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Neuropsychiatry of Pediatric Traumatic Brain Injury

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Synopsis

Pediatric traumatic brain injury (TBI) is a major public health problem. Psychiatric disorders with onset before the injury appear to be more common than population base rates. Novel (postinjury onset) psychiatric disorders (NPD) are also common and complicate child function after injury. Novel disorders include personality change due to TBI, secondary attention-deficit/hyperactivity disorder (SADHD), as well as other disruptive behavior disorders, and internalizing disorders. This article reviews preinjury psychiatric disorders as well as biopsychosocial risk factors and treatments for NPD.

Keywords

pediatric traumatic brain injury; novel psychiatric disorder; risk factors; treatment; review; brain imaging

Introduction

It is incumbent upon health practitioners including mental health practitioners to be familiar with the body of knowledge that is the “neuropsychiatry of pediatric traumatic brain injury.” This requirement is because of practical and theoretical concerns. The principal practical issue is related to the enormous independent and overlapping public health significance of pediatric traumatic brain injury (TBI) and psychiatric disorders. The primary theoretical importance relates to understanding brain-behavior relationships within a developmental biopsychosocial model of psychiatric disorder.

Epidemiology

Pediatric TBI is a major public health problem with an annual incidence of 400/100,000 accounting for an important cause of death and disability in the United States [1]. The male-to-female incidence rate ratio is approximately 1.8:1 and higher (2.2:1) in children aged 5-14. The incidence in males and females is similar in children aged 1-5 years (160 per 100,000 population), but then increases at a higher rate in males. Brain injury rates increase for males and decrease for females in late childhood and adolescence. Higher incidence rates are significantly related to median family income even when age and/or race/ethnicity is controlled [2]. The proportion of brain injury caused by motor vehicle-related accidents increases with age from 20% in 0-4 year old children, up to 66% in adolescents [3]. Bicycle-

related or pedestrian injuries more likely affect younger children while injury in adolescents is more often linked with motor vehicle accidents. Mechanism of injury in almost half of cases of infant, toddler, and young child TBI is related to assaults or child abuse, and falls. The distribution of brain injury by severity, ranges between 5-8% for severe, 7-8% for moderate, and 80-90% for mild brain injury.

Pathophysiology

Focal injuries including intracerebral, subdural, and epidural hematomas occur with a lower incidence in children (15%-20%) versus adults (30%-42%). The frequency of focal lesions occurs in a rostro-caudal rostro-caudal gradient. There is a higher frequency of children with lesions in the frontal lobe white matter, orbitofrontal region (orbital gyrus, gyrus rectus, and inferior frontal gyrus), and dorsolateral frontal region (middle and superior frontal gyri); a few lesions in the anterior temporal lobe; and isolated lesions in more posterior areas [4]. Skull fractures are evident in about 5%-25% of children and are less commonly associated with epidural hematomas (40%) versus adults (61%). Diffuse injury and cerebral swelling resulting in intracranial hypertension is more common in children than adults. The principal neuropathologic findings of a diffuse injury in children are diffuse axonal injury and/or vascular injury. Reviews of advances and challenges in the understanding of the pathophysiology of pediatric TBI as well as initial assessment, management, and treatment of pediatric TBI are available [5, 6]. Recognition and treatment of potential medical complications such as hypotension, hypoxemia, raised intracranial pressure, delirium, seizures, paresis, peripheral neuropathy, musculo-skeletal problems, and endocrine disorders are important to decrease morbidity.

Evaluation

The typical presentation of a child or adolescent with TBI to a mental health professional occurs at a variable amount of time after the injury. This, by necessity, requires a retrospective accounting of preinjury status and postinjury course of the presenting psychiatric syndrome. Asarnow et al. [7] have provided a useful template for thinking about determinates of behavioral syndromes in children and adolescents with TBI. The pathways to behavioral issues include the following. a) The behavior problem antedates the injury and may contribute to the risk for incurring the injury; b) a preexisting behavior problem is exacerbated by the brain injury; c) the behavior problem is a direct (biological) effect of a brain injury; d) the behavior problem is an immediate secondary effect of the injury (e.g., an emotional response to the accident, such as PTSD); e) the behavior problem is a long-term secondary effect of the injury (e.g., the conduct problems and decreased motivation from frustration produced by the cognitive impairments caused by brain injury); f) the behavior problems are caused by factors other than the injury.

As clinicians, our ability to make rational decisions in cases of pediatric TBI is enhanced by familiarity with the relevant scientific database on psychiatric disorders and their risk factors. The following review deals sequentially with methodological considerations, preinjury psychiatric status, and new-onset (postinjury) psychiatric disorders.

Methodological Concerns—There are only four published prospective studies of consecutive hospital admissions of children and adolescents with TBI in which standardized psychiatric interviews were used to assess psychopathology [8-11]; and only two of these studies had injured control children [8, 11, 12]. This small literature is complemented by a larger corpus that addresses postinjury behavioral changes reported by parents and teachers typically by questionnaires which tend not to be specific for the generating of psychiatric diagnoses or psychiatric treatment plans [13-17]. Most studies with rare exceptions [18]

exclude children with a history of non-accidental injury. Therefore this review refers only to accidental injury.

Preinjury Psychiatric Status—Prospective psychiatric TBI studies which have used standardized psychiatric interviews found that between one third and one half of children had a preinjury lifetime psychiatric disorder [8-11]. The finding that children who have a TBI are on average more behaviorally affected before their injury is supported by epidemiological data from a birth cohort with data points at age 5 and at age 10 [19]. Children who went on to sustain injuries (including mild TBI, lacerations, and burns) between age 5 and 10 had more behavioral problems, particularly aggression, before their injuries compared with uninjured children. One explanation for these findings involves a higher risk of injury in children with high impulsivity and risk-taking behaviors corresponding with diagnoses of externalizing disorders such as ADHD [20] in the absence of known preinjury brain damage.

Postinjury Psychiatric Status—The term novel psychiatric disorder (NPD) refers to two possible scenarios. In the first, a child who is free of preinjury lifetime psychiatric disorders may manifest a psychiatric disorder after injury. In the second, a child with a lifetime preinjury psychiatric disorder may develop a psychiatric disorder that was not present before the TBI. NPDs are heterogeneous, a fact that is not surprising given that the forces related to each injury and the eventual precise patterns of brain damage are different in each case. The categorical classification (NPD versus no NPD) reflects functional outcome in children and informs us about risk factors for psychiatric disorder in this population. However, research on the phenomenology and risk factors of specific NPDs or specific clusters of postinjury psychiatric symptoms is more useful both for the clinician who needs to tackle specific target symptoms and for the neuroscientist who seeks to understand brain-behavior relationships that may be applicable to both injured and non-injured children.

Novel Psychiatric Disorder (NPD)—NPDs recorded approximately 24 months after severe TBI has been present in 54% to 63% of children, and following mild/moderate TBI in 10% to 21% of children, and following orthopedic injury in 4% to 14% of children [8, 21, 22]. A recent study found that NPD was related to a lower fractional anisotropy in bilateral frontal and temporal lobes, bilateral centrum semiovale, and bilateral uncinate fasciculi [12]. In other studies, depending on time since injury, predictors of NPD have included severity of injury, preinjury psychiatric disorders, socioeconomic status/preinjury intellectual function, preinjury adaptive function, preinjury family function, and family psychiatric history [8, 22].

In recent years there has been a greater public awareness of pediatric mild TBI especially its overlap with sports concussion. Depending on study design, the rate of NPD in children with mild TBI varies from 10-100% [8, 21, 23-26]. However, in studies limited to consecutively treated children with mild TBI the range is narrower (10-40%) with larger studies generally finding higher rates. The rate at which children with mild TBI versus injured controls developed NPD was similar in one study [8] and higher, although not significantly so, in other small underpowered studies [21, 27]. In studies of TBI compared with uninjured controls, children with mild TBI had non-significantly higher [28], marginally higher [24], or significantly higher [23, 29] rates of NPD in four studies. Studies suggest that children with mild/moderate or mild TBI were at significantly higher risk for developing new-onset psychiatric disorder or an increase in post-concussion symptoms respectively in the first 3 months after injury if they had a preinjury psychiatric disorder or poorer preinjury behavioral adjustment [9, 30]. Children with mild TBI are more likely than orthopedic injured controls to demonstrate transient or persistent increases in post-concussive

symptoms in the first 12 months after injury especially if the injury was more serious [15, 31]. Post-concussive symptoms were unrelated to the apolipoprotein epsilon 4 allele [32]. The families of mild TBI children experienced more distress and burden than the families of orthopedic control children and this was closely linked with post-concussive symptoms [33].

The links between family function and psychiatric and/or behavioral function in children with mild to severe TBI are close. Typically family outcome is associated with lower preinjury family function, presence of NPD, more stressors and use of fewer sources of support [33-39].

Specific Psychiatric Disorders/Symptom Clusters—In this section findings related to specific NPDs are reviewed. Table 1 provides a summary of lesion-behavior correlates for NPDs and postinjury symptom clusters.

Personality change due to traumatic brain injury: The most common NPD after severe TBI is Personality change due to TBI (PC) [40, 41]. It cannot be overemphasized that PC is not a personality disorder. The diagnosis is made in the context of clinically significant symptoms of affective instability, aggression, disinhibited behavior, apathy, or paranoia reasonably judged to be caused by the injury. The Neuropsychiatric Rating Schedule (NPRS) [42] can reliably and validly guide the clinician to justify a diagnosis of PC. Approximately 40% of consecutively hospitalized severe TBI children had ongoing persistent PC an average of two years postinjury [40]. An additional approximately 20% had a history of a remitted and more transient PC. PC occurred in 5% of mild/moderate TBI but was always transient. The affective instability, aggressive, and disinhibited subtypes are common whereas the apathetic and paranoid subtypes are not common [40, 41]. Severity of injury is a significant predictor of PC in the first 2 years after TBI [10, 40, 41, 43]. More specifically, PC is associated with superior frontal gyrus lesions in the first year [10, 43]. This lesion correlate is consistent with prevailing models of affective regulation implicating the dorsal prefrontal cortex [44]. In the second postinjury year, PC was significantly associated with frontal white matter lesions and preinjury adaptive function [43]. This suggests that while affective regulation problems, associated initially with superior frontal lesions, decrease as other cortical areas subsume this function, subcortical network damage (lesioned white matter tracts) limits eventual recovery. For purposes of explanation, we might contemplate a mechanistic computer analogy. The analogy, in which a mother-board (representing cortex) and a wired network (representing a white matter network), would posit acceptable performance (appropriate affective regulation) with a mother-board replacement if that were the problem but not if the network itself was damaged. Furthermore, these findings suggest that similar to the idea of preinjury cognitive reserve [45], preinjury functional reserve such as higher preinjury adaptive function, predicts whether a child will have PC persisting through the second postinjury year. The later emergence of preinjury adaptive function as a correlate of PC can be understood through the metaphor of TBI as an “avalanche” and the individual as a structure that is covered over by the “avalanche.” If the structure is covered over but not destroyed by the snow, then with the passage of time and the melting of the snow pack, the tallest structures (i.e., higher premorbid function) would emerge (restore function) earlier. If the structure was destroyed then whatever factors led originally to the structure being among the tallest (e.g., genetics to environmental influences) would be operational in rebuilding the structure quickest. PC is also associated with a concurrent diagnosis of secondary attention deficit hyperactivity disorder, adaptive and intellectual functioning decrements, but not related to any psychosocial adversity variables [40]. PC tends to be the most debilitating psychiatric syndrome even when comorbid with other NPDs such as attention-deficit/hyperactivity disorder (ADHD) or oppositional defiant disorder (ODD).

Vignette 1: An 11 year old male with a severe TBI with preinjury ADHD and ODD had clinically significant moderate irritability (not caused by brain damage) before the injury. After the injury and for 12 months, he experienced significant worsening of his irritability. There were no major psychosocial stressors and his academic program was well suited to his abilities. A significant component of his affective instability was attributed to brain injury and therefore he was diagnosed with PC, affective instability subtype.

Secondary attention-deficit/hyperactivity disorder: Secondary attention-deficit/ hyperactivity disorder (SADHD) refers to ADHD that develops after TBI. The phenomenology of SADHD includes all ADHD subtypes [46]. SADHD is related to increasing severity of injury and intellectual function, memory, and adaptive function deficits as well as family dysfunction in samples of mild to severe TBI. When study cohorts are limited to severe or to severe/moderate TBI, adaptive deficits are still evident but findings regarding intellectual function outcome are mixed [20, 47]. Poorer preinjury family function and greater premorbid psychosocial adversity is associated with postinjury ADHD symptoms and SADHD [20, 48, 49]. Brain correlates of SADHD include right putamen or thalamic lesions [50, 51], and orbital frontal gyrus lesions [46]. These anatomical findings suggest that lesions in varied locations along specific cortico-striatal-pallidal-thalamic loops may generate a clinical syndrome of SADHD. Neurocognitive studies of SADHD compared with phenotypically-overlapping developmental ADHD have been reported but it is too early to reach definitive conclusions regarding their similarities and differences [49, 52-56] .

Vignette 2: Two Cases of SADHD and School Failure

- **a.** A 12-year old male with a severe TBI developed SADHD and significant problems with pragmatics of communication. Regulation of anger and sadness was unremarkable. Six months postinjury he was challenged more at school and fell behind his class. He experienced irritability, anger, and sadness and a diagnosis of an adjustment disorder with mixed emotional features was made. The clinician's formulation was that his affective instability was an indirect result of his TBI i.e. cognitive challenges led ultimately to school failure and his response included irritability and sadness.
- **b.** A 13-year old male with a severe TBI developed SADHD and significant challenges with pragmatics of communication. He was diagnosed with PC, affective instability subtype because regulation of anger and sadness was impaired in the hospital and persisted throughout the first year after the TBI. Six months postinjury he was challenged more at school and fell behind his class. He became even more irritable and sad but did not meet criteria for a major depression. The clinician's formulation was that his affective instability was a direct result of his TBI i.e. poor mood regulation and cognitive problems led to school failure and reduced his teacher's effectiveness in working with him.

Oppositional defiant disorder/Conduct Disorder: New-onset ODD and conduct disorder (CD) were reported respectively to occur in 9% and 8% of youth followed for 1 year after admission to a rehabilitation center [57]. The disorders/symptoms were associated with preinjury psychosocial adversity and concurrent symptoms of emotional lability. Similarly, in a consecutively hospitalized sample of mild-severe TBI, ODD symptoms in the first 12-months after TBI was related to social class, preinjury family function, and preinjury ODD symptomatology [58]. Greater severity of TBI predicted ODD symptoms two years after injury. Socioeconomic status influenced change (from before TBI) in ODD symptoms at 6, 12, and 24 months after TBI. Only at two years after injury was severity of injury a predictor of change in ODD symptoms. A report from a brain injury clinic sample showed that children who developed novel ODD/Conduct Disorder, when compared to children without

a lifetime history of the disorder, had significantly more family dysfunction, showed a trend toward a family history of alcohol dependence/abuse and suffered a milder TBI [59]. None of the studies of novel ODD/Conduct Disorder had orthopedic injury controls.

Post-traumatic stress disorder: Post-traumatic stress disorder (PTSD) and sub-syndromal posttraumatic stress disturbances occur despite neurogenic amnesia. Rates of novel PTSD range from 4%-13% although the presence of PTSD symptoms are relatively common (68%) in the first weeks after injury and decline (12%) by 2-years postinjury [60, 61]. Studies have shown significant predictors and/or correlates of PTSD symptomatology to include preinjury mood or anxiety disorder/symptoms, greater injury severity, female gender, early postinjury anxiety and depression symptoms, preinjury psychosocial adversity, and non-anxiety psychiatric diagnoses [60-62]. An imaging study found the PTSD criterion for “re-experiencing” was associated with a lower “lesion fraction” (volumetric fraction of a pre-defined atlas structure that overlapped with the participant's lesion) in the right limbic area, specifically the cingulum and hippocampus. The right limbic region is frequently activated in functional imaging studies of re-experiencing symptoms in PTSD [63]. In addition, PTSD hyperarousal symptoms were associated with left temporal lesions and absence of left orbitofrontal lesions [64].

Vignette 3: A 16-year old female was struck on the right temporal area by a discus thrown by a peer from 30 feet away. She experienced about 10 seconds of loss of consciousness and was seen in the emergency room and discharged. Imaging studies including an MRI 18-months postinjury were normal. Over the course of a few weeks she developed a fear of “flying objects” which expanded to include not only a discus but any ball kicked or thrown on a sports field and became fearful that the vehicle in which she was travelling would be hit by another vehicle. These fears were associated with a full range of PTSD re-experiencing symptoms, avoidance behaviors, and increased arousal. She developed a major depressive disorder with no suicidality. She was irritable but this seemed consistent with and fully accounted for by PTSD and major depression and therefore PC, affective instability subtype was not diagnosed. Only with intense effort was she able to maintain her preinjury grades and she had a full range of inattentive symptomatology and met criteria for a provisional diagnosis of ADHD, inattentive type. The diagnosis was provisional because it was unclear whether her inattention could be completely explained by her PTSD and major depression diagnoses. She also developed daily headaches which were partially responsive to low dose amitryptiline. She had a first-degree relative with panic disorder. She presented for treatment 18-months postinjury and responded well to cognitive behavioral therapy and a selective serotonin reuptake inhibitor (SSRI) but had to be strongly encouraged to expose herself to feared situations including driving. She did not require treatment for ADHD because symptoms resolved entirely with her treatment for PTSD and major depression.

Other Anxiety Disorders: Novel obsessive compulsive disorder occurs following TBI in adolescence [65, 66]. Frontal and temporal lobe lesions can precipitate the syndrome in the absence of obvious striatal injury [66]. New onset of obsessions are associated with female gender, psychosocial adversity, and mesial frontal and temporal lesions [67]. A wide variety of other anxiety disorders have been documented after childhood TBI. These include overanxious disorder, specific phobia, separation anxiety disorder, and avoidant disorder [9, 21, 22]. Preinjury anxiety symptoms and younger age at injury correlated positively with postinjury anxiety symptoms [65]. Furthermore, severity of brain injury and postinjury level of stress have been associated with mood/anxiety disorders [27]. Lesions of the superior frontal gyrus were significantly associated with postinjury anxiety symptoms [68] while orbitofrontal lesions were associated with fewer anxiety symptoms [64].

Mania/Hypomania: There are several published case reports on the development of mania or hypomania after childhood TBI [69]. Four of 50 children (8%) from a prospective study of consecutive children hospitalized following TBI developed mania or hypomania [70]. The phenomenology regarding the overlapping diagnoses of mania, PC, and ADHD must be considered in differential diagnosis [40]. Greater severity of injury, frontal and temporal lobe lesions, and family history of mood disorder may be implicated in the etiology of mania/hypomania secondary to TBI. Long lasting episodes and similar frequency of irritability and elation may be typical [70].

Depressive Disorders: In a retrospective psychiatric interview study [21] 1/4 of severe TBI children had an ongoing depressive disorder and 1/3 of the children had a depressive disorder at some point after the injury. TBI increased the risk of depressive *symptoms* especially among more socially disadvantaged children, and the depressive symptoms were weakly related to postinjury neurocognitive performance [71]. New-onset depression including disorders with no comorbid new anxiety disorder (non-anxious depression) and disorders with a comorbid new anxiety disorder (anxious depression) was related to left sided and right sided lesions and older age at injury compared with children who did not develop depression. Non-anxious depression was associated with left hemisphere lesions specifically in the left inferior frontal gyrus and temporal tip while anxious depression was associated with right hemisphere lesions specifically in the right frontal lobe white matter and also left parietal lobe lesions [72]. The association of non-anxious depression with left lesions and anxious depression predominantly with right lesions is similar to adult TBI findings [73]. Anxious depression was also associated with PC and a family history of anxiety disorder [72].

Psychosis and Autism: There have been only 2 cases of new-onset non-affective psychosis reported in 6 studies of consecutive admissions of children with TBI that used standardized psychiatric interviews [8, 11, 21, 22, 28, 43]. However, there has been interest in the possibility that early TBI increases the risk of psychosis in adult life [74, 75]. Autism after childhood TBI has not been described although other forms of brain injury have been implicated in the new-onset of autism in childhood, e.g., brain tumors [76]. It is important for clinicians to differentiate autism from qualitatively different disturbances of pragmatic communication and social communication that can be complications of severe TBI in young children [77, 78].

Treatment

Non-Pharmacologic Treatment Strategies

School: Academic functioning at school corresponds to occupational functioning for adults. Children, especially those with more serious TBI, are the beneficiaries of mandated services under the Individuals with Disabilities Education Act. Special education services target poor academic function related to 1) skill deficits in arithmetic, spelling, and reading; 2) emotional and behavioral disorders; or 3) a combination of the above with or without underlying difficulties of preinjury developmental learning problems in some children. For a more in-depth review of educational and related neuropsychological aspects of pediatric TBI the reader is referred to other references [79, 80].

Family-based treatment: One research laboratory is producing a growing body of pediatric TBI literature including randomized controls trials involving web-based family and teen problem-solving psychological therapies targeting behavioral problems rather than specific psychiatric disorders [81-86]. The research team's most recent therapeutic refinement is termed counselor-assisted problem solving (CAPS) which is a 6-month web-based, family-centered intervention that focusses on problem solving, communication, and self-regulation

[82]. After an initial in-person session with a therapist, follow up sessions with the therapist are conducted via Skype. These sessions proceed according to a pre-arranged standard plan with specific content and the treatment program is flexible in that supplementary sessions may be provided with content designed to address particular residual problems and needs of each family. Furthermore, the CAPS treatment arm provides access to a CAPS website which has self-directed didactic content regarding problem-solving skills, video clips modeling these skills, and exercises to practice the skills. The control group in the studies is an internet resource comparison (IRC) which involves the family and/or teen having access to key websites that provide self-directed didactic information about brain injury as well as modules about problem-solving around common issues, working with schools, and managing stress [82]. Among the positive results reported for CAPS is an improvement in parent-rated behavioral executive functioning in their children [82], an effect that is greater in the context of lower verbal intelligence of the children [81]. Furthermore, among older adolescents, CAPS was associated with greater improvement in multiple dimensions of externalizing behavior problems compared with IRC. The same research team earlier published on a treatment called Teen Online Problem Solving (TOPS) that appears to be closely related to CAPS. TOPS relative to IRC has been effective in improving problem-solving and depressive symptoms in parents, especially those with lower incomes [85]. TOPS resulted in improvement in parent-teen conflict generally and in parent and self-reported teen behavior problems particularly in adolescents with severe TBI [84].

Other approaches to treatment include cognitive behavioral therapy and restructuring the child's environment to maximize behavioral supports [80]. In addition, training parents to be more effective advocates for the child within the school system can be helpful [87].

Pharmacotherapies—The reader is referred to a recent comprehensive, albeit a bleak, review of neuropharmacology of pediatric brain injury [88]. In contrast to the promising developments in non-pharmacologic treatment strategies, that review concludes that evidence supporting the “off label” use of numerous agents for children with TBI is limited to nonexistent.

Personality change due to TBI – labile and aggressive subtypes: In the absence of treatment studies of children with PC, the following anecdotal guidelines are offered. The labile and aggressive types frequently co-occur [41] and respond similarly to treatment. Mood stabilizing anticonvulsants such as carbamezepine and valproic acid can be effective when combined with a behavior modification program targeting aggressive behavior. The addition of an SSRI can yield additional benefit.

Personality change due to TBI – disinhibited, paranoid, apathetic subtypes: The “disinhibited” subtype is very difficult to treat pharmacologically or behaviorally. The paranoid subtype is rare. Use of neuroleptic medication such as ziprasidone may be helpful in the acute hospitalization or rehabilitation unit if the child or adolescent is agitated or paranoid and the symptoms are impeding compliance with treatment regimens [89]. The potential risks from neuroleptics with regard to aberrations in neuronal recovery have been described in animal models [90]. The rare apathetic subtype may respond to stimulant medication or SSRIs.

There may be episodes when the child has intense lability, aggression, hyperactivity, and inattention, and meets criteria for overlapping syndromes of PC, mania or hypomania, and ADHD [9]. Mood stabilizers may help and stimulants should not necessarily be considered contra-indicated [91].

ADHD: Several reports of stimulants administered to children with TBI who have attention and concentration deficits show positive results although the data are mixed [92]. Anecdotal evidence from the author's practice suggests that children diagnosed with SADHD respond to stimulant medication. There have been no studies of bupropion or tricyclic antidepressant medication for SADHD. The use of bupropion is avoided because of the risk of seizures. Caution should be observed when prescribing the tricyclic antidepressants because of cardiac conduction side-effects.

Depression: There are no treatment studies of depressive disorders after pediatric TBI. Clinical experience suggests SSRIs are effective [93].

Emerging Treatment Approaches—Pharmacological research has been impeded by the difficulty in identifying and enrolling a sufficient number of children and adolescents with TBI with the same NPD at any single research site. Multicenter collaborations exemplified by the methodology of the Children's Oncology Group has been suggested to address the problem [88]. Expansion of the mission of existing research units in pediatric psychopharmacology (RUPP) to include multisite medication trials related to NPDs would rapidly advance our knowledge base. A related potential solution to this challenge has been initiated by means of a single patient trial (SPT)-published protocol across multiple sites for stimulant treatment for SADHD [94].

Advances in psychotherapy research for children and adolescents with TBI will include testing of treatment modalities that have been proven effective for behavioral, emotional, or family problems in uninjured populations. An example of an established treatment that may emerge as a treatment for a TBI cohort includes parent-child interaction therapy (PCIT) [95].

By far the most important ongoing and emerging intervention strategies involve prevention of injury. Education with regard to the use of bicycle helmets, enhancing motor vehicle safety, decreasing alcohol-related motor vehicle accidents, and decreasing the risk of child abuse and neglect are some of the methods to prevent or attenuate the morbidity caused by pediatric TBI [96].

Conclusions

Pediatric TBI is a major public health problem. The psychiatrist has a central role in working with affected children and adolescents because psychiatric disorders are common both preinjury and postinjury. There is a close relationship between psychiatric disorders and family function. Novel psychiatric disorders are associated with specific injury and psychosocial variables, including family dysfunction, which can be measured soon after injury. This allows for the potential recognition of children who are at high risk for psychiatric problems before they emerge. The categorization of behavioral complications of TBI into psychiatric syndromes permits a logical pharmacological and psychological treatment approach. Pharmacological research for novel psychiatric disorders is negligible while psychotherapy research is showing promise in the treatment of common domains of behavior such as self-regulation, communication, and aspects of family function but not specifically for novel psychiatric disorders. Cognitive function impairments complicate school re-entry and limit educational achievement. When cognitive function deficits are associated with psychiatric problems management is particularly challenging. Additional biological research e.g., with gene expression methodology, advanced imaging modalities such as magneto-encephalography and diffusion spectrum imaging as well as psychosocial research on injury risk and psychiatric outcome is necessary for promotion of effective primary and secondary prevention of behavioral morbidity.

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Acronyms

TBI	traumatic brain injury
NPD	Novel psychiatric disorders
SADHD	secondary attention-deficit/hyperactivity disorder
PC	Personality change
NPRS	Neuropsychiatric Rating Schedule
ADHD	attention-deficit/hyperactivity disorder
ODD	oppositional defiant disorder
CD	
PTSD	Post-traumatic stress disorder
SSRI	selective serotonin reuptake inhibitor
CAPS	counselor-assisted problem solving
internet	resource comparison
TOPS	Teen online problem solving
RUPPS	research units in pediatric psychopharmacology
SPT	single patient trial
PCIT	Parent-child interaction therapy

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Key Points

1. Pediatric traumatic brain injury (TBI) is a major public health problem.
2. Psychiatric disorders with onset before the injury appear to be more common than population base rates.
3. Novel (postinjury onset) psychiatric disorders (NPD) are also common and complicate child function after injury.
4. Novel disorders include personality change due to TBI, secondary attention-deficit/hyperactivity disorder (SADHD), as well as other disruptive behavior disorders, and internalizing disorders.

Table 1

Lesion-Psychiatric Correlates after Pediatric TBI

Disorder	Lesion Correlate (timing of outcome)	Source
Novel Psychiatric Disorder	Lower fractional anisotropy in bilateral frontal, temporal lobes, uncinate fasiculi, centrum semiovale (3 months)	[12]
Personality Change due to TBI	Superior frontal gyrus (6 and 12 months)	[10, 43]
	Frontal white matter (24 months)	[43]
ADHD	Right putamen, thalamus (12 months)	[20, 51]
	Orbital frontal gyrus (6 months)	[46]
PTSD (re-experiencing criterion)	Right limbic area (including cingulum, hippocampus) lower lesion fraction (12 months)	[63]
PTSD (hyperarousal symptoms)	Left temporal lesions and lower frequency of orbitofrontal lesions (12 months)	[64]
Obsessions	Mesial prefrontal and temporal (12 months)	[67]
Obsessive Compulsive Disorder	Frontal and temporal lobe (3-9 months)	[66]
Anxiety Disorder/subclinical anxiety disorder	Superior frontal gyrus (6 months) Lower frequency of orbitofrontal lesions (12 months)	[64, 68]
Non-Anxious Depressive Disorder/subclinical depressive disorder	Left inferior frontal gyrus and left temporal tip (6 months)	[72]
Anxious Depressive disorder/subclinical depressive disorder	Right frontal lobe white matter and left parietal lobe (6 months)	[72]
Mania/Hypomania	Frontal lobe and temporal lobe (3-24 months)	[70]