ERABI EVIDENCE-BASED REVIEW of moderate to severe ACQUIRED BRAIN INJURY

Clinical Guidebook

4. Pediatric Acquired Brain Injury Acute Care and Rehabilitation Interventions

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Pediatric Acquired Brain Injury Interventions

By the end of this chapter you should:

- Know the pharmacological and non-pharmacological, acute and rehabilitation interventions available to treat children and adolescents post injury.
- Be familiar with outcome measures available for a pediatric acquired brain injury population.
- Be able to identify the signs of non-accidental injury.

4.1 Introduction

Acquired brain injury (ABI) consists of both traumatic and non-traumatic causes that occur outside of the neonatal period. Traumatic brain injury (TBI) is the most common cause of interruption in normal child development and the leading cause of death in North America in those under the age of 19 (Guice et al., 2007; Kan et al., 2006; Kraus et al., 1990; Schunk & Schutzman, 2012). Common causes of TBI include falls, motor vehicle collision, bike related injuries, sporting injuries, and acts of violence (Schunk & Schutzman, 2012). In very young children, non-accidental injury (NAI; previously Shaken Baby Syndrome) is a frequent cause of injury. The worldwide incidence of pediatric TBI ranges from 12 to 486 children per 100,000 (Dewan et al., 2016).

While less common than TBI, non-traumatic brain injuries (nTBIs) still place a large burden on the healthcare system. Causes of non-traumatic brain injuries include, metabolic disturbances, anoxia, infections (encephalitis; meningitis), vascular and autoimmune disorders. In Ontario, Canada, between 2003 and 2010, 17,977 nTBIs requiring care were reported in patients under 19 years, with those 0-4 years and 15-19 years of age most affected (Chan et al., 2016).

The severity of a brain injury, often determined by Glasgow Coma Scale (GCS) score, is categorized as mild (GCS 13-15), moderate (GCS 9-12) or severe (GCS ≤8). The vast majority (90%) of children who sustain a TBI have mild brain injuries (Araki et al., 2017), with the symptoms resolving typically within days or weeks. Children with moderate to severe injuries often experience neurocognitive impairments, challenges with learning new information, deficits in executive function and psychosocial problems. Children who sustain diffuse injuries such as a traumatic injury, are most at-risk for disruption to typical development. Challenges may present at different developmental time points over the course of childhood.

There is a lack of high quality interventional studies being conducted for the pediatric brain injury population and very few clinical practice guideline recommendations are based on strong or moderate research evidence (Knight et al., 2019). Existing guidelines are primarily focused on general principles and service structure/organization (Knight et al., 2019). Given the heterogeneity within the pediatric ABI population, the influence of the developmental profile of the child at time of injury and the influence of family context, generalizing study findings can be a challenge. Moreover, the extrapolation of findings from adult studies needs to be done with great caution. The developmental age of a child in addition to their chronological age, should always be considered when planning interventions.

The purpose of this guideline chapter is to serve as a learning resource for residents and medical students. The content is based on available pediatric research literature, clinical guidelines and other clinical resources. Some key studies have been included within this chapter; however, study extractions for all pediatric ABI interventions meeting ERABI criteria can be found in the online module. The focus is primarily

on moderate to severe TBI. The Guidebook is not intended to be a prescriptive or exhaustive list of treatment options. Clinical judgment should always be used when deciding the best course of treatment for a patient. We encourage the reader to access and read the resources referenced, as well as the clinical guidelines cited, in more detail.

Click here to access the full ERABI Module for Pediatric Acute and Rehabilitation Interventions

4.2 Clinical Presentation

The Ontario Brain Injury Association defines ABI as, ***damage to the brain that occurs after birth from a traumatic or non-traumatic event but is not related to congenital disorders or degenerative disease.*** A head injury can also be described as focal/localized or diffuse. Focal injury means a specific location was damaged, such as with a stroke where a particular vascular territory is affected. Diffuse injury can occur with significant impact, often with acceleration/deceleration forces as well as from cerebral edema and pressure effects.

Primary and Secondary Injury. A head injury is often described with respect to primary and secondary injury. When a trauma occurs the primary injury may involve skull fracture, contusions, concussions, lacerations or diffuse axonal injury. Types of secondary injury are described in Table 1.

> ***Primary Injury:*** *"mechanical damage sustained immediately at the time of trauma from direct impact, or from shear forces when the gray matter and white matter move at different speeds during deceleration or acceleration" (p.400)(Schunk & Schutzman, 2012).*
>
> ***Secondary Injury:*** *"ongoing derangement to neuronal cells not initially injured during the traumatic event" (p.400) (Schunk & Schutzman, 2012). Occurs as an indirect result of the primary injury.*

Table 1. Secondary Mechanisms of Injury

Secondary Definition	Explanation
Cerebral Edema	Swelling of the brain
Ischemia	Inadequate blood flow
Hypoxia	Insufficient amounts of oxygen supplied to the brain
Hemorrhage or Hematoma	Bleeding or development of blood clots
Raised Intracranial Pressure	Increased pressure within the skull

Clinical Manifestations of an ABI. A child may present with seizures, speech problems, confusion, headache, vomiting, blurred vision, or an impaired level of consciousness. In infants, signs can include irritability, poor feeding and somnolence. Clinical sequelae of a brain injury can be broad and impact many aspects of a childs' life (Figure 1).

Figure 1. Clinical presentation of a brain injury.

Diagnosis of a brain injury. When a child presents with symptoms of a brain injury, a careful history and neurological exam are important in determining urgency for neuroimaging. CT scan and Magnetic Resonance Imaging are the modalities of choice. CT scan can be done quickly and is essential for the work up of a child with suspected severe traumatic injury. An MRI is used to identify patterns of injury to further aid in diagnosis, management and to some extent, prognosis. To look more specifically at vascular abnormalities, an MR angiogram and venogram can be done. An MRI with contrast is sensitive to inflammation and can be helpful in suspected infectious causes.

Injury Severity. ABI severity is usually classified according to the level of altered consciousness experienced by the patient following injury. Consciousness levels following ABI can range from transient

disorientation to coma or vegetative state. Common measures include the GCS, duration of unconsciousness, and duration of post-traumatic amnesia (PTA; the period following a trauma for which the patient has no recall of events). The GCS and measures to assess PTA are described in more detail in the next section.

Table 2. Definitions of Injury Severity

Mild	Moderate	Severe	Very Severe
• PTA <1 hour • GCS 13-15 • LOC 15-20 min	• PTA 1-24 hours • GCS 9–12 • LOC 15 min – 24 hours	• PTA 1–7 days • GCS between 3-8 • LOC 1-90 days	• PTA >7 days • LOC >90 days

4.3 Outcome Measures and Clinical Assessments

Outcome measurement is essential to clinical care. While there are many clinical outcome measures and assessment tools that can be used in pediatric brain injury, the availability of clinicians to administer the tools and local resources may influence which are used in different settings. A few common measures are highlighted below.

4.3.1 The Glasgow Coma Scale/Pediatric Glasgow Coma Scale

The GCS is based on eye opening, verbal and motor responsiveness and is a simple, objective assessment of level of consciousness (Teasdale & Jennett, 1974, 1976; Teasdale et al., 1978). The GCS is an observer rating scale consisting of 15 items in three basic categories: 1) motor response (6 items), 2) verbal response (5 items), and 3) eye opening (4 items). Points are awarded for the best response in each category and category scores are summed to provide a global GCS score (Sternbach, 2000; Wade, 1992). Total summed scores range from 3 (totally un-responsiveness) to 15 (alert, fully responsive).

For children two years of age or younger, a Pediatric GCS exists (James, 1986). While the scale is similar, the largest variation is in the verbal responses section, which includes coos, babbles and cries. The GCS is freely available, takes approximately 1 minute to administer and can be performed by all medical personnel (Oppenheim & Camins, 1992). Categorical divisions are used to differentiate patients in terms of initial severity of head injury:

- GCS scores 13-15 = mild
- GCS scores 9-12 = moderate
- GCS scores ≤8 = severe

4.3.2 Galveston Orientation and Amnesia Test and Children's Orientation and Amnesia Test

The Galveston Orientation and Amnesia test (GOAT) is a brief and simple mental status examination used to evaluate orientation (Levin et al., 1979). It consists of 10 items regarding orientation to person (name, address, and birthdate), place (city/town and building they are in) and time (current time, date, month, year & date of hospital admission), as well as memory of events both after and prior to the injury (Bode et al., 2000). The duration of PTA is defined as the period following coma in which the GOAT score is <75 (Levin et al., 1979). PTA is considered to have ended if a score ≥75 is achieved on three consecutive administrations (Novack et al., 2000; Wade, 1992; Zafonte et al., 1997).

Clinical Tip!

The GOAT should be used to determine when a patient is no longer in PTA and to guide the appropriateness of interventions.

The Children's Orientation and Amnesia Test (COAT), similar to the GOAT, was created to assess cognition serially for children and adolescents (Ewing-Cobbs et al., 1990). The COAT consists of 16 items assessing general orientation, temporal orientation (if between the ages of 8-15), and memory. It takes approximately 5-10 minutes to administer.

4.3.3 Rancho Los Amigos Levels of Cognitive Functioning Scale

The Rancho Los Amigos Levels of Cognitive Functioning Scale (RLA) provides a description of eight stages of cognitive function through which individuals with brain injuries typically progress during their stay in hospital and acute rehabilitative care (Hagen, 1982; Hagen et al., 1972). It is not considered an outcome measure but rather a scale and is a global index used to describe awareness, environmental interaction and behavioural competence (Timmons et al., 1987). The scale provides a quick and simple way to present an individual's level of recovery when communicating with families and other healthcare providers. This scale is typically used for individuals 14 years of age or older, as children's developmental differences at a very young age complicate accurate interpretation of the scale (Blosser & DePompei, 2003).

Clinical Tip!

There are resources available online that provide examples of appropriate responses for family members based on their loved ones RLA score, such as http://file.lacounty.gov/SDSInter/dhs/218115_RLOCFOriginalFamilyGuide-English.pdf

Table 3. Rancho Los Amigos Levels of Cognitive Functioning Scale (Hagen et al., 1972)

Level I	No Response	Patient does not respond to external stimuli and appears asleep.
Level II	Generalized Response	Patient reacts to external stimuli in nonspecific, inconsistent, and nonpurposeful manner with stereotypic and limited responses.
Level III	Localized Response	Patient responds specifically and inconsistently with delays to stimuli, but may follow simple commands for motor action.
Level IV	Confused-Agitated	Patient exhibits bizarre, nonpurposeful, incoherent or inappropriate behaviors, has no short-term recall, attention is short and nonselective.
Level V	Confused-Inappropriate	Patient gives random, fragmented, and nonpurposeful responses to complex or unstructured stimuli - Simple commands are followed consistently, memory and selective attention are impaired, and new information is not retained.
Level VI	Confused-Appropriate	Patient gives context appropriate, goal-directed responses, dependent upon external input for direction. There is carry-over for relearned, but not for new tasks, and recent memory problems persist.
Level VII	Automatic-Appropriate	Patient behaves appropriately in familiar settings, performs daily routines automatically, and shows carry-over for new learning at lower than normal rates. Patient initiates social interactions, but judgment remains impaired.
Level VIII	Purposeful-Appropriate	Patient oriented and responds to the environment but abstract reasoning abilities are decreased relative to premorbid levels.

4.3.4 A Common Set of Outcome Measures

A common set of outcome measures for TBI has been developed through a consensus process (McCauley et al., 2012). The outcome measures, which covered 14 broad domains, were categorized based on a three tier system: (1) core, (2) supplemental, and (3) emerging outcome measures (Table 4). While the list was intended for research purposes, it is thought to have clinical relevance as well. It has been suggested that if these measures are going to be used for benchmarking clinical centers a subset of core measures must be developed, as completing the current list of core measures in their entirety is impractical (Heneghan & Bell, 2018).

Table 4. Outcome measures proposed by the Pediatric Common Data Elements TBI workgroup (McCauley et al., 2012)

Domain	*Core*	*Supplemental*	*Emerging*
Academics	Child Behavior Checklist (CBCL-School Competence scale)	1. Woodcock-Johnson, 3rd Edition (WJ-III) 2. Gray Oral Reading Test, 4th Edition (GORT-4)	1. Comprehensive Test of Phonological Processing (CTOPP) 2. KeyMath-3 Diagnostic Assessment 3. Test of Word Reading Efficiency (TOWRE)
Adaptive and Daily Living	1. Pediatric Evaluation of Disability Inventory (PEDI – Self Care subscales) or 2. Functional Independence Measure for Children (WeeFIM)	Vineland-II	1. Adaptive Behavior Assessment System-Revised (ABAS-2) 2. Mayo-Portland Adaptive Inventory-4 (MPAI-4)
Family Environment	Family Assessment Device – General Function subscale (FAD - GF)	1. FAD (full version) 2. Family Burden of Injury Interview (FBII-interview format) 3. Conflict Behavior Questionnaire/ Interaction Behavior Questionnaire (CBQ/IBQ)	1. Family Burden of Injury Interview (FBII self-report version) 2. Child and Adolescent Scale of Environment (CASE)
Global Outcome	Glasgow Outcome Scale-Extended (GOS-E Peds)	PedsQL	Pediatric Test of Brain Injury
Health-Related Quality of Life	PedsQL (generic core)	None	1. Patient-Reported Outcomes Measurement Information System (PROMIS) 2. Neuro-QOL
Infant and Toddler Measures	1. Mullen Scales of Early Learning or 2. Bayley Scales of Infant and Toddler Development-III (full, not screen) 3. Brief Infant Toddler Social Emotional Assessment (BITSEA) or 4. CBCL	None	1. Shape School 2. Trails-P
Language and Communication	1. Wechsler Abbreviated Scale of Intelligence (WASI- Vocabulary subtest) 2. Caregiver Unintelligible Speech Rating	1. Comprehensive Assessment of Spoken Language (CASL) 2. Clinical Evaluation of Language Fundamentals (CELF-4) 3. Goldman-Fristoe Test of Articulation 4. Peabody Picture Vocabulary Test, 4th Edition (PPVT-4) 5. Percentage of Consonants Correct-Revised (PCC) 6. Verbal Motor Production Assessment for Children (VMPAC)	NIH Toolbox measure(s)

		7. Language Sample 8. Test of Language Competence Expanded (TLC-E)	
Neuropsychological Impairment Attention/Processing Speed	WISC-IV/WPPSI-III Processing Speed Index	1. Conners' Continuous Performance Test-Revised (CPT-2) 2. Test of Everyday Attention (Tea-Ch)	1. Flanker Test 2. NIH Toolbox measure(s)
Executive Functioning	Delis-Kaplan Executive Function System (D-KEFS) Verbal Fluency	1. Delis-Kaplan Executive Function System (D-KEFS) Trail Making Test 2. Behavioral Rating Inventory of Executive Function (BRIEF)\ 3. Contingency Naming Test (CNT)	1. Test of Executive Control (TEC) 2. Test of Strategic Learning (TOSL) 3. Functional Assessment of Verbal Reasoning and Executive Strategies – Student Version (FAVRES-S) 4. NIH Toolbox measure(s)
General Intellectual	WASI	None	None
Memory	1. Rey Auditory Verbal Learning Test (RAVLT) or 2. California Verbal Learning Test for Children (CVLT-C)	1. Wide-Range Assessment of Memory and Learning-Revised (WRAML-2) 2. Test of Memory and Learning Revised (TOMAL-2)	NIH Toolbox measure(s)
Motor/Psychomotor	None	1. Grooved Pegboard	NIH Toolbox measure(s)
Visual-Spatial	None	1. WISC-4/WPPSI-3 Block Design 2. Beery VMI	None
Physical Functioning	1. WeeFIM or 2. PEDI mobility subscale	1. Gross Motor Function Measure (GMFM-88, GMFM-66) 2. Peabody Developmental Motor Scales, 2nd Edition 3. Bruininks-Oseretsky Test of Motor Proficiency-2 (BOT-2)	1. PROMIS (mobility and upper extremity domains) 2. Neuro-QOL (mobility/ambulation domain) 3. NIH Toolbox measure(s)
Psychiatric and Psychological Functioning	1. CBCL Problem Behaviors or 2. Strengths and Difficulties Questionnaire	1. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) 2. Screen for Child Anxiety Related Emotional Disorders (SCARED) 3. Short Mood and Feelings Questionnaire (SMFQ) 4. UCLA PTSD Index 5. Alcohol, Smoking, and Substance Abuse Involvement Screening Test (ASSIST) 6. Children's Affective Lability Scale (CALS) 7. Children's Motivation Scale (CMS) 8. Modified Overt Aggression Scale (MOAS)	None

Recovery of consciousness	1. Children's Orientation and Amnesia Test (COAT) 2. Galveston Orientation and Amnesia Test (GOAT)	None	None
Social Role Participation and Social Competence	1. PedsQL (Social subscale) 2. Strengths and Difficulties Questionnaire (Peer Relations and Prosocial Behavior subscales)	1. Child and Adolescent Scale of Participation (CASP) 2. Social Skills Rating Scale (SSRS) 3. Child Behavior Checklist (Social Competence scale) 4. Vineland-II (Socialization scale) 5. PEDI Social Functioning Scales	None
Social Cognition	None	None	1. Interpersonal Negotiation Strategies (INS) 2. Reading the Mind in the Eyes Test-Child Version 3. Video Social Inference Test (VSIT)
TBI-Related Symptoms	Health and Behavior Inventory (HBI)	Post-concussion Symptom Inventory (PCSI)	None

Reprinted by permission from Mary Ann Liebert, Inc: Journal of Neurotrauma. Recommendations for the Use of Common Outcome Measures in Pediatric Traumatic Brain Injury Research. McCualey et al. 2012.

4.4 Acute Interventions for Pediatric Populations

This guidebook provides an overview of acute and sub-acute management for children with ABI, with particular focus on TBI management. Guidelines for the acute management of pediatric severe TBI have been recently published, as well as two acute care algorithms (Kochanek et al., 2019a; Kochanek et al., 2019b); the reader is referred to these resources for more detail. This section of the guidebook focuses mainly on the management of intracranial pressure (ICP), seizures and dysphagia. These topics are in no way exhaustive of acute interventions. An important topic not discussed is bowel and bladder management as often, post injury, children may need help re-establishing regular bowel movements and bladder emptying.

Components of Baseline Care (Kochanek et al., 2019b):

- Maintenance of appropriate level of analgesia and sedation
- Controlled mechanical ventilation
- Maintaining normothermic core temperature, preventing and treating fever
- Ensuring an appropriate intravascular volume
- Maintaining a minimum hemoglobin level for adequate oxygen delivery
- Treatment of coagulopathy
- Neutral Head positioning with head-of-bed elevation
- Antiepileptic drug therapy and use of continuous electroencephalography

Clinical Tip!

Acute Signs of Increased ICP:

- Cushing's triad: Hypertension, bradycardia, irregular or decreased respiration rate
- Fixed and dilated pupil
- Extensor posturing
- Acute change in LOC

Prevention of secondary insult to the brain from edema, hypoxemia and hypotension is critical following severe injuries. One of the most important concepts in the acute care of TBI focuses on controlling the rise in ICP that accompanies brain injury. Elevated ICP can be defined as ICP above 20 mm Hg, measured in any intracranial compartment (subdural, intraventricular, extradural, or intraparenchymal) (Sahuquillo & Arikan, 2006). Within the skull, the total volumes of brain tissue, cerebrospinal fluid and blood are fixed; an increase in one results in a decrease of the others (Pinto et al., 2019). Clinically, these shifts can result in a decrease in cerebral blood flow and put patients at-risk for brainstem herniation (Pinto et al., 2019). The body has the ability to regulate cerebral blood flow despite fluctuations in blood pressure through a process of cerebral autoregulation. Following brain injury, the typical mechanisms for autoregulation can be disrupted (Figure 3).

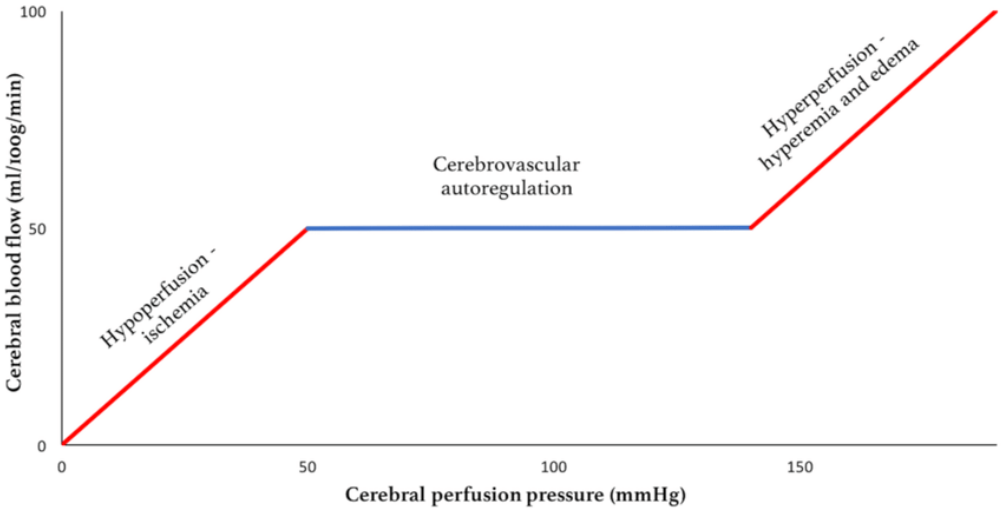


Figure 2. Cerebral autoregulation capacity (Harary et al., 2018)

Intracranial Pressure (ICP): the pressure inside the skull that is exerted based on the total volume of brain tissue, blood and cerebrospinal fluid.

Cerebral Perfusion Pressure (CPP): the pressure gradient that drives cerebral blood flow, calculated as the difference between the Mean Arterial Pressure (MAP) and the ICP.
CPP = MAP – ICP

Factors that contribute to increased ICP include an increase in brain water content, a decrease in cerebrospinal fluid reabsorption, an increase in cerebral blood volume, and mass lesions (Sahuquillo & Arikan, 2006). Elevations in ICP reduce cerebral perfusion pressure (CPP) thereby perpetuating secondary injury by reducing blood flow to the area. Symptoms of ICP may be blurred vision, vomiting, headache, issues with mobility, agitation, or change in behaviour. Elevated ICP has been shown to be associated with high risk of death and poor neurological outcomes (Kochanek et al., 2019b; Kukreti et al., 2014).

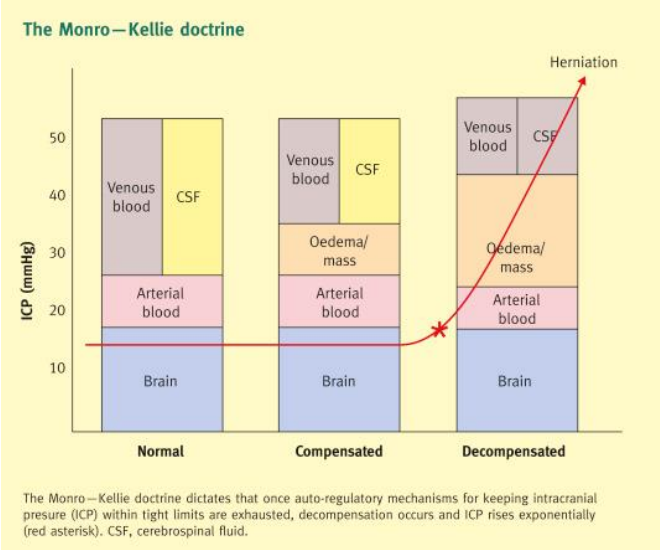


Figure 3. The Monro-Kellie doctrine. Reprinted with permission by Elsevier Ltd. (Wykes & Vindlacheruvu, 2015).

ICP monitoring is recommended in the Brain Trauma Foundation pediatric TBI guidelines; thresholds for ICP and CPP recommended in the guidelines are provided below (Kochanek et al., 2019b). Of note, for infants and young children an ever lower ICP threshold may be appropriate (Kochanek et al., 2019b). Monitoring ICP levels is challenging and invasive; however, hospitals that utilize ICP monitoring at greater rates have been shown to produce lower rates of mortality and severe disability following TBI (Bennett et al., 2012).

Factors that can negatively affect autoregulation and increase ICP

- Hypotension
- Hyperthermia (ie. fever)
- Hypoglycemia
- Seizures

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition, Brain Trauma Foundation (Kochanek et al., 2019b)

- *Treatment of ICP targeting a threshold of less than 20 mm Hg is suggested (Level III, p.S73).*
- *To improve overall outcomes. 1. Treatment to maintain a CPP at a minimum of 40 mm Hg is suggested. 2. A CPP target between 40 to 50 mm Hg is suggested to ensure that the minimum value of 40 mm Hg is not breached. There may be age specific thresholds with infants at the lower end and adolescents at or above the upper end of this range. (Both Level III, p.S73).*

4.4.1 Non-pharmacological Interventions for ICP Management

Q1. What are two non-pharmacological interventions for decreasing ICP in pediatric brain injury?

1. **Head Positioning** with head-of-bed elevation at 30°.
   There is limited evidence that head elevation may reduce ICP, but not CPP, in children post TBI.
2. **Hyperventilation** can transiently reduce ICP through cerebral arterial vasoconstriction via reduction in PaCO2. This is not a long-term intervention for ICP management but can be used at the bedside in urgent settings.

4.4.1.1 Head Position

For children who are critically ill as a result of an intracranial process such as TBI, the position of the head is important. The skull creates a fixed space in which the brain and the blood supplying it must co-exist, as such it is believed that elevation of the head, from 15° to 30°, encourages jugular venous drainage and a subsequent reduction in ICP (Bhalla et al., 2012; Marcoux, 2005). To avoid orthostatic hypotension, the child should be euvolemic prior to positioning (Marcoux, 2005), thus reducing the chance of impaired CPP with head elevation. The use of a neutral head position with an initial head-of-the-bed position at 30° is the most common practice recommended in clinical protocols (Kochanek et al., 2019a).

While the literature on head elevation is limited, a study by Agbeko and colleagues (2012) suggests that ICP may be lowered by head position alone without disrupting CPP pressure. The height and age of each individual should be accounted for before altering head elevation, as the decrease in ICP was associated

with the change in vertical distance from the base of the skull to the heart, rather than absolute degree of incline (Agbeko et al., 2012).

Key Study

Author/Year/ Country/Study Design/N	Methods	Outcomes
Agbeko et al. (2012) United Kingdom Pre-Post N=8	**Population:** TBI; Mean Age=10yr; Gender: Male=7, Female=1; Mean GCS=5.3. **Intervention:** Head elevation of patients was randomly increased or decreased by 10° at a time up to a max of 40° and down to a min of 0°. Data was collected over 18 protocol sessions. **Outcome Measure:** Intracranial Pressure (ICP) levels; Cerebral Perfusion Pressure (CPP) levels; mean arterial pressure.	1. ICP was significantly lower when head elevation was at a vertical height of 10cm (p<0.001). 2. CPP was not affected by head elevation (p=0.957). 3. A negative correlation was reported between the magnitude of ICP response and head height with a higher baseline ICP level associated with a lower magnitude of response (p=0.025). 4. Mean arterial pressure declined 3.9mmHg demonstrating a significant relationship with head elevation (p<0.001).

4.4.1.2 Hypothermia

Moderate therapeutic hypothermia (32-33°C) has been thought to reduce the onset of secondary injuries by preventing hyperthermia (body temperature >38-38.5°C) and decreasing cell death, excitotoxicity, metabolic demands and inflammation, to name a few (Kochanek et al., 2019b). However, several meta-analyses have shown hypothermia increased the risk of mortality (ranges 73%-87%) in pediatrics (Crompton et al., 2017; Ma et al., 2013; Zhang et al., 2015). It was also ineffective at improving Glasgow Outcome Scale scores (Zhang et al., 2015). The lowering of core body temperature can be harmful and put a child at risk for further complications.

Based on the evidence, hypothermia should be used with great caution in pediatric populations. Although there may be some benefits in the short-term, such as lowering immediate ICP, there does not appear to be significant long-term benefits. Early hypothermia is not recommended in management of pediatric TBI.

4.4.2 Pharmacological Interventions for ICP Management

Q2. What pharmacological interventions for managing pediatric intracranial hypertension are recommended in the Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, third Edition (Brain Trauma Foundation Guidelines)(Kochanek et al., 2019b)?

Answer

1. Continuous infusion hypertonic saline (3%, range from 0.1 and 1.0 mL/kg of body weight per hour, administered on a sliding scale) and bolus hypertonic saline (3%).

4.4.2.1 Hypertonic Saline

Mannitol is the drug most widely used in the treatment of intracranial hypertension in children; however, there is a lack of evidence supporting its use. Hypertonic saline (HTS) is used more frequently for acute ICP management. The administration of HTS results in an increase in serum sodium and osmolarity, creating an osmotic gradient that encourages passive diffusion of water out of cerebral cellular and interstitial spaces into blood vessels. This reduction in cerebral water content effectively lowers ICP (Khanna et al., 2000). HTS is used more frequently in children who are older, have intracranial hemorrhages and skull fractures, and severe injuries (Bennett et al., 2012).

A study comparing normal saline and HTS in children with severe TBI found that HTS lowered ICP and fewer additional interventions were needed (Fisher et al., 1992). Another study found an increase in favourable discharge disposition and a reduction in mortality in patients treated with HTS compared to those treated with a protocol that included mannitol (O'Lynnger et al., 2016).

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition, Brain Trauma Foundation (Kochanek et al., 2019b)

- *For ICP Control. Bolus HTS (3%) is recommended in patients with intracranial hypertension. Recommended effective doses for acute use range between 2 and 5 mL/kg over 10-20 min (Level II, p.S74).*
- *For ICP Control. Continuous infusion HTS is suggested in patients with intracranial hypertension. Suggested effective doses as a continuous infusion of 3% saline range between 0.1 and 1.0 mL/kg of body weight per hour, administered on a sliding scale. The minimum dose needed to maintain ICP less than 20 mm Hg is suggested (Level III, p.S74).*
- *For ICP Control. Bolus of 23.4% HTS is suggested for refractory ICP. The suggested dose is 0.5 mL/kg with a maximum of 30 mL (Level III, p.S74).*

4.4.2.2 Other Medications

Narcotics (fentanyl and morphine), barbiturates (pentobarbital), and midazolam are used in pediatric brain injury for sedation and analgesia and have been studied for their potential to reduce ICP levels (Guilliams & Wainwright, 2016). The use of analgesics and sedatives in pediatric populations is not recommended for ICP management; however, these medications are used for other treatment purposes as adequate sedation and analgesia is part of baseline care. Fentanyl and midazolam have been found to be ineffective in the literature in reducing ICP, and there is some evidence to suggest that they may even increase intracranial hemorrhaging (Welch et al., 2016). Shein et al. (2016) found that administration of 3% HTS yielded the fastest reduction in ICP and increase in CPP compared to Fentanyl (2µg/kg) and Pentobarbital (5mg/kg). Pentobarbital was shown to reduce ICP more gradually and without affecting CPP, whereas fentanyl decreased ICP but worsened CPP levels (Shein et al., 2016).

Laboratory studies have associated corticosteroid use with facilitation of synaptic transmission, reduction of lipid peroxidation, preservation of electrolyte distribution, enhanced blood flow, and membrane

stabilization (Grumme et al., 1995). In the pediatric population, corticosteroids (dexamethasone) were thought to reduce vasogenic cerebral edema and thereby ICP (Fanconi et al., 1988). The pediatric data highlights that dexamethasone suppresses endogenous production of glucocorticoids compared to controls (Fanconi et al., 1988; Kloti et al., 1987), and that it does not provide any benefit for children with acute TBI. The current pediatric guidelines recommend against corticosteroid administration for severe TBI (Kochanek et al., 2019b).

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition, Brain Trauma Foundation (Kochanek et al., 2019b)

- *For ICP control. With use of multiple ICP-related therapies, as well as appropriate use of analgesia and sedation in routine ICU care, avoiding bolus administration of midazolam and/or fentanyl during ICP crises is suggested due to risks of cerebral hypoperfusion (Level III, p.S74)*
- *For ICP control. High-dose barbiturate therapy is suggested in hemodynamically stable patients with refractory intracranial hypertension despite maximal medical and surgical management (Level III, p.S75).*
- *The use of corticosteroids is not suggested to improve outcome or reduce ICP (Level III)*

4.4.3 Surgical Interventions: Decompressive Craniectomies

The approach to management of individuals who sustain a severe TBI with refractory ICP and in the absence of a mass lesion, remains controversial. Decompressive craniectomies (DCs) are considered a last resort when trying to manage ICP (Kochanek et al., 2012; Ruf et al., 2003). If DC is the course of treatment, waiting in excess of 4 hours post admission and intraoperative blood loss greater than 300mL have been found to be predictors of poorer outcome and mortality (Khan et al., 2014) (Oluigbo et al., 2012). Further, surgery may result in complications such as ventilator associated pneumonia and site infection (Pechmann et al., 2015; Prasad et al., 2015).

Some research literature suggests that DCs are effective in reducing ICP and are associated with better outcomes in children following a severe TBI (Jagannathan et al., 2007; Weintraub et al., 2012). A RCT by Taylor et al. (Taylor et al., 2001) examined whether early DC was more effective than standard medical management in reducing ICP. While a greater reduction in ICP was found in the treatment group, the between group difference was not significant. This study also had several methodological limitations, therefore additional studies investigating the use of DCs are necessary. A systematic review has found that DCs resulted in favorable outcomes for pediatric populations regardless of the etiology of the ABI itself (Guresir et al., 2012). While the decision to use surgical interventions is complicated, often sicker children may need it.

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition, Brain Trauma Foundation (Kochanek et al., 2019b)

- *For ICP Control. DC is suggested to treat neurologic deterioration, herniation, or intracranial hypertension refractory to medical management (Level III, p.S75).*

4.4.4 Post-Traumatic Seizures

Q3. What are risk factors for post-traumatic seizures?

Answer

1. Location of lesion, cerebral contusions, retained bone and metal fragments, skull fracture, focal neurologic deficits, penetrating injury
2. Loss of consciousness
3. Severe TBI
4. Length of PTA
5. Age

Post Traumatic Seizures (PTS) may contribute to secondary injury following an ABI through the increase of metabolic demands and elevation of ICP (Chung & O'Brien, 2016). The incidence of early PTS (onset <1 week post-injury) in children has been reported to be between 12-18% (Liesemer et al., 2011; Thapa et al., 2010), but subclinical epileptiform activity has been detected with continuous EEG monitoring in up to 42.5% of children with head trauma (Arndt et al., 2013). Pediatric ABI is associated with greater volumes of post traumatic edema (Aldrich et al., 1992). This may affect the development of PTS as intracerebral fluid deposition has been postulated to be an important mediator in the pathogenesis of both early and late PTS (Willmore, 1990).

When examining the research literature for seizure prophylaxis, Phenytoin has been shown to be ineffective at preventing both early PTS (<1 wk of injury)(Young et al., 2004) and late PTS (>1 wk of injury) (Young et al., 1983) compared to placebo controls. Notably, there was also no difference observed in survival outcomes between phenytoin and placebo groups (Young et al., 2004). Using a different anti-seizure agent, levetiracetam, PTS was found to occur in 17.6-25% of the study population despite pharmaceutical prophylaxis (Chung & O'Brien, 2016; Vaewpanich & Reuter-Rice, 2016). Children that developed early PTS after levetiracetam prophylaxis were younger and had experienced abusive head trauma, compared to those that did not develop PTS (Chung & O'Brien, 2016; Vaewpanich & Reuter-Rice, 2016).

Key Studies

Author/Year/ Country/Study Design/PEDro Score/N	Methods	Outcome
Chung & O'Brien (2016) USA N=34	**Population:** TBI; Median Age=6.0yr; Gender: Male=20, Female=14; Median GCS=8. **Intervention:** Patients admitted to the pediatric intensive care unit were provided with 5-40mg/k per day of levetiracetam as a prophylaxis against post-traumatic seizures (PTS). Patients were monitored for up to 7d post injury. **Outcome Measure:** Incidence of PTS.	1. Six of the 34 patients (17.6%) developed PTS despite prophylactic levetiracetam. 2. Patients who developed PTS were significantly younger than those who did not (median age of 4 versus 10 respectively; p<0.0001). 3. Patients who developed PTS were significantly more likely to have experienced abusive head trauma (p=0.0004). 4. There was no significant difference in the dosage of levetiracetam between patients who did and did not develop PTS (p=0.87).
Young et al. (2004) RCT USA PEDro=6 N_I=102, N_F=69	**Population:** TBI; *Phenytoin (n=46):* Median Age=6.4yr; Gender: Male=31, Female=15; Mean Time Post Injury=34min; Median GCS=7. *Controls (n=56):* Median Age=5.9yr; Gender: Male=38, Female=18; Mean Time Post Injury=33min; Median GCS=7. **Intervention:** Patients were randomized to receive either phenytoin or a placebo. Those in the phenytoin group received a loading dose of 18mg/kg body weight followed by 2mg/kg body weight every 8hr for 48hr. Patients assigned to the placebo group received an equivalent volume at the same time points. All patients were kept under observation throughout the study. Median time to follow-up was 34.5d. **Outcome Measure:** Occurrence of seizure, Neurologic Outcome Score in Infants and Children (NOSIC).	1. Three patients from each group experienced a posttraumatic seizure. 2. The probability of a posttraumatic seizure was similar between groups with a median effect size of -0.015 (1.5%) higher seizure rate in the phenytoin group. 3. No significant difference was found between groups on the NOSIC (p=0.90).

Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines (Kochanek et al., 2019b).

- *For seizure prevention (clinical and subclinical). Prophylactic treatment is suggested to reduce the occurrence of early (within 7 d) PTS (Level III, p.S74).*
- *At the present time, there is insufficient evidence to recommend levetiracetam over phenytoin based on either efficacy in preventing early PTS (EPTS) or toxicity (p. S44).*

4.4.5 Dysphagia, Feeding and Nutrition

Q4. What are two predictive factors of dysphagia post TBI in children?

Answer
1. GCS score of less than 8.
2. A ventilation period of >1.5 days (Morgan et al., 2003).

The incidence of dysphagia among all children with TBI is 5.3% (Morgan et al., 2003); however, the incidence of dysphagia in children after a severe TBI is 68-76% (Morgan, 2010). Such a high rate is problematic as children already have difficulty meeting their metabolic demands following a brain injury, and problems with swallowing and feeding further attenuate the ability to obtain their nutritional goals (Morgan, 2010). The degree of injury to key brain regions, such as the brain stem and primary motor and sensory cortices, should be considered in identifying children who are at-risk for swallowing dysfunction (Mei et al., 2018).

Evidence- and Consensus-Based Guidelines for the Management of Communication and Swallowing Disorders Following Pediatric TBI (Mei et al., 2018).

- *Children with severe TBI and a ventilation period of >1.5 days should be screened by a SLP for swallowing deficits (Evidence-based recommendation).*
- *Children with moderate or severe TBI should be referred by a medical or health professional to a SLP during the acute phase (0-2 wk). Regular monitoring (i.e., on referral and transfer to rehabilitation, prior to discharge) should continue throughout inpatient and community rehabilitation where clinically indicated (Consensus-based recommendation).*
- *Instrumental assessments of voice or swallowing disorder (including fiber-optic endoscopic evaluation of swallowing or videofluoroscopy) should be used if clinically indicated (Consensus-based recommendation).*

Diagnosing a swallowing impairment should include a clinical bedside examination and a physiological assessment (Morgan et al., 2004). Commonly used assessments include Videofluoroscopic swallow study and fiberoptic endoscopic evaluation of swallow. The same interventions used in adult populations are available for pediatric treatment (i.e., nasogastric feeding tubes, enteral nutrition, and parenteral nutrition). While studies have found that total parenteral nutrition was superior to enteral nutrition in reducing mortality, several systematic reviews have mentioned that both feeding mechanisms provide an increase in survival when introduced early (48 hours)(Hadley et al., 1986; Perel et al., 2006; Taylor et al., 1999). For pediatric TBI, ***"initiation of early enteral nutritional support (within 72hr from injury) is suggested to decrease mortality and improve outcomes"*** **(S75)(Kochanek et al., 2019b).**

Additional nutritional interventions can include nitrogen supplementation, glutamine supplementation, and probiotic use. As children have high nutritional demands in general, it is important to complete an

individualized nutrition plan for each child, including consideration of who will be administering oral feeding, as that has been shown to have an impact on nutritional status (DeMatteo et al., 2002). Further, in the acute phase cognitive, physical and oromotor deficits can impact a child's ability to manage oral intake. Dieticians and Speech language pathologists are important members of the multi-disciplinary management of children following ABI. Dietician can help guide caloric intake while a Speech Pathologist can assist with bedside oral-motor examination.

Immunologic dysregulation, malnutrition, hypercatabolism and hypermetabolism pose a risk to children post injury (Briassoulis et al., 2006). Unfortunately, few studies have been conducted examining nutrition, feeding and dysphagia within a pediatric TBI population. Briassoulis et al. (2006) did study early enteral feeding with an immune enhancing or regular formula and the effect of the immune-enhancing diet on infection and metabolic indices. A decrease in interleukin-8 and early gastric colonization was shown with immunonutrition and the method was found to be clinically feasible and safe for children; however, this intervention was not advantageous over regular early enteral nutrition (Briassoulis et al., 2006). Further, the enhanced formula did not improve mean caloric and protein intake.

4.4.6 Agitation and Sleep Disruption

Pharmacological therapies are often used in the sub-acute phase of recovery as agitation and sleep-wake cycle disruption are frequent. Agitation and irritability can be common sequalea of a brain injury and a careful history in the sub-acute stage is important to assess pre- and post-injury changes. There is relatively little evidence to guide medication management in this population and extrapolation, with caution, is made from other populations.

Disruption to the sleep-wake cycle following a brain injury is likely due to injury as well as non-injury factors, including the critical care and hospital environment. **When evaluating sleep consider the following (Morse & Kothare, 2018):**

- Pre-injury sleep-wake patterns
- Contributing factors such as pain, environment, other medical conditions, psychiatric comorbidities, medication side-effects
- Effects of sleep-wake disturbances on fatigue, mood, cognitive and physical functioning
- Signs of specific sleep disorders such as snoring, apneas, hallucinations, nightmares, or limb movement

While self-reported sleep questionnaires are available, they may be difficult to use in a pediatric population. Polysomnography may also be an option.

Table 5. Treatment considerations for sleep disorders in patients following traumatic brain injury (Morse & Kothare, 2018).

Sleep Disorder	Treatment Options
Insomnia	
Primary	Sleep hygiene and CBT ± melatonin, sedatives/hypnotics, or acupuncture.
Secondary	
Due to PTSD	SSRIs, psychologic counselling, pain management counsel, CBT and sleep hygiene ± melatonin.
Due to pain	
Due to depression	
Due to medication	Remove offending medication, adjust dosing or time administered and consider offering sedating medicine at bedtime.
Nightmare disorder	Imagery rehearsal therapy, systematic desensitization, progressive deep-muscle relaxation training and prazosin.
Hypersomnia	Stimulant medications (i.e. methylphenidate, dextroamphetamine, modafinil, armomodafinil, strategic caffeine and naps.
Obstructive sleep apnea	Positive airway pressure (PAP) devices, surgical interventions, mandibular devices, and weight loss.
Central sleep apnea	PAP devices (including assisted servoventilation).
Periodic limb movements of sleep/restless-leg syndrome	Iron supplementation, dopamine agonists and gabapentin.
Circadian rhythm disorder	
Delayed sleep phase	Melatonin supplementation ± stimulant medication in daytime, ±hypnotic medication in the evening*, bright light therapy in the morning/reduced light exposure in the evening*, prescribed sleep-wake scheduling and sleep hygiene education.
Advanced sleep phase	Advanced chronotherapy (bright light therapy in the evening/reduced light exposure in the morning) ± melatonin, sleep hygiene education*, and prescribed sleep-wake scheduling.
Parasomnia	Safe sleep environment, scheduled awakenings, maintain a regular sleep schedule, benzodiazepines and anticonvulsant drugs.
Narcolepsy	Stimulant medications (i.e. methylphenidate, dextroamphetamine, modafinil, armodafinil), strategic caffeine and naps, and sodium oxybate.

4.5 Rehabilitation Interventions for Pediatric Populations

Behavioural, cognitive and motor deficits often exist post injury and each domain interacts with the others. While some deficits will be present immediately, the full impact of the injury may not be known until later on in the recovery period and will continue to unfold over the lifespan. Additional deficits may become apparent, as the child develops and approaches new developmental milestones. Recovery following brain injury is most pronounced in the first year post-injury but continues at a slower pace thereafter. Outcomes are impacted by age at the time of injury, severity of injury and degree of secondary complications as well as family factors. While this section is labelled rehabilitation, it should be noted that ***habilitation*** is also necessary among the pediatric TBI population, as children not only need to *relearn* previously held skills but there is also a need to learn new skills and adapt to new challenges.

Rehabilitation: regaining skills and abilities that may have been lost or impaired following the brain injury.

Habilitation: learning new skills expected for age in a way that accommodates areas of challenge and allows for continued developmental progress post injury.

Three key factors to remember when treating pediatric brain injury (Blosser & DePompei, 2003):

1. **The long-term effects can be cumulative**. For moderate and severe brain injuries, the injury often interferes with the individual's capacity to develop.
2. **There can be delayed onset of deficits**. Given that the brain is in the process of developing in childhood, it may be years before the deficits become apparent.
3. **Developmental stages and variability by age**.

Clinical Tip!

For children in care, additional attention to Attachment trauma and early adversity may also be important.

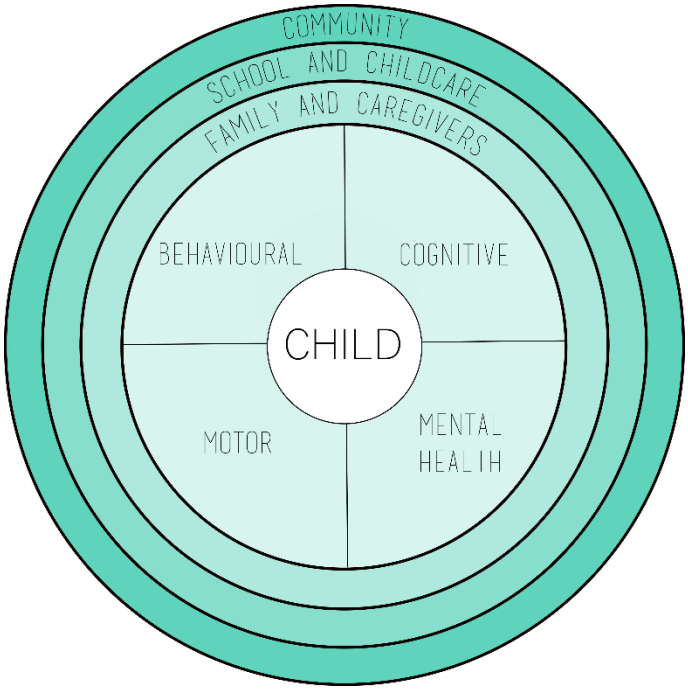
While specific interventions will be discussed below, the concept of resiliency is often overlooked. Resiliency refers to a "*system of intrapersonal protective factors, adaptational processes, and outcomes that operate in the context of different types of adversities" (King et al., 2018)*. As healthcare providers, it is important to promote resiliency and ultimately, a sense of self among young patients. In doing so, we encourage children's views of themselves as efficacious, optimistic and adaptable (King et al. 2018). There is growing literature around the importance of recognizing the perspective and capacity of children and youth following brain injury. Involving youth as active participants in their recovery is important for their further development and ultimate transition to young adulthood. Readers are encouraged to explore the resiliency framework in more detail (King et al., 2018).

4.5.1 Family Support

The family/caregiver play a critical role in a child's recovery and development following an ABI; family functioning is a significant moderator of child outcome following brain injury (Braga et al., 2005; Yeates & Taylor, 2005). While often family is thought to play a supporting role in a child's recovery, they need to be active participants and should be integrated into all stages of recovery.

Role of Family/Caregiver in a child's recovery (Savage et al., 2005)

1. Observer of the child's progress
2. Active participant in child's care and recovery
3. Insightful pre- and post- injury information regarding the child's abilities
4. Communicator with clinicians
5. Advocate for the child



Being the parent of a child with a brain injury can be a demanding and stressful experience. Parents and caregivers, themselves experience a psychosocial trauma. Post-injury parents are very grateful that their child is safe, however there can be a grieving process for the child they once knew in cases of severe injury (Roscigno & Swanson, 2011). Further, there may be feelings of guilt depending on how the child was injured. Parents may experience feelings of isolation, distress, relationship discord, anxiety, and engage in negative coping mechanisms such as avoidance and disengagement behaviours (Brown et al., 2013). The well-being and mental state of the caregiver needs to be taken into account as there is a bi-directional relationship between parent and child function: improvements in parental function are likely to have an effect on child adjustment and outcomes following an ABI and vice versa. Given this relationship, on an inpatient rehabilitation unit, the initial assessment of a patient should consider the family/caregiver's needs and available support systems, coping behaviours, levels of emotional distress and the general family functioning (Rivara et al., 2012). This should also be re-examined over time. Caregivers should be given educational materials on brain injury, peer networking opportunities, community-based resource lists and structured programming for coping strategies, problem solving and self-management (Rivara et al., 2012). Appropriate services should be provided to deal with the physical, psychological, emotional, and financial challenges that come from caring for a child with a brain injury. The injury may also impact how one parent's a child going forward. A detailed summary of family-supported interventions can be found in the online ERABI module.

Click here to access the full ERABI Module for Pediatric Acute and Rehabilitation Interventions

4.5.2 Behavioral Management

Significant increases in problematic behaviours such as ***aggression, disinhibition, impulsiveness, defiance, and non-compliance*** are commonly identified post injury (Gerring et al., 2009; Sohlberg, 2001), with the behavioural profile changing at different stages post injury. Children are also at a greater risk for developing ***internalizing behaviours, such as anxiety, depression, and personality changes*** after a TBI (Li & Liu, 2013). Often, these behaviours occur during the critical stages of rehabilitation, interrupting rehabilitation and education goals (Gurdin et al., 2005).

Clinical Tip!

To assess problem behaviours considering using:
Behavioural Assessment System for Children, Conners Comprehensive Behavior Rating Scale, Behavior Rating Inventory of Executive Function, Vineland Adaptive Behavior Scales or the Child Behavior Checklist.

Different behavioural profiles are typically seen at different stages after injury. For example, early behavioural consequences often include restlessness and agitation associated with confusion and disorientation. As recovery continues, problems with impulse control, cooperation with treatment activities and appropriate social interactions may emerge. Challenging behaviors have been related to both neurological (e.g. injury severity) and interpersonal (e.g., coping skills) factors, and several models have been put forward to describe the various influences on behavioral difficulties following ABI (Prigatano, 1992). Continued problematic behavior in children and adolescents after brain trauma is a major barrier to medical care, rehabilitation, and eventual independent living (Gerring et al., 2009). Causes of and contributors to behaviour problems can be multi-factorial.

Factors to consider as causes and/or contributors to behaviour problems:

- Pain: a verbal child can help localize the source; however, in a non-verbal child consider occult fractures, dental problems and constipation
- Sleep disruption (central or obstructive sleep apnea, restless leg syndrome, or delayed sleep phase)
- Dental abscess
- Vision Impairment
- Hearing Impairment
- Family stress and coping style
- Medication side-effect
- Attachment trauma
- Mismatch between expectations and abilities
- Seizures
- Frontal lobe syndrome
- Secondary ADHD
- Anxiety
- Depression
- Constipation

Approach to disruptive behaviour:

1. Is the behaviour atypical for age?
2. Is the behaviour atypical for developmental (i.e. Mental) age?
3. Characterize the behaviour: OPQRSTT
    - O - Onset
    - P - Progression
    - Q - Quality (intensity)
    - R– reactions (to the behaviour)
    - S – settings
    - T – triggers
    - T - treatments/strategies tried so far
4. Thorough medical review of systems
    - Vision or hearing impairment
    - Medication side-effect
    - Under treated or untreated pain
    - Chronic illness under-managed
    - Seizures
5. Characterize the impact on family and the family dynamic

Clinical Tip!

To engage a child in rehabilitation, make sure the interventions are aligned with their current developmental level and behavioural profile. A tool like the RLA can help determine appropriate expectations and level of neurocognitive recovery.

Behavioural therapies are directed at reducing or eliminating such problematic behaviours through the application of well-established behavioural and social learning principles. Behavioural interventions in infants and children will focus on responsiveness and behavioural management skills of the caregiver; however, interventions for adolescents often focus more on self-awareness and self-regulation (Wade, 2010). No one interventional approach will be effective for all ages.

4.5.2.1 Non-Pharmacological Interventions for Behavioural Disorders

Q5. What non-pharmacological therapies exist for the treatment of behavioral problems in children post brain injury outside of the acute phase?

Answers

1. **Cognitive Behavioural Therapy (CBT).**
   There is limited evidence that CBT may reduce anxiety, depression, and internalizing behaviour.
2. **Counsellor-Assisted Problem-Solving Groups.**
   There is conflicting evidence as to whether a counsellor-assisted problem-solving group yields superior outcomes compared to an internet resource intervention for management of externalizing, internalizing, and socialization behaviours in pediatric patients post TBI.
3. **Online Problem-Solving Programs**.
   There is strong evidence that online problem-solving programs with therapist assistance may be superior to internet resource comparison groups for targeting improvements in compliant behaviour and self-management in children post ABI, and for acutely improving anxiety, depression, and distress in the parents of children with ABI.

A common therapeutic intervention is Cognitive Behavioral Therapy (Pastore et al., 2011). Forms of compliance training protocols utilizing operant conditioning techniques such as positive reinforcement following social and cooperative behaviour, planned ignoring for disruptive behaviour, and a loss of reward for aggressive behaviour have also been studied (Pruneti et al., 1989; Slifer et al., 1993; Slifer et al., 1995; Slifer et al., 1997). Compliance training was found to be successful in lowering agitation scores (Slifer et al., 1997), lowering episodes of negative behaviours (Pruneti et al., 1989; Slifer et al., 1993; Slifer et al., 1995; Slifer et al., 1997), and encouraging the development of greater levels of autonomy (Pruneti et al., 1989). Finally, counsellor-assisted problem-solving and internet resource interventions may be effective at mitigating behavioural problems in pediatric patients post TBI; however, there is conflicting evidence as to which technique is superior and which patient would benefit most from each.

Cognitive behavioral therapy used in children who had sustained a severe TBI resulted in improved adaptive behaviour and reduced dysfunctional behaviours such an anxiety, depression, and internalizing behaviours, compared to controls (Pastore et al., 2011). Cognitive behavioural therapy was shown to be beneficial for children to attain adequate social reintegration following a severe TBI (Pastore et al., 2011). An important variable that differs widely across studies examining behavioural therapies is the time post injury. This is important because, as previously mentioned, different behavioural problems may appear at different stages of recovery. Majority of these therapies are studied on an adolescent sample and may be provided up to years post injury. Lastly, each intervention has varying cognitive requirements set as their inclusion criteria; for example, the study highlighted below required study

subjects to have an baseline full scale IQ of >75 in order to receive cognitive behavioural therapy (Pastore et al., 2011) .

Key Study

Author/Year/ Country/Study Design/PEDro Score/N	Methods	Outcome
Pastore et al. (2011) Italy Prospective Controlled Trial N=40	**Population:** TBI; *Cognitive Behavioural Therapy (CBT, n=28)*: Mean Age=10.9yr; Gender: Male=21, Female=7; Mean Time Post Injury=2.5yr; Mean GCS=5.5. *Controls (n=12)*: Mean Age=8.9yr; Gender: Male=10, Female=2; Mean Time Post Injury=2.5yr; Mean GCS=6.9. **Intervention:** All patients were offered CBT in order to reduce dysfunctional behaviours and increase functional behaviours. CBT ranged from 4-8mo in length with 2-3/wk lasting 45-60min. Parents also received a weekly session. Patients and families who did not participate in therapy agreed to return for follow-up as controls. Follow-up was conducted at 12mo. **Outcome Measure:** Child Behaviour Checklist (CBCL), Vineland Adaptive Behaviour Scales-Expanded Form (VABS).	1. Patients who received CBT reported significantly greater improvements on subscales: anxiety/depression, internalizing, social problems, somatic complaints, and withdrawal (all p<0.05) compared to controls. 2. After removing patients who received additional pharmacotherapy from the analysis, the aforementioned CBCL subscales remained significant, in addition to improvements in aggressive (p=0.002) and externalizing (p=0.004) behaviour. 3. CBT group demonstrated a significantly greater socialization skills score than controls (p<0.013) but no between group differences were found for communication and daily living skills.

4.5.2.2 Pharmacological Interventions for the Treatment of Behavioural Disorders

Q6. What pharmacological therapies have been studied for the treatment of behavioral problems in children post brain injury?

Answers

1. **Amantadine**.
   There is limited evidence that the use of amantadine can decrease the amount of aberrant behaviours .
2. **Methylphenidate.** There is conflicting evidence regarding whether methylphenidate improves cognitive behavioural function compared to placebo in children following TBI.

Pharmacological interventions are often introduced to treat aggressive or agitated behaviour post TBI (Suskauer & Trovato, 2013). To date, no medication has proven to be effective in modifying outcomes in a child with a brain injury. Investigators have studied the role of the psychostimulant methylphenidate and other dopamine enhancing medication, such as amantadine, and the efficacy of these medications on aggression and agitation.

Amantadine has been shown to be safe to administer to children (Green et al., 2004). Although there were unfavourable side effects, such as aggression and nausea, these side effects remitted upon modification of dosage, cessation of amantadine treatment (Green et al., 2004) or persistence of treatment beyond 2

days (Beers et al., 2005). In terms of efficacy, amantadine administration at a mean of 0.9 years post injury reduced the frequency of negative behaviours associated with frontal lobe injuries after 12 weeks of treatment (Beers et al., 2005). Subjective chart review of observed behaviours in children (alertness, verbalizations, agitation) also revealed improvement in patients treated with amantadine; however, it is unknown whether such improvements were due to the medication or natural recovery (Green et al., 2004).

Methylphenidate, a psychomotor stimulant, is an established treatment of attention deficit/hyperactivity disorder (ADHD) in children. Similar executive function deficits can be seen in children who have sustained a significant brain injury including: attention deficits, hyperactivity and impulsivity (Leonard et al., 2004). In addition, for children with pre-exisiting ADHD, the deficits can be accentuated post-TBI. The effect of methylphenidate for children post TBI is conflicting, with studies varying in terms of dosage given, time post injury and duration of pharmacological treatment. While no improvements in memory, behaviour, speed of processing, or attention were found after methylphenidate treatment (Williams et al. 1998), a study by Hornyak et al. (1997) found methylphenidate improved cognitive and behavioural function. The imporvements were associated with increased participation in therapy at school and improvements in behaviours at home (Hornyak et al. 1997). Further corroborating those findings, a pre-post test noted that immediate-release methylphenidate improved disruptive behaviour at home and at school and was associated with either no or few side effects in patients with TBI or ADHD (Ekinci et al., 2017). Finally, Nikles et al. (2014) found that stimulants (methylphenidate or dexamphetamine) had a small effect on improvement of ADHD symptoms, such as attention and concentration. Although reported as an improvement, the difference compared to the placebo phase was not statistically significant (Nikles et al., 2014).

4.5.3 Cognitive Therapies

Q7. What are common neurocognitive deficits following TBI? Name an intervention with evidence for each.

Answer

1. Attentional deficits – Amsterdam Memory and Attention Training for children program.
2. Learning and Memory – Pager systems and diary use.
3. Executive Functioning – Counsellor Assisted Problem-Solving Therapy.
4. Communication – Peer-group training of pragmatic language skills.

Common cognitive consequences of childhood ABI include deficits in attention, memory, problem-solving, communication, processing speed, executive function and academic difficulties (Sohlberg, 2001). In general, children with more severe head injuries tend to have broader deficits than those with mild injuries (Rivara et al., 2011). Cognitive abilities that are being developed at the time of injury are more compromised than those that are fully developed (Gaines & Soper, 2018). Mastery of certain functions that are disrupted while in-development may not always be possible (Gaines & Soper, 2018). Moreover, assessing cognitive recovery in children is challenging as improvements in task

Clinical Tip!
Interventions for cognitive deficits should be integrated into children's classroom experience.

performance does not imply recovery, given that developmental expectations are ongoing and incremental (Van't Hooft, 2010).

4.5.3.1 Remediation of Attentional Deficits

Almost half of children post TBI will experience either persisting, worsening, or develop attention issues (Backeljauw & Kurowski, 2014). There is currently a scarcity of interventions available to target the rehabilitation of attention in children that have sustained an ABI. Attention has no agreed upon definition; it is a multifaceted construct and is difficult to assess. One-way attention may be defined as sustained and selective attention. Sustained attention involves the level of arousal, alertness, and vigilance, and involves concentrating on an activity or focus on one thing for extended periods of time. Selective attention involves the ability to discriminate and filter between relevant and irrelevant sensory stimuli. Attentional deficits in children can be detrimental to academic, social, and psychological function (Park et al., 2009).

Various programs have been studied to try to treat attention deficits following brain injury with mixed results. A challenge in evaluating specific programs is discerning the effect of the training from the potential co-intervention of being provided support. One such program is the Amsterdam Memory and Attention Training for Children (AMAT-c). The intervention consists of 3 phases, each targeting sustained attention, selective attention, or mental tracking, respectively. As the child progresses through the program, they complete increasingly difficult assignments and games with the assistance of a coach (Catroppa et al., 2015; Dvorak & van Heugten, 2018).

Four studies evaluated the effectiveness of the Amsterdam Memory and Training for children (AMAT-c) intervention in mixed brain injury populations (Catroppa et al., 2015; Hooft et al., 2005; van't Hooft et al., 2003; van 't Hooft et al., 2007). In majority of the studies sustained attention did not improve compared to baseline or controls (Catroppa et al., 2015; Hooft et al., 2005; van 't Hooft et al., 2007). In terms of selective attention, the results were also conflicting; three studies reported that selective attention improved in the AMAT-c intervention (Hooft et al., 2005; van't Hooft et al., 2003) and was maintained by 6-month follow-up (van 't Hooft et al., 2007). Memory improved in all studies.

Key Study

Author/Year/ Country/Study Design/PEDro Score/N	Methods	Outcome
Hooft et al.(2005) Sweden RCT PEDro=6 N_I=40, N_F=38	**Population:** ABI: TBI=21, Brain Malignancies=14, Encephalitis=2, Anoxia=1; *Amsterdam Memory and Attention Training for Children (AMAT-c, n=18)*: Mean Age=11.7yr; Gender: Male=12, Female=6; Mean Time Post Injury=2.2yr; Severity: Mild/Moderate=7, Severe=5. *Controls (n=20)*: Mean Age=12.6yr; Gender: Male=10, Female=10; Mean Time Post Injury=2.6yr; Severity: Mild/Moderate=6, Severe=3. **Intervention:** Patients were randomly allocated to perform an interactive activity for 30mins, 6d/wk over 17wk using the AMAT-c program or to an interactive program chosen by the patient, teacher and parents. The AMAT-c was completed in three	1. At post-treatment, children in the AMAT-c group had significant improvements on the GDS (p=0.01), but not on any other measure of sustained attention (ART and VRT, p=0.38 and p=0.52 respectively) compared to controls. 2. On selective attention measures, the AMAT-c group performed significantly better from baseline to post-treatment on both TMT A and B (p=0.002 and p=0.006 respectively), WISC-III Coding scale (p=0.002), Stroop Test 1 (p=0.02) but not Stroop Tests 2 and 3 (p=0.08 and p=0.27 respectively), and BCT number of correct answers (p=0.002) but not BCT reaction time (p=0.53).

Author/Year/ Country/Study Design/PEDro Score/N	Methods	Outcome
	phases; sustained attention, selective attention, and mental tracking. Assessments were completed at baseline and at post-treatment. **Outcome Measure:** Wechsler Intelligence Scales for Children (WISC-III) Coding and Digit Span tests, Visual Reaction Time (VRT), Auditory Reaction Time (ART), Gordon Diagnostic System (GDS), Stroop Tests, Trail Making Tests A and B (TMT A and B), Rivermead Behavioural Memory Test (RBMT), Rey-Osterrieth Complex Figure (ROCF), Binary Choice Test (BCT), 15 Word Test.	3. Performance on memory tasks significantly improved in the AMAT-c group at post-treatment compared to controls on WISC-III Digit Span (p=0.0004), ROCF (p=0.003), RBMT (p=0.00004). Immediate recall on the 15 Words Test was not significantly different between groups (p=0.39) but delayed recall on the test was significant greater in the experimental group (p=0.02).

Considerations for Inpatient Rehabilitation Based on the Quality of Care Indicators for the Rehabilitation of Children with TBI (Rivara et al., 2012).

- *Interventions employed to improve attention or executive functions in children with TBI should train meta-cognitive strategies.*
- *Interventions employed to improve attention or executive functions in all children with TBI should be applied to functional activities, such as:*
  a. completing school work, b. keeping track of medical information, c. keeping track of personal information, d. planning daily activities or schedules, and e. other activities relevant to the child's needs if specifically documented in the child's goals.
- *Interventions employed to improve attention in all children with TBI should document training of external strategies, such as: a. environmental modifications (eg, removal of distractions such as TV), b. fatigue management (eg, frequent breaks), c. a formal low sensory stimulation protocol.*

4.5.3.2 Remediation of Learning and Memory

Memory impairment is one of the most debilitating symptoms following brain injury and it is estimated that time and cost of care would be reduced if effective medical treatments were found to improve memory (Hooft et al., 2005; McLean et al., 1991). In the broadest sense, learning and memory deficits are defined as ***problems with the encoding, consolidation, and/or retrieval of new or old information***. Typically, memory performance is tackled by: (1) restoration/retraining of memory and (2) compensation.

Table 6. Examples of Learning and Memory Interventions

Intervention	Evidence
Pager • provided messages containing memory and planning cues	There is limited evidence that the use of a pager system may improve memory and planning activities compared to having no pager system in adolescents post TBI (Wilson et al., 2009).
Memory Rehabilitation Program • 6, 1.5hr sessions involving self-instruction and diary entry training	There is limited evidence that rehabilitation focused around diary entries and self-instructional training may temporarily improve memory deficits in children post TBI (Ho et al., 2011).
Cognitive Rehabilitation Therapy • Focused on alertness, attention, concentration, perception, memory skills, and problem solving.	There is limited evidence that biweekly sessions of cognitive rehabilitation may improve memory skills in pediatric patients post TBI (Brett & Laatsch, 1998).

Wilson et al. (2009) used a pager as a memory aid to help children remember and attain their everyday tasks more consistently. All participants improved in their percentage of targeted behaviours achieved throughout the day when using the pager. These improvements were maintained (to a slightly lesser degree) when the pager was removed (Wilson et al., 2009). Another memory aid that has been tested is the use of a diary, specifically when used in combination with self-instructional training that focused on developing self-regulation and self-awareness skills (Ho et al., 2011). Children in this study experienced improvements in their daily memory deficits; however, unlike with the pager system, these improvements were not maintained at follow-up. Furthermore, the number of diary entries was significantly correlated with improvement in memory deficits. In a case series completed by Brett and Laatsch (1998), 10 school aged children were offered biweekly session of cognitive rehabilitation for 20 weeks. Pre- and post-testing results revealed a modest improvement in memory skills only. This was attributed to engagement in a variety of verbal memory strategies (repetition, clustering, and semantic processing).

4.5.3.3 Remediation of Executive Functioning

Executive functions refer to higher-level cognitive functions that are primarily mediated by the frontal lobes. These functions include ***insight, awareness, judgment, planning, organization, problem solving, multi-tasking, and working memory*** (Lezak, 1983). Executive deficits are particularly relevant following TBI from both a pathophysiological as well as a psychosocial perspective. Bilateral frontal lobe involvement occurs frequently in TBI, in contrast to unilateral lesions following vascular injury (Greenwald et al., 2003). Direct contusions to the frontal and temporal lobes, as well as diffuse axonal injury, can affect executive functioning. Patients with a TBI may present with cognitive and behavioral deficits in the presence of minimal physical impairment because of these patterns of injury.

Counsellor Assisted Problem Solving Therapy

Problem-solving therapies have shown promise for rehabilitating deficits post TBI in pediatric populations (Krasny-Pacini et al., 2014; Kurowski et al., 2014; Wade et al., 2014). In particular, Counsellor Assisted Problem Solving Therapy (CAPS), a web-based problem-solving program, has gained status as an effective intervention used to improve cognitive and behavioural deficits in children post TBI. Multiple studies have compared CAPS to other internet-based interventions and have found evidence supporting its benefit in the executive functioning of pediatric patients post-TBI, particularly adolescents (Kurowski et al., 2013;

Tlustos et al., 2016; Wade et al., 2015; Wade et al., 2014). Linden et al. (2016) conducted a meta-analysis that confirmed that the CAPS intervention was beneficial in remediating executive functioning but that only a small to medium effect size was found. A clinically important effect on the patients was deemed to be unlikely. Counsellor-assisted problem solving should be considered to help remediate executive function for those over the age of 14, as well as those with a severe TBI.

Another large body of evidence was found discussing the effects of metacognitive therapies for improving executive function post-TBI in pediatric populations. There is evidence that metacognitive therapies such as the Strategic Memory Advanced Reasoning Training (SMART) program improves higher-order cognitive functioning and reasoning in pediatric populations.

4.5.3.4 Rehabilitation of Communication Deficits Post ABI

During childhood, language and communication skills are continuously maturing and when brain injuries occur, there may be an abnormal delay in the emergence of skills, or a reduction in eventual mastery levels (Didus et al., 1999). It is known that pragmatic language skills are developing until at least the age of 12 years. ***Pragmatic language skills refer to the social language skills used during social communication and includes what is said, how it's said, non-verbal communication and appropriateness of the interaction.*** When these skills are impaired and proper development does not occur, in addition to impaired communication, the child's ability to effectively interact with peers is affected, in turn impacting upon social processes (Didus et al., 1999; Savage et al., 2005).

Several aspects of communication have been described; among them are the use of listening, speaking, reading, writing and gesturing to understand an idea or to express thoughts. 'Speech' refers to the production of sounds that make up words and sentences; however, 'language' implies the use of words or ideas to express or interpret thoughts. Finally, 'cognitive communication' refers to the use of language and underlying processes (attention, problem solving etc.) to communicate effectively. There are 3 types of language abilities (receptive, expressive and pragmatic) that can be affected by an ABI (Savage et al., 2005), either individually or as a group (DePompei & Hotz, 2001). Several interventions have been explored for individuals whose communication has become impaired as a result of an ABI. The most common approach is therapy targeting accommodations, but other therapies include targeting remediation and metacognitive strategies (Turkstra et al., 2015). In terms of remediating communication skills, younger children benefit more from behaviour-based approaches whereas older adolescents benefit from reasoning strategies (Shaw, 2016).

Types of communicative competencies (Rivara et al., 2012):

- Active listening
- Turn taking
- Topic initiation
- Topic management
- Verbal organization
- Non-verbal communication behaviours (eye contact)

For communication deficits specifically there is limited evidence in the pediatric literature. One study has demonstrated that electropalatography treatment may be effective at improving articulation post-TBI in pediatric populations (Morgan et al., 2007). While a second study has demonstrated that a peer-group

language skills training may also be effective for improving communication in children (Wiseman-Hakes et al., 1998). It should be noted that both of these studies only provide limited evidence.

4.5.4 Motor Rehabilitation

Q8. What interventions have been shown to be effective in the pediatric population for improving motor deficits post-ABI?

Answer

1. Constraint induced movement therapy
2. Walking and balance exercises
3. Physiotherapy
4. Robot mediated therapy
5. Virtual reality training (ie. Nintendo Wii)

Improvements in motor function have been reported in children after sustaining an ABI; however, differences in gait velocity, stride length, and hand function may persist in the long term (Kuhtz-Buschbeck et al., 2003). Baque et al. (2016) conducted a systematic review on motor rehabilitation and found both physiotherapy and virtual reality result in favourable outcomes in the pediatric population.

Home based exercise programs are effective at improving motor function in children who have sustained an ABI (Katz-Leurer et al., 2008; Katz-Leurer et al., 2009). Both of the home based exercise programs studied were considered short term intensive programs and were implemented in the chronic phase of brain injury rehabilitation. In the 2008 study, balance and motor coordination (Sit-stand-sit, step-up exercises) and walking performance (2 Minute Walk Test, Walking Speed) improved within the group of children that received exercise therapy, but there was no generalized effect for unpracticed motor skills (i.e., grasping action) (Katz-Leurer et al., 2008). When compared to a group of children who continued with daily activities, children in exercise therapy still improved in their functional balance performance (Time up and Go Test), aerobic capacity (repetitions in the sit-to-stand, and step-up sideways on preferred and non-preferred leg movements) but not in walking performance (2 Minute Walk Test, Walking speed) (Katz-Leurer et al., 2009). These improvements were maintained immediately after the conclusion of the program, but not at the six week follow-up within the exercise group (Katz-Leurer et al., 2009). Overall, home based exercise programs seem to improve coordination, dexterity and aerobic capacity more significantly than simple regular daily activities in the short-term, however these benefits may not be maintained for longer than 6 weeks.

Key Study

Author/Year/ Country/Study Design/PEDro Score/N	Methods	Outcome
Katz-Leurer et al. (2009) (Katz-Leurer et al., 2009) Israel RCT PEDro=7 N_I=20, N_F=9	**Population:** ABI: TBI=10, Cerebral Palsy=10; *Home-based exercise (n=10)*: Mean Age=8.2yr; Gender: Male=7, Female=3; GCS Score=<8. *Control Group (n=10)*: Mean Age=9.2yr; Gender: Male=7, Female=3; GCS Score=<8. **Intervention:** Patients were randomly assigned to receive either a home based exercise program (sit-to-stand and step-up exercises; 5d/wk for 6wk) or instructions to maintain regular daily activities. Assessments were conducted at baseline, post-treatment and at 6wk follow-up. **Outcome Measure:** Timed Up and Go Test (TUG), Functional Reach Test (FRT), Two-minute Walk Test (2MWT), walking speed, number of repetitions for sit-to-stand and step-up exercises.	1. Patients in the exercise group demonstrated a significantly greater improvement in TUG scores, FRT forward, FRT preferred hand (p=0.01 for all) compared to controls from baseline to post-treatment. 2. No significant differences reported for FRT non-preferred hand subscore, 2MWT or walking speed from pre to post-treatment. 3. Within group, the exercise group performed significantly more sit-to-stand, step-up sideways on preferred/non-preferred leg movements from baseline to post-treatment. Step-up exercises performed forwards, regardless of preferred/non-preferred leg did not yield significant improvements. 4. No significant differences were found on any measures for the exercise group from post-treatment to 6wk follow-up.

4.5.4.1 Constraint Induced Movement Therapy

Constraint induced movement therapy (CIMT) has two key components: first, the limb that is least or not at all impaired is constrained. Following this, a therapist leads the patient in a program of intensive, repetitive daily motor movements that are performed with the affected limb (Cimolin et al., 2012). The mechanism underpinning this approach involves using the impaired limb to promote neuroplasticity and cortical reorganization (Gordon & Di Maggio, 2012).

Cimolin et al. (2012) found that motor function improved post intervention in the hemiparetic limb of each child who had sustained a TBI. Prior to treatment, movements with the affected arm were slower and took longer. Post intervention, improvement was noted in the arm's overall range of motion and the execution of movement. Gross motor function also improved significantly following CIMT therapy compared to baseline, however the authors suggest that such improvement may be attributed to spontaneous recovery over time. Despite findings from Cimolin et al. (2012), there are concerns for CIMT in the pediatric population, such as tolerability of such intense treatment, inability to deal with psychological effects from frustration, and difficulties with bimanual movements (Cimolin et al., 2012). To date the evidence on CIMT is limited.

4.5.4.2 Technological Aids in Motor Rehabilitation

Technological aids in motor rehabilitation for children are primarily in two categories: virtual reality-based, or robot mediated therapies. Virtual reality therapy consists of creating simulated environments where individuals can practice cognitive and/or motor skills in a controlled environment. The most commonly used systems today include the Nintendo Wii and Wii-Fit software (Gil-Gómez et al., 2011). Robotic assisted therapies for upper and lower limb have also been studied minimally.

There is limited evidence that use of a Nintendo Wii console can improve motor coordination, as well as the amount and intensity of physical activity that a patient participates in, in children post ABI (De Kloet et al., 2012). There is also limited evidence that walking and balance exercises performed in a virtual reality environment can improve pelvic and ankle kinematics, but not knee flexion, compared to healthy controls in children post ABI (Biffi et al., 2015). The current literature suggests that simulators are a user-friendly, safe and motivating tool that can be used as part of a therapeutic intervention, however further studies are required to support their use as main-stays in motor therapy post ABI. Beretta et al. (2015) used a body-weight supported treadmill in combination with physiotherapy to re-train gait performance in children following an ABI. There was a global improvement in both motor and functional abilities of the lower limbs in children who received robotic assistance and physiotherapy compared to those who received standard physiotherapy alone.

Key Studies

Author/Year/ Country/Study Design/N	Methods	Outcomes
Beretta et al. (2015) Italy Prospective Controlled Trial N=23	**Population:** ABI: TBI=11, Tumor=7, Ictus=4, Anoxia=1; Robotic-Aided Gait Training (RAGT; n=23): Mean Age=11.8yr; Gender: Male=12, Female=11. Controls (n=11): Mean Age=10.4yr; Gender: Male=7, Female=4. **Intervention:** Patients assigned to the RAGT group (45min/d for 5d, for 4wk) were provided the use of an exoskeleton designed to perform a walking pattern on a treadmill, in addition to 20 sessions of physiotherapy. The control group received physiotherapy only. **Outcome Measure:** 6-Minute Walk Test (6MWT), Gross Motor Function Measure (GMFM), Functional Assessment Questionnaire (FAQ), 3D Gait Analysis.	1. The RAGT group improved significantly in overall gross motor function on the GMFM ($p<0.001$). 2. Subgroup analyses of ambulant patients revealed that the RAGT group improved significantly on the FAQ ($p=0.007$), 6MWT ($p<0.005$), GMFW Dimension C ($p=0.006$) D and E (both $p=0.001$), whereas control patients only improved significantly on the GMFW Dimension C ($p<0.05$).

4.5.4.3 Spasticity

Q9. Which pharmacological agent has the strongest evidence for use in pediatric populations for the treatment of spasticity?

Answer.

1. Botulinum toxin type A.

Spasticity has been defined as "*a velocity-dependent increase in tonic stretch reflexes*" and is one component of the upper motor neuron syndrome (pg S182) (O'Brien, 2002). For some individuals who sustain an ABI, spasticity post injury can present as a mild to severe range of motion restriction, repetitive spasms, and/or pain. The treatment of spasticity ranges from physiotherapy (to stretch muscles) to the administration of medication. Unfortunately, the research into bracing and stretching is limited.

Two studies evaluated the effectiveness of botulinum toxin type A (BTX-A) for the management of spasticity in children with an ABI. Overall, BTX-A improved spasticity and range of motion in children and adolescents with an ABI (Guettard et al., 2009; van Rhijn et al., 2005). When BTX-A for both upper and lower extremities was paired with other therapies (physical, occupational and exercise therapy) improvements were seen not only in spasticity and range of motion, but also voluntary motor control. Due to the lack of comparison groups, conclusive statements about the efficacy of BTX-A are difficult to make. Currently, it is unclear if the improvements in spasticity and mobility were due to the combination of therapy, BTX-A alone, or the standard therapy. Importantly, BTX-A treatment was not associated with any adverse side effects for injection doses under 10 U/kg of botulinum toxin (Guettard et al., 2009; van Rhijn et al., 2005). As such, Intra-muscular BTX-A injections may be considered a safe treatment for children with severe brain injury, and effective when used in combination with orthotic devices and specific functional exercise programs.

Key Study

Author/Year/ Country/Study Design/N	Methods	Outcome
Van Rhijn et al. (2005) Belgium Prospective Controlled Trial N=21	**Population:** TBI; Age Range=2.7yr-19.8yr; Gender: Male=15, Female=6. *Group 1 (n=4)*: Mean Time Post Injury=35.8mo. *Group 2 (n=10):* Mean Time Post Injury=11.3mo. *Group 3 (n=7):* Mean Time Post Injury=18.0mo. **Intervention:** Patients in Group 1 (spastic quadriparesis with impaired consciousness) received bilateral injections of botulinum toxin type A (BTX-A) to the hip adductors, knee and plantar flexors. Group 2 (patients with upper limb spasticity) received unilateral injections to the elbow, fingers, wrist flexors, and/or shoulder muscles. Group 3 patients with lower limb spasticity) received bilateral and unilateral injections to the plantar, knees, hip flexors, and/or hip adductors. Following the injections, all patients received a cast or an orthosis with Groups 2 and 3 receiving additional physiotherapy, ergotherapy and functional exercises. Assessments were conducted at baseline, 1mo, 3mo and 5mo. **Outcome Measure:** Modified Ashworth Scale (MAS), range of motion (ROM) goniometry assessment.	1. All groups demonstrated improvements in spasticity on MAS from baseline to 1mo. 2. At 3mo follow-up, Group 1 demonstrated the greatest level of improvement in spasticity on MAS compared to baseline. Groups 2 and 3 also demonstrated improvements from baseline to 3mo. 3. At 5mo follow-up, Group 2 continued to demonstrate improvements in spasticity on MAS compared to baseline. Groups 1 and 3 also exhibited improvements compared to baseline, but improvements had declined in comparison to 3mo follow-up. 4. Group 2 exhibited the greatest level of improvement in ROM with mean increases of 23°, 36° and 53° at 1mo, 3mo and 5mo follow-ups compared to baseline. 5. ROM in Group 3 improved by a mean of 4° from baseline to 1mo follow-up but then experienced a -6° decline at 3mo follow-up and a -3° decline at 5mo follow-up compared to baseline ROM. 6. Group 1 exhibited moderate improvements in ROM with mean increases of 5°, 7° and 2° at 1mo, 3mo and 5mo follow-ups compared to baseline.

4.5.5 Vestibular Recovery

Q10. Define Vestibular dysfunction and identify some of its symptoms.

Answer.
1. Vestibular dysfunction is when the brain does not receive proper sensory information from the inner ear, and results in balance and eye movement problems.
2. The primary symptoms of vestibular dysfunction are vertigo, dizziness, imbalance and spatial disorientation, vision disturbances, hearing changes, and cognitive or psychological changes.

Vestibular dysfunction is commonly overlooked in the pediatric population post ABI. Symptoms may include vertigo, balance problems, visual complaints (double vision, blurriness), and nausea. Mann and Black (1996) noted that the most common persisting vestibular symptom after TBI is positional vertigo (symptoms provoked by head movement). Head trauma has been shown to be the third most common cause of childhood vertigo, accounting for 14% of all cases (Gioacchini et al., 2014). Common assessments used when evaluating vestibular dysfunction are caloric testing (cold water injected into the inner ear), electronystagmography, and the Dix-Hallpike maneuver (Cifu & Caruso, 2010).

4.6 Non-Accidental Injury

Q11. What age are children most likely to present with a non-accidental injury, and what are the mortality rates associated with this type of trauma?

Answer.
Children most often experience a non-accidental injury between 2.5-4 months old when the colic period is at its highest. Approximately 13-50% of NAI cases result in death.

The constellation of injuries associated with non-accidental trauma sustained during infancy, such as retinal hemorrhage, intracranial and musculoskeletal injuries has been referred to as shaken baby syndrome, whiplash-shaken infant syndrome, shaken impact syndrome, infant shaken impact syndrome, non-accidental or abusive head injury (Dias et al., 2005). NAI occurs when a child is shaken in an angular movement repeatedly. This acceleration and deceleration motion causes the brain to rotate within the baby's skull, resulting in high gravitational forces transmitted to the brain (Deputy, 2003; Macdonald & Helfrich, 2001; Tsao et al., 2002).

Occurrences of NAI tends to increase between 2.5 to 4 months when the period of "colic" is at its highest (Goulet et al., 2009). Due to the anatomy of an infant, they are at an elevated risk of developing long-term disabilities, impairments, injury and even death as a result of brain injuries (Gutierrez et al., 2004). Deaths from NAI account for 13-50% all non-accidental pediatric deaths recorded (Dias et al., 2005; Goulet et al., 2009; Lancon et al., 1998), and for the infants that survive, severe neurological impairments and physical disabilities are recorded in over half of cases (50-75%)(Dias et al., 2005; Goulet et al., 2009). NAI can result in many possible long-term consequences such as "*permanent brain damage, visual impairments,*

developmental delays, disabilities and motor impairments, paralysis, eye damage, hearing loss, blindness, decreased movement from spastic muscles, seizures and even death" (Carbaugh, 2004).

Risk Factors of Non-Accidental Injury (Carbaugh, 2004; Goulet et al., 2009; Lewin, 2008)

- Frequent and inconsolable crying (colic or purple crying)
- Male gender
- Difficult infant temperaments
- Prematurity
- Low-birth weight
- Special needs
- Medical fragility

Diagnosis and Clinical Findings

As the clinical symptoms of NAI are non-specific, each case tends to vary in its presentation. Minor symptoms of NAI can be mistaken for other childhood illnesses which lead to challenges in recognizing the syndrome. Common clinical signs include irritability, seizures, impaired consciousness, bulging fontanelle, abnormal eye movements, vomiting, lethargy, poor feeding, apnea and muscle weakness (Altimier, 2008; Carbaugh, 2004; Duhaime et al., 1998; Lewin, 2008). Brain swelling, subdural hemorrhage (SDH) and retinal hemorrhaging are three classic symptoms that can indicate an infant has been abused (Mian et al., 2015). As there is no one sign or symptom of NAI, high clinical vigilance is needed when assessing infants with altered neurological status.

Assessments such as neurologic and ophthalmologic examinations, skeletal survey, CT and MRI of the head are used to diagnose NAI (Coody et al., 1994; Duhaime et al., 1998). CT scans have been shown to be superior to MRI when viewing the damage to the infant's brain, especially since findings like intracranial hemorrhage, hairline skull fractures, and compression fractures in the skull are all visible on CT scan (Coody et al., 1994).

Table 7. Diagnostic Findings in Non-Accidental Injury (Carbaugh, 2004) (p.110).

Test	Findings Consistent with Non-Accidental Injury	
Computerized Tomography (CT)	• Subdural hematomas • Subarachnoid haemorrhage • Cerebral contusions • Cerebral edema	• Subtle skull fractures • Ventricular enlargement • Brain atrophy (chronic finding) • Hypodense areas
Magnetic Resonance Imaging (MRI)	• Subdural haematomas • Subarachnoid haemorrhages • Cerebral contusions • Cerebral edema • Subtle skull fractures	• Ventricular enlargement • Brain atrophy (chronic finding) • Hypodense areas • Intraparenchymal lesions • Chemical state changes of haemoglobin that substantiate repeated injuries
Skeletal Survey	• Long bone injury • Traction fractures (corner and bucket handle) • Periosteal striping	• Long bone bruising • Skull fractures • Rib fractures

	• Metaphyseal fracture • Shaft fracture	• Fractures in various stage of healing
Ophthalmologic Examination	• Retinal haemorrhages • Vitreous haemorrhage • Papilledema • Retinal detachment • Anisocoria (unequal pupils) • Orbital and lid ecchymosis • Subconjunctival haemorrhage	• Hyphema • Sixth nerve palsy • Disruptions of contents of the eye • Optic nerve haemorrhage • Optic nerve scleral junction haemorrhage • Orbital fat haemorrhage • Disconjugate eye movements

Treatment

Acute management of NAI, particularly if the infant is unconscious, may include intubation, ventilation, fluid resuscitation and anticonvulsant therapy (Duhaime et al., 1998).

Education and Prevention

The largest formally evaluated education program is the Period of PURPLE Crying Prevention initiative. The PURPLE program has strong evidence for improving maternal behaviors such as walking away during inconsolable crying and sharing information on the dangers of NAI.

Key Study

Author/Year/ Country/Study Design/PEDro Score/N	Methods	Outcomes
Barr et al. (2009b) USA RCT PEDro=5 N=2738	**Population:** *PURPLE (n=1374)*: Gender: Male=0, Female=1374. *Control Group (n=1364)*: Gender: Male=0, Female=1364. **Intervention:** Mothers of newborn infants were randomly assigned to receive the Period of PURPLE Crying prevention material package consisting of a DVD and an 11-page booklet, or a DVD on injury prevention and two brochures as part of a control group. All mothers completed a 4-day diary of the infant's behaviours at 5wk post-birth followed by a telephone survey at 2mo. Mothers were assessed on their knowledge of crying and shaking, and their behavioural responses to stressful situations. Assessments were conducted at post-treatment. **Outcome Measure:** Baby Day Diary (BDD), telephone survey.	1. Mothers who received the PURPLE intervention scored higher on the Crying Knowledge and Shaking Knowledge scales of the telephone survey compared to the control group. 2. Sharing advice with other caregivers about walking away during inconsolable crying and the dangers of shaking was more frequent for the treatment group than the controls but no between group differences for sharing advice on infant crying. 3. Responses to crying scores on the telephone survey were higher in the PURPLE group for crying, inconsolable crying, and self-talk compared to the control group (non-significant). 4. The PURPLE group documented significantly more infant distress in the BDD compared to the control group ($p<0.05$).

Overall the largest impact on NAI is to be made through education. Programs that are administered within the hospital and provided through a healthcare professional are effective in communicating the dangers of shaking an infant (Altman et al., 2011; Bechtel et al., 2011; Deyo et al., 2008; Dias et al., 2005; Simonnet et al., 2014), and helping parents change their behaviour, such as "taking a break if frustrated with a crying infant" (Bechtel et al., 2011).

The PURPLE intervention has been shown to improve maternal knowledge of infant crying compared to an infant safety information control group (Barr et al., 2009a; Barr et al., 2009b; Fujiwara et al., 2012); however, improvements in knowledge regarding infant shaking was only shown in one study (Barr et al., 2009a). Mothers reported walking away from infant with inconsolable crying more than the control group (Barr et al., 2009b; Fujiwara et al., 2012), and more mothers shared this information with other caregivers (Barr et al., 2009a; Barr et al., 2009b; Fujiwara et al., 2012).

4.7 Case Study

Patient Snapshot:

Aaron
Is a 14-year-old boy who sustained a TBI after falling 25 feet from a tree. The fall was witnessed by bystanders and he was unconscious for several minutes. He was transferred to the local trauma centre and cared for in the Pediatric Intensive Care unit where he remained intubated for 7 days. It is now two weeks post injury and Aaron has been transferred from the Pediatric Intensive Care unit to the General Pediatrics Ward for further therapy, under your care.

Lifestyle Factors: Aaron is currently a student, with no history of alcohol abuse or smoking. He has a parental support system at home as he lives with his mother (Karen) and father (Jim), as well as four younger siblings. He is entering grade 9 in the fall.

Medical History: Aaron had an initial GCS of 5. Neuroimaging showed subarachnoid hemorrhage over the right parietal-occipital lobe and evidence of microhemorrhage and diffuse axonal injury of the frontal lobes bilaterally. There was trace hemorrhage in the occipital horns of the lateral ventricles, but no hydrocephalus. There was no significant mass effect. There was no c-spine injury. He had no complications in PICU and ICP was managed with 3% saline in the first 24 hours. He also had a minor liver laceration, but no intervention was required.

He was diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) at age 7 but is not currently taking any medication. He has a history of Asthma. He has had no prior hospitalizations or surgeries. He fractured his elbow at age 4, falling down a slide.

Signs & Symptoms: On your initial assessment of Aaron's mental status, you determine that he:

- Can recognize his family members but is not consistently orientated to date or location
- He has difficulty remembering events from the day prior
- He often makes comments that are off-topic or out of context to the situation
- He can ambulate and when left unattended, attempts to leave the room
- He sleeps for short periods in the day and is awake for 1-3 hours at a time over night
- He requires reminders and support for the sequence of his daily activities (i.e. brushing his teeth).

Q1. Based on the Rancho Los Amigos Scale, at which level is Aaron functioning?

Level V – Confused, inappropriate

His parents are very concerned about their son's inappropriate behaviour/memory problems and what this means for his recovery. What can you do to help them understand the recovery process?

Provide the family with a copy of the family RLA and suggest:

1. Repeat things as needed. Don't assume that he will remember what you tell him.
2. Tell him the day, date, name and location of the hospital, and why he is in the hospital when you first arrive and before you leave.
3. Keep comments and questions short and simple.
4. Help him organize and get started on an activity
5. Bring in family pictures and personal items from home.
6. Limit the number of visitors to 2-3 at a time.
7. Give him frequent rest periods when he has problems paying attention.

The next day on rounds, the nurses communicate that Aaron often chokes during means. What should you do next?

1. Consult a speech-language pathologist for bedside assessment and to determine need for modified barium swallow study.
2. Given Aaron's confusion, a bedside assessment is recommended first.

After another 2 weeks in hospital, the neuropsychologist has cleared Aaron from PTA. He has been working with the occupational therapist on daily activities. The Neuropsychologist has recommended a screen assessment of cognitive skills to help with transition planning.

Q2. What are some common neurocognitive areas of deficit following pediatric TBI?

1. Pragmatic language
2. Executive functions
3. Attention
4. Impulse control
5. Processing speed

Aaron continues to experience disruption in his sleep with significant difficulties in sleep onset and maintenance. What are some additional medical causes that may contribute to poor sleep post TBI?

Possible causes include: Periodic limb movement, Restless leg syndrome, obstructive sleep apnea, medication side-effects, pain.

Q3. What are some non-pharmacological interventions that could be done?

1. Regulate day/night cycle with opening curtains during the day
2. Allowing for activity as tolerated during the day
3. Limit nursing interventions needed during sleep
4. Ensure dark sleeping environment
5. Provide relaxation strategies

Six months later Aaron has returned home after completing inpatient rehabilitation at a pediatric centre. He has returned to school 3 days a week. He is in grade 9 at a new high school. He completes his work in the resource room and receives some one on one instruction. The school has voiced concerns with Aaron's ability to learn and feel his inattention and impulsivity are significant barriers. His parents have a similar difficulty at home with having Aaron follow through with requests; he needs frequent reminders to stay on task and they have given up trying to do homework. He is in regular conflict with his younger sister.

Q4. What are two standardized tools you could use to assess Aaron's behaviours?

- Behavioural Assessment System for Children
- Conners Comprehensive Behavior Rating Scale
- Behavior Rating Inventory of Executive Function
- Child Behavior Checklist

As Aaron had a premorbid diagnosis of ADHD, it would be important to review these symptoms in multiple contexts and in relation to his pre-morbid function. Questionnaires should be completed by both school and parents. If parents are separated, ensure you gather information from each parent.

You are seeing Aaron in your clinic and you review his parents' concerns with behaviour. What medical considerations should you screen for on your history and physical to look for contributors or causes of poor attention & problem behaviours (other than his pre-morbid ADHD)?

1. Sleep disruption/disorder
2. Neuroendocrine dysfunction – especially thyroid function, growth hormone and cortisol
3. Seizure disorder
4. Pain or headaches
5. Undertreated chronic disease (i.e. asthma)
6. Substance use (in adolescent population)

On review of systems, Aaron eats well and is growing. He does not have any pain or headaches. He still requires his puffers with frequent colds and often coughs at night even without illness. He is not restless at night and has no snoring. His parents have not noticed any abnormal movements or signs of a seizure.

He has had no syncope. He takes a long time to settle to sleep at night because he is still 'on the go'. His parents have trouble setting a consistent bedtime. He does not nap during the day but does seem quite tired after school. He has not had any bowel or bladder problems. His gait has been normal.

Aaron has a normal physical exam.

He does not take any regular medications; he was previously on an inhaled corticosteroid for his asthma when he was younger, but his parents stopped that about a year ago. He has no allergies and his immunizations are up to date.

Q5. What are possible mental health or neurocognitive considerations for his poor attention and problem behaviours?

- Depression, anxiety, post-traumatic stress
- Slow processing speed
- Pragmatic language impairment
- Executive function deficit following TBI
- Exacerbation of pre-morbid ADHD
- Frontal lobe syndrome
- Family dysfunction

Q6. What are some family or school factors which may be contributing to Aaron's behaviour?

- Lack of routine or explicit expectations for Aaron both at home and/or school
- Lack of education for teachers around strategies to support children with TBI (use of visuals, clear expectations, low distractions)
- Change in parenting style to more permissive parenting following the trauma of seeing their child injured
- Mis-match between academic expectations and Aaron's abilities

You start with counseling the family around setting expectations, especially at bedtime, reinforcing the importance of good sleep hygiene. As sleep problems following TBI and in children with pre-existing neurodevelopmental disorders are common, you also suggested they try melatonin. You arrange to follow up in 3 months.

Q7. What is the evidence for treatment of sleep disorders in pediatric TBI?

- No randomized clinical trials
- Role for both pharmacological and non-pharmacological interventions
- Consider restless leg syndrome, OSA and nocturnal seizures
- Identify modifiable environmental factors such as setting limits, creating a routine and ensuring dark and quiet room
- Limit screen time before bedtime to no more than two hours before desired bedtime

Aaron and his parents return for follow up in 3 months. He is sleeping better with Melatonin 5 mg. He now is asleep by 10 pm. He still has significant impulsivity and difficulty initiating and completing tasks, even with visual supports, planners and school supports. You review questionnaire data from home and school and determine that Aaron has many un-treated symptoms of ADHD. You compare to

questionnaires you did prior to his injury and see a similar pattern but with more impairment. His parents ask about medication options.

Q8. What is the role of medication in the treatment of this child's deficits? What other treatment recommendations can you make?

The evidence for medications to target disruptive behaviour, impulsivity and attention deficits in children following TBI is mixed with much heterogeneity in study population and medications studied. In this case, Aaron has a pre-exisiting diagnosis of ADHD and exacerbation of executive dysfunction following TBI is well described. A trial of a long-acting stimulant could be considered, following best practice for treatment of ADHD.

Counsellor led behaviour strategies should also be explored to assist Aaron in building his problem-solving strategies around conflict resolution.

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