

# The difficult concussion patient: what is the best approach to investigation and management of persistent (>10 days) postconcussive symptoms?

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## ABSTRACT

**Background** Concussion in sport typically recovers clinically within 10 days of injury. In some cases, however, symptoms may be prolonged or complications may develop. The objectives of the current paper are to review the literature regarding the difficult concussion and to provide recommendations for an approach to the investigation and management of patients with persistent symptoms.

**Methods** A qualitative review of the literature on concussion in sport was conducted with a focus on prolonged recovery, long-term complications and management including investigation and treatment strategies. MEDLINE and Sports Discus databases were reviewed.

**Results** Persistent symptoms (>10 days) are generally reported in 10–15% of concussions. This figure may be higher in certain sports (eg, ice hockey) and populations (eg, children). In general, symptoms are not specific to concussion and it is important to consider and manage coexistent pathologies. Investigations may include formal neuropsychological testing and conventional neuroimaging to exclude structural pathology. Currently, there is insufficient evidence to recommend routine clinical use of advanced neuroimaging techniques or genetics markers. Preliminary studies demonstrate the potential benefit of subsymptom threshold activity as part of a comprehensive rehabilitation programme. Limited research is available on pharmacological interventions.

**Conclusions** Cases of concussion in sport where clinical recovery falls outside the expected window (ie, 10 days) should be managed in a multidisciplinary manner by healthcare providers with experience in sports-related concussion. Important components of management, after the initial period of physical and cognitive rest, include associated therapies such as cognitive, vestibular, physical and psychological therapy, assessment for other causes of prolonged symptoms and consideration of a graded exercise programme at a level that does not exacerbate symptoms.

## INTRODUCTION

Over the past decade, recommendations for the management of concussion in sport have centred on physical and cognitive rest until symptoms resolve and then a graded programme of exertion prior to medical clearance and return to play.<sup>1–3</sup> This basic approach works well for the majority of concussions where clinical features resolve progressively within 10 days. In a number of cases, however, recovery can be prolonged or complications may develop.

Persistent symptoms following concussion are a cause of significant morbidity and frustration to the athlete and pose a management challenge to the clinician. While there has been an explosion of studies on the acute management of concussion over the past decade, data on the management of prolonged recovery remain sparse. The current management approach to the difficult concussion is largely based on anecdotal evidence or extrapolation from studies on moderate-to-severe traumatic brain injury (TBI).

The objectives of the current study were to review the literature regarding the difficult concussion and to provide recommendations for an approach to the investigation and management of patients with persistent symptoms.

## METHODS

Searches of MEDLINE (ISI Web of Science, PubMed) and SportDiscus databases were undertaken using the key words ‘concussion’, ‘mild traumatic brain injury’, ‘head injury’ and ‘sport’ or ‘athlete/athletic’. These terms were combined with the following keywords to identify the literature for difficult concussions and key aspects of investigation and management: ‘symptoms’, ‘complex’, ‘difficult’, ‘prolonged’, ‘persistent’, ‘post-concussion syndrome’, ‘investigation’, ‘imaging’, ‘biomarker’, ‘gene/genetic’, ‘treatment’, ‘medication’, ‘management’, ‘exercise’ and ‘rehabilitation’.

The search was limited to the English language and focused on original papers published in the past 10 years. Reference lists from retrieved articles were searched for additional articles, and the authors’ own collections of articles were included in the search strategy.

## RESULTS

### Persistent postconcussion symptoms

Concussion typically results in a range of symptoms and signs in a number of different domains.<sup>1–3</sup> The clinical features vary, but commonly reported symptoms include headache, nausea, dizziness and balance problems, blurred vision, confusion, memory disturbance, mental ‘fogginess’ and fatigue.<sup>4–9</sup> Prospective cohort studies and systematic reviews have consistently demonstrated that the majority of cases of concussion in adult populations resolve within 10 days of injury.<sup>6 9–12</sup> A ‘difficult concussion’ can be described as one in which clinical recovery falls outside the expected window (ie, 10 days).

The incidence of prolonged clinical recovery following concussion varies depending on the cohort

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**Table 1** Summary of studies reporting symptoms at baseline

Paper	Subject characteristics	Scale used	Results	Common symptoms reported
Covassin <i>et al</i> <sup>26</sup>	1209 Collegiate athletes	PCS (ImPACT)	Mean total symptom score ( $\pm$ SD): males: 7.3 ( $\pm$ 11.5), females 7.9 ( $\pm$ 12.4)	Fatigue, headache, sleep disturbance, difficulty concentrating
Lovell <i>et al</i> <sup>50</sup>	1746 High school and university student athletes	PCS (ImPACT)	Mean total symptom score ( $\pm$ SD): males 4.6 ( $\pm$ 7.7), females 7.9 ( $\pm$ 11.5)	NR
Shehata <i>et al</i> <sup>51</sup>	260 University athletes	SCAT	Mean total symptom score: males 3.52, females 6.39	Fatigue/low-energy, drowsiness, neck pain, difficulty concentrating, difficulty remembering
Piland <i>et al</i> <sup>27</sup>	1065 Collegiate athletes	HIS	Mean total symptom score ( $\pm$ SD): 4.72 ( $\pm$ 6.07) No significant differences between males and females	Fatigue, drowsiness, headache, trouble falling asleep, difficulty concentrating
Schneider <i>et al</i> <sup>52</sup>	4193 Youth hockey players	SCAT2	Median total symptom score 0–8 (range 0–108) No significant difference between males and females	Fatigue/low energy, headache
Jinguji <i>et al</i> <sup>53</sup>	214 High school athletes	SCAT2	Average number of symptoms score=2.25 No significant differences between males and females	Fatigue, trouble falling asleep, difficulty concentrating, difficulty remembering

HIS, Head Injury Scale (9 items, 7-point Likert scale); NR, not reported; PCS, Postconcussion Symptom Scale; SCAT, Sport Concussion Assessment Tool.

being investigated (as well as the time frame used to define ‘prolonged’). Studies have shown that approximately 10–15% of collegiate and professional American football players have symptoms beyond 10 days.<sup>7 10 13</sup> Similar figures have been demonstrated in Australian football.<sup>4 9</sup> Higher rates of prolonged recovery (ie, over 30% of cases) have been reported following concussion in ice hockey,<sup>6</sup> and in cohorts of high school athletes.<sup>14 15</sup>

Common persistent symptoms include headache, depression, ‘difficulty concentrating’, ‘fatigue or low energy’, ‘difficulty sleeping’ or ‘feeling not quiet right, in a fog or slowed down’.<sup>4 7 9 10 13 16</sup> These symptoms are non-specific and may be reported in healthy athletic populations at baseline (table 1) and in patients with other injuries, illnesses or neuropsychiatric conditions. These same symptoms have also been reported in general trauma patients, individuals with anxiety or depression, patients with chronic pain syndromes, soldiers with combat stress and individuals who are involved in litigation regardless of the type of injury.<sup>17–25</sup>

When assessing postconcussion symptoms, it is important to consider that reporting of symptoms may be affected by a number of factors including sex, socioeconomic factors, concurrent illness or musculoskeletal injury and moderate-to-high intensity exercise.<sup>18 26–29</sup> Studies in patients with mild TBI have also demonstrated that symptom reporting can be influenced by general health status,<sup>30</sup> other medical conditions such as migraines<sup>31</sup> and psychological factors such as coexisting anxiety and depression.<sup>32</sup>

The method used for symptom reporting can also impact on the results. For example, Krol and Mrazik<sup>33</sup> performed a cross-sectional study in 117 athletes comparing self-reported symptoms to symptoms endorsed during an interview. The authors found a higher number of symptoms reported and a greater overall symptom score in the self-administered condition.<sup>33</sup> They also found that athletes reported more symptoms when the interviewer was woman.<sup>33</sup> Similarly, Iverson *et al*<sup>34</sup> demonstrated a higher reporting of symptoms on a self-administered questionnaire when compared with a structured interview in a cohort of athletes with concussion.

General health questionnaires that incorporate patient-reported outcome measures in a number of domains

(eg, depression, anxiety, etc) have been used in the study of retired players.<sup>35 36</sup> Given the complex nature of postconcussion symptoms, similar questionnaires may also be beneficial in the assessment of difficult concussions. Domains that should be considered in this assessment include:

- ▶ Depression and anxiety (eg, Hospital Anxiety and Depression Scale, Beck Depression Inventory, Depression Anxiety Stress Scale, Profile of Moods States);
- ▶ Headache and migraine (Headache Impact Test, Migraine Disability Assessment);
- ▶ General health and disability (eg, Short-form 36 Health Survey Questionnaire, Health-Related Quality of Life);
- ▶ Sleep (eg, Medical Outcomes Study Sleep Scale Survey);
- ▶ Drug and alcohol use/abuse (eg, Drug Abuse Screening Test, Alcohol Use Disorders Identification Test).

The advantages of a more detailed, semiquantitative assessment are that it may help identify other causes or contributing factors to the individual’s symptoms and may facilitate monitoring over time. While specific patient-reported outcome measures have yet to be validated in concussion, they may serve as useful clinical and research assessment tools.

### Role of investigations

The assessment of recovery following concussion is currently limited by the absence of simple and reliable direct measures of brain function. Instead, clinicians must rely on indirect measures to inform clinical judgement, such as the symptoms and signs of concussion (including neurological and balance assessments), in addition to the use of brief neuropsychological tests to estimate the recovery of cognitive function.

### Neuropsychological testing

Computerised screening neuropsychological test batteries have become an important component of concussion assessment.<sup>1–3</sup> The test batteries have been shown to be sensitive to changes in cognitive function following concussion. Moreover, they have been shown to detect cognitive deficits in a significant proportion of individuals even after the symptoms have resolved.<sup>9 37</sup>

Although formal neuropsychological testing is also recommended in cases of concussion with persistent symptoms, there

is no literature on the test properties (sensitivity, specificity, predictive value, etc) in this setting.

#### Advanced imaging and investigation techniques

Advanced imaging and investigation techniques have demonstrated changes in brain function, activation patterns and white matter fibre tracts in cases of concussion with prolonged symptoms (table 2A). Often, these changes exist even when the athlete has recovered clinically and returned to sport (table 2B). As such, the significance of these changes remains unclear at this time. Nevertheless, advanced imaging and investigation techniques (such as Diffusion Tensor Imaging, functional MRI, MR spectroscopy, quantitative EEG, etc) may hold hope for future assessment protocols in concussion. In the short term, their use in the research setting should continue to be encouraged.

#### Genetic testing

Preliminary research reveals a potential association between genetics and long-term outcome following concussion. Apolipoprotein E (APOE) has been the most extensively studied gene in TBI. Jordan *et al*<sup>38</sup> demonstrated a relationship between APOE4 genotype and chronic TBI score, particularly in high exposure boxers (ie, more than 12 professional bouts). Similarly, Kutner *et al*<sup>39</sup> studied the potential influence of APOE4 genotype in a cohort of 53 active professional American footballers and found that players with at least one copy of the APOE4 allele scored lower on tests of attention and information processing speed and accuracy. In a neuropathological study of athletes with Chronic Traumatic Encephalopathy (CTE), an increased frequency of the APOE4 allele was noted among cases of pathologically confirmed CTE.<sup>40</sup> Recently, however, a large case series did not find a definite relationship between the APOE genotype and CTE, especially in lesser grades of CTE.<sup>41</sup>

Other genes that have been considered include the APOE promoter and Tau, with no consistent findings regarding an effect on outcome following concussion in sport.

Despite the methodological limitations of these studies, they provide preliminary evidence of a complex inter-relationship between head injury, genetics and the risk of cumulative damage. However, more research is required in this area before genetic testing can be recommended as part of the clinical work-up of concussion.

#### Management of structural injuries masquerading as concussion

Any athlete that sustains a head injury is at risk of having a structural brain injury (eg, brain contusion). One of the critical roles of the initial medical assessment is to examine the player neurologically for such injuries. There are well described and validated guidelines for the use of imaging in the acute stage following head injury (eg, the Canadian CT head Rule or the New Orleans Criteria).<sup>42 43</sup> Furthermore, in athletes with persistent symptoms or cognitive deficits, consideration should be given to conventional neuroimaging to investigate for an underlying structural injury.

To date, there are no published studies evaluating treatment strategies in athletes who sustain structural head injuries. Consequently, decisions regarding their management, including return to play, should be made by a clinician experienced in structural brain injury and based on the type of injury (eg, fracture and haemorrhage), relative risks associated with return to sport and the presence of ongoing sequelae (eg, symptoms, signs, cognitive deficits). Structural brain injury is not a

concussion. It requires further consideration outside of the realm of sport medicine expertise.

#### Treatment of persistent symptoms

##### Non-pharmacological treatment

The current treatment approach for difficult concussions is based largely on an extension of the guidelines for acute injuries (ie, rest until symptoms resolve, followed by the use of combined clinical measures of recovery to determine the timing of return to play). While an initial brief period of rest may be important in the management of acute concussion, there is limited evidence that further rest is beneficial in cases where clinical features are prolonged.

Conversely, preliminary evidence suggests that an active rehabilitation programme is useful for the management of concussion where the symptoms are prolonged (table 3). The rehabilitation programme is started even in the presence of symptoms.

The graded exercise test has also been demonstrated to have good inter-rater and test-retest reliability.<sup>44</sup>

When dizziness or disequilibrium is a prominent feature of persistent symptoms following concussion, vestibular rehabilitation may be useful.<sup>45</sup> In a cohort of individuals with blast-related mild TBI, Gottshall and colleagues demonstrated improvement in symptoms after an 8-week period of vestibular physiotherapy.<sup>46</sup>

Other treatments have been used anecdotally for the management of specific symptoms. For example, manual or physical therapy may be used to treat myofascial pain or neck trigger points contributing to headaches; cognitive therapy including memory tasks as well as learning coping skills may be useful for some patients with persistent cognitive symptoms; and those who have problems with anxiety, panic attacks or other psychological or emotional problems may benefit from meditation, biofeedback or psychological therapy. At present, however, there are limited data on these techniques in the management of prolonged symptoms following concussion.

##### Pharmacological treatment

Numerous medications are available to treat the range of symptoms that are observed following concussion.<sup>47</sup> Many of these medications have been investigated in patients with moderate or severe TBI, but there are few trials that have been conducted in mild TBI or concussion.

In a small cohort of volunteers diagnosed with major depression following mild TBI, Fann *et al*<sup>48</sup> demonstrated an improvement in symptoms and function with the use of sertraline.

In a recent retrospective study, Reddy *et al*<sup>49</sup> examined the effects of amantadine in 25 adolescent athletes with postconcussion symptoms that persisted longer than 21 days. Individuals were compared with historical controls, and all individuals were assessed using a computerised neurocognitive test battery. The authors showed that the group treated with 100 mg of amantadine twice per day demonstrated greater improvements in their reaction time, verbal memory and symptom reporting.<sup>49</sup>

A number of different antimigraine treatments have been assessed in small studies of patients with headaches following mild TBI (table 4). The studies all report moderate to good results, but the findings have not been confirmed in larger randomised control trials, and nor have they been trialled specifically in patients with persistent symptoms following concussion in sport.

#### Components of a comprehensive concussion clinic

Current consensus advocates a multifaceted clinical approach to the assessment of concussion. This is perhaps even more

**Table 2** Changes observed on advanced imaging and investigation techniques

Paper	Study type/ setting	Subject characteristics	Inclusion criteria	Investigation	Findings/results
<i>A. Athletes with persistent symptoms following concussion</i>					
Chen <i>et al</i> <sup>54</sup>	Prospective cohort	9 Concussions, 6 healthy controls	Persistent symptoms following concussion	fMRI (working memory task)	Significantly reduced task-related BOLD changes in the prefrontal cortex in athletes with prolonged symptoms following concussion Activation patterns improved as symptoms improved on follow-up
Cubon <i>et al</i> <sup>55</sup>	Cross-sectional	10 Collegiate students with prolonged symptoms compared to 10 healthy controls and 5 TBI patients (2 moderate TBI and 3 severe TBI)	Persistent symptoms 1 month postinjury	Diffusion tensor imaging (MD and FA analysed using tract-based spatial statistics)	Significant increase in MD in concussed individuals Similar results were observed in the moderate but not severe TBI patients when compared to controls
Gosselin <i>et al</i> <sup>56</sup>	Cross-sectional	14 Patients with mild TBI—recruited from 2 tertiary trauma centres 23 Controls	Persistent symptoms following mild TBI	ERP, fMRI (working memory task)	Attenuated BOLD signal changes and reduced amplitude for the working memory task were observed in the mild TBI group BOLD signal changes were correlated with symptom severity
Tallus <i>et al</i> <sup>57</sup>	Cross-sectional	19 Individuals with mild TBI (11 with persistent symptoms, 8 recovered) and 9 healthy controls	Injury sustained 5 years earlier, GCS 13–15 on admission, normal MRI	MT (measured using navigated transcranial magnetic stimulation and electromyography)	MT was higher in some (but not all) mild TBI individuals compared to controls Changes were observed even in individuals who had recovered clinically The results suggest that subtle prolonged changes may exist in some patients following mTBI and that in a proportion of these patients the changes may be 'compensated'
<i>B. Athletes with concussion whose symptoms had resolved</i>					
Vagnozzi <i>et al</i> <sup>58</sup>	Prospective (multicentre) cohort	40 Concussions 30 Healthy controls	Recent concussion; age 16–35	MRS Used single voxel (ROI: right frontal lobe), and chemical shift techniques to analyse data	Self-reported symptoms recovered within 3–15 days Significant differences between concussed and control groups were observed in metabolite ratios at day 3 postinjury. Metabolite changes gradually recovered to control levels within 30 days of injury
Henry <i>et al</i> <sup>59</sup>	Prospective cohort	College athletes 10 Concussions 10 controls	Recent concussion	MRS (ROI: prefrontal and primary motor cortex)	Neurometabolic differences between concussed and control groups were observed in the acute phase (lower <i>N</i> -acetylaspartate:creatine levels in the prefrontal cortex and lower glutamate:creatine levels in the motor cortex) as well as the delayed phase (increase in the myoinositol levels in the motor cortex)
Slobounov <i>et al</i> <sup>60</sup>	Cross-sectional	College athletes 17 concussions 17 controls	Recent concussion, clinically recovered	rsfMRI (ROI: right dorsolateral prefrontal cortex, bilateral precuneus, bilateral primary visual cortex, bilateral hippocampus)	All concussion individuals were asymptomatic at rest and had no NP deficits rsfMRI revealed disrupted functional network both at rest and in response to a graded physical test
Baillargeon <i>et al</i> <sup>61</sup>	Cross-sectional	48 Concussions 48 Controls	Concussion assessed >6 months postinjury	EEG (visual 3-stimulus oddball paradigm)	Concussed athletes had lower P3b amplitudes than the control athletes Adolescent athletes showed persistent deficits in working memory
Johnson <i>et al</i> <sup>62</sup>	Cross-sectional	Collegiate athletes 14 Concussions 15 Controls 9 Additional concussions	Recent concussion, recovered clinically	rsfMRI (measured the default mode network)	Significant default mode network connectivity differences were observed between concussed and control groups Regression analysis revealed a significant reduction in magnitude of connection between various structures in the brain as a function of the number of concussions

BOLD, blood oxygenation level-dependent; ERP, event-related brain potential; FA, fractional anisotropy; fMRI, functional magnetic resonance imaging; NP, neuropsychological; MD, mean diffusivity; MRS, MR spectroscopy; MT, motor threshold; ROI, regions of interest; rsfMRI, resting state fMRI; TBI, traumatic brain injury.



**Table 3** Active rehabilitation

Paper	Study type/setting	Subject characteristics	Inclusion criteria	Outcome measures	Findings/results
Gagnon <i>et al</i> <sup>63</sup>	Prospective cohort (tertiary referral centre)	N=16 Children and adolescents (aged 10–17 years)	Postconcussion symptoms >4 weeks	Symptoms checklist, clinical examination, balance testing, coordination testing	Used a graded rehabilitation programme (beginning with submaximal aerobic training that is, 15 min on a treadmill or stationary bike, then introducing sports-specific training drills for 10 min) Found a significant increase in exercise tolerance and reduction in symptom score (30.0±20.8 at presentation to 6.7±5.7 at discharge) Mean duration of intervention 4.4±2.6 weeks
Leddy <i>et al</i> <sup>64</sup>	Prospective cohort (University concussion clinic)	N=12 (6 athletes, 6 non-athletes)	Symptoms >6 weeks following concussion (5 sports related, 1 motor vehicle accident)	Graded symptom checklist, graded exercise treadmill test (Balke protocol)	Exercise at an intensity of 80% of the maximum heart rate achieved on the treadmill test before the exacerbation of symptoms 10 of the 12 reported being symptom-free at rest Athletes recovered faster than non-athletes Rate of symptom improvement was directly related to exercise intensity achieved
Baker <i>et al</i> <sup>65</sup>	Retrospective case series	N=91 (63 had follow-up phone assessment 4–73 months postinjury)	Symptoms >3 weeks	Subjective symptom reporting, graded exercise treadmill test (Balke protocol)	41/57 Who completed the exercise programme returned to full daily functioning

important in the setting of prolonged symptoms, where the diagnosis is not always clear (ie, there are other causes of prolonged symptoms) or when superimposed factors lead to a pattern of deterioration rather than the expected improvement. Some components of a comprehensive concussion clinic are summarised in table 5, although the list is by no means complete and expands with time and experience. For instance, access to expertise such as sport psychology, physiatry, psychiatry, occupational therapy, social work and educational consultants are now included in such a list. In addition, in the setting of the difficult concussion, access to appropriate rehabilitation strategies, both physical and cognitive, is important and identification of programme leadership and coordination is key. Community resources may be incorporated in addition to medical facilities.

Ideally, the concussion clinic would also have a central role in athlete and public education and health advocacy participating in collaborative efforts. Access to academic studies, as well as participating in and benefiting from research findings, helps to nurture the future directions of such a programme and benefits the injured athlete. The physical and administrative structure and support to the programme will facilitate excellence in the provision of care.

## SUMMARY AND RECOMMENDATIONS

A 'difficult concussion' can be described as one in which clinical recovery falls outside the expected window (ie, 10 days in the adult population).

### Assessment of persistent symptoms

Persistent symptoms are non-specific and may be caused by or contributed to by other conditions (such as migraine, mental health issues, concurrent injuries, etc). The assessment of persistent symptoms therefore requires a careful history (including both past and family history) and examination (including assessment of the cervical spine and vestibular function). The current postconcussion symptom checklist on the SCAT2 alone is insufficient for the assessment of persistent symptoms, without a detailed history of the symptoms. The addition of patient-reported outcome measures to the assessment battery in prolonged or difficult cases (especially in the case of the retired player with ongoing cognitive issues) would provide a more comprehensive, quantifiable approach to assessment and may allow identification of other causes or contributing factors to the patient's symptoms.

**Table 4** Pharmacotherapy for persistent post-traumatic headache

Paper	Study type/setting	Subject characteristics	Treatment	Findings/results
Weiss <i>et al</i> <sup>66</sup>	Case series	14 Mild TBI and 7 whiplash injury patients diagnosed with migraines postinjury	Propranolol and/or amitriptyline	'Dramatic reduction' in the frequency and severity of headaches in 70%
McBeath and Nanda <sup>67</sup>	Case series	34 Patients referred to headache clinic with headache as part of a postconcussion syndrome	Repeat intravenous dihydroergotamine and metoclopramide	Reported a good-to-excellent response in 29 of 34 patients. Also noted improvement in memory symptoms, sleep disturbance and dizziness
Packard <sup>68</sup>	Retrospective cohort	100 Patients with chronic daily headache of between 2 and 6 months duration following mild TBI	Valproate	60% Reported mild-to-moderate improvement after 1 month of treatment. The remaining 40% either showed no response (26%) or stopped treatment because of side effects

TBI, traumatic brain injury.

**Table 5** Components of a comprehensive concussion clinic

Component	Purpose/role
<b>Personnel</b>	
▶ Sports medicine physician, neurologist, neurosurgeon	▶ Detailed assessment and treatment outline for patient
▶ Neuropsychologist	▶ Comprehensive neuropsychological assessment
▶ Certified athletic trainer/exercise physiologist	▶ Coordination of subsymptom threshold programme
▶ Physical therapist	▶ Vestibular rehabilitation
▶ Psychologist	▶ Management of expectation/education
▶ Psychiatrist	▶ Perform and interpret imaging
▶ Neuroradiologist	▶ Coordinate research programmes
▶ Research coordinator	
▶ Access to subspecialties	
▶ Social worker	
▶ Education specialist/consultant	
<b>Equipment</b>	
▶ CT/MRI scanner	▶ Imaging
▶ Treadmill/heart-rate monitor	▶ Exercise stress testing
▶ Balance testing	▶ Other investigations
▶ Reaction time	
▶ Others: bloods, genetic marker kits	
▶ Access to research protocols	

### Role of investigations

Neuropsychological testing remains as an important component of assessment following concussion. Formal neuropsychological testing should be encouraged in the difficult concussion, although there are limited data to support its recommendation at present.

Conventional imaging should be considered in any athlete with persistent symptoms or cognitive deficits to investigate for an underlying structural injury.

Advanced imaging and investigation techniques have demonstrated changes in small cohorts of patients with persistent symptoms, as well as in individuals after clinical recovery following concussion. At present, the clinical significance of these changes remains unclear. The current literature does not support the use of these investigation tools in the routine clinical management of athletes with concussion. Advanced imaging and investigation techniques do, however, contribute to our understanding of the pathophysiology of concussion, and ongoing use should be encouraged in the research setting.

### Treatment

Currently, there is no evidence that prolonged rest is beneficial for patients with persistent symptoms. Preliminary studies demonstrate that an active rehabilitation programme may be useful for the management of cases where symptoms are prolonged.

The important components of an active rehabilitation programme include:

- ▶ Commencement even in the absence of complete symptom resolution;
- ▶ Prescriptive advice regarding the intensity, duration and timing of exercise;
- ▶ Working to a level that does not aggravate the symptoms (subsymptom threshold exercise);
- ▶ Slow progression of rehabilitation with monitoring of clinical outcome.

Currently, there is limited evidence for the use of pharmacotherapy in concussion. Medications should be limited to cases that do not resolve with a conservative approach, or those with

severe symptoms at rest that preclude the start of a graded rehabilitation programme. Medications generally should be restricted to the management of related syndromes (eg, migraine, sleep disturbance, etc).

Difficult concussions should be managed in a multidisciplinary manner. Ideally, this is in the setting of a concussion clinic with access to expertise in a wide range of areas.

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### REFERENCES

- 1 Aubry M, Cantu R, Dvorak J, *et al*. Summary and agreement statement of the 1st International Symposium on Concussion in Sport, Vienna 2001. *Clin J Sport Med* 2002;12:6–11.
- 2 McCrory P, Meeuwisse W, Johnston K, *et al*. Consensus statement on concussion in sport: the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. *Br J Sports Med* 2009;43:176–84.
- 3 McCrory P, Johnston K, Meeuwisse W, *et al*. Summary and agreement statement of the 2nd International Conference on Concussion in Sport, Prague 2004. *Br J Sports Med* 2005;39:196–204.
- 4 McCrory PR, Ariens M, Berkovic SF. The nature and duration of acute concussive symptoms in Australian football. *Clin J Sport Med* 2000;10:235–8.
- 5 Erlanger D, Kaushik T, Cantu R, *et al*. Symptom-based assessment of the severity of a concussion. *J Neurosurg* 2003;98:477–84.
- 6 Benson BW, Meeuwisse WH, Rizos J, *et al*. A prospective study of concussions among National Hockey League players during regular season games: the NHL-NHLPA Concussion Program. *Can Med Assoc J* 2011;183:905–11.
- 7 McCreary M, Guskiewicz KM, Marshall SW, *et al*. Acute effects and recovery time following concussion in collegiate football players—the NCAA Concussion Study. *JAMA* 2003;290:2556–63.
- 8 Lovell MR, Collins MW, Iverson GL, *et al*. Recovery from mild concussion in high school athletes. *J Neurosurg* 2003;98:296–301.
- 9 Makkissi M, Darby D, Maruff P, *et al*. Natural history of concussion in sport markers of severity and implications for management. *Am J Sports Med* 2010;38:464–71.
- 10 Guskiewicz KM, McCreary M, Marshall SW, *et al*. Cumulative effects associated with recurrent concussion in collegiate football players—the NCAA Concussion Study. *JAMA* 2003;290:2549–55.
- 11 Belanger HG, Vanderploeg RD. The neuropsychological impact of sports-related concussion: a meta-analysis. *J Int Neuropsychol Soc* 2005;11:345–57.
- 12 Broglio SP, Puetz TW. The effect of sport concussion on neurocognitive function, self-report symptoms and postural control—a meta-analysis. *Sports Med* 2008;38:53–67.
- 13 Pellman EJ, Viano DC, Casson IR, *et al*. Concussion in professional football: injuries involving 7 or more days out—part 5. *Neurosurgery* 2004;55:1100–16.
- 14 Iverson G. Predicting slow recovery from sport-related concussion: the new simple-complex distinction. *Clin J Sport Med* 2007;17:31–7.
- 15 Lau BC, Kontos AP, Collins MW, *et al*. Which on-field signs/symptoms predict protracted recovery from sport-related concussion among high school football players? *Am J Sports Med* 2011;39:2311–18.
- 16 Cantu RC, Guskiewicz K, Register-Mihalik JK. A retrospective clinical analysis of moderate to severe athletic concussions. *PM R* 2010;2:1088–93.
- 17 Lees-Haley PR, Fox DD, Courtney JC. A comparison of complaints by mild brain injury claimants and other claimants describing subjective experiences immediately following their injury. *Arch Clin Neuropsychol* 2001;16:689–915.
- 18 Mickeviciene D, Schrader H, Obelieniene D, *et al*. A controlled prospective inception cohort study on the post-concussion syndrome outside the medicolegal context. *Eur J Neurol* 2004;11:411–19.
- 19 Alla S, Sullivan SJ, McCrory P. Defining asymptomatic status following sports concussion: fact or fallacy? *Br J Sports Med* 2012;46:562–9.
- 20 Meares S, Shores EA, Batchelor J, *et al*. The relationship of psychological and cognitive factors and opioids in the development of the postconcussion syndrome in general trauma patients with mild traumatic brain injury. *J Int Neuropsychol Soc* 2006;12:792–801.
- 21 Meares S, Shores EA, Taylor AJ, *et al*. Mild traumatic brain injury does not predict acute postconcussion syndrome. *J Neurol Neurosurg Psychiatry* 2008;79:300–6.
- 22 Meares S, Shores EA, Taylor AJ, *et al*. The prospective course of postconcussion syndrome: the role of mild traumatic brain injury. *Neuropsychology* 2011;25:454–65.

- 23 Cooper DB, Kennedy JE, Cullen MA, *et al.* Association between combat stress and post-concussive symptom reporting in OEF/OIF service members with mild traumatic brain injuries. *Brain Inj* 2011;25:1–7.
- 24 Iverson GL. Misdiagnosis of the persistent postconcussion syndrome in patients with depression. *Arch Clin Neuropsychol* 2006;21:303–10.
- 25 Iverson GL, McCracken LM. 'Postconcussive' symptoms in persons with chronic pain. *Brain Inj* 1997;11:783–90.
- 26 Covassin T, Swank CB, Sachs M, *et al.* Sex differences in baseline neuropsychological function and concussion symptoms of collegiate athletes. *Br J Sports Med* 2006;40:923–7.
- 27 Piland SG, Ferrara MS, Macciocchi SN, *et al.* Investigation of baseline self-report concussion symptom scores. *J Athl Train* 2010;45:273–8.
- 28 Gaetz MB, Iverson GL. Sex differences in self-reported symptoms after aerobic exercise in non-injured athletes: implications for concussion management programmes. *Br J Sports Med* 2009;43:508–13.
- 29 Alla S, Sullivan SJ, McCrory P, *et al.* Does exercise evoke neurological symptoms in healthy subjects? *J Sci Med Sport* 2010;13:24–6.
- 30 McLean SA, Kirsch NL, Tan-Schriner CU, *et al.* Health status, not head injury, predicts concussion symptoms after minor injury. *Am J Emerg Med* 2009;27:182–90.
- 31 Gunstad J, Suhr JA. "Expectation as etiology" versus "the good old days": postconcussion syndrome symptom reporting in athletes, headache sufferers, and depressed individuals. *J Int Neuropsychol Soc* 2001;7:323–33.
- 32 Lange RT, Iverson GL, Rose A. Depression strongly influences postconcussion symptom reporting following mild traumatic brain injury. *J Head Trauma Rehabil* 2011;26:127–37.
- 33 Krol AL, Mrazik M. Self-report of concussion symptoms in collegiate athletes. *Arch Clin Neuropsychol* 2009;24:506–6.
- 34 Iverson GL, Brooks BL, Ashton VL, *et al.* Interview versus questionnaire symptom reporting in people with the postconcussion syndrome. *J Head Trauma Rehabil* 2010;25:23–30.
- 35 Guskiewicz KM, Marshall SW, Bailes J, *et al.* Association between recurrent concussion and late-life cognitive impairment in retired professional football players. *Neurosurgery* 2005;57:719–24.
- 36 Guskiewicz KM, Marshall SW, Bailes J, *et al.* Recurrent concussion and risk of depression in retired professional football players. *Med Sci Sports Exerc* 2007;39:903–9.
- 37 Broglio SP, Macciocchi SN, Ferrara MS. Neurocognitive performance of concussed athletes when symptom free. *J Athl Train* 2007;42:504–8.
- 38 Jordan BD, Relkin NR, Ravdin LD, *et al.* Apolipoprotein E epsilon4 associated with chronic traumatic brain injury in boxing. *JAMA* 1997;278:136–40.
- 39 Kutner KC, Erlanger DM, Tsai J, *et al.* Lower cognitive performance of older football players possessing apolipoprotein E epsilon 4. *Neurosurgery* 2000;47:651–7.
- 40 McKee AC, Cantu RC, Nowinski CJ, *et al.* Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. *J Neuropathol Exp Neurol* 2009;68:709–35.
- 41 McKee A, Stein TD, Nowinski C, *et al.* The spectrum of disease in chronic traumatic encephalopathy. *Brain* 2013;136:43–64.
- 42 Papa L, Stiell IG, Clement CM, *et al.* Performance of the Canadian CT Head Rule and the New Orleans Criteria for predicting any traumatic intracranial injury on computed tomography in a United States Level I trauma center. *Acad Emerg Med* 2012;19:2–10.
- 43 Stiell IG, Wells GA, Vandemheen K, *et al.* The Canadian CT Head Rule for patients with minor head injury. *Lancet* 2001;357:1391–6.
- 44 Leddy JJ, Baker JG, Kozlowski K, *et al.* Reliability of a graded exercise test for assessing recovery from concussion. *Clin J Sport Med* 2011;21:89–94.
- 45 Gottshall K. Vestibular rehabilitation after mild traumatic brain injury with vestibular pathology. *Neurorehabilitation* 2011;29:167–71.
- 46 Gottshall KR, Hoffer ME. Tracking recovery of vestibular function in individuals with blast-induced head trauma using vestibular-visual-cognitive interaction tests. *J Neurol Phys Ther* 2010;34:94–7.
- 47 Petraglia AL, Maroon JC, Bailes JE. From the field of play to the field of combat: a review of the pharmacological management of concussion. *Neurosurgery* 2012;70:1520–33.
- 48 Fann JR, Uomoto JM, Katon WJ. Sertraline in the treatment of major depression following mild traumatic brain injury. *J Neuropsychiatry Clin Neurosci* 2000;12:226–32.
- 49 Reddy CC, Collins M, Lovell M, *et al.* Efficacy of amantadine treatment on symptoms and neurocognitive performance among adolescents following sports-related concussion. *J Head Trauma Rehabil* (in press).
- 50 Lovell MR, Iverson GL, Collins MW, *et al.* Measurement of symptoms following sports-related concussion: reliability and normative data for the Post-Concussion Scale. *Appl Neuropsychol* 2006;13:166–74.
- 51 Shehata N, Wiley JP, Richea S, *et al.* Sport concussion assessment tool: baseline values for varsity collision sport athletes. *Br J Sports Med* 2009;43:730–4.
- 52 Schneider KJ, Emery CA, Kang JA, *et al.* Examining Sport Concussion Assessment Tool ratings for male and female youth hockey players with and without a history of concussion. *Br J Sports Med* 2010;44:1112–17.
- 53 Jinguji TM, Bompadre V, Harmon KG, *et al.* Sport Concussion Assessment Tool-2: baseline values for high school athletes. *Br J Sports Med* 2012;46:365–70.
- 54 Chen JK, Johnston KM, Petrides M, *et al.* Recovery from mild head injury in sports: evidence from serial functional magnetic resonance imaging studies in male athletes. *Clin J Sport Med* 2008;18:241–7.
- 55 Cubon VA, Putukian M, Boyer C, *et al.* A Diffusion Tensor Imaging Study on the white matter skeleton in individuals with sports-related concussion. *J Neurotrauma* 2011;28:189–201.
- 56 Gosselin N, Bottari C, Chen JK, *et al.* Electrophysiology and functional MRI in post-acute mild traumatic brain injury. *J Neurotrauma* 2011;28:329–41.
- 57 Tallus J, Lioumis P, Hamalainen H, *et al.* Long-lasting TMS motor threshold elevation in mild traumatic brain injury. *Acta Neurologica Scandinavica* 2012;126:178–82.
- 58 Vagnozzi R, Signoretti S, Cristofori L, *et al.* Assessment of metabolic brain damage and recovery following mild traumatic brain injury: a multicentre, proton magnetic resonance spectroscopic study in concussed patients. *Brain* 2010;133:3232–42.
- 59 Henry LC, Tremblay S, Leclerc S, *et al.* Metabolic changes in concussed American football players during the acute and chronic post-injury phases. *BMC Neurol* 2011;11:105.
- 60 Slobounov SM, Gay M, Zhang K, *et al.* Alteration of brain functional network at rest and in response to YMCA physical stress test in concussed athletes: rsfMRI study. *Neuroimage* 2011;55:1716–27.
- 61 Baillargeon A, Lassonde M, Leclerc S, *et al.* Neuropsychological and neurophysiological assessment of sport concussion in children, adolescents and adults. *Brain Injury* 2012;26:211–20.
- 62 Johnson B, Zhang K, Gay M, *et al.* Alteration of brain default network in subacute phase of injury in concussed individuals: resting-state fMRI study. *Neuroimage* 2012;59:511–18.
- 63 Gagnon I, Galli C, Friedman D, *et al.* Active rehabilitation for children who are slow to recover following sport-related concussion. *Brain Injury* 2009;23:956–64.
- 64 Leddy JJ, Kozlowski K, Donnelly JP, *et al.* A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. *Clin J Sport Med* 2010;20:21–7.
- 65 Baker JG, Freitas MS, Leddy JJ, *et al.* Return to full functioning after graded exercise assessment and progressive exercise treatment of postconcussion syndrome. *Rehabil Res Pract* 2012;2012:705309.
- 66 Weiss HD, Stern BJ, Goldberg J. Post-traumatic migraine: chronic migraine precipitated by minor head or neck trauma. *Headache* 1991;31:451–6.
- 67 McBeath JG, Nanda A. Use of dihydroergotamine in patients with postconcussion syndrome. *Headache* 1994;34:148–51.
- 68 Packard RC. Treatment of chronic daily posttraumatic headache with divalproex sodium. *Headache* 2000;40:736–9.



## The difficult concussion patient: what is the best approach to investigation and management of persistent (>10 days) postconcussive symptoms?

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