CHAPTER 1

History, Diagnostic Considerations, and Controversies

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Mild traumatic brain injury (mTBI)—which also traditionally incorporates terms such as *concussion*, *minor head injury*, *minor brain injury*, or *minor head trauma*—occurs when a forceful motion of the head (with or without impact) results in a transient alteration of mental status, such as confusion or disorientation, loss of memory for events immediately before or after the injury, or brief loss of consciousness. Traumatic brain injury (TBI) in children has garnered increasing attention among clinicians, researchers, parents, educators, communities, and sports- and recreation-related professionals working with children in recent years, as data indicate that the rates of hospital admissions and emergency department visits for head injuries are indeed higher among children than the general adult population, particularly among children under 5 years and in adolescents ages 15–19 (Faul, Xu, Wald, & Coronado, 2010). In addition to mechanisms such as motor vehicle crashes and falls, each year an estimated 135,000 cases of TBI, treated in emergency departments, occur due to sports and recreation injuries in children ages 5–18 years (Centers for Disease Control and Prevention, 2007). mTBI accounts for the overwhelming majority (at least 75%) of all TBI in the United States (Sosin, Sniezek, & Thurman, 1996)—though, due to lack of data on individuals who do not seek immediate medical attention, this is a probably an underestimate of the true incidence of mTBI. Despite growing acknowledgment of the potential for long-term disability in at least a subset of children and adolescents with mTBI, the long-term consequences of pediatric mTBI have been difficult to estimate.

This chapter provides a brief introduction to early research findings that have influenced current methodology in pediatric mTBI research, and we review general trends in current literature in contrast to literature from approximately two to three decades ago. Diagnostic considerations and commonly used criteria are introduced in the context of developmental considerations in children. Finally, a series of remaining controversies in the field of pediatric mTBI are briefly introduced.

TRENDS IN mTBI RESEARCH IN CHILDREN

Historically, mTBI has not received a great deal of scholarly attention because it was generally accepted as clinically benign (Echemendia & Julian, 2001; Segalowitz & Brown, 1991). Until more recently, lukewarm interest, a lack of controlled studies, and underestimation of the sequelae of mTBI all presented significant obstacles to developing a solid understanding of its long-term consequences. However, highly publicized sports-related mTBI and media focus upon military-related mTBI in the adult literature have aroused an interest in the consequences of this condition at all ages, including in children and adolescents, as demonstrated by a dramatic increase in published studies in pediatric mTBI in recent years (see Figure 1.1). Nevertheless, some aspects of early methodological design continue to exert a notable influence on current studies in this area.

Early History

Modern research on mTBI in children was pioneered by child psychiatrist Michael Rutter and his associates. Following earlier investigation of outcomes of depressed skull fracture with dural tears, using a retrospective design (Shaffer, Chadwick, & Rutter, 1975), these investigators shifted their focus to prospective investigation of children who sustained closed-head trauma (Brown, Chadwick, Shaffer, Rutter, & Traub, 1981; Chadwick, Rutter, Brown, Shaffer, & Traub, 1981a; Chadwick, Rutter, Shaffer, & Shrout, 1981b; Rutter, Chadwick, Shaffer, & Brown, 1980). This seminal series of studies was distinguished by longitudinal designs that involved serial assessments of children at 4 months, 1 year, and 2.5 years postinjury. Secondly, these investigators used a "dose–response" strategy of comparing outcomes of children

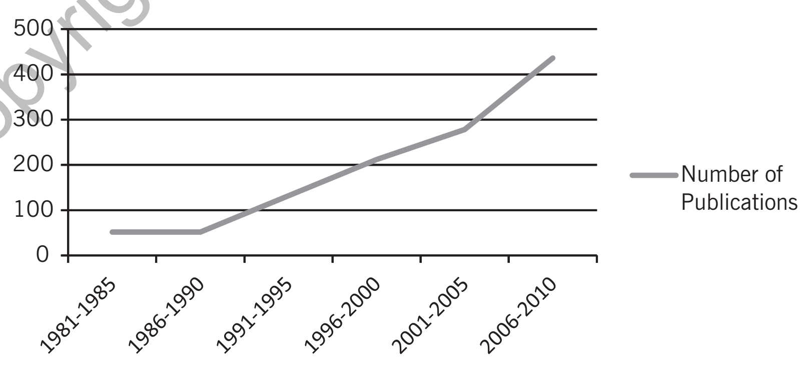

FIGURE 1.1. Results of a PubMed search for articles related to mTBI in children between the years 1981 and 2010 by 5-year increments, indicating a steady increase in publications in the last 20 years. The most dramatic increase occurs in the last 5 years.

who sustained mild head injury with children who sustained severe head injury. In addition, a group of children who experienced orthopedic injury without trauma to the head were also studied to control for more general injury-related risk factors. Standard interviews with the parents shortly after the injury were conducted to obtain information about preinjury medical history and psychiatric disorder in addition to characterizing the family environment. Serial Performance IQ scores showed a recovery curve after severe head injury, whereas repeated assessment of children in the mTBI group revealed little change in performance over time. Rutter inferred that a threshold for brain injury was exceeded in the severe head injury group, but not in the patients with mild head injury. Although the rate of preinjury psychiatric disorder was highest in the mTBI group (31%) relative to the severe TBI (14%) and control (11%) groups, the rate of novel psychiatric disorder in the postinjury assessments was markedly increased only in the children who sustained severe TBI. These studies also called attention to the contribution of preinjury comorbidities to psychiatric sequelae of the injuries and the effects of disadvantageous environment, which were controlled through this study design. The legacy of Rutter's research is seen in contemporary studies on mTBI in children that have incorporated aspects of the earlier work.

One focus of studies in the early 1990s was related to the epidemiology and incidence of mTBI. The 1991 National Health Survey revealed that motor vehicle accidents were responsible for 28% of brain injuries, sports and physical activities were responsible for 20%, and assaults were responsible for 9%. The study highlighted the fact that the risk of sustaining brain injury was highest among teens, young adults, males, and people with low income who lived alone (Sosin et al., 1996). Although the national survey did not separately categorize mTBI and moderate brain injury, the study did begin to highlight the magnitude of the issue. In another study from this era, Segalowitz and Brown (1991) reported that 2–3% of high-school-age adolescents (14–18 years) were hospitalized for mTBI. However, when the authors conducted a survey in a high school with a sample size of 616, they found that reports of mTBI (including nonhospitalized cases) in the same age group were almost 10 times higher than hospital-reported incidence.

In addition to incidence and prevalence, assessment of the cognitive sequelae (e.g., Levin, Eisenberg, Wigg, & Kobayashi, 1982; Winogron, Knights, & Bawden, 1984) and behavioral outcome (e.g., Boll & Barth, 1983; Stern, Melamed, Silberg, Rahmani, & Groswasser, 1985) in children was a focus of mTBI research from early on. Segalowitz and Brown (1991) reported that adolescents with mTBI between 14 and 18 years of age displayed problems with hyperactivity, stuttering, mixed handedness, and dislike of mathematics. On the other hand, Knights et al. (1991) reported few behavioral changes in children ages 5–17 years with mTBI. Interestingly, and consistent with the general trend at the time, this study did not utilize a control group, reflecting the notion that children with mTBI were appropriate controls for children with moderate and severe brain injury.

Advances in technology, especially in regard to brain imaging and measures of the brain injury associated with abnormal neuropsychological outcomes, have also played a role in bolstering interest in mTBI. For example, between 1981 and 1990, electroencephalograghy (EEG) was used to demonstrate abnormalities not visualized by clinical computer tomography (CT) scans (Sugiura et al., 1981). EEG was also used to distinguish minor and mild concussions, with a reported potential value of determining the risk of later posttraumatic epilepsy (Geets & Zegher, 1985). The reliance on EEG to assess brain abnormalities postinjury lessened somewhat thereafter, as routine clinical use of EEG post head trauma was shown to be unrevealing in some instances and initiated concern related to the burden of unnecessary diagnostic procedures (Oster, Shamdeen, Gottschling, Gortner, & Meyer, 2010). Near the late 1980s, mTBI research shifted to the use of magnetic resonance imaging (MRI) as a measure to assess structural alterations of the brain postinjury (Levin et al., 1987, 1989). In one study, MRI scans revealed 44 more intracranial lesions than did concurrent CT scans in 85% of patients (Levin et al., 1987). In comparison to EEG, the higher density of prognostic information obtained from MRI proved it superior to electrophysiological testing (Wedekind, Fischbach, Pakos, Terhaag, & Klug, 1999). In addition, the use of MRI seemed to more accurately detect specific types of brain injury, namely, diffuse axonal injury found in the cerebral white matter (Yokota, Kobayashi, Nakazawa, Tsuji, & Taniguti, 1989). This finding, among others, revealed the presence of injuries possibly associated with neuropsychological outcomes that required more sensitive measures.

Recent Trends in Research

In contrast to the paucity of research on pediatric mTBI 30 years ago, recent research on mTBI has flourished and covers a more diverse range of topics, including epidemiology, research methodology, diagnostic techniques such as behavioral assessment and brain imaging, neurocognitive and social outcomes, and consequences of brain imaging techniques on children's health.

Advances in technology continue to facilitate the advancement of research in mTBI, especially the development of more sensitive, noninvasive, advanced MRI techniques such as diffusion tensor imaging (DTI). This MRI technique reveals potential alteration in white matter microstructure, and has been cited as a promising prognostic tool (Inglese et al., 2005). The use of DTI in adult mTBI has grown particularly rapidly in recent years, but has also been used in children and adolescents. In addition to advanced structural MRI techniques, Keightley et al. (2011) investigated the effect of sports-related mTBI using functional MRI and the Head Impact Telemetry (HIT) System to localize and assess the changes in neural activity in the brain as a result of mild injury. Moreover, HIT allowed the detection and recording of the magnitude and location of head impacts during sport activities. With the aid of technology, the head impact location can now be assessed, as well as the possible neural networks affected by mTBI. Other forms of advanced structural and functional neuroimaging are also being used in the study of pediatric mTBI and are the focus of a later chapter.

Technological developments have paved the way not only for improvement in brain imaging techniques, but also for the analysis of mTBI at a molecular level (Menascu, Brezner, Tshechmer, & Rumeny, 2010). For example, Filippidis, Papadopoulos, Kapsalaki, and Fountas (2010) reviewed studies examining the role of the S100B serum biomarker in the treatment of children who sustained mTBI. Although the specificity of that particular marker has yet to be demonstrated in mTBI in children (see Geyer, Ulrich, Grafe, Stach, & Til, 2009; Piazza et al., 2007), such studies suggest that serum protein biomarkers may be eventually identified that could facilitate diagnosis and avoid unnecessary head CT scans to alleviate the risks of radiation exposure in children (Klig & Kaplan, 2010).

Another topic of recent research is the emphasis on long-term outcome from childhood mTBI in terms of neurocognitive and sociocognitive functioning, as well as later neuroimaging. For example, Beauchamp et al. (2011) investigated the changes in hippocampal, amygdalar, and global brain volume 10 years after childhood TBI in patients with a range of severity that included mTBI. This group of investigators has also examined persistent changes in the corpus callosum in relation to social skills (Beauchamp et al., 2009) and predictors of educational skills in long-term outcome following injury during childhood (Catroppa et al., 2009). Anderson, Brown, Newitt, and Hoile (2011) have investigated consequences of head injury in the domains of intellectual ability, personality, and quality of life.

Another appealing feature in recent research has been the increased acknowledgment of children's phenomenological experience following mTBI. For example, Woodrome et al. (2011) investigated children's coping strategies after mTBI and reported that coping strategies collectively account for 10–15% of the variance in children's posttraumatic symptoms over time.

As noted above, research on pediatric mTBI has undergone a noticeable proliferation. Technological developments and acknowledgment of mTBI as a more serious health concern have ignited interest in the topic and helped shape the direction of research. New techniques to measure brain injury, although progressively more advanced than the methods used 30 years ago, still aim to answer some of the fundamental questions sought from the start: that is, to examine the scope of the problem, accurately assess outcome, identify any persistent sequelae, understand the mechanism underlying any persistent deficits, and reveal factors that influence recovery.

DIAGNOSTIC CONSIDERATIONS IN mTBI

This section is included to inform clinical investigators and clinicians who retrospectively obtain information about the acute phase of injury based on medical record review and/or parent interview. However, readers are referred to pediatric neurosurgical sources for more detailed information on the clinical guidelines for assessment and management of acute TBI in children (see Luerssen, 1994).

Definition of mTBI

Definitions of mTBI used by clinicians and investigators vary significantly (Culotta, Sementilli, Gerold, & Watts, 1996). As noted by Yeates and Taylor (2005), various definitions and terminologies, published by professional organizations representing different medical specialties, and have contributed to a lack of consensus about what is referred to here as *mild traumatic brain injury* (mTBI). The American Academy of Pediatrics (1999) published treatment guidelines for "minor closed head injury," which are described in Table 1.1. Although symptoms are presented, no mention is made of altered brain function. In contrast to the AAP definition, which includes "normal mental status on initial examination," the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine (1993) refers to this clinical condition as mTBI and includes alteration of consciousness in the definition (see Table 1.2) with the presumption of a "physiological disruption of brain function." The World Health

TABLE 1.1. American Academy of Pediatrics Definition of "Minor Closed Head Injury"

Inclusion criteria

- Normal mental status on initial examination
- No abnormal or focal neurological findings
- No physical evidence of skull fracture
- Loss of consciousness < 1 minute
- May have had a seizure immediately after injury
- May have vomited after injury
- May exhibit other signs and symptoms (e.g., headaches, lethargy)

Exclusion criteria

- Multiple trauma
- Unobserved loss of consciousness
- Known of suspected cervical spine injury
- Suspected intentional head trauma

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Organization (WHO) specifies several *International Classification of Diseases*, 10th revision (ICD-10) codes as mild closed-head injury, including a concussion (code 850), which is referred to as a "transient impairment of function as a result of a blow to the brain." The ICD-10 also has diagnostic codes to specify whether a mild closed-head injury is associated with loss of consciousness, skull fracture, or brain lesions.

Age and Developmental Issues in Assessments during the Acute Phase of mTBI

Assessment of Impaired Consciousness

Historically, clinicians and investigators have classified TBI as mild, moderate, and severe using the Glasgow Coma Scale (GCS), a widely used scoring system to assess impaired consciousness and coma (Teasdale & Jennett, 1974). Patients with scores of 8 or less are classified as "severe," scores of 9–12 are "moderate," and scores of 13–15 are "mild." Alteration of consciousness is a key diagnostic feature of mTBI, but administering the verbal component of the GCS assumes that comprehension

TABLE 1.2. American Congress of Rehabilitation Medicine Definition of "Mild Traumatic Brain Injury"

Inclusion criteria (at least one must be present)

- Any loss of consciousness
- Any loss of memory for events immediately before or after the accident
- Any alteration in mental state at the time of the accident
- Focal neurological deficits that may be transient

Exclusion criteria

- Loss of consciousness > 30 minutes
- Glasgow Coma Scale score < 13 after 30 minutes
- Posttraumatic amnesia > 24 hours

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of language is sufficiently developed to reliably assess the ability to follow simple commands. Consequently, modifications of the GCS and use of pediatric scales to measure impaired consciousness have been proposed for use with infants. For example, among children under 36 months, a pediatric coma scale that is intended to approximate the GCS can be used (Simpson, Cockington, Hanieh, Raftos, & Reiley, 1991). Assessment of "confusion," the level of verbal response immediately below "oriented" on the verbal component of the GCS, is also age-dependent. Although an experienced pediatric clinician might be capable of evaluating confused speech in a young child, reliance on temporal orientation could be problematic because this ability is not reliably developed until approximately age 8 years. Despite these caveats, the GCS continues to be widely used in emergency centers that treat children with mTBI (Kapapa, Konig, Pfister, Sasse, & Woischneck, 2010).

Assessment of Posttraumatic Amnesia

Postraumatic amnesia (PTA) refers to the interval following injury for which the child has no recall of events. mTBI may be diagnosed based on PTA and confirmation of trauma to the head even without loss of consciousness. Evaluated in real time, PTA could extend to the circumstances of injury, the immediate postinjury period, arrival of first responders, and transport to hospital. Later evaluations rely on the child's recall of the aforementioned events surrounding the injury and the events immediately before the injury (e.g., climbing a tree, prior play preceding injury in a football game), which may be vulnerable to retrograde amnesia. With dependence on orientation to person, place, and time, developmental status must be considered in the clinical assessment of PTA. Consequently, Ewing-Cobbs, Levin, Fletcher, Miner, and Eisenberg (1990) designed the Children's Orientation and Amnesia Test (COAT) to evaluate PTA during the acute and subacute phases of TBI in children ages 3–15 years. Measures of PTA developed for use with adults (e.g., Galveston Orientation and Amnesia Test) could be given to adolescents 16 years and older. The COAT evaluates general orientation (e.g., person and place), temporal orientation, and short term memory. Scoring of the COAT is referenced to control data obtained in typically developing children. Items pertaining to temporal orientation are not included in the assessment of children younger than 8 years because this capacity is not well developed in young children. A total score falling two standard deviations or more below the mean for the child's age is interpreted as evidence for residual PTA. Repeated administration of the COAT could show resolution of PTA over time, which corresponds to 24 hours or less in mTBI. During the resolution of PTA, cognitive performance is typically variable and often limited by fatigue and poor attention. Deferring more comprehensive neuropsychological assessment until after PTA resolves, postconcussion symptoms diminish, and the child returns home from the emergency center is advisable to obtain reliable data.

CONSIDERATIONS AND CONTROVERSIES

Despite significant advances in the field of pediatric mTBI, several important considerations and controversies remain, including a number related to clinical assessment and research methodology.

Complicated versus Uncomplicated mTBI in Children

As noted earlier, the results of CT are not typically considered in most definitions of mTBI, and variation exists across emergency centers in the clinical guidelines for obtaining CT in mTBI. However, estimates are that 14% of children with GCS scores of 13–15 show evidence of pathology on CT scans acquired within 24 hours after sustaining TBI associated with mild impairment of consciousness (Simon, Letourneau, Vitorino, & McCall, 2001). In a longitudinal study of cognitive recovery in 80 children ages 5–15 years who underwent CT within 24 hours of sustaining a TBI associated with mild impairment of consciousness, the data obtained on four occasions over the first 12 months were compared to 32 children with pathology on CT scan and 48 children with normal CT (Levin, Hanten, Roberson, Li, & Ewing-Cobbs, 2008). Evidence of slower or reduced recovery of episodic memory, resistance to cognitive interference, visual–motor speed, and academic achievement was apparent in the group of children whose mTBI was complicated by pathology on the CT scan. These authors proposed that presence of early CT abnormalities may indicate the need for follow-up examination and increase the risk for neurobehavioral sequelae of an otherwise mTBI.

Influence of Multiple or Repeat mTBI

Although multiple mTBI has not been a very popular research area among scholars, the prevalence and outcome of the condition beg for further interest and research. For example, Zemper (2005), in a large prospective cohort study that included a total of 15,304 football players age 18 years or less, reported that individuals with a concussion history were almost 6 times more likely to have another concussion and almost twice as likely to include loss of consciousness. In another study of collegiate football players, repeated head injuries were also associated with slower recovery (Guskiewicz, McCrea, Marshall, Cantu, & Randolph, 2003). For example, in this study, 30.3% of the participants with one previous concussion recovered in less than a day, whereas none of the patients with three or more previous concussion displayed such rapid recovery. Moreover, the recovery was prolonged (i.e., more than 7 days) for 30% of the patients with three or more previous concussions, whereas only 9% of patients with one previous concussion showed prolonged recovery. Whether children and adolescents demonstrate an increased vulnerability to subsequent injury, the degree to which this vulnerability changes over the developmental spectrum throughout childhood and adolescence, and alteration of the expected trajectory of recovery with repeat injury remain topics of controversy.

Some researchers investigating high school and collegiate athletes have reported that the level of cognitive impairment as a result of repeated mTBI is no different than cognitive impairment caused by a single mTBI (e.g., Broglio, Ferrara, Piland, Anderson, & Collie, 2006; Iverson, Brooks, Lovell, & Collins, 2006; Macciocchi, Barth, Littlefield, & Cantu, 2001). On the other hand, other studies report that a history of multiple previous concussions results not only in lingering consequences, as demonstrated in inferior performance on baseline preseason testing on a neuropsychological battery (e.g., Collins et al., 1999), but also in differences in on-field signs/symptoms, such as greater likelihood of loss of consciousness and confusion in high school athletes (Collins et al., 2002).

A recent meta-analysis by Belanger, Spiegel, and Vanderploeg (2009) aimed to measure the magnitude of cognitive impairment caused by multiple mTBI in athletes. They analyzed eight studies, all conducted with athletes, which involved 614 cases of multiple mTBI and 926 control cases of a single mTBI with no previous history. These two groups were evaluated across seven cognitive domains: attention, executive functioning, fluency, memory acquisition, delayed memory, motor abilities, and postconcussion symptom reporting. Although the overall effect on neuropsychological functioning was not significant, exploratory follow-up analyses showed that multiple mTBI was associated with deficits on measures of executive functioning and delayed memory, although the effect sizes were small (0.24 and 0.16, respectively). In general, this meta-analysis revealed that in studies to date, sustaining two or more mTBI has modest association with cognitive performance in only a few domains that may last several months after the most recent TBI.

Although it is intuitive that multiple mTBI should have greater adverse effect on cognitive functioning than a single mTBI, as reviewed above, the literature presents conflicting results. This discrepancy might be caused by the methodological variability among the studies (Macciocchi, Barth, & Littlefield, 1998), especially regarding age and postinjury time variables. Age at injury is important because age seems to have an effect on the recovery from mTBI (Field, Collins, Lovell, & Maroon, 2003). Additionally, *second-impact syndrome* is a commonly discussed postconcussion clinical sequela that is reported to occur when an athlete sustains a second head injury before fully recovering from the first head injury (Cantu, 1998), presumably from diffuse cerebral swelling that does not resolve prior to a second concussion. To date, this phenomenon has been observed mostly in children and teenagers. However, the existence of a second-impact syndrome has been a source of some controversy because of its rarity and the lack of closely spaced concussions in most observed cases (McCrory & Berkovic, 1998; Randolph, 2011). Diffuse cerebral swelling is also a well-documented phenomenon in the neurosurgical literature following a single minor brain trauma (Mandera, Wencel, Bazowski, & Krauze, 2000; Snoek, Minderhoud, & Wilmink, 1984).

Finally, potential methodological variability concerning the interval between recurrent concussions may affect results. For example, there plausibly may be a difference between sustaining consecutive traumas within a short time frame (i.e., within a single game) as opposed to over a longer time frame (i.e., months or years apart). However, the outcome of recurrent concussions with longer intervals and in children at specific developmental stages remains incompletely understood.

As noted, studies with human subjects cannot provide a clear picture of the outcome of repeated mTBI due to methodological constraints. Animal models, on the other hand, can shed light on this topic because animal studies lack some confounding variables that are associated with human subjects (see Obenaus et al., Chapter 4, and Babikian, DiFiori, & Giza, Chapter 5, this volume). For example, studies on adult animal models for repeated head traumas suggest that multiple concussions, compared to single concussion, result in impaired cognitive performance (e.g., Kanayama et al., 1996; Laurer et al., 2001). Taken together, the animal and human literature suggests that the effect of multiple mTBI, both in cognition and pathophysiology, appears more pronounced in patients with three or more concussions.

However, the literature review above indicates that conclusions regarding the effect of multiple mTBI on cognitive functioning are premature. Several reasons can be cited to direct scholarly attention to this topic. Distinct populations from different backgrounds sustain multiple mTBI regularly; it is of value to determine the consequences of repeated head trauma in each of these populations for implementation of intervention, which may lead to more effective rehabilitation. As noted above, the current literature on multiple head injuries is currently limited to sports-related injuries. Underprivileged populations, such as children with a history of abuse and prison inmates, are also subject to repeated head trauma. For example, a study by Diamond, Harzke, Magaletta, Cummins, and Frankowski (2007) reported that of the 998 prison inmates who were interviewed for the study, 82.8% reported having had one or more head injuries during their lifetime. Recurrent mTBI incidents have not yet been shown definitively to have an additive effect that can lead to cognitive deficits comparable to sequelae of more severe TBI. Although knowledge on repeated sports-related head injuries is increasing, we cannot safely argue that other sources of repeated head trauma (e.g., blast exposure, abuse) result in the same pathophysiology and related neurobehavioral phenotype. Given that the existing literature on the effects of multiple mTBI has yielded equivocal findings, it is important to identify the source of this variation for proper diagnosis, prognosis, and rehabilitation, particularly as it relates to infants, children, and adolescents.

Importance of Time Postinjury in Cognitive Symptom and Imaging Resolution in Acute mTBI

Despite widespread agreement that mTBI may be associated with initial neuropsychological problems and changes detectable on some forms of advanced imaging in *some* patients, disagreement continues about the frequency and relevance of these findings, even in the acute phase of recovery, as well as their persistence. Knowledge surrounding the time course underlying recovery also remains incomplete, as do the factors that may influence this pattern in any given child. The inconsistency in reported findings likely results from several factors, including the absence of a standard definition of mTBI and differences in selection criteria, sample characteristics, and methodology. Impaired attention, concentration, information-processing speed, and memory continue to be cited as the most common initial and persistent complaints following mTBI, with other common symptoms including headaches, dizziness, nausea, fatigue, and emotional problems such as impulsiveness and mood swings. We note that considerable variability exists in the frequency with which individuals with mTBI report postinjury complaints, and clearly further study is warranted.

Imaging studies of acute mTBI in children have also struggled to identify the direction, time course, and persistence of parenchymal, or brain tissue, changes associated with mTBI. For example, some researchers utilizing advanced modalities such as DTI with children and adolescents have reported initial increases in metrics such as fractional anisotropy and decreases in measures of mean diffusivity or apparent diffusion coefficient, which have been ascribed to cytotoxic edema or inflammation in the acute or subacute stage (Wilde et al., 2008; Wu et al., 2010). In contrast, others have reported an opposite pattern in DTI-related metrics in a subacute stage in adults with poor outcome (e.g., Messe et al., 2011). In addition to the direction of change, the persistence of these changes remains unknown, particularly in pediatric populations, and additional understanding of the pattern and time course of these changes is needed.

Outcome Measures

The question as to whether pediatric mTBI results in long-term deficits has been controversial, and study results have been mixed. Perhaps not surprisingly, comprehensive review articles on this topic have failed to conclusively resolve the issue (Beers, 1992; Boll & Barth, 1983; Carroll et al., 2004; Satz, 2001; Satz, Zaucha, McCleary, & Light, 1997), but they have served to highlight many of the shortcomings of work in this area. In addition to persistent problems, including the lack of a consistent definition of mTBI and the lack of agreement on appropriate groups to be used for comparison, numerous other factors that limit progress have been cited, such as wide age ranges of study samples, relatively short follow-up duration, narrow age ranges of instruments hampering longitudinal follow-up, fundamental differences in constructs of cognitive abilities over the developmental spectrum (e.g., executive function in a toddler vs. an adolescent), demonstrated validity of an instrument's use in TBI, and the sensitivity of some instruments (although standardized) in detecting impairment following mTBI in particular. Additionally, the sources of information regarding emotional/psychiatric features, cognition, and behavioral disturbance can greatly influence the quality and veridicality of the data. For example, how well can a very young child estimate and report his or her own level of fatigue or thinking more slowly, and so forth? Conversely, a parent may have difficulty accurately estimating the severity of his or her child's somatic and emotional symptoms, as these are purely subjective experiences that cannot be precisely assessed by an informant. Clinical lore suggests that parent and child reports often result in contradictory symptom pictures. Although it is beyond the scope of this chapter to address these issues, it is obvious that if persisting deficits indeed do occur following mTBI in some children and adolescents, the selection of the most appropriate outcome measures is paramount.

In an effort to advance the field of TBI more quickly, an interagency Common Data Elements (CDE) initiative was recently formed (Thurmond et al., 2010), and the TBI Outcomes Workgroup was charged with the task of selecting a set of instruments recommended for use in TBI (Wilde et al., 2010). However, the original CDE workgroup did not include measures appropriate for infants, children, and adolescents with TBI, so an additional set of measures was later selected to specifically address this gap (McCauley et al., 2012). The intent of the pediatric CDE is to present a starting point to stimulate further research and also to highlight the limitations of existing measures in certain domains, in order to lead to further test development. Newly developed measures may help to clarify the presence or absence of long-term deficits in infants, children, and adolescents with mTBI. At present, the CDE acknowledges the need for specific recommendations for mTBI, and additional work is planned. Further information on specific measures for the assessment of mTBI in children and adolescents is contained in chapters that follow.

Suboptimal Effort and Negative Impression Management

In mTBI literature in adults, consideration is often given to suboptimal effort and symptom exaggeration in the context of secondary gain, often related to litigation and financial compensation. However, in children, this issue has received much less attention, presumably due to the assumptions that youth are less capable of deception than adults and that examiners can readily detect suboptimal effort in youth.

Additionally, the role that external and psychological incentives may play in symptom report and performance on testing in youth has been assumed to be different than that of adults. Consequently, few studies in mTBI in children have specifically examined the role of effort validity.

Two recent studies have suggested that suboptimal effort may indeed require further consideration in both clinical practice and research, at least in children older than 8 years. Kirkwood and Kirk (2010) examined performance on the Medical Symptom Validity Test (MSVT) in 193 consecutively referred patients with mTBI, ages 8–17 years, and reported a base rate of suboptimal effort of 17%, based upon failure of at least one of the three primary effort indices of the MSVT. A comparison of the groups that passed versus failed the MSVT revealed no difference in gender, ethnicity/race, maternal education, history of premorbid learning disability, attention-deficit/hyperactivity disorder or reading problems, litigation status, time since injury, or whether the injury was associated with loss of consciousness or neuroimaging pathology. In a subsequent report that utilized a larger sample of approximately the same age range, 18.5% of the sample failed at least one of the three primary effort indices of the MSVT (Kirkwood, Yeates, Randolph, & Kirk, 2011). Again, the samples of children that failed versus passed symptom validity measures did not differ in terms of demographic variables, history of premorbid conditions, litigation status, or injury severity. The underlying reasons for suboptimal effort in children with mTBI may not be readily apparent, but the authors of the above studies indicate that factors may include both conscious and unconscious processes and attempts to obtain external gains (e.g., additional support at school) or to fulfill internal psychological needs (e.g., somatization). It is also possible that failure on symptom validity tests in children simply reflects noncompliance or other factors that increase performance variability.

Appropriate Comparison Groups in Pediatric mTBI Research

The question of the appropriate control group is important in the study of mTBI, and premorbid conditions and factors not directly related to injury must be carefully considered to gain a clear understanding of the consequences of mTBI (Asarnow et al., 1995; Bijur, Haslum, & Golding, 1990). Many recent studies of pediatric TBI have used children with orthopedic injuries as a comparison group. This approach derives from the impetus to control for confounds on measures of outcome by factors ancillary to brain injury, such as risk factors that predispose to injury (Stancin et al., 1998) or the psychological impact of trauma (Basson et al., 1991).

Risk factors for TBI can be broadly divided into personal and demographic characteristics of the injured person and general effects of the trauma experience. Among personal and demographic factors, socioeconomic status (SES), psychiatric status, race, gender, and family environment have been identified as relevant to TBI. For example, lower SES is associated with greater propensity for injury of any type (Collins, 1990), including TBI (Selassie, Pickelsimer, Frazier, & Ferguson, 2004; Yates, Williams, Harris, Round, & Jenkins, 2006), a pattern that has been ascribed to greater exposure to more physically demanding occupations, neighborhood violence, and less safe residences or vehicles (Hoofien, Vackil, Gilboa, & Donovick, 2003). In children with TBI, lower SES is associated with poorer psychosocial outcome (e.g., Taylor et al., 1999) and worse performance on tests of cognition (e.g., Hanten et al., 2009). Stancin et al. (1998) found that even among children with orthopedic injuries alone, preinjury family status predicted later parental and family distress. Thus, SES is an important variable to consider, both in studies of incidence and outcome of children with TBI and in the effect of injury on the family. Other demographic factors shown to influence incidence and outcome of TBI include gender and age, with older children having an advantage over younger children (depending on injury severity), and race, with African American or American Indian populations being more affected than European American (Bazarian et al., 2005; Rutland-Brown, Langlois, Thomas, & Xi, 2006).

Controlling for demographic variables, however, may not be sufficient to account for non-injury-related effects, especially on outcome research. Babikian et al. (2011) studied the outcome of three groups of children well matched on age, gender, race, and socioeconomic status: those with mild TBI (n = 124), other injuries not involving the head (n = 115), and a demographically comparable group of children without injuries (n = 145). On measures of memory, verbal learning, and executive function, the authors found that for five of the six variables on which there were differences between the mTBI group and the noninjury control group, the other-injury group also showed deficits, suggesting that the impairment observed in the TBI group could be due to the general effects of trauma, rather than to brain injury. Notably, however, the other-injury group had Abbreviated Injury Scale scores that were significantly higher than the mTBI group, and the mTBI was not verified or classified by neuroimaging data. Nonetheless, other studies of children who have experienced trauma and hospitalization have revealed effects of the experience that could potentially confound outcome measures of mTBI (Daviss et al., 2000).

Psychiatric status has been implicated as a factor in TBI research. For example, attention-deficit/hyperactivity disorder has been associated with the propensity to sustain injury (Bruce, Kirkland, & Waschbusch, 2007; Ozer, Gillani, Williams, & Hak, 2010; Schwebel & Gaines, 2007), including TBI (Gerring et al., 1998). On the other hand, studies have reported effects of depression (Han et al., 2011), anxiety (Max et al., 2011), and posttraumatic stress disorder (PTSD) on recovery after injury (Holbrook et al., 2005), which have been found to be related to quality of life. Daviss et al. (2000) reported that of 83 children hospitalized for trauma, 69% showed posttraumatic stress symptoms at baseline, and 59% at 6 months postinjury. In a study of children with mTBI, Hajek et al. (2010) found higher PTSD in orthopedically injured children at baseline, as compared to children with TBI, but did not find that symptoms persisted in either group. Literature linking PTSD to reading and academic achievement (Delaney-Black et al., 2002) highlights the importance of controlling for psychiatric variables when studying cognitive outcomes of TBI.

Although the consensus for a number of years has been that children with orthopedic injury are well matched to those with TBI on many of the above-mentioned factors, some evidence suggests that the risk factors may not equate between groups. Loder, Warschausky, Schwartz, Hensinger, and Greenfield (1995) investigated the relation of premorbid family environment and behavioral profiles of children who had sustained orthopedic trauma. They reported significantly higher rates of premorbid social problems and behavioral dysfunction in the orthopedically injured children than in the general population, although the direct comparison to children with TBI was not made.

Other studies also suggest that orthopedic injury groups may not be equitable (at least quantitatively) to children with TBI on some risk factors. For example, Basson et al. (1991) used a parent interview to assess behavior problems of children with TBI, children with general traumatic injuries (not involving the head), and children who had undergone emergency appendectomies. They found that the greatest behavioral change was experienced by the group of children with general trauma, which exceeded that of children with TBI. In contrast, none of the children with appendectomies met criteria for behavior change, suggesting that the experience of trauma itself may lead to behavior change, and that the propensity for behavior change may differ in children with orthopedic injuries (or general trauma) and children with TBI.

CONCLUSION

In many respects, the field of pediatric mTBI is still in its infancy, with less than a half century of research behind it. However, interest in this topic is rapidly increasing in both depth and breadth, and significant advances in understanding have emerged in the last 20 years. Nonetheless, significant unresolved issues remain regarding the classification and diagnostic criteria for mTBI, and these are particularly worthy of further consideration in infants and young children, where traditional assessment of signs and symptoms is difficult. Additionally, several existing and emerging controversies are apparent in current research related to the use of an appropriate control group; the impact of repeat mTBI in terms of increased vulnerability to subsequent injury; the existence and selection of appropriate outcome measures for use mTBI with infants and children who have sustained mTBI; the assessment of suboptimal effort in children; and the magnitude, direction, and persistence of change on imaging-related indices and measures of symptoms and cognitive performance, particularly in the acute or subacute period.

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