Neurocognitive Testing in Concussion Management

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ABSTRACT

The role of neurocognitive testing in the clinical management of concussion remains under debate. Although professional sports teams frequently use automated computerized testing, there is strikingly little evidence of the benefit of testing in clinical decision-making at this time. In addition, one study has shown normalization of computerized tests while formal neuropsychological testing continues to detect deficits in performance. We will review current evidence for the use of such testing.

1.0 MILD TBI

Neurocognitive Deficits

Neurocognitive deficits are commonly detected following concussion. For most people, symptoms usually resolve within days or weeks but between 5 and 20% of those injured may have persistent clinical sequelae and evolve into having persistent Post-Concussion Syndrome (PCS) weeks or months later (Kraus and Chu 2005; Ruff and Weyer Jamora 2009). Neurological symptoms and signs and associated neurocognitive dysfunction are key indicators of injury severity and subsequent recovery trajectory. The immediate symptoms of mTBI/concussion include headache, dizziness and nausea as well as physical signs, which may include unsteady gait, slurred speech, poor concentration and slowness when answering questions (McCrory et al. 2005). Even where there is an absence of post-traumatic amnesia (PTA) and/or loss of consciousness (LOC), neurocognitive

abnormalities may be detected in the immediate aftermath of a suspected concussion (McCrea et al. 2002). Up to 15% of those with mTBI may have ongoing symptoms (Marshall et al. 2012). In one study in the UK, nearly half of a cohort of youth and adults with mild head injuries experienced disability 1 year after injury (Thornhill et al. 2000), confirmed by a second study (Limond et al. 2009). However, these participants, although noted as having a "mild" injury, may have had more "complicated" injury as they were typically hospitalized for observation for over a day. Other studies have found clinical sequelae are significant over 2 years post-injury for mild TBI. Hawley et al. (2004a,b) found that children with mild TBI were significantly more anxious compared to controls, and behavioral and school-related problems were reported by families of mildly injured children as well as moderate and severely injured children at just over 2 years post-injury. As factors accounting for young age potentially being linked to more symptom severity are not well understood.

There is much debate about whether persistent symptoms are related to neurological or psychological factors, and what role there is for pre-morbid status (Alexander 1995; Lishman 1988; Carroll et al. 2004b). Neurocognitive domains span a wide gamut of mental functions. The following are key functions: executive functions—control of planning, organizing, self-awareness, and control of impulsiveness; sustained attention—the ability to concentrate on tasks; divided attention—the ability to handle two or more different tasks simultaneously; and memory—the ability to encode, store and retrieve information. There are two main reasons for conducting neurocognitive assessment for concussion—to determine the presence of cognitive impairment for early diagnosis of mTBI and to monitor recovery over time (Barth et al. 1989; Macciocchi et al. 1996; Davis et al. 2009).

Although military mTBI has been in the news over the past few years, most research findings have come from sports concussions, which have informed clinical practice. Systems developed for evaluating sports concussion have been adapted for military use. The guiding principle of testing is to ensure that those injured are removed from game play or from combat duties until they are free of concussion symptoms and are fit to return to play, work, school, or duty. Neurocognitive testing complements clinical evaluation (which remains the gold standard for return to activities). Athletes are typically tested before the sports season begins to obtain a baseline against which subsequent post-injury testing results are compared. As they are their own controls, any significant decline in performance compared to baseline suggests cognitive deficits following concussion have yet to resolve. If there is no baseline test to compare, post-injury performance against normative (group) baselines can be used. Of note, computerized neurocognitive testing was found to have returned to baseline levels after 7 days, even in athletes who had persistent cognitive deficits detectable by in person neuropsychologist testing (Belanger and Vanderploeg, 2005).

Testing needs to be specific, sensitive, reliable and valid for identifying mTBI/PCS (Iverson et al. 2005). Validity is measurement accuracy or how closely the test measures what it is supposed to be measuring. Sensitivity and specificity refer to the likelihood of identifying either true positives or negatives, respectively. Sensitivity is the probability that someone who is concussed is properly identified by the test. If a test has a high specificity, it will reliably predict those who have a concussion versus those who do not. Reliability refers to measurement consistency for each occasion the test is used with the same participants given the same testing conditions. Test–retest reliability is especially important for baseline testing since variations could falsely identify someone with a concussion as normal and vice versa. Test-retest reliability can be estimated by comparing test results carried out at different times and calculating a correlation coefficient. However, repeat testing has been reported to lead to practice effects, with the participant performing better in subsequent tests due to a learning effect (Collie et al. 2003). Use of alternate versions of tasks can limit practice effects (Collie et al. 2001).

If a test is known to have practice effects, then a Reliable Change Index (RCI) can be used to calculate the expected improvement from baseline to post-concussion testing, and then an adjustment can be applied to factor

in improvement (Hinton-Bayre and Geffen 2002). The RCI is calculated by using a control group to establish the average change between tests and an additional correction is made for test variability and reliability to generate a standard score (Z).

Neurocognitive Assessment: Development of Methodology

Recovery of neurocognitive functioning following concussion has been extensively examined in studies of athletes (see Barth et al. 1989; Macciocchi et al. 1996; Echemendia et al. 2001). Traditional neuropsychological tests are written tests requiring 4 to 6 hours to administer. A comprehensive testing battery is required because the cognitive deficits following concussion are variable (Echemendia et al. 2001). Frequently administered tests include: Digit Span (Lezak 1995), which tests working memory with mental rotation; Speed of Comprehension and Language Processing (Lezak 1995), which tests general cognitive level and speed of processing information; Trail Making Tests A and B (Lezak 1995), which test sustained and divided attention; Stroop Color and Word (Lezak 1995), which tests executive skills (especially inhibition); and Symbol Digit Modalities Test (SDMT), which measures visual-spatial and motor speed and accuracy (Smith 1982). Shorter test versions have been developed and are sensitive to the mild cognitive problems accompanying acute concussion—such as attention, reaction time, and complex memory (Barth et al. 1989; Macciocchi et al. 1996; Boll and Barth 1983; Hughes et al. 2004). These tests provided objective data, which were more effective than subjective reports in distinguishing between those concussed, compared to those without concussion at 48 hour after injury (Echemendia et al. 2001).

Computerized tests were introduced in the last two decades, offering some advantages over conventional methods (Campbell et al. 1999). Computerized systems provide a more accurate measurement of reaction times (RTs), known to be impaired following a concussion (Pellman et al. 2004). Computers allow for either a standardized presentation of stimuli or random presentations of a large number of alternate forms, improving test–retest reliability (Schatz and Browndyke 2002). Automated tests include the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) (Maroon et al. 2000), a computerized neuropsychological test battery designed to measure a range of cognitive functions including attention and processing speed. Other software packages designed to diagnose post-concussion cognitive deficits in sports include HeadMinder™ (Erlanger et al. 1999) and CogSport™ (Cogstate 1999). CogState Sport™ measures simple and complex attention, reaction times and accuracy, as well as memory and problem solving ability (Schatz and Zillmer 2003) to create a composite score. This score then determines pass or failure. The US Department of Defense uses the Automated Neurocognitive Assessment Metrics (ANAM) (Rice et al. 2011) and the US Navy and Army developed the Defense Automated Neurobehavioral Assessment (DANA) (Lathan 2013). Computerized testing was originally considered to be less likely to show practice effects compared to traditional testing, but these have been reported (Collie et al. 2003). Practice effects typically arise after the first few times taking the test after which performance plateaus (Falletti et al. 2006).

Other key advantages of computerized testing include the ability to administered self-reported measures of clinical symptoms and other surveys and the ability to test multiple people simultaneously in a room or other setting. In contrast, traditional neuropsychological tests require one-to-one testing as well as interpretation by a qualified individual. Computerised testing can be carried out with one technician who is adept at administering tests (rather than requiring a neuropsychology background, although supervision by a neuropsychologist is required at some level), remotely if the test is a web-based one, and either individuals or groups or individuals can be tested at one time. Interpretation of test results is ideally done by a neuropsychologist (Echemendia et al. 2009). It should be noted that concussion is a clinical diagnosis and computerized testing may aid in this diagnosis by identifying domains of cognition, which are impaired, but computers cannot be solely relied upon in the absence of other clinical data to make a diagnosis of concussion (Schatz and Putz 2006). Other factors,

such as distractions in the testing environment, can affect results. One other aspect of computerized testing is a focus on briefer test batteries, which may not be as detailed as traditional testing (Gualtieri and Johnson 2008). Thus, it is unlikely that computerized testing will completely replace individual one-on-one testing.

Studies have been conducted comparing computerized to traditional tests. Iverson et al. (2005) examined the construct validity of ImPACT™ with the SDMT (Smith 1982), reporting that both were good measures of Processing Speed and Reaction Time. CogSport™ has been evaluated on 300 professional Australian football players as well as hundreds of healthy controls across a wide range of ages (Makdissi et al. 2001). ANAM has been taken by over 1.2 million US military service members while DANA, a more recently developed test battery, has been taken by several hundred.

Neuropsychological Functioning After Concussion

Sports Studies

There are many sports studies showing that a person typically recovers completely from a single concussion without detectable neurocognitive deficits (Wall et al. 2006). A meta-analysis of neuropsychological testing in sports concussion identified 21 studies between 1970 and 2004, which used a baseline comparison (Belanger and Vanderploeg, 2005). They reported mild-to-moderate effect of concussion in the first 24 hours on global test measures and larger effects on memory (acquiring and delayed recall). However, return to baseline on neuropsychological testing was noted, by 7–10 days post-injury. Practice effects of testing were identified that might have led to an underestimate of concussion effects. Also studies in which persons that had a remote history of a prior concussion were excluded showing smaller effect sizes than those not excluding such athletes. These findings suggested that prior head injury was associated with greater cognitive sequelae in subsequent injury. McCrea et al. (2003) followed concussed (n = 94) and uninjured control (n = 56) American college football players selected from a cohort study of 1,631. They were tested during pre-season, then immediately after injury, at 3 hours following injury, and again 1, 2, 3, 5, 7, and 90 days post-injury. By 7 days, basic assessment on the Standard Assessment of Concussion (SAC), a brief screening cognitive battery typically given on a sports field sideline as part of in game concussion testing, showed no significant group effect between the non-concussed and concussed groups. However, mild impairments in cognitive processing speed and verbal memory were noted for the concussed athletes at 2 and 7 days post-injury, and verbal fluency on traditional neurocognitive tests was still affected in the concussed group at 7 and 90 days post-injury. There was no evidence of other persistent clinical symptoms at 90 days. They also reported that 10% of players required greater than a week for symptoms to resolve. A large research effort examining the chronic effects of sports concussion is now underway partnering the US NCAA (collegiate sports) with the Department of Defense military service academies.

Studies have also examined the cumulative effects of multiple concussions. Wall et al. (2006) showed that jockeys with multiple lifetime concussions had impaired executive functions and attention compared to those with a single lifetime concussion. Younger age accounted for much of the variance in decrement in attention, suggesting that younger age of injury, or repeat injury within a shorter time span, may be an important consideration. A meta-analysis of 10 studies between 1970 and 2009 by Belanger et al. (2010) indicated that two or more mTBIs had minimal long-term cognitive deficits, suggesting that people returned to baseline. Thus, the effects of repeat concussion, remain unclear (Williams et al. 2010). Several factors have been identified to be associated with delayed recovery including prior concussion, multiple concussions within a short period, greater-than-1 min LOC, longer duration and severity of initial symptoms, greater number of symptoms, younger age, presence of mental health conditions such as depression, and use of medications such as psychotropic drugs (McCrory et al. 2009).

Comparison Between Athletes and Non-Athletes

There are key differences between athletes and non-athletes. Athletes may discount or ignore clinical symptoms and have a strong motivation to return to play (Ruff and Weyer Jamora 2009). Also, with awareness of long-term consequences of concussion, including chronic traumatic encephalopathy, concussion protocols to remove players from the game have been implemented. In non-athletes, other factors may affect outcome, including pre-morbid conditions (educational, socio-economic, etc.), injury characteristics (mechanisms, forces, etc.) and degree of post-injury support. Another major difference between sports and general populations is that there are typically no baseline measures available for non-athletes. The interpretation of post-injury test scores based on normative data lowers sensitivity and specificity of injury detection.

Studies in Non-Athletes

One early, well-controlled study of non-athletes compared 22 people with mTBI with 19 uninjured, matched controls showing that a single minor head injury was associated with mild but clinically non-significant cognitive impairment 1 month after injury (Dikmen et al. 1986). This study applies to those without pre-existing health conditions. Neurocognitive problems included problems with concentration and new learning, but these were not detectable 1 year after injury.

A meta-analysis of neurocognitive studies (from 1970 to 2004) of patients with mTBI by Belanger and Vanderploeg (2005) identified 39 studies where participants sought medical attention and severity of injury was identified. Of eight cognitive domains assessed, problems were mostly confined to verbal fluency (executive skills) and delayed memory, and there was no difference to controls at 90 days post-injury, although litigation was a moderating factor. Another meta-analysis by Schretlen and Shapiro (2003) indicated that cognitive performance of mTBI patients could not be distinguished from matched controls at 1 month post-injury. These findings have led to the interpretation that recovery should be complete by 3 months after injury (Binder 1997; Frencham et al. 2005). Pertab et al. (2009) reported that some injured persons may have ongoing neurocognitive sequelae.

How early factors relate to persistent clinical symptoms has been studied. Shreedy et al. (2006) investigated prediction of post-concussion symptoms using an emergency department assessment examining neuropsychological and balance deficits and pain severity in 29 concussed individuals. Thirty individuals with minor orthopedic injuries and 30 controls were recruited for this study. Concussed participants and those with orthopedically injuries were followed up by telephone at 1 month to assess symptom severity. In the emergency department, concussed subjects performed worse on some neuropsychological tests and had impaired balance compared to controls. They also reported significantly more post-concussive symptoms at follow-up. Neurocognitive impairment, pain and balance deficits were all significantly correlated with severity of post-concussion symptoms. The findings suggest that a combination of clinical variables may be useful in predicting which individuals will develop persistent post-concussion symptoms.

Imaging and Neurocognitive Testing

There is some evidence linking neurocognitive dysfunction to neuroimaging findings after concussion. A study of 20 complicated mTBI (based on GCS falling between 13 and 15 with abnormal CT scan results) and uncomplicated mTBI patients revealed that the complicated patients performed worse on memory tasks (visual reproduction and verbal learning) (Lange et al. 2009). An MRI study of neuropsychological functions in 30 mTBI patients compared to matched controls indicated that patients with traumatic lesions performed worse on neurocognitive tasks of concentration and attention within 4 days of injury compared to those with non-specific lesions or no lesions (Kurca et al. 2006).

Functional imaging studies have provided further evidence of systems implicated in mTBI. In an fMRI study of 18 mTBI patients up to 1 month post-injury, there were significant changes in activation patterns (McAllister et al. 2001). The patient group, compared to controls, had differential activation patterns—in bilateral frontal and parietal areas—on working memory tasks under moderate load. An fMRI study of working memory task with concussed athletes (15 symptomatic participants who had sustained their last injury 1 to 14 months previously) revealed differential activity patterns compared to a control group (Chen et al. 2004). They had weaker activity in areas related to self-monitoring—such as prefrontal cortex. Chen and colleagues conducted fMRI imaging for working memory task on athletes 1 month post-injury that had self-rated for severity of symptoms—(a low (n = 9) symptoms group and a moderate (n = 9) symptoms group, and a control group). The moderate group showed less activation in the ROI identified in controls for the tasks—the dorsolateral prefrontal cortex. Both concussed groups had increased activation in the left temporal area (Chen et al. 2007). These findings suggest that it may be possible to detect physiological changes in neurological systems linked to changes in cognitive functions.

Utility of Cognitive Testing

There is still much debate about the use of computerized neurocognitive testing. Ideally having a baseline would enable post-injury results to be compared. One concern is someone not giving full effort in order to have post-injury test results compared to baseline shows more rapid improvement. Tests of effort embedded into computerized tests can identify falsely low performers. The utility of existing computerized tests, though, has not been proven. In comparisons between different tests most do not have good test-retest validity (Cole et al. 2013). In US military populations, there was a post-deployment effect on testing; so routine testing is not recommended in the absence of a clinical suspicion of concussion (Haran et al. 2013). Similarly others have found moderate reliability with low specificity and moderate sensitivity of computerized tests (Lau et al., 2011; Nelson et al., 2015, 2016; Chin et al. 2016).

Children and Adolescents

In contrast to adults, recovery from concussion in children may be different and tends not to be characterized by problems with neurocognitive functioning but rather with behavioural difficulties. Hawley et al. (2004a, b) showed that for children between 5 and 15 years, with an average of 2.2 years since the time of injury, late sequelae could still emerge with increased risk associated with greater initial injury severity. However, the evidence is not strong, and there are methodological problems with many earlier studies (Carroll et al. 2004a, b), particularly with regard to lack of control groups and consideration of pre-morbid and non-injury factors. In general, post-concussion symptoms are usually transient.

A study by Wrightson et al. (1995) followed pre-school children who had sustained mTBI from soon after injury to 6 months and a year. There was an orthopaedic control group. They found no differences after injury on a range of cognitive tasks, but at 6 months and 1 year, the children with mTBI scored less well on tasks of visual problem solving. A prospective, longitudinal follow-up at 23 years post-injury study by Hessen and colleagues (Hessen et al. 2007) identified PTA as a particularly important factor in mTBI in childhood injuries. They tested 45 and 74 adults who had injuries 23 years previously as children or adults, respectively. Those who had injuries in childhood, and had a PTA of half an hour or more, were at risk for developing chronic, mild, neuropsychological dysfunction. They note that here was no control group, but they had taken account of pre-injury factors in analysis. Cognitive outcomes, and the effect of education, were investigated by Ponsford et al. (1999). They found that initial symptoms had resolved by 3 months, but children with previous head injury or learning difficulty had ongoing problems. Cognitive reserve—a resilience issue—was examined in a study by Fay et al. (2010). They found that children with lower cognitive ability with complicated mTBI (as determined using MRI) were especially prone to cognitive symptoms. The needs of children and families were addressed by

Hawley (2003) who found that across severity of TBI there were significant problems associated with anxiety over time with no significant resolution of problems when comparing mTBI and moderate to severe TBI groups. Family functioning variables are also strong mediators of outcome both pre- and post-injury (Yeates and Taylor 2005) and these have to be considered. Tonks et al. (2011) have studied a range of mediating variables of recovery from various forms of Acquired Brain Injury in childhood—including age of injury, underlying cognitive factors and socio-emotional functioning. The development and refinement of measures that are sensitive to mTBI groups would be important for children, who appear to develop subtle executive and higher level cognitive and socio-behavioural difficulties.

2.0 SUMMARY AND CONCLUSIONS

Neurocognitive functions appear to recover rapidly early after concussion. Studies linking radiographic neuroanatomic data and neurocognitive functions suggest functional changes in brain activation may resolve quickly. There appears to be concordance between neurological findings and neurocognitive functions early after injury, but, with time, such associations disappear. Compared to adults, neurocognitive assessment of children and adolescents with mTBI can be affected by other factors. Computerized testing can complement a clinical examination but never substitute. Existing computerized tests have moderate reliability and validity.

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