Sports Concussion and the Clinical Neurologist, Part II

Neurologists, who increasingly will confront patients diagnosed with sports concussion, must be adept at identifying and managing the condition. Part II of a series reviews screening modalities.

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The greatest focus when it comes to sports concussion has been in the attempt to develop diagnostic testing to evaluate athletes who are suspected of having suffered a concussion. Testing ranges from simple sideline evaluation tools to complex neuroimaging studies. None of the diagnostic studies are completely objective and should never be used as the sole means of assessment or in deciding when to return an athlete to play. The best way to assess an athlete or any individual who has sustained a concussion is still a comprehensive neurological history and detailed neurological examination performed by a properly trained physician.

Sideline Concussion Assessment Tool (SCAT2)

Developed in 2008 to replace the original sideline assessment tool SCAT1, SCAT2 is intended to assess individuals aged 10 and older and can be used by almost anyone after a brief training session.[1] It is used by a number of professional and amateur sports organizations and is usually given at the start of the season and repeated if an athlete sustains a concussion. The test has many of the same components of the standard neurological exam, with eight subsections including; symptoms, physical signs, Glascow coma score, Maddock's score, cognitive assessment, balance assessment, coordination and a standardized concussion assessment (Glascow coma score and Maddock's score do not apply if using the test as a baseline assessment). Many concussion experts do not use the Glascow coma scale because loss of consciousness is present in less than 10 percent of all athletes. Portions of the test have not been validated and therefore SCAT2 should never be used as the sole measure to return an athlete to play, or as a substitute for a physician-performed neurological evaluation.

Computerized Testing

Most professional, college, and some high school sports teams use computerized testing IMPACT, Headminder Concussion Resolution Index (CRI) (New York, NY), CogSport (CogState, Melbourne, Australia), and the Automated Neuropsychological Assessment Metric (ANAM) [Center for the Study of Human Operator Performance, The University of Oklahoma, Norman]. Athletes are tested by a trainer or neuropsychologist prior to the start of the season and during the season if a concussion is reported. These tests are useful tools for evaluating athletes, and despite being validated with formal neuropsychological testing, they should never be used as the sole means for returning an athlete to play and should never be substituted for a comprehensive history and neurological examination.

The most widely used computerized test is IMPACT, however most tests measure multiple aspects of cognitive functioning, including: Attention span, working memory, sustained and selective attention, response variability, non-verbal problem solving. Issues with computerized testing include: Lack of initial effort (i.e., pre-season) whereby the athlete will actually score better after sustaining a concussion;[2] An inability to address associated symptoms (i.e., headache, sleep disorders);[3] Reaction time testing is marginal and does not simulate game conditions. The tests are also influenced by symptoms, such as headache and lack of sleep, which are very common with concussion.[4-7]

Furthermore, the tests do not appear to accurately reflect the metabolic recovery of the injured brain, as most high school and collegiate athletes displayed functional/cognitive recovery at approximately six days following a sports-related concussion, while the professional athletes displayed recovery within three days.[8] This is inconsistent with physiological recovery, which takes between 14-28 days.[9] Finally, as the tests are often administered on consecutive days, improvements in concussed athletes may be partially associated with learning effects and not with injury recovery.[10-13]

Neuropsychological Testing

Formal paper and pencil neuropsychological testing is the best method to evaluate cognition in athletes who have sustained concussion. The tests have been validated in studies with non-athletes,[14,15] but, surprisingly, there are very few studies in concussed athletes.[16-18] Due to cost, length of testing, and access, neuropsychological testing is mainly used in athletes with prolonged cognitive symptoms. Testing tends to focus on assessment of sustained and divided attention, reaction time, visual and auditory processing speed, and working memory. Intelligence, problem solving and language are also tested.[16-18]

> **Definition of Sports Concussion**
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> A prolonged transient alteration in neuronal function caused by a blow to the athlete's head and/or body with transmission of force to the head, resulting in rotational and/or translational (i.e., angular and lateral) movement of the head resulting in neurological symptoms that resolve sequentially over time.

Balance, Agility and Reaction Time Testing

After concussion, communication between sensory systems is lost in the majority of individuals, causing moderate to severe postural instability in either the anterior-posterior direction, medial-lateral direction, or both.[19-21] Concussed athletes have demonstrated balance deficits using both high-tech and clinical methods of assessment.[22-24] Decreases in postural stability persist for up to three days following injury, after which time the athletes gradually recover to approximately the scores of matched control subjects by day 10 post-injury.[19,23] Vestibular deficits are related to problems with sensory integration, whereby the concussed athlete fails to use their visual and vestibular systems effectively. Studies have demonstrated difficulties with task switching in concussed athletes.[21] A number of tests are currently available or in development including Balance Error Scoring system (BESS), Sensory Organization Testing (SOT), Gait Testing, Virtual Reality Testing, and Instrumented Agility Task Testing.[23,25] In addition, there are components of the neurological exam including Rhomberg (i.e. sway), finger-nose-finger, fine finger testing, rapid alternating movement testing, and tandem gait alone or in conjunction, that may be useful in evaluating concussed athletes but still need to be validated. The Balance Error Scoring System (BESS) uses three different stances (double, single, and tandem) which are completed twice—once while on a firm surface and once while on piece of medium-density foam.[23] Studies have revealed greater differences between injured and uninjured subjects when the balance tasks became more challenging, such as by adding a foam surface and narrowing the base of support.[22] The test is also part of SCAT2, and the only part of BESS to be validated is the single leg stance portion.[26] BESS is most sensitive at time of injury up to three to five days post-concussion.[23]

Concussed athletes have also demonstrated balance deficits using a sensory organization testing (sophisticated force plate systems).[27] These tests provide a more technical or refined measure of balance performance by challenging and altering information sent to the various sensory systems. Testing is limited to use off the field and in academic centers secondary to size and technology needs.

Others have attempted to assess athletes using high-tech virtual reality testing.[28] Finally, researchers at the University of Michigan are in the process of testing a "puck drop test" where a long stick weighted with a hockey puck is dropped and the athlete tries to catch it as quickly as possible. Marks on the stick measure how quickly the athlete was able to react. Seven of eight Division I athletes who had suffered a concussion showed significantly slowed reaction times with the device, which is currently undergoing further testing.[29]

Eye Movement Testing

Galetta et al. have developed the King-Devick test (K-D) to assess eye movement abnormalities in concussed athletes.[30,31] The test involves reading aloud a series of single digit numbers on three test cards from left to right. The sum of the three test card time scores and the number of errors are scored. The test is hypothesized to measure impairment of eye movements, attention, and language. They administered the test to a cohort of boxers (n = 27) and MMA fighters (n = 12) pre- and post-fight. Post-fight K-D time scores were significantly higher (worse) for participants who had head trauma (59 vs. 41 seconds), and those with LOC had higher post fight K-D scores than those without LOC (65.5 vs. 52.7 seconds). Abnormal post-fight scores also correlated with abnormal MACE scores. The authors suggested that the test could serve as a rapid sideline screening test.[31] The study has not been validated in other populations, i.e. ice hockey, football etc., and there are issues with the timing of the post-testing, including the time immediately after the fight, when the athlete is physically fatigued and dehydrated. Fatigue and dehydration are well known to effect cognitive function and cognitive testing.[32] In addition, giving the test immediately after the fight when the athlete's motivation may not be as high as pre-fight and there are significant external distractions can affect outcome.

The ID Coaches Sideline tracker is another test that can measure eye movement abnormalities in concussed athletes. The test looks for gaze abnormalities and is given after an athlete is suspected of being concussed. Blurred/double vision or inability to focus may be indicative of concussion.

Electrophysiological Testing

McCrea et al.[33] used Quantitative EEG Q-EEG in a prospective, non-randomized study of 396 high school and college football players, which included a cohort of 28 concussed athletes and 28 matched controls. All underwent preseason baseline testing including postural stability testing, cognitive testing and Q-EEG. Clinical testing was repeated on the day of injury. They found injured athletes performed poorer on neuro-cognitive testing than controls on the day of injury but not at days eight or 45. However, concussed athletes had abnormal electrical activity noted on the day of injury and day eight, but not day 45. They concluded that the duration of physiological recovery may last longer than observed clinical recovery. Dupuis et al. 2000 looked at event-related potentials (ERP) to assess cerebral activity in 20 college athletes with MTBI. They found that concussed athletes had a decrease in the P300 amplitude and concluded that this may reflect alterations in attention and concentration.

Biomarkers

The biotechnology industry and military are currently looking at a number of biomarkers to measure mTBI, both on the battle ground and in the clinic.

Apolipoprotein E (APOE), APOE promotor gene, Catechol-o-methyltransferase (COMT), Dopamine

D2 receptor (DRD2) (ANNK1 gene), Interleukin p53, Angiotensin converting enzyme (ACE), CACNA1A, SB100, have been or are currently being evaluated. The two most widely studied are Apolipoprotein and SB-100 with the later showing minimal efficacy in detecting concussion in sports.[34-37]

Apolipoprotein has been looked at in a number of studies in both athletes and non-athletes and has been correlated as a marker for chronic injury. Zhou et al.[38] performed a meta-analysis and looked at 14 cohort studies. There was no correlation of the Â4 allele with initial injury severity. However, the Â4 allele was associated with poorer outcome at six months after injury. Terrell et al. looked at 195 college athletes, mainly football and soccer players. The cross-sectional study investigated the association between APOE, APOE promoter, and tau polymorphisms and a self-reported history of concussion over a prior eight-year period. There was a three-fold increase in risk of concussion in those with the TT genotype of G-219T polymorphism relative to the GG genotype, and a four-fold increased risk in those a with self-reported history of concussion associated with loss of consciousness. There was, however, no association with APOE or tau genotypes.

Kristman, et al.[39] in a prospective cohort study of 318 collegiate athletes in various sports, compared concussion rates in athletes with and without APOE Â4 allele. They found no association between Â4 allele and sustaining a concussion Finally, Tierney et al.[40] looked at 196 college athletes (163 male football and 33 female soccer players) in a multi-center cross-sectional study evaluating the association of carrying 1 or more APOE rare (or minor) alleles (APOE Â2, APOE Â4 and T allele of G-219T APOE promoter polymorphism) and a self-reported history of concussion. Athletes carrying all three rare alleles were 9.8 times more likely to report a previous concussion. Athletes carrying the T allele of the APOE promoter gene were 8.4 more likely to report multiple concussions and the authors concluded that carriers may be at greater risk for multiple concussions.

Neuroimaging

Athletes who sustain concussion do not require routine imaging. Exceptions include those with loss of consciousness, increasing lethargy, and focal neurological findings on their neurological exam. If the athlete requires imaging, CT and conventional MRI are both useful in detecting intracranial and subdural bleeds, however they are usually without findings. Conventional MRI with gradient echo is also useful in detecting micro-bleeds and Diffuse Axonal Injury (DAI) in more severely injured patients. More advanced imaging such as Positron Emission Tomography (PET), Functional MRI (fMRI), Magnetic Resonance Spectroscopy (MRS), and Diffusion Tensor Imaging (DTI) hold the most promise for quantitative assessment of sports related concussion. Ideally, imaging needs to provide quick, reliable, and longitudinal capabilities, and be easily employed in the community setting.

Positron Emission Tomography (PET) scanning measures brain metabolism by using radio nucleotides with short half-lifes. It is useful in measuring quantitative brain glucose uptake and regional oxygenation and therefore can demonstrate metabolic disturbances after brain injury.[41] There is little data on athletes who have sustained concussion.

AAN Sports Neurology Position Statement

1. Any athlete suspected of suffering a concussion should be removed from participation until evaluated by a physician.
2. No athlete should be allowed to participate in sports if they are still experiencing symptoms of a concussion.
3. Following a concussion a physician, preferably a neurologist, should be consulted prior to clearing the athlete to return to participation.
4. A certified coach or athletic trainer should be present at all sporting events, including practices, where risk of concussion is involved.
5. Education efforts should be maximized to improve the understanding of concussion by all athletes, parents, and coaches.
6. An athlete must be completely asymptomatic (cognitively/physically), off of any concussion related medications) and complete a graded protocol prior to RTP.

Note: This is an updated version of the original released in 2010. Point #6 has since been added.

One study looked at 19 boxers and eight normal controls. The study demonstrated hypometabolic areas, i.e., decreased glucose uptake in the bilateral posterior parietal lobes that extended to the lateral occipital lobes, bilateral frontal lobes, bilateral cerebellar hemispheres, and posterior cingulate cortex.[42] There are also a few studies in patients with mTBI that demonstrated correlation between metabolic dysfunction and neuropsychological performance.[43-45] Potential disadvantages include study duration, arterial sampling for quantitative studies, lack of available units in the community, the need to produce isotopes on site/locally. The most important disadvantage is that in patients with mild traumatic brain injury, PET imaging studies appear to remain abnormal after the recovery phase. The potential in sports related concussion assessment is in the academic setting to study brain physiology and metabolic derangements associated with sports concussion.

Magnetic Resonance Spectroscopy (MRS) uses metabolite data from regions of the brain to provide an assessment of neuro-chemical alterations after brain injury. Metabolites typically include N-acetylaspartate NAA (neuronal specific metabolite and a marker for neuronal health), myoinositol (glial marker), choline (marker of inflammation), lactate (indirect marker for ischemia and hypoxia), creatinine and phosphocreatinine (stable brain metabolite and marker of cellular energy status).[46] Vagnozzi et al.[47] looked at athletes with sports related concussion and found a diminished NAA/creatinine ratio 12 days after the athletes reported symptomatic recovery. The major drawback with MRS is its relative availability in the community due to scanner requirements and software costs.

Functional MRI (fMRI) measures changes in regional blood oxygenation that are usually quantified based on Blood Oxygen Level Dependent activity (BOLD). Following injury, decreases in blood flow are therefore speculated to represent impaired functional capacity.[46] The study usually requires a patient to perform a task while being imaged. Limited studies using fMRI in sports related concussion (Lovell et al.) have demonstrated abnormal BOLD activity, which correlated with symptom scores and neuropsychological testing. The studies also demonstrated improvement in BOLD activity in patients whose symptoms had resolved, implicating fMRI as a tool to possibly assess recovery from concussion.

In addition, athletes who displayed hyperactivation on a cognitive task in the acute phase had prolonged recovery times relative to those athletes who demonstrated typical activation in the acute phase implicating fMRI could be used to predict who will recover quicker.[48] Functional MRI has also been used in defining areas of the brain affected in sports concussion. Jantzen et al.[49] found increased activation in the areas of the parietal, lateral frontal, and cerebellar regions. Major limitations are software cost and the duration of the test. Therefore, its use will be limited to academic institutions and professional sports teams.

Near Infrared Spectroscopy is a non-invasive technique that evaluates cerebral blood volume and oxygenation. The technology is based on the transmission and absorption of near-infrared light as it passes through tissue. Cote, et al. monitored cerebral hemodynamics during acute exercise following concussion in 14 male university hockey players and found cerebral oxygenation was reduced up to 35 percent on day one following concussion. Blood volume increased immediately following a concussion at rest and during exercise at day one and returned to baseline by day seven. The authors concluded that there is an increased demand for oxygenated blood following concussion. This technology uses a hand held scanner and has the potential to be used in office as a screening technique.

Diffusion tensor magnetic resonance imaging (DTI/MRI) uses state of the art high Field MRI (1.5T and 3.0T) to evaluate the speed and direction of water movement within axons, which is termed fractional anisotropy or FA. DTI is based on the diffusion of water molecules. Water tends to move faster along nerve fibers rather than perpendicular to them. In healthy individuals, white matter diffusion is more organized in a specific direction; this is known as anisotropy. FA is believed to reflect many factors, including the degree of myelination and axonal density/integrity. FA Values range from 0 to 1, where 0 represents isotropic diffusion or lack of directional organization and 1 represents anisotropic diffusion or diffusion restricted to one direction. In most studies FA is decreased in patients with mTBI and TBI.[50] The technology is a modification of diffusion weighted imaging and determines white matter integrity and is sensitive to changes in white matter microstructure. It's also specific to each individual scanner and therefore prior to institution, each imaging center must develop their own set of normal values and specific DTI protocol, which the operator and radiologist will then use to manually outline the specific regions of interest.[50] Most imaging centers use region of interest analysis (ROI) where white matter FA is measured in specific regions of the brain. The measured FA is then compared to a database of normal patients. ROI is useful for testing hypotheses regarding the relation of white matter integrity in a specific neuro-anatomical region to an outcome variable, and a 1.5 to 2 standard deviation in the FA is considered abnormal.[50]

A majority of the studies using DTI have been in patients with mTBI and TBI. The Kraus paper, published in *Brain* in 2007,[51] is considered the landmark paper for DTI methodology with respect to TBI. Region of interest analysis included the anterior and posterior corona radiata, corticospinal tracts, cingulum, external capsule, forceps major and minor, genu, corpus callosum, inferior fasciculus, superior longitudinal fasciculus. The primary objective was to characterize white matter integrity utilizing DTI across the spectrum of chronic TBI of all severities. Secondary objectives included examining the relationship between white matter integrity and cognition. The researchers looked at 20 mild and 17 moderate/severe TBI patients and 20 controls who underwent DTI and neuropsychological testing with FA being the primary measure of white matter integrity. Moderate to severe TBI patients showed decreased white matter FA in all ROI. Mild TBI patients showed decreased FA in the corticospinal tracts, sagittal stratum and superior longitudinal fasciculus. Cubon, et al. 2011[52] assessed WM fiber tract integrity using tract-based spatial statistics (TBSS) in 10 varsity college athletes and controls. They also included moderate and severe TBI patients and controls. Athletes still symptomatic one month after sports-related concussion demonstrated increased mean diffusivity (MD) in several WM tracts in the left hemisphere including the inferior and superior longitudinal fasciculus, fronto-occipital fasciculi, retrolenticular part of internal capsule, posterior thalamic and acoustic radiations. There was no difference in fractional anistropy (FA) between athletes and controls, however FA decreased with the level of severity. This could be interpreted that the athletes FA's were abnormal as the study's controls actually had moderate to severe TBI. The researchers concluded that FA may be more sensitive in detecting severe injury and MD may be more sensitive in detecting mild injury. In a similar study Henry et al 2011[53] investigated the effects of sports concussion on white matter integrity using three different Diffusion Tensor Imaging measures (FA, axial diffusion AD, and MD) by comparing a group of 10 non-concussed athletes with a group of 18 concussed athletes of the same age (mean: 22.5 years) and education (mean: 16 years) using a voxel-based approach (VBA) within both the acute and chronic post-injury phases, i.e. at one to six days post-concussion and again six months later. FA was increased in dorsal regions of both cortical spinal tracts (CST) and in the corpus callosum in concussed athletes at both time points. AD at both time points was elevated in the right cortical spinal tracts. MD values were decreased in concussed athletes in the cortical spinal tracts (CST) and corpus callosum at both time points. Although there was some limitation in the technique used to image large fiber tracts, the authors concluded that sports concussions result in changes in diffusivity in the corpus callosum and CST of concussed athletes.

Conclusion

There are a number of tools to assist the physician in assessing and returning an athlete to play. Computerized and formal, i.e. paper and pencil, neuropsychological testing have been the most widely studied and validated. Neuroimaging studies especially DTI MRI hold significant promise as an objective measure for the future. However none of the testing is completely objective and therefore should never be used alone when evaluating and considering returning an athlete to play. ■

Part III of this series will appear in the January/February edition. Part I appeared in September/October. Visit PracticalNeurology.net to download the entire three-part article.

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