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Chapter 59: Cognitive Impairments After TBI

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INTRODUCTION

Traumatic brain injury (TBI) causes several types of damage to the brain that affect the cerebral cortex, subcortical nuclear structures, and their widespread white matter connections (see chapters by Kochanek et al. and Hovda for more details). The resulting cascade of pathological changes disrupts neural functioning at multiple levels, from individual cellular and vascular structures to the larger brain networks they comprise (see Figure 1). This rapid deformation of brain anatomy and physiology leads to clinical neurological and neurobehavioral impairments that affect a person's cognition, vegetative and emotional functions, as well as social behaviour capacities (1). This chapter is organized to provide an overview and synthesis of the cognitive impairments that are commonly associated with TBI in adults. Cognitive and behavioral symptoms are often major concerns in all types of TBI, as indicated by the many other chapters relating to cognition and behavior, including Kreutzer (*Neuropsychological Assessment and Treatment Plans*), Cicerone (*Cognitive Rehabilitation*), Murdoch (Assessment and Treatment of *Speech and Language Disorders*), Coelho (*Cognitive-Communication Deficits*), McAllister (*Emotional and Behavioral Sequelae)*, and Arciniegas (*Pharmacotherapy of Cognitive Impairments)* among others. The importance of these topics stems from the fact that rehabilitation outcomes and any long-term effects of TBI on personal, social and occupational functioning can often be related to cognitive abilities along with behavioral and emotional control. Indeed, cognitive measures are among the most important predictors of patients' return to work and independent living, even among those with good medical recoveries (2, 3).

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TBI and post-concussion syndromes occur along a spectrum recognized *as mild to severe*, with clinical profiles increasingly recognized as a rational and expected "hierarchy" (or cluster) of

clinical symptoms, mainly determined by the intensity, severity and location of the injury in the brain along a "gradient" of disturbances. In addition to these direct brain-behavior effects of TBI, clinicians and families must realize that there can be many complicating medical and psychological conditions that can contribute to post-TBI cognitive, behavioral and emotional impairments. These complicating factors are detailed in several chapters throughout the text and underscore the complex and nature of TBI. Despite their prevalence, cognitive impairments must be carefully evaluated on an individual basis, as they can be influenced by pre-existing conditions (e.g., learning disabilities, attention deficit hyperactivity disorder, substance abuse, prior head trauma), co-morbid conditions (e.g., seizures, major depression, pain, and medication side-effects) and differences in TBI damage and recovery. As an example, recent study identified a significant effect of major depression in lowering cognitive functions after TBI (4), with similar effects occurring with chronic headache and other pain, dizziness, diplopia, sleep disturbance, and stress vulnerability. Hence, a multidisciplinary and comprehensive approach to TBI and specifically to cognitive and behavioral impairments is necessary for best treatment outcomes. This is particularly important as TBI is considered a significant predisposing factor in the dementia literature.

NEUROCOGNITIVE EVALUATION

Neurocognitive (or neuropsychological) assessment encompasses clinical and psychometric testing procedures that survey and objectively measure the effects of cerebral damage on cognitive, behavioral, social and emotional functioning (5,6). These procedures help identify and define the nature and extent of TBI effects utilizing standardized cognitive tests and survey instruments, together with comprehensive interview and clinical assessment. Neuropsychological

test scores can change in different ways depending upon TBI pathophysiology. To this end, a variety of specific assessment techniques have been developed to evaluate a patient's relative strengths and weaknesses in multiple domains such as memory, speech and language, attention-concentration, spatial cognition, executive functions, and social cognition (see chapter by Kreutzer for further details). Scores are then interpreted in reference to available normative data that provide the typical range and variation in test performance.

Interpretation of neuropsychological test scores is meant to identify the type and severity of cognitive impairments that in turn reflect general location and severity of brain injury. Most clinicians employ a flexible battery approach that focuses on specific problem areas identified through clinical exam and observation. The flexible battery approach emphasizes evaluating the patient's *pattern* of performance; that is, the possible causes for their impaired test score. For example, impaired memory test scores may reflect attentional and encoding deficiencies, working memory limitations, memory consolidation deficits, poor access to and retrieval of information or some combination of these underlying cognitive difficulties. Delineating specific processing impairments will also provide a more direct and efficient approach to remediation services that target impaired processes. Therefore, neuropsychological assessment, along with assessments provided through diverse medical and therapy services, is geared toward identifying how best to detect, characterize, and intervene in the remediation of cognitive, behavioral, social and emotional impairments that are caused by TBI. The following sections cover specific cognitive processing domains that are particularly important in TBI.

REACTION TIME

Information processing measures are designed to determine the speed and accuracy of basic sensory-perception and perceptual-motor responses. These processes are mediated by diverse cortical and subcortical regions along with white matter connections that are vulnerable to TBI-related damage. Head trauma may alter reaction time capacities in several ways. Sarno et al. (7) demonstrated that severe TBI was associated with prolonged simple and choice reaction times to visual, auditory and tactile stimuli. Tactile stimuli presented particular difficulty in comparison to vision and audition (i.e., sensory-specific deficit) as well as in combination with those modalities (i.e., cross-modal deficits). This is an important study emphasizing acquired change in the typical sensory detection and integration processes that are critical for consistent functioning within stimulating and changing environments. Investigators have confirmed that reaction time can also be compromised after mild TBI (8,9), particularly as task difficulty increased and when inter-hemispheric transfer of information was required. Tinius (9) considered such results to be similar to adults with attention deficit disorder. Even when simple reaction time tasks are completed in normal fashion after TBI, deficits can emerge under conditions of increasing task difficulty, greater informational load, and even fatigue (10) that lead to inconsistent, slowed, and erroneous responses.

ATTENTION AND WORKING MEMORY

Attentional and working memory (WM) problems after TBI are among the most common cognitive impairments reported by patients, family members and clinicians, constituting a significant limitation in speed and efficiency of cognitive processing (11). Attention and working memory (WM) are sometimes considered to be overlapping processes, though most investigators separate them based on theoretical terms or specific task requirements. For example, many tests

of attention are externally-directed (e.g., detection of stimuli or repeating materials) whereas many WM measures depend upon an additional internally-directed dimension aimed at attentional and other processing resources for the purpose of holding or manipulating presented materials in the midst of problem-solving or completion of an action (such as in dual-task, n-back and calculation paradigms). Several kinds of attentional and WM components have been identified and examined in TBI, with troubling deficits often found to pose serious threats to everyday cognitive functions. In clinical practice, these deficits can be evident on specific tests of attention and WM (e.g., digit span, letter-number sequencing, continuous performance measures, n-back and go no-go tasks) as well as on tests where attention and working memory are important components (e.g., Trail making Part B, Stroop, Wisconsin Card Sorting etc.).

Zoccolotti and colleagues (12) sought to compare multiple attentional and WM measures in 106 patients with generally more severe TBI drawn from multiple European sites. The sample was tested at least 5 months after injury (allowing for recovery of acute effects) and 80% of participants suffered coma $\geq$8 days. Four computerized tasks were compared. The first 2 tasks required rather straightforward or *intensive attention* and included measures of (1) alertness (reaction time with and without a tonal warning) and (2) sustained attention to horizontal bar movements. The final 2 tasks were considered measures of *selective attention* (i.e., working memory) based upon keeping certain rules in mind and allocating attentional resources between dual tasks. These were hypothesized to be more problematic after TBI and included: (3) selective attention on go no-go and design detection tasks, and (4) divided attention to simultaneous visual and auditory tasks, each to detect a specific pattern during continuous stimulus presentations. Results confirmed that patients showed considerably more difficulty in the

selective attention tasks requiring go no-go responding (combining working memory with inhibitory control) and divided attention (increasing the working memory load), with up to one-half of the sample demonstrating deficits. Some difficulties were also evident in the more straightforward intensive attention conditions, varying between 9–33% of patients. Analyses also indicated considerable variability in performance amongst patients. This is not unexpected given the diverse trauma and personal characteristics of the sample. At least three subgroups were identified:

- A severely impaired subgroup, with a similar attention deficit profile as the overall sample (greater impairment in selective and divided attention tasks). This subgroup, comprising nearly 50% of the sample, also had more severe trauma and longer length of coma. While all patients with mild and moderate levels of coma completed the divided attention task, 5% of severe and 26% of very severe coma patients were unable to complete the task.
- A less impaired subgroup with a large dissociation between normal alertness scores and poor divided attention scores. Nearly 44% of the sample showed this pattern of performance that argues against a nonspecific or generalized slowing of performance and supports the possibility of a specific divided attention and WM-related deficit. We have encountered such deficits commonly in clinical practice, where the complaints can be described as disorganized behavior, inability to multi-task, losing track of objects, paperwork and activities, and being able to undertake ‘only one activity or task at a time’.
- A third possible subgroup (comprising only 7% of the sample) included those with very long reaction times in both alertness and divided attention tasks, suggesting significantly slowed psychomotor speed.

Given their fundamental and widespread role in cognition, attentional and WM deficits

essentially constrain most aspects of intelligent and adaptive human behavior and hence can have pervasive effects within home, community and occupational settings. WM tasks have been examined during functional brain imaging studies (fMRI) as a measure of neurophysiological integrity. These experiments have been particularly important because structural imaging is not always revealing after TBI. In most studies fMRI activation patterns appear to be different after TBI, revealed often by increased activation in expected WM-related brain areas and/or activation in additional brain regions even when task performance is similar to controls. Increased fMRI responses have been found to be correlated with symptom severity in concussed athletes (13) and to be associated with longer recovery times (14). These results suggest that TBI patients must exert greater mental and neural effort in cognitive and occupational tasks that may have been managed more easily prior to injury. This can lead to increased physical and mental fatigue, even muscle tension and headaches that may be mistaken for simply stress effects. In these cases, a reduced work load and schedule is usually recommended. In some TBI cases, the degree of attentional change is sufficient to warrant evaluation of attention deficit-type symptoms. This is typically undertaken with a combination of standardized tests of attention (such as the Working Memory Index from the Wechsler Adult Intelligence Scale and continuous performance tasks) and behavioral survey of attentional behaviors (such as the Brown Adult ADD Scale). Treatment of adult TBI patients with low dose stimulants and alternatives can be of significant benefit to their occupational and daily functioning, particularly when combined with cognitive compensatory strategies.

UNAWARENESS OF DEFICITS (ANOSOGNOSIA)

Anosognosia (meaning, literally, “without knowledge of disease,” a term introduced by Babinski

(15) is a common behavioral disorder occurring in neurological conditions, characterized by limited acknowledgement or frank denial of neurological symptoms that may include memory and cognitive deficits, hemiparesis, visual and other sensory disturbances, gait disorder and deficits of naturalistic action/limb apraxia (16, 17).

Patients' inability to recognize functionally-relevant problems is known to be a major barrier to rehabilitation after closed-head injury (18). Disavowal of neurological impairment can take several forms, including lack of emotional concern for acknowledged deficits (anosodiaphoria), verbal denial of deficits that are implicitly acknowledged (e.g. patients claim that they can walk but never actually attempt to get out of bed), combined explicit and implicit denial of deficits, denial of ownership of an impaired body part (asomatagnosia or somatoparaphrenia), and, at the far end of the continuum, dislike or hatred of a dysfunctional body part (misoplegia) (16, 19). Patients with this disorder can evidence dramatic abnormalities in behavior, such as throwing themselves from their beds "in order to get rid of that awful leg." Although occurring in conjunction with other clinical syndromes such as spatial neglect, amnesia, and even thought disorders, dissociations of awareness of deficit from each of the associated clinical syndromes are reported, and thus anosognosia may be best characterized as an independent syndrome, at this time without a single neuroanatomic basis.

Impact of Anosognosia

Although there are no formal studies of the possible contribution of anosognosia to a delay in seeking medical attention after closed head injury, numerous anecdotal reports suggest that unawareness of deficit (sometimes theorized to be partly due to a functional adaptation, e.g.

"shock") may keep patients from presenting promptly to a medical care provider or emergency room after head injury, especially if patients lack other bodily injuries. Currently, no treatments for closed head injury are available that depend critically upon initiation within a short period after an injury occurs, but this remains a real possibility within the near future, similar to acute thrombolytic therapies after stroke.

The most relevant impact of anosognosia on rehabilitation after TBI is in patients' acceptance of the rationale for participation in treatment (engagement in the rehabilitative program), and in their ability to participate in the program once having agreed to do so (16, 19). It is reasoned that patients may thus put forward inadequate or inconsistent effort, preventing gains in strength and endurance. However, anosognosia and decreased motivation has not in formal studies been universally associated with a poorer rehabilitation outcome (20). The scope of rehabilitation for anosognosic patients may be more limited because of safety and supervision needs, and fewer challenging tasks may be attempted in order to ensure that patients will not expose themselves to further harm or attempt to perform tasks of which they are incapable. Lastly, anosognosia presents a barrier to studying outcomes in head trauma rehabilitation. After TBI, patients consistently report better cognitive, physical and emotional outcomes than do their loved ones and clinicians (21). This creates problems in interpretation of patient self-report data, which might under other circumstances be considered to be of greater validity than that of external observers.

Mechanisms of Anosognosia

Weinstein and Kahn (22) first proposed that psychological denial may produce inability to

acknowledge neurological deficits after stroke such as hemiparesis. Important clinical observations, however, are inconsistent with the psychological defense mechanism hypothesis. A coping strategy should be more utilized as recovery progresses, cognition improves, and chronic losses become apparent. Anosognosia is most apparent immediately post-injury, and gradually improves (16, 18, 19, 21). A denial syndrome should be most severe for deficits posing the greatest potential ego threat, and less marked for deficits not likely to produce disability. However, modular dissociations in anosognosia not clearly based on subjective deficit severity (e.g. unawareness of visual problems but awareness of gait problems) are reported after head injury (19, 23). In subjects without brain injury, anosognosia can be induced by selective hemispheric anesthesia (16), but in the same individuals, this occurs more commonly after right- than left-sided injection. This asymmetry is difficult to explain on a psychological basis. Most critically, in brain-injured patients, it is unclear that anosognosia confers even temporary functional advantage, either in reducing subjective distress or in improving function , which is central to the concept of a psychological defense. Schacter and Prigatano (24) summarized the controversy this way:

Although most observers agree that defensive denial of a kind that can be observed in non-brain-damaged patients plays some role in the unawareness phenomena exhibited by some brain-damaged patients, the nature and extent of the contribution is still the subject of debate . . . The critical problem . . . is to develop adequate criteria for distinguishing between defensive and nondefensive forms of unawareness and to delineate the underlying bases for them.

Management and Treatment of Anosognosia

Unfortunately, large controlled trials of specific management and treatment methods for subjects with anosognosia after closed head injury are not yet available. A number of clinical approaches are reported to be symptomatically useful. These include *explicit* techniques in which therapists have subjects self-assess and then perform straightforward, quantifiable tasks and help them to

measure assessment-performance discrepancies, *implicit* techniques in which subjects are asked to perform in both preserved and deficient areas in order to experience the contrast between these abilities, and techniques involving *external and off-line feedback*, such as videotaping and later viewing task performance, and reviewing it in a group setting with performance assessment from other group members. Related to the external/off-line method is *intervention based on third person assessments*, in which patients make judgments about pictured scenaria in which others fail to perform tasks, preselected to resemble their impairments (25). Although reinforcement with these methods has traditionally been behavioral, positive results have been reported when increased accuracy of self-assessment is reinforced with monetary rewards. A general difficulty with these clinical reports, however, is that although patients' awareness of deficit may have improved, the effect on daily living activities has not been well-studied. In at least one instance, there was a failure of the improved self-awareness to generalize to untrained tasks (26). Therefore, further studies are needed to identify the most effective interventions for anosognosia after TBI. In typical practice, such interventions are team-based and often require continued efforts by therapists and educated caregivers after hospital discharge.

INTELLECTUAL FUNCTIONING

Measures of intelligence are frequently employed in the neuropsychological assessment of brain-injured patients to ascertain a broad range of cognitive capacities (27). It is important to consider estimated premorbid intellectual ability when assessing current intelligence. These estimates can be accomplished through standardized word reading tests (e.g., Wechsler Test of Adult Reading), employment records, academic achievement data, and multifactorial formula (e.g., Barona Index; 28). Although several instruments have been designed for the purpose of evaluating intelligence,

the Wechsler scales are favored by most clinicians. In its most updated versions, the Wechsler Adult Intelligence Scale [WAIS-III and IV] has several important features:

- It surveys a broad range of verbal and nonverbal cognitive abilities with standardized instructions and materials
- Test items are presented in order of ascending difficulty and they are usually discontinued after a certain number of incorrect responses, allowing for assessment of many different abilities without undue frustration for patients. Increasing item difficulty allows the evaluator to determine the patient's base level [i.e., floor] and frustration level [i.e., ceiling]; that is, such scores help determine patient functioning relative to the varying demands that patients may experience in different contexts. These measures may also shed some light on patient efforts in testing.
- Interpretation of multiple subtest and composite scores (i.e., Full Scale, General Ability, Verbal Comprehension, Perceptual Organization/Reasoning, Working memory, Processing Speed etc.),is possible through extensive normative data that provide statistical comparisons, enhancing the strong reliability and validity indicators of the scale.

Interpretation of IQ tests requires highly trained clinical expertise particularly because there is no single or specific profile of intellectual impairment that results from brain damage (29). From available studies, however, it is possible to identify several common patterns associated with TBI effects, as follows:

1. A generalized pattern of intellectual decline is most likely to be observed in patients whose TBI is at least moderate to severe (30).
2. The Wechsler Working Memory and Processing Speed indexes are comparatively more

sensitive to TBI effects than measures of crystallized knowledge and reasoning-based measures such as Vocabulary, Similarities, and Matrix Reasoning (30, 31).

3. A large discrepancy between index scores is not always synonomous with brain damage; nor does it necessarily imply damage to one hemisphere versus the other. For example, a lower Perceptual Reasoning Index score may be related to slowed visuomotor processing speed rather than right hemisphere damage per se, and a lower Working Memory Index score may be related to impaired attention and concentration rather than specific left hemisphere damage. Indeed, large discrepancies have been identified among some non-TBI "normal" adults as well (32), though the frequency is low. Nonetheless, discrepancies of 15 points or more deserve close scrutiny for acquired cognitive dysfunction and possible relationship to brain trauma-related variables such as coma, post-traumatic amnesia, brain imaging, and electroencephalography. This entails ruling out other premorbid or concurrent causes of cognitive dysfunction and test impairment and supporting any inferences about localized brain damage with additional specific indicators.
4. In reasoning about and explaining any left vs. right hemisphere disparities in intellectual processing, investigators have emphasized that the left hemisphere tends to fundamentally process information in more sequential and component fashion (e.g., mental arithmetic, digit span, vocabulary) whereas the right hemisphere engages in more simultaneous and holistic information processing (e.g., block design, matrix reasoning, picture completion). Thus, on the WAIS-III for example, left vs. right hemisphere deficits, at least as expressed through verbal vs. performance IQ score differences, should not be interpreted as simply verbal vs. visuospatial differences; rather, they may reflect

different levels and cognitive approaches to information processing.

5. Impairment on the block design subtest has been associated with damage to the parietal lobes regardless of the side of cerebral dysfunction (29).
6. Vocabulary and picture completion subtests have been employed in estimating premorbid intellectual functioning because of their robust resistance to brain injury.
7. Deficits on the similarities subtest have been associated predominantly with left frontal injury because of its reliance on verbal concept formation and abstraction.
8. In interpreting intellectual test scores and patterns, the important contributions of unique personal attributes must be assessed including educational level, premorbid functioning, learning disability, cultural/linguistic factors and others that are likely to affect IQ test scores.

The foregoing summary should not be considered immutable; rather, clinicians engaged in assessing intellectual functioning among TBI patients utilize these principles to guide interpretation and hypotheses about related functional deficits, their causes and their remediation. Similarly, the cognitive strengths observed in IQ testing may point clinicians in the direction of harnessing intact patient abilities to compensate for possible limitations. In our clinical experience, we do not rely on one cognitive measure, sign or symptom of TBI as being sufficient for rendering diagnosis and understanding of the patient's complaints. Similarly, the presence of atypical IQ scores by itself should not be assumed to reflect cerebral impairment without further investigation. For individuals with unusual IQ profile scores, review of their health history, development, and school testing records can disclose significant pre-existing discrepancies in verbal and mathematical/spatial abilities. Competent neuropsychological evaluations take many factors into account as part of understanding TBI effects. IQ scores, therefore, should not be

considered in isolation from measures of attention, memory, language, etc; similarly, test data should not be emphasized in the absence of a clear patient history, neurological evaluation and related data from other service providers.

LEARNING AND MEMORY

Learning and memory are among the most fundamental and important cognitive capacities that underlie human development and everyday adaptation. The neurobiological bases of how we acquire and subsequently retain vast amounts of information and experiences remain enigmatic though there is increasing understanding of the neural structures and processes that mediate functional memory systems. In scientific and clinical studies of TBI there is increasing evidence for both damaging alterations to memory-related structures and disruption of memory processing. The effects of post-traumatic memory impairments can be disabling and significantly limit an individual's ability to live independently, handle a job, and interact productively with others (33). Subjective complaints of memory impairment after TBI are quite common, even among those with mild TBI and good medical recovery (34). Although not always substantiated by standardized memory testing, the physiological brain changes underlying such complaints are becoming somewhat clearer. The controversy arises in part from the wide individual variability in the effects of TBI on brain networks and in different methods across studies. For example, there are differences in the ways patient are sampled (e.g., consecutive series vs. select patients referred for assessment), in how learning and memory are assessed, in the length of time post-injury, age of injury, and severity of TBI. There are also complicating effects of TBI that include chronic pain, sleep disturbance, depression, stress due to loss of income etc. that are known to affect learning and memory capacities, and must be considered in both etiology and treatment

plans. Despite these many cautions, reliable correlations have been reported between memory impairments and TBI pathophysiology. Specifically, decreased hippocampal and temporal white matter volumes were found to be significantly related to measured memory impairments in adults with mild TBI (35). Furthermore, despite normal MRI or CT imaging in 15 of 20 patients with mild TBI, Umile et al. (36) reported that dynamic brain imaging (i.e., SPECT and PET) detected abnormalities in 18 of the 20 patients, with 15 of 20 having abnormalities in the temporal lobe, primarily the hippocampal region. There are also important functional imaging data suggesting that the brain activity patterns of TBI patients become altered during tasks of memory retrieval. Specifically, patients had to engage increased levels of frontal, anterior cingulate and occipital lobe activity during memory tasks while showing reduced right dorsomedial thalamic activation and attenuated hemispheric asymmetry that was characteristic of healthy controls (37).

Post-Traumatic Amnesia

Post-traumatic amnesia (PTA) refers to the immediate and dramatic amnesic effects of TBI. Patients can be described as *confused*, *agitated*, *repeating questions*, and *disoriented* in this acute/post-acute phase. PTA is defined as the period during which patients are not effectively encoding or retaining any new information and experiences, which can last from a few moments to several weeks and even months after TBI. Although patients are awake and alert during this period, they subsequently recall little to no information regarding the accident and such post-traumatic events as transportation to the hospital, medical evaluation, and even visits of family members. Patients with PTA are disoriented to time, place and reason for hospitalization, and may even think that they are at school or in another town. As described previously, they may

show anosognosia during this period as well as a range of behavioral control difficulties and agitation.

PTA is variable in both extent of amnesia and pattern of recovery. It is considered a general marker of neurological impairment and in most cases gradually improves. Sometimes the term 'shrinking post-traumatic amnesia' is used to refer to the gradual reduction in severity and temporal extent of amnesia (in both retrograde and anterograde spheres). PTA can be assessed with standardized instruments such as the Galveston Orientation and Amnesia Test (38). Recovery of orientation and short-term memory can be reliably predicted from early daily screening and is generally a strong indicator of functional independence upon discharge (39, 40). It is important during this period to rule out exacerbating effects of sleep disturbance, pain medications, and other complicating factors on post-traumatic attention and memory deficits.

An interesting implication of PTA concerns its relationship to post-traumatic stress disorder (PTSD). That is, does loss of consciousness and memory after TBI protect against the development of PTSD symptoms that typically involve the re-experiencing of the traumatic events as well as heightened emotion with anxiety and avoidance behaviors? If the event cannot be remembered, can PTSD symptoms still be possible? PTSD symptoms were surveyed in 53 TBI respondents (out of a sample of 371 cases) and compared to their TBI trauma memories. Results indicated that those with traumatic memories of the TBI event (n = 26) reported the highest and most intrusive psychological distress followed by those with no traumatic memories at all (n = 14, although the most severe TBI cases overall) who reported less severe PTSD symptoms that were generally non-intrusive. Those with non-traumatic memories (n = 13) did

not report any PTSD symptoms. Reviews by Bryant (42) and Harvey et al. (43) have generally favored the view that PTA and PTSD can co-exist though in ways that may be different than in non-TBI PTSD cases. The latter review underscored a number of caveats to the view that PTSD occurs after TBI despite inability loss of consciousness and PTA issues, related either to imprecise criteria for TBI and/or limited assessment of stress-related symptoms (PTSD and acute stress disorder). Further research is needed to clarify the causes and management of these co-morbid conditions.

Cognitive Aspects of Learning and Memory

There are multiple systems of memory that have been described along different axes such as declarative and procedural, short-term and long-term, anterograde and retrograde, as well as material-specific divides such as verbal and visuospatial. There is strong scientific and clinical support for these variations in the diagnosis and treatment of post-traumatic memory impairments, irrespective of the specific cause of the TBI. There are several well-standardized and comprehensive tests of learning and memory and these are often the first step in the objective identification of specific learning and memory impairments.

Information processing approaches to memory systems and the brain have identified 3 principal aspects: *encoding, consolidation* and *retrieval*. Encoding typically refers to learning processes that underlie the acquisition of new information and experiences through sensory-perceptual, cognitive and attentional mechanisms. Encoding is thought to be mediated by subcortical-cortical sensory-perceptual systems together with prefrontal attentional/executive resources that are allocated according to the load of information, its difficulty, prior knowledge, interest in the

material etc. Thus *how information is processed* (e.g., in shallow, brief fashion vs. more in-depth) has considerable influence on its subsequent activity in the brain. Consolidation pertains to those biological mechanisms that are necessary to *maintaining* a memory trace, thought to involve interactive processing between cortical sensory association areas and limbic system structures, particularly the hippocampus and its other limbic connections. Retrieval refers to the access and recovery of memory traces either through recall and recognition processes. The neural basis of retrieval remains unclear but may involve executive search processes mediated by the prefrontal cortex as well as comparison of perceptual familiarity. Given this model of learning and memory and the evident diversity of neural structures and connections that subserve memory, it is somewhat clearer why memory complaints may be so common after TBI. That is, large scale coordination of cortical, subcortical and limbic system structures is usually required to mediate the attentional, sensory-perceptual, cognitive and executive processing underlying the multiple memory systems. When these systems are impaired, the behavior of patients typically regresses to a default mode, whereby they act upon previous knowledge and habits, without incorporating new information, events and contingencies. Hence, patients may be quite capable in routine situations because of well-learned habits and behaviors, but very limited in their new current circumstances because personal and situational information is not updated and retained.

Studies investigating TBI and memory continue to show diverse results. While some reports have identified principally encoding deficits, others have identified consolidation and retrieval deficits (45, 46). It is more likely the case that there are identifiable subgroups of memory impaired TBI patients that can present with greater encoding, consolidation or retrieval deficits (47). Particularly in patients with mild TBI, memory impairments may not be apparent on some

standardized testing but do become evident under certain conditions such as when patients must divide their attention during the encoding phase, manage a greater load of information, and maintain their learning over the course of a meeting, class or non-routine assignment (48). This can give rise to greater *variability* in learning and memory, a more subtle form of memory impairment. There are a number of other cognitive and learning parameters that can both affect and aide memory retention in patients. For example, strategies of clustering similar semantic information (e.g., chunking) require greater effort but once acquired can improve verbal retention, while spaced repetition of words can also contribute to more effective learning. An important clinical guideline that is emerging from extant literature is the realization that there are interactive effects of processing speed, working memory, and EF on episodic memory impairments that may combine to influence functional levels of learning and memory capacities in naturalistic settings (49). Thus it is important to consider treatment options of both cognitive remediation strategies and cholinergic medications in recovery of learning and memory impairments after TBI (50, 51; see also chapters 61 and 73).

CONFABULATIONS AND DELUSIONS

TBI can cause both confabulations and delusions. These disorders lie at the interface of memory, self-awareness/ self-monitoring, visual perceptual and executive function abilities after TBI and can occur as direct effects of TBI. Some patients show confabulations within the context of significant amnesia, attempting to fill in gaps of memory loss with overlearned knowledge about themselves and others. This kind of confabulation is thought to involve a combination of amnesia and disinhibited responding, usually associated with temporal and frontal lobe dysfunction. Several delusional misidentification syndromes have been described, centering

around altered ability to recognize persons well-known to the patient and the belief that strange people are disguising themselves in some way to look like the patient's spouse or another family member. These unusual symptoms have been associated with combined damage to frontal (usually bilateral frontal) and right posterior cortical regions. Examples include Capgras syndrome, defined as the impaired belief that someone well known to the patient has been replaced with a look-alike imposter (also described as reduplicative paramnesia) (52), and Fregoli syndrome in which the patient believes that a stranger, sometimes another patient or a staff member, is actually disguised and acting as a familiar person such as their mother (53). Confabulations and delusions generally resolve over time, but are also know to persist chronically. Challenging patients's false beliefs is often not helpful in recovery and family members as well as providers often must accommodate to these fixed beliefs. A single delusion can occur or there may be several co-occurring delusions, not necessarily inter-related. Misidentification and delusional syndromes can occur after TBI without other features of pyschosis. Curiously, patients often do not appear distressed by these symptoms nor do they act upon them in any real way.

SPATIAL COGNITION

Spatial cognition subserves a variety of adaptive behaviors, from navigation within diverse environments to spatial-related attention, memory and problem-solving. Spatial cognition is obviously critical to daily activities such as driving, ambulation, dressing, self-care and keeping track of items maintained in home and work settings. TBI infrequently causes the striking hemispatial neglect syndrome often associated with right parietal lobe damage, but can lead to changes in attention to spatial cues, visuomotor scanning that underlies spatial search,

constructional praxis, and learning/memory of places as well as various spatial patterns and complex scenes (46, 54). Exploratory deficits and other motor-intentional spatial disorders commonly occur after TBI, associated with medial frontal cortical dysfunction and hypokinesia (55). Most often, spatial cognitive deficits associated with TBI have not been singled out per se, but rather discussed within the context of attention, intelligence, memory and executive functions. Spatial representational and spatial-motor dysfunction after TBI have been less fully investigated.

CHEMICAL SENSES

TBI can dramatically affect both olfaction and taste. Olfactory deficits have been associated with multiple types of trauma to the head as well as trauma to the nasal cavity, olfactory epithelium, and the olfactory nerve as it travels through the cribiform plate to the olfactory bulb. Brain pathophysiology from inflammation, white matter shearing, hemorrhage, contusion and other effects can cause particular damage to the main olfactory structures of the brain including the olfactory bulb, tract, and interconnected subcortical and piriform cortical regions in the basal and medial aspects of the frontal and temporal lobes (56). In a comprehensive study of 268 patients with TBI, studied at a specialty smell and taste center, Doty and colleagues (57) reported that 66.8% showed anosmia (complete loss of smell) and 20.5% demonstrated microsmia (partial loss of smell). The incidence of these deficits was higher than other reports probably because of specialty center referral patterns. Performance was based on scores from the University of Pennsylvania Smell Identification Test, a 40-odorant scratch and sniff, multiple choice recognition test. About one-half of the cases suffered head trauma from motor vehicle accident, with head trauma from falls the second most likely cause. Follow-up testing of 66 patients,

varying from 1 month to 13 years later (mean follow-up period was 5.5 years, with mean age 41 years, and the sample 55% male), showed that 36% improved slightly while 45% experienced no change and 18% worsened in their olfactory deficit. Three patients actually regained normal olfaction although none had anosmia to begin with. The incidence of parosmia (olfactory distortions) decreased from 41% to 15.5% over an 8-year follow-up period. Parosmias varied from transient to intermittent to persistent in severity. There were no significant effects of age, sex or time since injury on olfactory deficits. Other changes in olfaction include decreased threshold, hallucination (usually associated with post-traumatic epilepsy), and decreased recognition memory.

Taste can be affected by TBI in a variety of ways, although usually not as severe as olfaction. Quantitative changes in gustation include altered threshold levels and decreased intensity of taste that are often described as ageusia or hypogeusia (58). Occasional increased sensitivity or hypergeusia can occur as well. Changes in taste are typically measured in relationship to detection and recognition of the four basic taste stimuli: salty, sweet, sour, and bitter. Qualitative changes in gustation are often described as onset of unpleasant tastes such as bitterness, metallic and even rancid, and as a loss of typical taste preferences. Deems et al. (59) reported that 18% of all taste problems evaluated at a specialty smell and taste clinic were related to trauma. These disorders are generally not amenable to treatment once other modifiable causes have been ruled out (e.g., oral hygiene, sinus, oral secretions, toxic exposures, smoking). Subcortical-cortical gustatory regions and pathways are less vulnerable to damage from head trauma than olfaction. Complaints of decreased taste can be related in many cases to olfactory loss, leading to decreased detection and perception of flavors rather than gustatory deficit per se (see chapter 48 for further

details).

EXECUTIVE FUNCTIONS

Executive functions (EF) encompass cognitive, behavioral and emotional processes that underlie many aspects of decision-making, adjustment, and achievement. These processes have often been defined in terms of complex cognitive activities such as planning, judgment, problem-solving and anticipation that require the coordination of multiple sub-processes to organize behavior from one action to another and achieve pertinent goals. Associated cognitive operations in EF include working memory, prospective memory, strategic planning, cognitive flexibility, abstract reasoning and self-monitoring. Executive functions have also been implicated in the goal-directed *regulation* of attentional and cognitive resources, sensory-perception, and actions in order to manage transitions from one activity to another throughout the day, over extended intervals of time, and across diverse settings (1, 6, 60-63).

The neural systems involved in executive functions include the prefrontal cortex most prominently, together with interconnected neural circuitry forming prefrontal-cortical and subcortical networks. Some of these networks have been described under the terms *dorsolateral*, *orbital* and *medial* (64, 65). In minor and moderate TBI, the traumatic forces are more frequently localised to the *orbitofrontal* and *temporal polar* zones including the amygdala and anterior hippocampus (see Figure 2 for underlying anatomy). The clinical manifestations in these cases

INSERT FIGURE 2 ABOUT HERE

are often a mixture of behavioural, cognitive and affective symptoms that include personality disintegration, coping disturbances and impulsive control of behaviour, besides the more easily

recognisable attentional impairments and executive function deficits. Even minor or moderate TBI cases manifest in a distinctive pattern of symptoms referred to as “disinhibited” and “pseudopsychopathic” behaviour with characteristics of egocentrism, childishness, stubbornness as well as tactless, aggressive and abusive behaviors. Many of these symptoms are difficult to measure with precision. Usually a combination of behavioral examinations and clinical analysis *of real-world functioning* is required. The orbital prefrontal region has been implicated mainly in social and emotional aspects of behavior including certain kinds of value-driven decision-making, theory of mind, reward-based learning and social judgment. The medial prefrontal circuit has been related to social cognition, motivational and attentional processes including social judgment, self-other evaluations, initiation, inhibition and maintainence of motivated behavior. In studies of TBI-related pathology, orbital and medial regions of the prefrontal cortex have been found to be especially vulnerable to damage by mechanisms of shearing and stretching of fibers as well as direct injury from impact against the irregular base of the skull. The orbital-medial prefrontal region is especially affected by strong blunt impact as well as physical acceleration/deceleration forces. Applied force vectors and tissue compliance influence the intensity of the coup, countercoup, angular and rotational forces that stretch and lacerate brain tissue centrifugally, from midline sagittal aspects (i.e., medial and orbital pre-frontal cortex impacting against the lamina cribrosa and the roof of the orbit as well as against the wing of the sphenoid bone) toward the surface of the cortex (lateral prefrontal cortex) and the deep connections with the striatum, thalamus and other subcortical nuclei such as the amygdala.

As injury becomes more *severe*, patients are more likely to have an abulic or a dysexecutive syndrome in which, the traumatic damage can extend toward more medial and subcortical frontal

areas, involving the corpus callosum and the brain stem. TBI patients develop disinterest, lethargy, reduced drive and lack of initiative, clinically resembling an abulic, amotivational or pseudo-depressed state. When traumatic lesions involve dorsolateral prefrontal cortex and disruption of their cortico-cortical and subcortical-cortical connections, patients may show significant impairments of executive functions, including working memory deficits, lack of insight, reduced reasoning and set-shifting, poor divided attention, and defective linguistic abilities (66, 67). The dorsolateral prefrontal network mediates many higher cognitive aspects of behavior such as abstract reasoning, planning and working memory. Some clinical disorders such as distractability and impulsivity have been found to be related to measured attentional and executive function deficits (68, 69). Significant correlations between measures of executive functions and regional cerebral glucose metabolism have been found in the mesial and lateral prefrontal regions and the cingulate gyrus. Interesting, the correlations were evident despite the absence of detectable structural lesions on brain MRI. These findings confirmed those reported previously by Goldenberg et al. (70) who also noted correlation of executive measures with reduced blood flow in the thalamic region. Hence, impairments of executive functions may be related not only to focal traumatic lesions of the prefrontal cortex but also to white matter disconnection (i.e., traumatic axonal injury) of prefrontal-related networks that link to the thalamus and other important cortical and subcortical regions. White matter damage, as well as the interruption of white matter tracts, has been frequently shown to be directly associated with cognitive-behavioural sequelae in TBI. Diffusion tensor imaging tractography is extremely sensitive to white matter changes following TBI including changes in the microstructure of white matter fibers, and represents a promising methodology for studying TBI.

Some behavioral disorders after TBI have not been linked to cognitive deficits per se and may be due to alterations in emotion-related processing. For example, Rolls et al. (71) reported that patients with ventral frontal damage after TBI had particular difficulty in reward-based contingency learning. That is, after successfully learning an initial stimulus-reward association, they were impaired in both reversal learning (when the stimulus signaling reward was reversed) and in extinction learning (when the stimulus no longer signaled reward). The impairments were correlated to surveyed behavioral deficits that included disihibition, social difficulties, lack of initiative and perseveration. Interestingly, the behavioral deficits were not correlated with verbal IQ, paired associate learning or Tower of London performance. Emotion processing may also be an integral part of value-driven decision-making capacities when one must rely on judgment of chance and probability of consequences such as applying for and taking a new job, prioritizing most important tasks, investment decisions, and gambling. This has been operationalized into a standardized task (The Iowa Gambling Task) in which subjects must learn to choose cards from stacks that are rigged to have different levels of risk and reward, varying from high risk-high win to low risk-low win (72). Patients with ventral frontal damage performed poorly on this task, choosing high risk options that led to huge losses. Furthermore, many did not generate the anticipatory skin conductance responses that might typically signal risk-taking effects. Damage to these regions is common after TBI and such associated deficits may lead patients to make hasty decisions with little anticipation of negative outcomes.

Both focal and diffuse frontal lesions after TBI disrupt activities of daily living (ADL) and EF impairments may represent a main component of ADL failure (73, 74). In particular, executive abilities of planning, self-monitoring and self-correction, decision-making and judgment are

considered critical for independent, adaptive functioning within real world settings (75).EF deficits of inattentiveness, mental slowing, impulsivity, and lack of prospective memory can all contribute to major functional impairments after TBI. The impact of such impairments can be viewed as damaging a complex cognitive-emotional *macrostructure* or *managerial knowledge unit* (including strategic planning, procedural memory, working memory) that underlies most multi-step requirements of real life, such as meal preparation or a recreational activity (74, 76). Meal preparation or going to a movie may well be more difficult than cognitive tasks presented during a formal clinical testing session because the former situations require a patient to develop and implement a plan and invest executive resources in accomplishing the many aspects of the task (60, 61, 76, 77). In cognitive testing the patient typically is administered a single problem with instructions provided by the examiner, learning trials may be short, initiation is prompted and feedback is often given at the end of the task. Certainly it is not the same in real world settings, where situational constraints, priorities and requirements are not always clear, and success depends on timely, internally-generated and self-monitored processing without the benefit of feedback. Most neuropsychological tests do not specifically explore strategic planning, competitive skills, or prospective memory. A notable exception to this is the experimental Strategic Management Simulation technology that has shown promise in detecting executive impairments in TBI patients with good medical recovery and few neuropsychological test deficits as well as in remediation of persisting EF deficits (78, 79). An important priority in both assessment and linkage to cognitive remediation is the development of further paradigms that tap multiple problem solving variables in real time and with varying degrees of structure and feedback.

Social Cognition and Behavior

Humans are naturally social creatures, born to live and thrive within social settings with many complex forms of interaction that have emotional coloring and context. Hence, an important facet of human cognition and executive functioning extends beyond the strictly intellectual endeavors of planning, concept formation, and problem-solving to domains such as metacognitive thinking, social skills, moral beliefs, personality traits, and "theory of mind", a special faculty of the human brain that mediates interpretation and appreciation of other people's feelings and mental states (6, 80). Frontotemporal damage from TBI can lead to dramatic alterations of conduct, personality, and psychosocial integration, at times leaving most cognitive and sensory-motor functions relatively intact. From a clinical standpoint, there is often a spectrum of social-behavioral symptoms associated with TBI rather than definite syndromes. Some patients become puerile, profane, facetious, irresponsible, irascible, and aggressive as forms of social disinhibition. Others lose spontaneity, initiative, curiosity, and develop mental and behavioral inertia as forms of abulia and apathy (81). Still others develop lack of awareness and insight, loss of creativity and emotional vitality. Some of these deficits are expressed as loss of pragmatic aspects of communication, loss of empathy and inability to understand and appreciate sarcasm, jokes, irony, and other vital social communication tools (82, 83). Another facet of social related processing involves recognition of common forms of emotional expressions. Hornak et al. (84) showed that ventral frontal damage from head trauma (and other etiologies as well) was associated with deficient recognition of emotional facial expressions and correlated with subjective emotional change and social behavior of patients.

Although many of these social-emotional deficits are difficult to objectively evaluate and measure with current instruments, some progress has been made in developing tests of social

judgment, theory of mind, emotional intelligence, and social adaptation. These are important and problematic sequelae of TBI that must be examined in further studies and managed with a combination of patient and family interventions. The combined use of clinical interview with patient and family members and behavioral inventories can uncover many of these deficits. Experimental measures of social judgment, theory of mind abilities, social knowledge and emotion-related processing are beginning to shed light on deficits underlying these real-life problems and are increasingly targeted in experimental intervention programs.

SUMMARY

Cognitive impairments after TBI often present significant challenges for recovery and return to premorbid levels of occupational and social functioning. In early stages, patients' lack of awareness of their deficits (anosognosia), impaired self-regulation, and post-traumatic amnesia constitute major limitations to participation in rehabilitation services and safety. Often there is a combination of attentional, memory, perceptual, processing speed, executive function and social-emotional deficits that require multi-modal therapy services and a gradual return to independent daily activities. Cognitive and social-emotional deficits are frequently slower to recover than physical injuries and require outpatient therapy services with medical follow-up care. Education of caregivers is particularly important for monitoring and continued remediation of such impairments within home and community settings. When cognitive deficits remain persistent, individualized therapy is usually required combining aspects of skill retraining, compensatory strategies, and environmental supports to optimize functional cognitive capacities.

REFERENCES

1. Zappalà G. The frontal lobes: Executive and behavioural control of human reasoning. Implications for understanding brain injury. *Rivista Italiana di Neurobiologia 2008;* 54: 195-202.
2. Dikmen SS, Ross BL, Machamer JE et al. One year psychosocial outcome in head injury. *J Intl Neuropsychol Soc* 1995; 1:67–77.
3. Drake AI, Gray N, Yoder S. Pramuka M, Llewellyn M. Factors predicting return to work following mild traumatic brain injury: A discriminant analysis. *J Head Trauma Rehabil* 2000; 15: 1103–1112.
4. Rapoport MJ, McCullagh S, Shammi P, Feinstein A. Cognitive impairment associated with major depression following mild and moderate traumatic brain injury. *J. Neuropsychiat Clin Neurosci* 2005; 17: 61-65.
5. Jones RD, Anderson SW, Cole T, Hathaway-Nepple J. Neuropsychological sequelae of traumatic brain injury. In Rizzo M, Tranel D (Eds.) *Head Injury and Postconcussive Syndrome* 1996; New York, NY: Churchill Livingstone, 395-414.
6. Eslinger P, Grattan L, Geder L. Neurologic and neuropsychologic aspects of frontal lobe impairments in postconcussive syndrome. In Rizzo M, Tranel D (Eds.) *Head Injury and Postconcussive Syndrome* 1996; New York, NY: Churchill Livingstone, 415-440.
7. Sarno S, Erasmus L-P, Lipp B, Schlaaegel W. Multisensory integration after traumatic brain injury: A reaction time study between pairings of vision, touch, and audition. *Brain Injury* 2003; 17: 413–426.
8. Mathias JL, Beall JA, Bigler ED. Neuropsychological and information processing deficits following mild traumatic brain injury. *J intl Neuropsychol Soc* 2004; 1: 286–297.

9. Tinius T. The Integrated Visual and Auditory Continuous Performance Test as a neuropsychological measure. *Arch Clin Neuropsychol* 2003; 18: 439–454.
10. Stuss DT, Stethern LL, Hugenholtz H, Picto T, Pivik J, Richard MJ. Reaction time after head injury: Fatigue, divided and focussed attention and consistency of performance. *J Neurol Neurosurg Psychiat* 1989; 52: 742–748.
11. McAllister TW, flashman LA, Sparling MB, Saykin AJ. Working memory deficits after traumatic brain injury: Catecholaminergic mechanisms and prospects for treatment – a review. Brain Injury 2004; 18: 331-350.
12. Zollolotti P, Matano A, DeLoche G et al. Patterns of attentional impairment following closed head injury: A collaborative European study. *Cortex* 2000; 36: 93–107.
13. Pardini JE, Pardini DA, Becker JT, Dunfee KL, Eddy WF, Lovell MR, Welling JS. Postconcussive symptoms are associated with compensatory cortical recruitment during a working memory task. *Neurosurgery* 2010; 67: 1020-1028.
14. Lovell MR, Pardini JE, Welling JS et al. Functional brain abnormalities are related to clinical recovery and time to retrun to play in athletes. Neurosurgery 2007; 61: 352-360.
15. Babinski J. Contribution a l'etude dies troubles mentaux dans l'hemiplegie organique cerebrale (anosognosia). *Revue Neurologique* (Paris) 1914;27:845–847.
16. Adair JC, Schwartz RL, Barrett AM. Anosognosia. In Heilman KM and Valenstein E (Eds). *Clinical Neuropsychology, Fourth Edition* 2003; New York, NY: Oxford University Press, 185-214.
17. Hart T, Giovannetti T, Montgomery MW, Schwartz MF. Awareness of errors in naturalistic action after traumatic brain injury. *J Head Trauma Rehabil* 1998;13:16–28.
18. Prigatano GP, Schacter DL. *Awareness of Deficit After Brain Injury: Clinical and*

Theoretical Issues. 1991; New York, NY: Oxford University Press.

19. Giacino JT, Cicerone K. Varieties of deficit unawareness after brain injury. *J Head Trauma Rehabil 1998;* 13:1–15.
20. Fleming JM, Strong J, Ashton R. Cluster analysis of self-awareness levels in adults with traumatic brain injury and relationship to outcome. *J Head Trauma Rehabil* 1998;13:39–51.
21. Powell JM, Machamer JE, Temkin NR, Dikmen SS. Self-report of extent of recovery and barriers to recovery after traumatic brain injury: A longitudinal study. *Arch Phys Med Rehabil* 2001;82: 1025–1030.
22. Weinstein EA, Kahn RL. *Denial of Illness: Symbolic and Physiological Aspects.* Springfield, IL: Charles C. Thomas, 1955.
23. Dalla Barba G, Bartolomeo P, Erigs AM, Boisse MF, Bachoud-Levi AC. Awareness of anosognosia following head trauma. *Neurocase* 1999; 5: 59–
24. Schacter DL and Prigatano GP, 1991. Forms of unawareness. In Prigatano GP, Schacter DL (Eds). *Awareness of Deficit after Brain Injury: Clinical and Theoretical Issues.* New York: Oxford University Press, 1991.
25. McGlynn SM, Schacter DL. Unawareness of deficits in neuropsychological syndromes. *J Clin Exp Neuropsychol* 1989;11: 143–205.
26. Sohlberg MM and Rawlings-Boyd J. *Picture this! Strategies for Assessing and Increasing Awareness of Memory Deficits*. San Antonio, TX: The Psychological Corporation. 1996.
27. Fisher DC, Ledbetter MF, Cohen NJ, Marmor D, Tulsky DS. (2000). WAIS-III and WMS-III profiles of mildly to severely brain-injured patients. *Appl Neuropsychol*

2000;7:126–132.

28. Green REA, Melo B, Christensen B, Ngo L, Monette G, Bradbury. Measuring premorbid IQ in Traumatic Brain Injury: An Examination of the Wechsler Test of Adult Reading (WTAR). *Journal of Clinical and Experimental Neuropsychology* 2008; 30, 2:1-10
29. Lezak MD. *Neuropsychological Assessment (3rd ed.)*. New York: Oxford University Press, 1995.
30. Martin TA, Donders J, Thompson E. Potential of and problems with measures of psychometric intelligence after traumatic brain injury. *Rehabil Psychol* 2000;45:402–408.
31. Axelrod BN, Fichtenberg NL, Liethen PC, Czarnota MA, Stucky K. Performance characteristics of postacute traumatic brain injury patients on the WAIS-III and WMS-III. *Clin Neurosychol* 2001; 15:516–520.
32. Brooks BL, Strauss E, Iverson GL, Slick DJ, Sherman EMS. Developments in Clinical Neuropsychological Assessment: Refining Psychometric and Clinical Interpretive Methods. *Canadian Psychology* 2009; 50, 3:196-209.
33. Drake AI, Gray N, Yoder S, Pramuke M., Llewellyn M. Factors predicting return to work following mild traumatic brain injury: A discriminant analysis. *J Head Trauma Rehabil* 2000;15: 1103–12.
34. Rimel RW, Giordani B, Barth JT, Boll TJ, Jane JA. Disability caused by minor head injury. *Neurosurg* 1981;9:221–8.
35. Bigler ED, Anderson C V, Blatter DD, Anderson CV. Temporal lobe morphology in normal aging and traumatic brain injury. *Am J Neuroradiol* 2002;23:255–66.
36. Umile EM, Sandel ME, Alavi A, Terry CM, Plotkin RC. Dynamic imaging in mild traumatic brain injury: Support for the theory of medial temporal vulnerability. *Arch Phys*

Med Rehabil 2002; 83:1506–13.

37. Levine B, Carbeza R, McIntosh AR, Black SE, Grady CL, Stuss DT. Functional reorganisation of memory after traumatic brain injury: A study with H(2)(15)O positron emission tomography. *J Neurol Neurosurg Psychiat* 2002;73:173–81.
38. Levin HS, Benton AL, Grossman RG. Neurobehavioral Consequences of Closed Head Injury. 1982; New York, NY: Oxford University Press.
39. Tate RL, Perdices M, Pfaff A, Jurjevic L. Predicting duration of post-traumatic amnesia (PTA) from early PTA measurements. *J Head Trauma Rehabil 2001*;16:525–42.
40. Alderso AL, Novack TA. Measuring recovery of orientation during acute rehabilitation for traumatic brain injury: Value and expectations of recovery. *J Head Trauma Rehabil* 2002; 17:210–9.
41. Turnbull SJ, Campbell EA, Swann IJ. Post-traumatic stress disorder symptoms following a head injury: Does amnesia for the event influence the development of symptoms? *Brain Injury* 2001;15: 775–85.
42. Bryant RA. Post-traumatic stress disorder and traumatic brain injury: Can they co-exist. *Clin Psychol Rev* 2001;21:931–48.
43. Harvey AG, Brewin CR, Jones C, Kopelman MD. Co-existence of post-traumatic stress disorder and traumatic brain injury: Towards a resolution of the paradox. *J Intl Neuropsychol Soc* 2003;9:663–676.
44. DeLuca J, Lengenfelder J & Eslinger PJ: Memory and learning, In Rizzo M, Eslinger PJ (Eds.), *Principles and Practice of Behavioral Neurology and Neuropsychology*, 2004; Philadelphia, PA: Elsevier, 247-266.
45. DeLuca J, Schultheis MT, Madigan NK, Christodoulou C, Averill A. Acquisition versus

retrieval deficits in traumatic brain injury: Implications for memory rehabilitation. *Arch Phys Med Rehabil* 2000;81:1327–33.

46. Vanderploeg RD, Curtiss G, Schinka JA, Lanham RA. Material-specific memory in traumatic brain injury: Differential effects during acquisition, recall, and retention. *Neuropsychol* 2001;15: 174–84.
47. Curtiss G, Vanderploeg RD, Spencer J, Salazar AM. Patterns of verbal learning and memory in traumatic brain injury. *J Intl Neuropsychol Soc* 2001;7:574–85.
48. Mangels JA, Craig FI, Levine B, Schwartz ML, Stuss DT. Effects of divided attention on episodic memory in chronic traumatic brain injury: A function of severity and strategy. *Neuropsychologia* 2002;40:2369–85.
49. Perbal S, Couillet J, Azouvi P, Pouthas V. Relationships between time estimation, memory, attention, and processing speed in patients with severe traumatic brain injury. *Neuropsychologia* 2003;41:1599–1610.
50. Griffin SL, vanReekum R, Masanic C. A review of cholinergic agents in the treatment of neurobehavioral deficits following traumatic brain injury. *J Neuropsychiat Clin Neurosis* 2003;15:17–26.
51. Morey CE, Cilo M, Berry J, Cusick C. The effect of Aricept in persons with persistent memory disorder following traumatic brain injury: A pilot study. *Brain Injury* 2003;17:809–15.
52. Alexander MP, Stuss DT, Benson DF. Capgras syndrome: A reduplicative phenomenon. *Neurology* 1979;29:334–339.
53. Box O, Laing H, Kopelman M. The evolution of spontaneous confabulation, delusional misidentification and a related delusion in a case of severe head injury. *Neurocase*

1999;5:251–262.

54. Skelton RW, Bukach CM, laurance HE, Thomas KG, Jacobs JW. Humans with traumatic brain injuries show place-learning deficits in computer-generated space. *J Clin Exp Neuropsychol* 2000;22:157–75.

55. Heilman KM. Intentional neglect. *Frontiers in Bioscience* 2004.

56. Eslinger PJ, Damasio AR, Van Hoesen GW: Olfactory dysfunction in man: Anatomical and behavior aspects. *Brain and Cognition* 1982;1:259–85.

57. Doty RL, Yousem DM, Pham LT, Kreshak AA, Geckle R, Lee WW. Olfactory dysfunction in patients with head trauma. *Arch Neurol* 1997;54:1131–1140.

58. Pritchard TC, Eslinger PJ, Wang J, Yang Q. Smell and taste disorders. In Rizzo M & Eslinger PJ (Eds.) *Principles and Practice of Behavioral Neurology and Neuropsychology*; Philadelphia, PA: Saunders, 335-360.

59. Deems DA, Doty RL, Settle RG et al. Smell and taste disorders: A study of 750 patients from the University of Pennsylvania Smell and Taste Center. *Arch Otolaryngol Head Neck Surg* 1991;117: 508–528.

60. Shallice T, Burgess PW. Deficits in strategy application following frontal lobe damage in man. *Brain* 1991;114:727–741.

61. Levine B, Dawson D, Schwartz ML, Boutet I, Stuss DT. Assessment of strategic self-regulation in traumatic brain injury: Its relationship to injury severeity and psychosocial outcome. *Neuropsychol* 2000;14:491–500.

62. Eslinger PJ. Conceptualizing, describing, and measuring components of executive function. In Lyon GR, Krasnegor (Eds.) *Attention, Memory, and Executive Function* 1996; Baltimore, MD: Paul H. Brookes, 367-396.

63. Andres P, Van der Linden M. Are central executive functions working in patients with focal frontal lesions? *Neuropsychologia* 2002;40:835–845.

64. Eslinger PJ, Geder L. Behavioural and emotional changes after focal frontal lobe damage. In Bogousslavsky J, Cummings JL(Eds). *Behavior and Mood Disorders in Focal Brain Lesions* 2000; Cambridge, UK: Cambridge University Press, 217-260.

65. Barbas H. Connections underlying the synthesis of cognition, memory and emotion in primate prefrontal cortices. *Brain Res Bull* 2000;15:319–330.

66. Grafman J, Jones B, Salazar A. Wisconsin Card Sorting performance based on location and size of neuroanatomic lesion in Vietnam veterans with penetrating head injury. *Percept Mot Skill* 1990;74:1120–22.

67. Allegri RF, Harris P. Prefrontal cortex in memory and attention processes. *Rev Neurol* 2001;32:449–453.

68. Baddeley A, Della Sala S, Papagano C, Spinnler H. Dual task performance in dysexecutive and nondysexecutive patients with a frontal lesion. *Neuropsychol* 1997;11:187–94.

69. Burgess PW, Alderman N, Evans J, Emslie H, Wilson BA. The ecological validity of tests of executive function. *J Intl Neuropsychol Soc* 1998;4:547–558.

70. Goldenberg G, Oder W, Spatt J, Podreka I. Cerebral correlates of disturbed executive function and memory in survivors of severe closed head injury: A SPECT study. *J Neurol Neurosurg Psy*chiat 1992;55:362–8.

71. Rolls E.T, Hornak J, Wade D, McGrath J. Emotion-related learning in patients with social and emotional changes associated with frontal lobe damage. *J Neurol Neurosurg Psychiat* 1994;57: 1518–24.

72. Bechara A, Tranel D, Damasio H, Damasio AR. Failure to respond autonomically to anticipated future outcomes following damage to prefrontal cortex. *Cereb Cortex* 1996;6: 215–225.

73. Eslinger PJ, Damasio AR. Severe disturbances of higher cognition after bilateral frontal lobe ablation: Patient EVR. *Neurol* 1985;35:1731–41.

74. Fortin S, Godbout L, Braun CMJ. Cognitive structure of exeutive deficits in frontally lesioned head trauma patients performing activities of daily living. *Cortex* 2003;39:273–291.

75. Acker MBA. Review of ecological validity of neuropsychological tests. In D E Tupper and K D Cicerone (Eds). *The Neuropsychology of Everyday Life: Assessment and Basic Competencies* 1990; Boston, MA: Klucer Ac. Publ., 19-55.

76. Grafman J. Similarities and distinctions among current models of prefrontal cortical functions. *Ann NY Acad Sci* 1995;769: 337–368.

77. Channon S, Crawford S. Problem-solving in real-life type situations: the effects of anterior and posterior lesions on performance. *Neuropsychologia* 1999;37:757–70.

78. Satish U, Streufert S, Eslinger PJ. Measuring executive function deficits following head injury: An application of SMS simulation technology. The Psychological Record 56: 181-190, 2006.

79. Satish, U, Streufert S, Eslinger PJ. Simulation-based executive cognitive assessment and rehabilitation after traumatic frontal lobe injury: A case report. Disability and Rehabilitation Research, 30: 468-78, 2008.

80. Stuss DT, Gallup GG, Alexander MP. The frontal lobes are necessary for "theory of mind". *Brain* 2001;124:279–86.

81. Trexler LT, Zappalà G. Neuropathological determinants of acquired attention disorders in traumatic brain injury. *Brain Cogn* 1988;8:291–302.
82. Eslinger PJ. Neurological and neuropsychological bases of empathy. *Eur Neurol* 1998;39:193–9.
83. McDonald S, Flanagan S. Social perception deficits after traumatic brain injury: Interaction between emotion recognition, mentalizing ability, and social communication. *Neuropsychol* 2004; 18:572–9.
84. Hornak J, Rolls ET, Wade D. Face and voice expression identification in patients with emotional and behavioral changes following ventral frontal lobe damage. *Neuropsychologia* 1996; 34:247–61

Key Clinical Points

1. Traumatic brain injury is associated with often persisting cognitive deficits that interfere with return to occupational, school, and social roles.
2. Common areas of cognitive deficit include attention, working memory, executive functions, word retrieval, learning and memory, and social cognition.
3. In addition to cognitive deficits themselves, patients may lack awareness of their deficits and functional limitations (anosognosia), further compounding their adjustment to injury and recovery.
4. Cognitive, behavioral and emotional deficits after TBI are related to the underlying damage to the brain, including cortical, subcortical, limbic and brainstem regions.
5. In cases of mild TBI, deficits may become evident mainly under conditions of time pressure, fast processing speed, multiple tasks requiring divided attention, persistent accuracy in

responding, working memory load, and need to monitor errors.

6. Cognitive difficulties are more common in non-routine situations that require novel problem-solving approaches and less common in routine actions and situations.

7. Cognitive deficits often require continued rehabilitation services that extend from acute and post-acute care to extended follow-up outpatient care.

Key References