddles (an MRI-safe 'mouse' with left and right buttons only).
5. Have the subject insert ear plugs.
6. Have the subject lie down on scanner bed.
7. Position the head in the head coil and stabilize the head using foam inserts and a reminder strap across forehead. Should the participant require corrective lenses to see the computer screen, fit them with MRI-compatible goggles with the appropriate prescription strength.
8. Move the scanner bed into the scanner.
9. Place video screen outside bore of scanner and orient subject to mirror on head coil where the working memory task will be projected.
10. Obtain T1 weighted structural image using 3D spoiled gradient with inversion preparation (3D SPGR-IRprep) (see Table 1 for a complete description of scan parameters).
11. Administer the working memory task and collect functional MRI images using single-shot T2*-weighted imaging with spiral in/out readout[7].
12. Obtain FLAIR image.
13. Obtain PD/T2 weighted image using dual-echo fast spin echo (2D-FSE-XL) using ASSET. ASSET is turned off if white matter hyperintensities are seen on FLAIR image.
14. Obtain T2*-weighted structural images using gradient-recalled echo (GRE).
15. Obtain 2 diffusion tensor imaging (DTI) datasets (3 if time permits) using single shot echo-planar imaging with dual-spin echo.
16. Remove subject from scanner.

3. Recording the Force and Direction of Hits to the Head using the Head Impact Telemetry (HIT) System

1. Obtain a proper fit for the hockey helmet on subject's head.
2. Remove batteries from helmet and charge fully, then return to helmet.
3. Ensure that the helmets and HIT system are transmitting and receiving data, respectively, prior to collecting game data.
4. Collect data during game play, recording each hockey period's stop and start time.
5. Send data for processing via sync mechanism to Simbex using internet connection.

4. Performing Post-mTBI Neuropsychological Follow-up Testing

1. On the same day as an injury report is received, complete the Hit Injury Report Form with the parent to obtain clinical and functional details regarding the injury.
2. Administer the PCS-R to subject and determine current severity of symptoms.
3. Approximately day 1 post-injury: administer PCS-R. If symptoms are unresolved (i.e. have not returned to baseline levels), do not administer full neuropsychological test battery.
4. If subject's symptoms permit, complete the balance assessment (refer to 1.3 and 1.4) and jump test (refer to 1.6).
5. If subject's symptoms permit, administer leg maximal voluntary contraction test (refer to 1.7).
6. If subject's symptoms permit once physical testing is completed, administer the verbal and visual working memory task.
7. Continue to administer the PCS-R until symptoms have resolved (i.e. return to baseline levels) according to the schedule outlined in Table 2.
8. Approximately day 5 post-injury: administer PCS-R. If symptoms are unresolved repeat testing sequence above (refer to 4.3 to 4.6).
9. If symptoms are still unresolved after 7 days post-injury, continue to administer PCS-R weekly until symptoms resolve.
10. For subjects whose symptoms have resolved, repeat steps 1.2 to 1.9.
11. Proceed to structural and functional MRI follow-up scanning session (refer to Section 5).

5. Acquiring Structural and Functional MRI Post-mTBI Follow-up Images

1. Schedule subject for follow-up scanning session within 72 hours post-injury.
2. Repeat steps 2.2-2.16 listed above.

3. If symptoms are unresolved at the time of the first follow-up scanning session, schedule a second follow-up scanning session once symptoms are resolved and repeat steps 2.2-2.16 as listed above.

6. Performing Matched Control Subject Neuropsychological Follow-up Testing

1. Examine ages (i.e. years and months) of all subjects enrolled in experiment and generate a list of potential age and gender-matched control subjects according to birthdates corresponding to within 3 months in the same calendar year for each mTBI subject.
2. Contact control subjects and schedule testing session.
3. Replicate testing protocol to the matched mTBI subject with respect to the timing and number of follow-up sessions. Repeat steps 1.2-1.16 above, as indicated. For example, if the mTBI subject's symptoms were resolved within 24 hours and they only completed one follow-up testing session that included the entire neuropsychological battery, then replicate this protocol with the matched control subject.
4. Proceed to structural and functional MRI follow-up scanning session (refer to section 7).

7. Acquiring Structural and Functional MRI Matched Control Subject Images

1. Repeat steps 2.2-2.16 listed above.
2. If the control subject is matched to a mTBI subject who completed two follow-up scanning sessions due to unresolved symptoms, schedule a second testing session matching the time interval between sessions (i.e. number of days) and repeat steps 2.2-2.16 as listed above.

8. Data Analyses

1. Calculate descriptive statistics (mean and standard deviation) for magnitude and number of hits to the head for each player as obtained from the HIT system, normalizing data per player per game.
2. Calculate the change score from baseline for each neuropsychological test score across all mTBI and matched control subjects.
3. Perform a matched samples t-test with group as the between subjects factor (i.e. mTBI versus control) and change in neuropsychological test performance as the dependent variable to analyze the effect of mTBI on neuropsychological function.
4. Use the clinical PD/T2-weighted image sets to generate whole-brain volumetric measures to measure global swelling in the brain immediately post-mTBI.
5. For each mTBI subject, the T1-weighted images are used to calculate focal changes in tissue volume using two complimentary calculations of nonlinear deformation fields. First, register baseline scans to each of the follow-up scans. Second, calculate the deformation between consecutive pairs of scans, to capture short-term scan-to-scan differences.
6. Correct the DTI data for eddy-current distortions and head motion, and reorient the gradient directions prior to calculating the diffusion tensor parameters. For mTBI versus non-mTBI group studies, use the method of tract-based spatial statistics (TBSS), recently introduced by the Oxford group[8].
7. Identify any white matter hyperintensities on the FLAIR images and microbleeds on the GRE images to separate regions of normal appearing white matter from those that have experienced damage post-mTBI[9]. Use these locations to extract quantitative measures derived from DTI (fractional anisotropy, FA, mean diffusivity, D, and radial diffusivity, DR).
8. For the DTI analyses, correlate TBSS voxel values with the HITS telemetery data (i.e. magnitude and number of hits to the head), using the multivariate Partial Least Squares analysis method[10 - 13]. Partial Least Squares (PLS) is a multivariate technique that can identify whole-brain patterns of activity that vary with experimental conditions or behaviour.
9. Pre-process fMRI images via spatial coregistration to an early fiducial volume from the first imaging run to correct for head motion, followed by a 3D Fourier transform interpolation.
10. Spatially normalize motion-corrected images to an in-house fMRI spiral template using a 12-parameter affine transform with sinc interpolation and smooth with a Gaussian filter of 6 mm full-width-at-half-maximum to increase the signal-to-noise ratio.
11. Remove the initial five image volumes in each run, in which transient signal changes occur as brain magnetization reaches a steady state.
12. Perform univariate analyses using Statistical Parametric Mapping 2 (SPM2) where vectors identifying the image corresponding to the onset time of each event are convolved with the hemodynamic-response-function (HRF) and entered into a voxel-wise multiple linear regression [14].
13. Compute parameter estimates for each of the covariates which reflect changes in BOLD signal per event-type, relative to baseline.
14. Use voxel-level t-statistics to perform contrasts comparing activity brain regions that are differentially engaged across tasks (e.g. working memory versus control task) and groups (e.g. mTBI versus controls).
15. Combine information from the HIT system (i.e. average magnitude of head impacts for each player) with structural and functional neuroimaging data. To assess these interrelations, use PLS analysis.
16. Use the average magnitude of head impacts for each player to run a behavioural PLS which will relate the average magnitude to differences in brain activity patterns during performance on the working memory task.

9. Representative Results

Head Impact Telemetry System

Table 3 depicts quantitative data recorded for corresponding impacts illustrated in Figure 2. Peak linear acceleration is the maximum linear acceleration of a player's head during impact. The units are g's. A g is the acceleration of gravity at sea level (9.8 meters per second squared). Peak rotational acceleration is the maximum rotational acceleration of a player's head during impact. The units are radians per second squared. Azimuth is a measure of impact location. Azimuth is defined from -180° to 180° with 0° at the back of the head and positive azimuth to the right side of the head. Elevation is the other measure of impact location. Elevation is defined from 0° (horizontal plane passing through the head center of gravity) to 90° (crown of the head).

Functional MRI

Figure 3 depicts serial fMRI results from a) concussed athletes with symptom resolution and b) with no symptom resolution. Note: task-related brain activities in the frontal region are clearly observed only in athletes with symptom resolution.

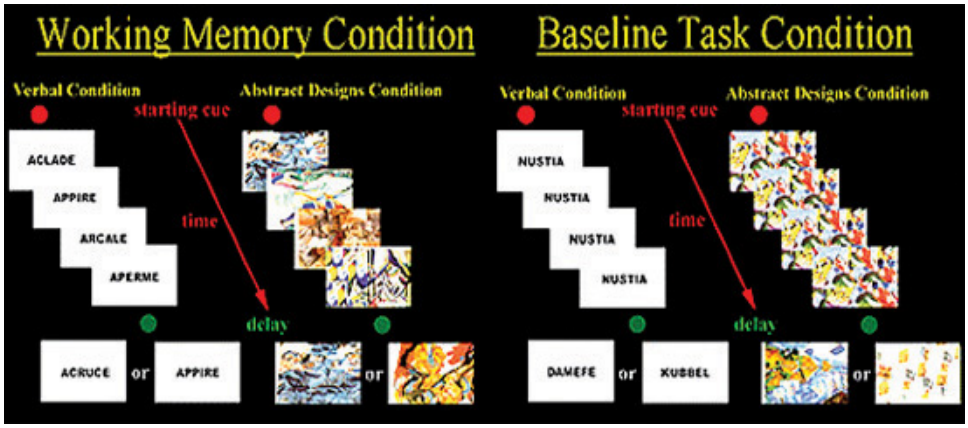

Figure 1. Schematic diagram of the externally ordered working memory task.

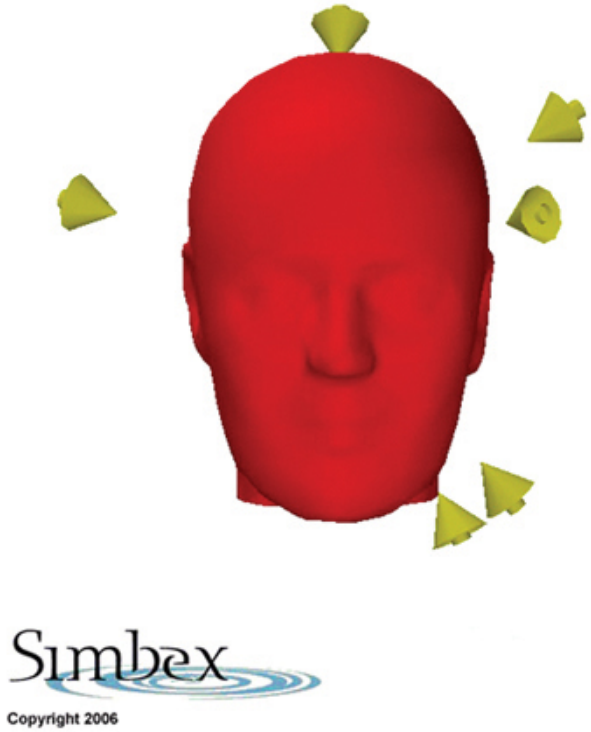

Figure 2. Example of HIT System data interface showing directional vectors indicating the location for the six hits described in Table 3. Simbex 2006.

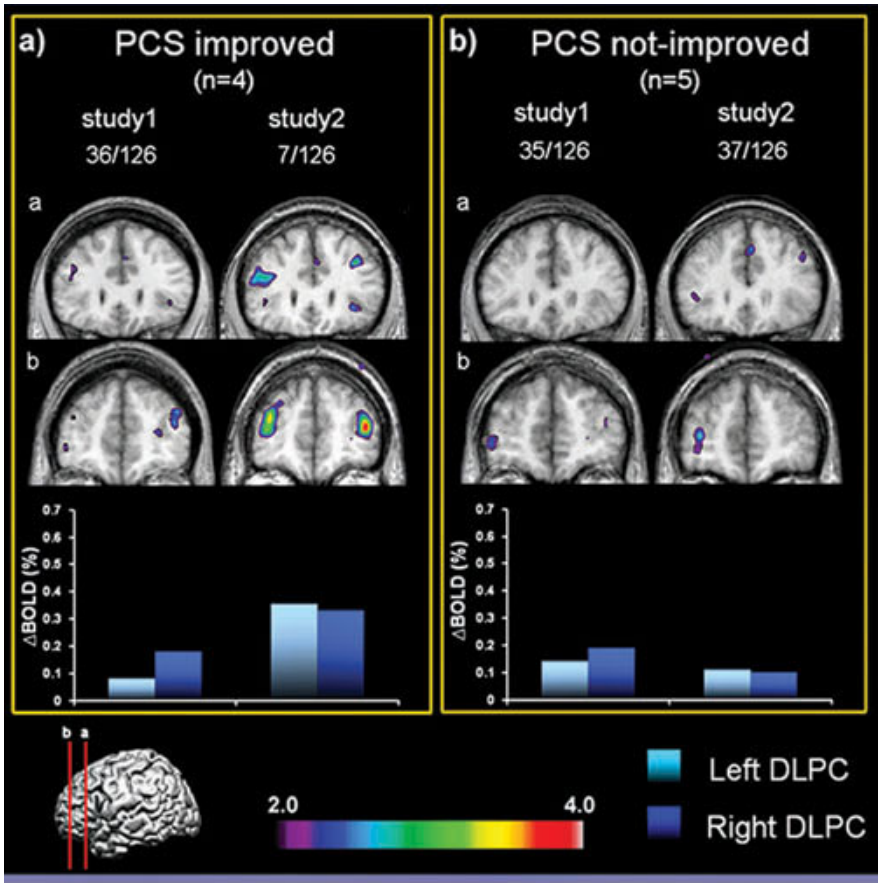

Figure 3. Serial fMRI results from a) concussed athletes with symptom resolution and b) with no symptom resolution. PCS=post-concussion symptoms; n=number of subjects; ▲BOLD = change in blood oxygenation level dependent signal; DLPC = dorsolateral prefrontal cortex.

Scan Type	Sequence	TE/TR/TI/FA1	Matrix/ FOV(cm)2	NEX3	Slice Thickness/ # Slices	Other	Scan Time
T1 weighted	3D spoiled gradient echo with inversion preparation (SPGR-IRprep)	5.9/1.3/300/20	256 160/22	2	1.4/128		7:30
PD/T2 weighted	Dual-echo fast spin echo (FSE)	20,102/2.9s/	256 192/22	2	3/48	interleaved	12:00
FLAIR	FSE-IRprep	140/9.3s/2.2s/	256 192/22	1	3/48		4:12
Diffusion Tensor	Single-shot echo planar imaging, with dual spin echo	min/~9s/	128 128/33	2	2.6/50+	b-value:1000 s/ mm2 Gradient orientations:23 B0:2 peripheral gating	6:30
T2*	Gradient echo	20/350/ /20	256 192/22	1	3/48	interleaved	4:30
fMRI	Single-shot T2*, with spiral in/out readout	30/2s/ /70	64 64/20		5/26	peripheral monitoring: respiration, cardiac	12:00-15:00
qT2	Poon & Henkleman	10/2500/	128 128/24	4	4/1		21:00
						TOTAL	**70:42**

Table 1. Details of Scan Parameters For Clinical and Functional MR Sequences at 3T.

[1] TE (echo time); TR (repetition time); TI (inversion time); FA (flip angle)
[2] FOV (field of view)
[3] NEX (number of excitations)

Time	Post-Concussion Symptom Scale (PCS)	Working Memory Task	Balance	Coordination	Neuropsychological Assessment
Baseline Year 1	X	X	X	X	X
Post-Concussion (PC) Day 1	X	X	X	X	
PC Day 2	X				
PC Day 3-4	X				
PC Day 5-6	X	X	X	X	
PC Day 7	X				
Weekly after Day 7	X				
PCS Resolution	X	X	X	X	X
Baseline Year 2	X	X	X	X	X

Table 2. Administration of Neuropsychological Measures for All Subjects.

Note: Each individual concussed subject will be matched with orthopedic and no injury control subjects. The control subjects will be administered the measures for the same time frame as the concussed subject they are matched with. For example, if a concussed subject experienced resolution of PCS symptoms on day 14, an orthopedic control subject as well as a no injury control subject would also be administered the full neuropsychological assessment on day 14 (i.e. treated as though their 'PCS' symptoms resolved on day 14) in order to match data points.

Event Date	Event Time	Peak Linear Acceleration	Peak Rotational Acceleration	Azimuth	Elevation
2006-10-29	15:39:01:410	22.45	2842.32	-67.30	29.05
2006-10-29	15:47:02:120	7.09	478.66	-116.53	-61.24
2006-10-29	16:21:40:190	15.25	1288.01	-83.96	-52.09
2006-10-29	16:48:31:910	8.91	603.32	-134.04	16.33
2006-10-29	16:48:32:060	18.18	1256.09	60.36	10.36
2006-10-29	17:04:50:110	20.18	1093.22	-4.47	50.31

Table 3. Sample of data collected from one player with one helmet.

Discussion

We predict that those youths who show the greatest impact on brain white matter will show the greatest reorganization of brain activity, and the longest behavioural and neural recovery periods. This research will provide a better understanding of pediatric post-concussion events and have a significant impact on medical care, as it will allow us to establish a recovery protocol based on research evidence that is specific to children and youth. Such a protocol can then be translated to stakeholders, including parents, coaches and doctors. To achieve these goals, we will characterize and quantify further the neuropsychological and neural sequelae in concussed pediatric athletes. We also measure cognitive improvement and changes in brain structure and activity patterns that accompany behavioural recovery. In addition, the study will provide a new look at the impact of concussion and repeated non-concussive head impacts on long-term brain plasticity and development in youth.

Disclosures

No conflicts of interest declared.

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