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

14. Pediatric Acquired Brain Injury Acute Care and Rehabilitation Interventions

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Key Points

Head elevation may lower intracranial pressure, but have no effect on cerebral perfusion pressure in children post TBI.

Therapeutic hypothermia delivered for 24, 48, or 72 hours can decrease intracranial pressure more than normothermia treatment for at least 24 hours in children post TBI, however, intracranial pressure may increase during the re-warming period.

Therapeutic hypothermia delivered for 24 or 48 hours is not different than normothermia in terms of mortality, unfavourable outcomes, or complications (arrythmias, coagulopathies, infections) in children post TBI.

Therapeutic hypothermia delivered for 24 hours can cause a decrease in heart rate, blood pressure, and cerebral perfusion pressure compared to normothermia treatment in children post TBI; further, decreases in blood pressure and cerebral perfusion pressure are associated with the development of unfavourable outcomes.

Therapeutic hypothermia delivered for 48 or 72 hours increases anti-oxidant markers, and decreases brain injury markers in the cerebrospinal fluid compared to normothermia treatment in children post TBI.

Enacting a protocol change to have cooling blankets placed on the patient's bed prior to arrival in the pediatric ABI inpatient unit may decrease duration of hyperthermic states and acetaminophen administration.

Spine injury severity, midline shift on CT scan, fixed pupils, abdominal injury, and subarachnoid hemorrhage are associated with mortality and unfavourable outcomes at 3 months post-TBI in a pediatric population that underwent hypothermia treatment.

Treatment with hypertonic saline or Lactate Ringer's solution may decrease intracranial pressure and increase cerebral perfusion pressure proportional to the increase in serum sodium in children post ABI. However, hypertonic saline may cause lower rates of acute respiratory distress syndrome and a shorter hospital length of stay compared to Lactate Ringer's solution.

Hyperosmolar therapy (3% hypertonic saline and mannitol) may not improve intracranial pressure, cerebral perfusion pressure, or serum osmolarity in children post TBI.

Hypertonic saline treatment might lower intracranial pressure acutely (30 min, 7.5% hypertonic saline) and for up to 72 h (3% hypertonic saline) in children refractory to standard therapy (Intracranial pressure>20 mmHg) post TBI, however, both concentrations increase cerebral perfusion pressure, serum sodium, and serum osmolarity.

Hypertonic saline (7.5%) treatment might cause hypernatremia, kidney injury, acute respiratory distress syndrome, and severe neurological impairment in children post TBI refractory to standard therapy (Intracranial pressure>20 mmHg)

A hypertonic saline-based protocol could increase favourable discharge disposition, but not neurological outcomes compared to non-protocol guided therapy in children post TBI.

Early (<30 min post episode) hypotensive treatment may reduce mortality in pediatric patients post TBI.

Compared to fentanyl (2µg/kg) and pentobarbital (5mg/kg), 3% hypertonic saline may reduce intracranial pressure and increase cerebral perfusion pressure more rapidly in pediatric patients post TBI.

The effect of fentanyl on intracranial pressure and cerebral perfusion pressure in pediatric patients post TBI is unclear, however, high-dose fentanyl and low-dose midazolam, used either alone or in combination, may increase intracranial pressure.

Pentobarbital administration may lower intracranial pressure and cerebral perfusion pressure in pediatric patients with refractory intracranial pressure post TBI.

It is unclear whether dopaminergic agents, including amantadine, improve emergence from disorders of consciousness post ABI, however, an amantadine protocol of 4mg/kg/d for a week followed by 6mg/kg may be a safe and effective regiment to follow.

Administration of dexamethasone can inhibit endogenous production of glucocorticoids in children post TBI.

Administration of dexamethasone likely increases the risk of bacterial pneumonia, but does not improve intracranial pressure, neurological outcomes, or blood pressure in pediatric patients post TBI.

N-Acetylcysteine and probenecid administration likely increases N-Acetylcysteine cerebrospinal fluid levels and is not associated with adverse events or hospital length of stay, in pediatric patients post TBI.

Magnesium sulfate may not adversely affect intracranial pressure, cerebral perfusion pressure, or mean arterial pressure in children post TBI.

The presence of abusive head trauma, high PRISM III score, and low post-admission GCS score may be associated with mortality in pediatric patients post TBI, however, anemia and blood transfusions are not.

Coagulation assessments performed upon admission to the pediatric TBI inpatient unit may be prognostic indicators of favourable outcomes post TBI.

A decompressive craniectomy may improve intracranial pressure, cerebral perfusion pressure and be associated with improved GCS scores in children post TBI compared to those who do not receive the procedure.

A decompressive craniectomy may be just as effective as standard therapy at reducing intracranial pressure in pediatric patients post TBI.

A decompressive craniectomy may be associated with secondary complications such as infections, formation of hygroma, and insertion of a cerebrospinal fluid shunt, in children post TBI.

Predictors of poor outcomes after a decompressive craniectomy might include non-accidental head trauma, delay (>4 hours) in surgery following admission, and intraoperative bleeding that exceeds 300 mL, in children post TBI.

Supraciliary "keyhole" small craniotomies for the treatment of anterior frontal space occupying lesions may not be associated with major operative or post-operative complications in pediatric patients post ABI.

A burr-hole craniotomy without continuous drainage for the treatment of either a chronic subdural hematoma or a subdural hygroma may not be associated with complications in pediatric patients post ABI.

There may be no difference in mortality between pediatric patients with TBI who sustained a penetrating injury and were treated at either an adult or pediatric trauma center.

Cognitive behavioural therapy may reduce internalizing behaviour disorders and improve socialization in pediatric patients post ABI, especially in patients not receiving adjunct pharmacotherapy.

Self-monitoring training might improve on-task behaviour, but not accuracy in completing assignments or task engagement, in pediatric patients post TBI.

Behavioural therapies might reduce problematic behaviours, lower agitation, and increase autonomy in pediatric patients post ABI.

Counsellor-assisted problem-solving and internet resource interventions may be effective at mitigating behavioural problems in pediatric patients post TBI, however, conflicting evidence exists as to which is superior and who benefits the most.

Mental health services are commonly underutilized within the first two years of a TBI, regardless of treatment (counsellor-assisted problem-solving versus internet resource comparison), gender, race, age, or socioeconomic status.

Online parenting skills workshops may be superior to internet resources in acutely reducing caregiver stress, depression, or self-efficacy. However, such workshops are likely not effective at improving parent-child communication post ABI.

An online problem-solving program with therapist assistance may be superior to an internet resource comparison group at improving compliant behaviour and self-management in children post TBI.

Web-based teen problem solving intervention programs are effective in reducing parental depression, anxiety, and distress compared to an internet resource comparison group, especially in families with lower socioeconomic status.

Family-based interventions benefit children, adolescents, and their families following brain injury.

An app-based coaching intervention may be effective in raising confidence and participation in activities following a pediatric TBI or brain tumor.

"Stepping Stone Triple P with Acceptance and Commitment Therapy" may improve parental outcomes and short-term behavioural problems in children post ABI.

Face to face family problem solving therapy may improve internalizing behavioural problems in children post TBI, however, it may not impact parental distress or relationship satisfaction.

Family based rehabilitation might be superior to clinician-directed care to improve cognitive and physical outcomes in children following a TBI.

A family focused inpatient social work program may be just as effective as a usual care intervention in reducing feelings of trauma and grief in parents/caregivers of children post-TBI. However, parents/caregivers undergoing an inpatient social work program may report increased confidence in managing pediatric TBI and feelings of more supportive counselling, increased family resources, and awareness of medical issues than a usual care intervention.

Use of community resource coordinators post discharge may not improve functional outcomes in children post TBI.

Multidisciplinary outpatient programs may improve functional outcomes for children following ABI.

Online family problem solving interventions likely improve everyday functioning, specifically in the school and community domains, but not at home, in adolescents who have sustained a TBI.

Interventions directed at improving social interactions might be beneficial in children post TBI.

A dedicated hospital to school transition program may not provide any more benefit than increasing special education and behavioural service access (usual care) in children post TBI.

Amantadine appears to be safe and efficacious in decreasing undesirable behaviours and improving the rate of recovery in children post TBI

The Amsterdam Memory and Training program may improve selective, but not sustained attention in pediatric patients post ABI.

The Attention Improvement and Management (AIM) program may improve sustained, but not selective, attention skills in pediatric patients with TBI compared to healthy controls.

Attention-specific neuropsychological training improves cognition, attention and behavioral skills in pediatric patients post TBI.

A cognitive computerized training (CCT) program may be feasible for pediatric patients post TBI.

Evidence regarding the efficacy of methylphenidate in improving cognitive and behavioural function following pediatric TBI is conflicting.

Utilization of a pager in adolescents post TBI may help improve memory.

Utilization of a diary in combination with self-instructional training might temporarily improve memory in children post TBI.

Cognitive rehabilitation can improve intellectual function for children following brain injury.

Counsellor assisted problem solving programs may be effective in improving executive function in adolescents post TBI; especially older adolescents (14-17 years), adolescents who suffered a severe TBI, and those with poor speech.

The Strategic Memory Advanced Reasoning Training (SMART) intervention may improve high-order cognitive functioning in adolescents post ABI.

Goal management therapy may reduce parental ratings of their child's executive dysfunction.

Therapist-assisted metacognitive treatment programs for pre-adolescents likely improve executive function and increase the use of metacognitive learning strategies post ABI.

Interventions that target problem solving may be effective at improving executive function and metacognitive abilities post ABI.

Speech therapy using electropalatography might improve articulation in children post TBI.

Peer-group training of pragmatic language skills might improve communication in children post ABI.

Injury-related information provided to participants and parents may not have an effect upon deficit self-awareness in children post TBI.

It is unclear whether upper limb lycra splints improve the quality of movement in children post TBI.

Constraint induced movement therapy may improve upper limb function in children post TBI, however, further research is required.

Virtual reality-based therapy focused on walking and balancing exercises may improve certain movements (pelvic and ankle kinematics) but not others (knee flexion) in pediatric patients post ABI.

Movement therapy using a Nintendo Wii console might improve motor coordination, as well as engagement and intensity of physical activity in pediatric patients post ABI.

Body-weight supported treadmill training with an exoskeleton combined with physiotherapy may be superior to physiotherapy alone at improving gait and motor function in pediatric patients post ABI.

A wearable ankle robot combined with a computer game interface might reduce spasticity and improve balance in pediatric patients post ABI.

Robot Mediated Therapy (RMT) combined with goal-oriented reaching tasks might improve upper limb motor function and spasticity in pediatric patients post ABI.

Botulinum toxin type A, when used in combination with adjunct therapy (physiotherapy and occupational therapy), may effectively reduce upper and lower limb spasticity to improve movement range of motion, in children and adolescents following ABI.

Intrathecal baclofen pumps may reduce upper and lower limb spasticity in children with hypoxic brain injuries, however, intrathecal pump implantation may be associated with complications such as infections and skin protrusions. Side effects may be mitigated by subfascial pump implantation.

Home based exercise programs likely improve functional balance, aerobic capacity, and dexterity in children with an ABI, however, after 6 weeks, they have similar effects.

Prophylactic phenytoin likely does not reduce early (< 1 week post injury) or late (>1 week post injury) seizures in children post ABI.

Patients receiving prophylactic levetiracetam may be more likely to develop post traumatic seizures if they are younger and have experienced abusive head trauma.

Enhanced immune enteral feeding formulas may not be superior to regular formulas in regards to improving caloric and protein intake, however, may have beneficial anti-inflammatory properties.

Initiating nutritional support earlier may result in a decrease in mortality and better outcomes in a pediatric population post ABI.

The PURPLE intervention for shaken baby syndrome may increase knowledge about crying and the effects of shaken baby syndrome among caregivers. It may also increase protective behaviours among caregivers, such as walking away during a period of inconsolable crying in their infant.

Education programs on infant crying and safety may be effective at informing parents about the dangers of shaken baby syndrome, helping change their behaviour, and reducing the number of shaken baby syndrome.

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Abbreviations

ABI	Acquired Brain Injury
ADHD	Attention Deficit/Hyperactivity Disorder
AMAT-c	Amsterdam Memory and Attention Training for Children
BTX-A	Botulinum Toxin Type A
CAPS	Counsellor Assisted Problem Solving Therapy
CPP	Cerebral Perfusion Pressure
DC	Decompressive Craniectomy
GCS	Glasgow Coma Scale
HTS	Hypertonic Saline
ICH	Intracranial Hypertension
ICP	Intracranial Pressure
I-InTERACT	Internet-Based Interacting Together Everyday
IRC	Internet Resource Intervention
nTBI	non-Traumatic Brain Injury
PCT	Prospective Controlled Trial
PTS	Post Traumatic Seizure
RCT	Randomized Controlled Trial
RH	Retinal Hemorrhage
SBS	Shaken Baby Syndrome
SMART	Strategic Memory Advanced Reasoning Training Program
TBI	Traumatic Brain Injury

Pediatric Interventions in Acquired Brain Injury Rehabilitation

14.0 Introduction

Acquired brain injuries can be separated into two broad categories based on their etiology: Traumatic brain injuries (TBI) and non-traumatic brain injuries (nTBI). TBI is commonly caused by motor vehicle accidents, falls, assaults, gunshot wounds, and sport injuries (Greenwald et al., 2003) while nTBIs often caused by focal brain lesions, anoxia, tumors, aneurysm, vascular malformations, and infections of the brain (Braga et al., 2005) Module 1: Introduction and Methodology).

Unfortunately, interruptions to normal child development are frequently caused by TBI. In the United States alone, it is estimated that 500, 000 children and adolescents with TBI are seen at hospitals every year (McCradden et al., 2019). TBI accounts for 9.6% of pediatric deaths (0-19) in Canada and 40% of pediatric deaths in the US (White et al., 2001). Overall, TBIs are considered 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; Young et al., 2004). Importantly, children under the age of 6 who sustain a TBI are at a greater risk of resultant mortality compared to children who sustain a TBI at an older age (Lichte et al., 2015). While not as common as TBI, nTBIs still place a large burden on the healthcare system. In Ontario, Canada, between 2003/04 and 2009/10 alone, approximately 17,977 nTBI episodes requiring care were reported in patients under 19 years (82.3 per 100,000 children and youth 19 years and under in Ontario, Canada) (Chan et al., 2016). The age group most likely to sustain an nTBI during this time were babies (0-4 yr), followed by late adolescents (15-19 yr) (Chan et al., 2016).

In several regions around the world the main cause of TBI in children is motor vehicle accidents, including North America (Asemota et al., 2013), Saudi Arabia (Alhabdan et al., 2013), Italy (Gazzellini et al., 2012), the Netherlands (De Kloet et al., 2012), Australia (Amaranath et al., 2014), and South Africa (Okyere-Dede et al., 2013; Schrieff et al., 2013). Other causes of TBI include falls, bike related injuries, sport related injuries, and acts of violence (Schunk & Schutzman, 2012). Males are twice as likely as females to experience a TBI. Male children are more likely to experience an intentional injury (i.e., physical assault), and adopt risk-taking behaviour that may lead to injury, or a fall from great heights, whereas female children are more likely to experience a TBI in the home due to small falls (falls <2m) (Collins et al., 2013). Non-accidental trauma represents <10% of pediatric TBI with the highest rates being reported in Nigeria (10%) and Malaysia (9%), while only 1-8% of pediatric TBI in the United States is attributed to non-accidental trauma (Dewan et al., 2016). Although the majority of ABI cases and research centers around TBIs, nTBI rates in Ontario between 2003-2010 were reported as high as 22.7 cases/100,000 due to substance toxicity, 18.4/100,000 for primary brain tumour cases, and 15.4/100,000 for meningitis cases (Chan et al., 2016). Despite clear evidence of high rates of nTBIs, proper treatment and epidemiological literature is lacking in most types of nTBIs, and nTBIs as a whole. For example, there is currently very little epidemiological research and healthcare utilization on primary brain tumours in pediatric patients, in spite of the fact that they are the leading cause of cancer death in patients under 19 (Brain, 2018).

The early years of childhood are a time of much growth and change, during which the body and brain are growing and developing daily. A brain injury interrupts this complex pattern of growth and development and may lead to substantially increased variability in baseline skills. As such, there is a need for age/stage

appropriate testing and rehabilitation programming, as well as longitudinal follow-up to address the increasing gap between the skills of the child and age appropriate peers. Further complicating rehabilitation, many children that sustain a TBI have behavioral problems, learning difficulties, and show a lack of restraint (Anderson et al., 2013). Mental health problems that are common post pediatric ABI include aggression, internalizing disorders, post-traumatic stress disorder, attention deficit hyperactivity disorder, and personality changes (Schachar et al., 2015). The residual effects of ABI are different between children and adolescents, perhaps due to the difference in developmental stage at the time of the brain injury. Older children more often have headaches, cognitive impairments, and behavioural disorders post TBI compared to younger children (Choe, 2016). The majority (90%) of children who sustain a TBI have mild brain injuries (Araki et al., 2017), however, those with more severe brain injuries have the potential for significant deterioration immediately post injury and further complications during rehabilitation (Schunk & Schutzman, 2012).

Due to the fact that the nervous system is still developing, treatment of a child with a TBI is quite distinct from the typical treatment of an adult with a brain injury. Rehabilitation for those who sustain head injuries can have a significant positive impact on not just the speed of recovery, but can also help to improve functional outcomes beyond what is expected from spontaneous recovery (Cope, 1995).

14.1 Acute Interventions

A brain injury is often discussed in two phases, the primary injury and the resulting secondary injury. The primary injury is defined as "*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*" (Schunk & Schutzman, 2012). A secondary injury is defined as the "*ongoing derangement to neuronal cells not initially injured during the traumatic event.* This ongoing injury results from *"processes initiated by the trauma: hypoxia, hypofusion, metabolic derangements, expanding mass and increased pressure and edema.*" (Schunk & Schutzman, 2012). Surviving a severe TBI requires a very rapid response in the acute phase (Gazzellini et al., 2012). This first section will discuss the treatments that may be used in the acute stages of TBI in a pediatric population.

One of the most important concepts in the acute care of TBI is the rise in intracranial pressure (ICP) that accompanies brain injury, and perpetuates secondary injury by increasing pressures within the cranium and reducing blood flow to the area (Doyle et al., 2016). Cerebral perfusion pressure (CPP) is the pressure gradient that drives cerebral blood flow. CPP is determined, in part, by intracranial pressure (ICP). Elevations in ICP reduce CPP and therefore reduce cerebral blood flow with the hypoxia ultimately resulting in substantial secondary injury post TBI. It is therefore crucial to take steps to reduce the frequency, amplitude and duration of raised ICP episodes in the acute phase post-TBI to mitigate the risk of secondary injury and negative outcomes. According to clinical guidelines, CPP should be no lower than 40mmHg and ICP no higher than 20mmHg for children post-TBI in order to prevent detrimental effects (Kochanek et al., 2012). Monitoring ICP levels is challenging as doing so requires invasive measurement. 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). In addition, ICP monitoring may be effective in the early detection of elevated ICP, therefore reducing poor outcomes after pediatric TBI (Kochanek et al., 2012). It is also known that children with severe TBI's (Glasgow Coma Scale (GCS)<8) are at higher risk of intracranial hypertension (ICH) (Dixon et al., 2016). Current guidelines recommend ICP monitoring in the acute phase post TBI for children whose brain injury is classified as severe (Kochanek et al., 2012). Accordingly, in practice it has been observed that older children and those with more severe TBI's are more likely to have their ICPs monitored (Sigurta et al., 2013).

Elevated ICP has been shown to be associated with high risk of death and poor neurological outcomes post TBI (Kochanek et al., 2012; Kukreti et al., 2014). Specifically, ICP>20mmHg at any time and increased numbers of hours spent with ICP above target have been shown to be associated with worse outcomes post TBI (Miller Ferguson et al., 2016). As such, once appropriate monitoring/investigation has led to a diagnosis of ICH, steps should be taken to reduce ICP. Multiple interventions to reduce ICP have been explored, including regulation of head position in bed, treatment with hypertonic saline, and treatment with decompressive craniectomies.

14.1.1 Non-Pharmacological Interventions

14.1.1.1 Head Position

For children who are critically ill as a result of an intracranial processes such as a TBI, tumor, infection, or hydrocephalus, the position of the child's 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). Of course, head elevation can also reduce the flow of blood into the intracranial space and consequently reduce cerebral blood flow - a complication which further exacerbates the original brain injury. As such, it is recommended that the clinician ensures that the child is "*euvolemic prior to placing him or her in this position is important to avoid orthostatic hypotension*" (pg 222; (Marcoux, 2005), thus reducing the chance of impaired CPP with head elevation. Despite a substantial body of research looking at effects of head elevation in adults who have sustained a TBI, little is known of its efficacy in children; existing studies are presented in Table 14.1.

Table 14.1 Head Elevation for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcomes
Agbeko et al. (2012) United Kingdom Pre-Post N=8	**Population:** TBI; Mean Age=10.0yr; 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 maximum of 40° and down to a minimum of 0°. Data was collected over 18 protocol sessions. **Outcome Measure:** Intracranial Pressure (ICP) levels, Cerebral Perfusion Pressure (CPP) levels, Mean Arterial Pressure (MAP).	1. ICP was significantly lower when head elevation was at a vertical height of 10 cm ($p<0.001$). 2. CPP was not affected by head elevation ($p=0.957$). Only one patient experienced a significant change in CPP after an increase in head elevation ($p=0.006$), and in fact CPP increased. 3. A negative correlation was reported between the magnitude of ICP response and baseline ICP, with a higher baseline ICP level associated with a lower magnitude of response ($p=0.025$). 4. MAP declined 3.9 mmHg, demonstrating higher head elevations are associated with a decrease in MAP ($p<0.001$).

Discussion

Agbeko and colleagues (2012) examined the impact of head elevation on ICP by randomly altering head position and measuring ICP and CPP responses. Results suggest that ICP decreased when the head of the bed was elevated by a minimum of 10 cm. If the head was elevated by a lower amount, ICP was found to increase. It is important to note that this effect occurred in most children, but not all (Agbeko et al., 2012).

CPP was not found to change significantly as a result of adjusting the head of the bed, which contradicts the aforementioned concerns of decreased CPP after head elevation (Bhalla et al., 2012). 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). While the results of this study provide promising evidence supporting head elevation in pediatric patients post TBI, the lack of controls and randomization make it difficult to draw solid conclusions from the study. Further randomized, controlled studies are suggested to investigate this intervention.

Conclusions

There is level 4 evidence that head elevation may reduce intracranial pressure, but not cerebral perfusion pressure, in children post TBI.

Head elevation may lower intracranial pressure, but have no effect on cerebral perfusion pressure, in children post TBI.

14.1.1.2 Hypothermia

A number of pathological mechanisms determine the extent and duration of traumatic brain injury in pediatric and adult populations. These mechanisms often involve the formation of free radicals, changes in ionic flux that lead to damage, ischemia, upregulation of neuroinflammatory pathways, neurotransmitter release (excitotoxicity), metabolic and mitochondrial dysfunction, as well as swelling (edema) (Kochanek et al., 2012; Olah et al., 2018). Many of these mechanisms are temperature sensitive, whereby increased temperature accelerates these processes leading to further injury and neurodegeneration (Olah et al., 2018). In this sense, therapeutic hypothermia has gained increasing interest as a possible neuroprotective strategy to attenuate the pathological mechanisms of TBI (Olah et al., 2018).

In animal models of TBI, moderate therapeutic hypothermia (32-33 °C) has been shown to prevent the onset of secondary injuries caused by hyperthermia (body temperature 38-38.5°C) (Zhao et al., 2017) (Bramlett & Dietrich, 2012) (Feng et al., 2010) (Dietrich et al., 2009). However, human clinical trials have led to more controversial results. In adults, clinical trials have demonstrated a relationship between hypothermia and improved neurological outcomes (increased Glasgow Outcome Scale scores) (Clifton et al., 1993; Marion et al., 1997). While in the pediatric population, there appears to be an association between hypothermia and an elevated risk of mortality post TBI (Sundberg et al., 2011). Furthermore, a meta-analysis conducted by Zhang et al. (2015) found that hypothermia was ineffective in improving neurological outcomes and increased the risk of mortality, as well as arrhythmias in children who sustained a TBI.. In this sense, lowering core body temperature may be harmful and put a child at risk for further complications. Therefore, it is important to conduct more clinical trials to understand the proper onset, duration, and outcomes of therapeutic hypothermia. Current hypothermic protocols vary and are administered over a period of 24, 48 and 72 hours, however further research is necessary to evaluate its safety and efficacy in pediatric TBI.

Table 14.2 Hypothermia for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcomes
Onset of Hypothermia Treatment		
Lovett et al. (2017) USA Retrospective N=71	**Population:** *Preintervention Group (N=47):* Median Age=4.6yr; Gender: N/A; Mean time post injury=acute; Median GCS=6. *Intervention 1 Group (N=9)*: Median Age=9yr; Gender: N/A; Mean time post injury=acute; Median GCS=3. *Maintenance Group (N=6)*: Median Age=4.5yr; Gender: N/A; Mean time post injury=acute; Median GCS=3. *Intervention 2 Group (N=9)*: Median Age=8yr; Gender: N/A; Mean time post injury=acute; Median GCS=3. **Intervention:** Retrospective chart review of a hyperthermia reduction protocol on a pediatric TBI inpatient unit. The preintervention phase cohort was analyzed before the implementation. The intervention 1 group had a cooling blanket placed on the patient bed prior to arrival and turned on when their temperature rose above normothermia. The maintenance phase focused on sustaining the results of intervention 1 group. The intervention 2 group focused on total prevention by initiating the cooling blanket immediately upon patient arrival. **Outcomes:** median duration of hyperthermia, acetaminophen administration, neurosurgical intervention, mortality, and lengths of stay.	1. The median duration of hyperthermia in the preintervention group was 135 min, down to 45 min in the Intervention 1 group, rose to 88.5 min in the Maintenance group, and declined to 0 min in the intervention 2 group. This was a statistically significant reduction based on phase of the study (p=0.04) 2. There was significantly less acetaminophen administered in the intervention and maintenance groups compared to the preintervention group (p=0.04). 3. There were no significant group-differences in measures of neurosurgical intervention, mortality, and lengths of stay.
Hypothermia Treatment Duration of 24hrs		
Hutchison et al. (2010) *A post-hoc analysis of* Hutchison et al. (2008)	**Intervention:** A post-hoc analysis of aforementioned study to determine the relationship between cerebral perfusion pressure (CPP), hypotension, and outcomes following hypothermia treatment in children post-TBI. **Outcome Measure:** Hypotension, Pediatric Cerebral Performance Category (PCPC), Unfavorable Outcomes, Cerebral Perfusion Pressure (CPP).	1. CPP was significantly higher in the hypothermia group at 8hr and 12hr post-treatment than it was in the normothermia group (p<0.050). 2. A lower CPP was noted in the hypothermia group 32-60hr post treatment compared to the normothermia group (p<0.050). 3. Hypothermia patients experienced significantly more episodes of hypotension within 24hr post injury (p=0.030) and low CPP 25-72 hr post injury (p=0.020) compared to normothermia patients 4. One or more episodes of hypotension (low systolic pressure) or low CPP levels within 25-72 hr post-injury for the hypothermia group was significantly associated with unfavourable outcomes (p=0.040 and p=0.030 respectively).
Hutchison et al. (2008)	**Population:** TBI; *Hypothermia Group (n=108)*: Mean Age=9.8yr; Gender: Male=70, Female=38; Mean Time Post Injury=6.3 hr; Median GCS=5. *Normothermia Group (n=118)*: Mean Age=10.2yr; Gender: Male=71, Female=47; Median GCS=5. **Intervention:** Patients were randomly assigned to either a hypothermia therapy group (where a mean	1. Thirty-two of 102 patients (31%) in the hypothermia group and 23 of 103 (22%) in the normothermia group had an unfavorable outcome at 6 mo. (p=0.140). 2. A total of 23 deaths were recorded among the hypothermia group in contrast to the 14 deaths

Author Year Country Study Design Sample Size	Methods	Outcomes
Canada RCT PEDro=7 N=225	temperature of 32.5°C was maintained via surface cooling techniques for 24 hr) 8 hours after treatment, or a normothermia group (where a mean temperature of 37°C was maintained). After 24 hr, hypothermia patients were warmed 0.5°C every 2 hr. Outcomes were assessed at 6mo follow-up. **Outcome Measure:** Pediatric Cerebral Performance Category (PCPC), Mortality Rates, Intracranial Pressure (ICP) , Cerebral Perfusion Pressure (CPP) , Blood Pressure rates, Heart Rate.	among the normothermia group, however the difference was not significant (p=0.060). 3. Intracranial pressures were lower during the cooling period and higher during the rewarming period in the hypothermia group compared to the normothermia group at 16 hours (P=0.020), 24 hours (P=0.010), 48 hours (P=0.010), and 72 hours (P=0.030). 4. At 24hr post-treatment, heart rate was significantly lower in the hypothermia group compared to the normothermia group (p<0.001) 5. At 25-72hr post-treatment, CPP and mean blood pressure were significantly lower amongst hypothermia patients compared to normothermia patients (both p<0.001) whereas heart rate was no longer significantly different.
Hypothermia Treatment Duration of 48hrs		
Adelson et al. (2013) USA RCT PEDro=7 N=77	**Population:** TBI; *Hypothermia Group (n=39)*: Median Age=9.7yr; Gender: Male=21, Female=18; Time Post Injury=<6 hr; Median GCS=6. *Normothermia Group (n=38)*: Median Age=12.5yr; Gender: Male=27, Female=11; Time Post Injury=<6 hr; Median GCS=6. **Intervention:** Patients were randomly assigned to either the hypothermia group or the normothermia group. The hypothermia group was cooled with iced intravenous saline to 34-45°C then surface cooled to 32-33°C. This was maintained for a 48hr period at which time all were rewarmed. Those in the normothermia group were maintained at 36.5-37.5°C. A 3mo follow-up was conducted. **Outcome Measure:** Mortality rate, Glasgow Outcome Scale (GOS), Glasgow Outcome Scale-Extended Pediatrics (GOS-E Peds).	1. No significant difference was reported between the two groups (p=0.150) in mortality rates at 3mo. 2. Six patients in the hypothermia group died and two patients in the normothermia group died over the course of the study (p=0.150). 3. No significant differences were found between the two groups in GOS and GOS-E Peds scores (p=0.900, p=0.730 respectively) at 3mo follow-up.
Bayir et al. (2009) USA RCT PEDro=6 N=28	**Population:** TBI; *Hypothermia Group (n=13)*: Mean Age=6.8yr; Gender: Male=9, Female=4; Time Post Injury=<24 hr; Mean GCS=6.3. *Normothermia Group (n=15)*: Mean Age=5.1y r; Gender: Male=8, Female=7; Time Post Injury=<24 hr; Mean GCS=6. **Intervention:** Patients were randomized into one of two conditions: hypothermia or normothermia. Both groups received temperature monitoring via a rectal probe with the hypothermia group maintained at a temperature of 32-33°C and normothermia patients maintained at 36.5-37.5°C for 48 hr. Data was collected over 3 d of treatment. **Outcome Measure:** Cerebrospinal fluid (CSF) Protein Sulfhydryls (Prot-SH), CSF Glutathione concentrations, CSF F2-isoprostane levels, CSF Anti-oxidant Reserve (AOR) levels.	1. The effect of temperature was not significant on CSF prot-SH (p=0.104) or CSF F2-isoprostane levels (p=0.104). 2. An inverse relationship between temperature and AOR was reported (p=0.022) with the hypothermia group demonstrating significantly greater AOR levels. 3. Glutathione concentration in CSF and temperature were inversely related (p=0.002).
Adelson et al. (2005) USA RCT	**Population:** TBI; Phase 1 (HYPO 1): Gender: Male=27, Female=21. *Hypothermia Group (n=23)*: Mean Age=6.92yr; Mean Time Post Injury=4.62 hr; Mean GCS=5.74. *Normothermia Group (n=25)*: Mean	1. In HYPO 1, the hypothermia group demonstrated lower mortality rates than the normothermia group but the difference was not

Author Year Country Study Design Sample Size	Methods	Outcomes
PEDro=6 N=74	Age=6.86yr; Time Post Injury=<6 hr; Mean GCS=5.64. Phase 2 (HYPO 2): Gender: Male=17, Female=9. *Hypothermia Group (n=13):* Mean Age=7.17 yr; Mean Time Post Injury=15.03 hr; Mean GCS=6.42. *Normothermia Group (n=13):* Mean Age=5.6 yr; Time Post Injury=6-24 hr; Mean GCS=6.23. **Intervention:** Patients were randomized into one of two conditions, hypothermia or normothermia. HYPO 1 – Both the hypothermia group (32-33°C) and normothermia group (36.5-37.5°C) maintained via a surface temperature control unit with a rectal probe. Information about complications was collected daily for the first 5 d. HYPO 2 – Patients who did not meet inclusion criteria but followed the same study protocol as HYPO 1. Assessments were conducted at 3 and 6 mo follow-ups. **Outcome Measure:** Mortality rates, complication rates, Glasgow Outcome Scale (GOS), Intracranial Pressure (ICP) , Cerebral Perfusion Pressure (CPP) .	statistically significant. In HYPO 2, both groups reported three deaths. 2. Within the first 24 hr of treatment, hypothermia patients had significantly lower ICP than normothermia patients (p=0.024). However, this difference was no longer significant after 24 hr. 3. Although there were no significant differences between groups on GOS scores, patients with good GOS outcomes had significantly lower ICP levels (p=0.036) and lower CPP levels (p=0.010).
Biswas et al. (2002) USA RCT PEDro=7 N=21	**Population:** TBI; *Hypothermia Group (n=10)*: Mean Age=5.9yr; Mean Time Post Injury=4.1 hr; Mean GCS=4.7. *Normothermia Group (n=11)*: Mean Age=6.5yr; Mean Time Post Injury=4.5 hr; Mean GCS=5.7. **Intervention:** After randomization to receive either hypothermia or normothermia treatment, all patients were administered sedatives, analgesics and neuromuscular blocking agents during the first 48 hr of hospital admission. In the hypothermia group, rectal temperature was lowered and maintained at 32°-34°C for a period of 48 hr. Follow-ups were conducted at 3, 6 and 12 mo. **Outcome Measure:** Glasgow Outcome Scale (GOS), Pediatric Cerebral Performance Category (PCPC), Pediatric Overall Performance Category (POPC), Intracranial Pressure (ICP), Cerebral Perfusion Pressure (CPP), White Blood Cell Count.	1. There were no significant differences in GOS, PCPC or POPC scores between both groups. 2. There were no significant differences between treatment groups regarding changes in ICP over time (p=0.730) and overall ICP level (p=0.770). 3. In both groups CPP declined slowly before increasing after 60 hr but the rate of increase was not significant. 4. All patients demonstrated a significant decrease in white blood cell count (p<0.001) during the study but there was no statistical significance between groups.
Hypothermia Treatment Duration of 72hr		
Beca et al. (2015) Australia RCT PEDro=7 N_I=55, N_F=50	**Population:** TBI; *Hypothermia Group (n=24)*: Mean Age=11.0 yr; Gender: Male=11, Female=13; Mean Time Post Injury=5.3 hr; Mean GCS=5.5. *Normothermia Group (n=26)*: Mean Age=9.5 yr; Gender: Male=16, Female=10; Mean Time Post Injury=5.0 hr; Mean GCS=4.5. **Intervention:** Individuals in the normothermia group maintained a body temperature between 36° and 37°C. The hypothermia group was maintained at a body temperature between 32 and 33°C followed by rewarming. Both groups were monitored for 72 hr. Outcomes were analyzed at 12 mo follow-up. **Outcome Measure:** Development of Comorbidities, Death, Hospital/intensive Care Unit (ICU) Length of Stay (LOS).	1. There was no significant difference between groups for unfavourable outcomes (p=0.700), death (p=0.340), ICU LOS (p=0.870), or hospital LOS (p=0.70). 2. There was no significant difference between groups in the need for mechanical ventilation (p=0.770). 3. There was no significant difference between groups for any type of infection (p>0.250), bleeding (p>0.480), arrhythmia (p=0.480) or acute respiratory distress syndrome (p=0.230).

Author Year Country Study Design Sample Size	Methods	Outcomes
Li et al. (2009) China RCT PEDro=6 N=22	**Population:** TBI; *Hypothermia Group (n=12)*: Age Range=0.7-8.0yr; Mean Time Post Injury=7.2 hr; Mean GCS=6.4. *Normothermia Group (n=10)*: Age Range=0.5-9.0; Mean Time Post Injury=6.8 hr; Mean GCS=6.5. **Intervention:** Patients were randomized to either a localized hypothermia treatment using a cooling cap on the patient's head and maintained at an intracranial temperature of 34.5°C or a normothermia group maintained at 38°C for 72 hours. Data was collected at 8, 24, 48 and 72 hr intervals. **Outcome Measure:** Intracranial Pressure (ICP), Neuron-specific Enolase (NSE) Levels, S-100 levels, Brain-specific Creatine Kinase (CK-BB) levels, Blood Pressure.	1. The hypothermia group demonstrated lower ICP values which were statistically significant at 8, 24, 48 and 72 hr (all p<0.050). 2. S-100 levels were significantly lower in the hypothermia group compared to the normothermia group at 8, 24 and 48 hr post-treatment (all p<0.010). 3. At 24, 48 and 72 hr post-treatment, patients in the hypothermia group had significantly lower NSE and CK-BB levels (all p<0.050 and p<0.0001 respectively) compared to the normothermia group. 4. There was no significant difference between groups with regards to blood pressure.
Outcomes after Hypothermia Treatment		
Rosario et al. (2018) USA Secondary RCT Analysis N=77	**Population:** *TBI Group (N=77):* Median Age=11yr (IQR, 3 – 15); Gender: Male=62%, Female=38%; Mean time post injury=acute; Median GCS=6 (IQR, 5-7). **Intervention:** Children from a severe TBI unit were enrolled in a therapeutic hypothermia clinical trial. Study authors investigated characteristics associated with unfavorable outcomes on the GOS-E and mortality at 3-months post-TBI. Bivariate and stepwise regression analyses were used. **Outcomes:** Mortality, Glasgow Outcome Scale – Extended (GOS-E).	1. No demographic, clinical, or CT characteristics in the bivariate analysis were associated with mortality. In the stepwise regression analysis, abbreviated injury severity spine (3.48 [1.14-10.58]) and midline shift on CT (8.35 [1.05-66.59]) were significantly associated with mortality. 2. Characteristics in the bivariate analysis associated unfavorable GOS-E scores were: two fixed pupils (14.17 [3.38-59.37]), abdominal abbreviated injury (2.03 [1.19-3.39]), and subarachnoid hemorrhage (3.36 [1.30-8.70]). In the stepwise regression analysis, both 1 and 2 fixed pupils, hypoxia (5.22 [1.02-26.67]), and subarachnoid hemorrhage were associated with unfavorable GOS-E scores.

Discussion

Several RCTs have investigated the efficacy of therapeutic hypothermia in children with severe TBI. All treatments were initiated within 24 hours of TBI onset and methods of delivering hypothermia included a blanket (Adelson et al., 2005; Adelson et al., 2013; Bayir et al., 2009; Beca et al., 2015; Hutchison et al., 2010; Hutchison et al., 2008) or cooling cap for localized treatment (Li et al., 2009). The duration of treatment was 24, 48 or 72 hours.

In a study by Hutchinson et al. (2008), hypothermia treatment began a mean time of 6.3 hours post-admission and was maintained for 24 hours. The study found that despite a trend towards increased unfavourable outcomes and a higher mortality, patients in the hypothermia group were not significantly different than the normothermia group. Furthermore, it was reported that ICP was significantly lower in the hypothermia group during cooling (16, 24 hr) and significantly higher during rewarming (48, 72 hr) compared to the controls. Hypothermia treatment was also associated with a lower heart rate (at 24 hr), CPP (25-72 hr), and blood pressure (25-72 hr) compared to the normothermia group. A post-hoc analysis

of the original study went on to discuss that patients in the hypothermia group experienced more episodes of hypotension (at 24 hr post treatment) and low CPP (at 25-72 hr) than the normothermia group, and that these outcomes were significantly associated with the development of unfavourable outcomes (Hutchison et al., 2010). Similarly, in a retrospective cohort study, systolic blood pressure <75th percentile was significantly associated with a higher risk of in-hospital mortality after isolated severe TBI in children (Suttipongkaset et al.).

The majority of studies reviewed implemented a hypothermia protocol delivered for 48 hours (Adelson et al., 2005; Adelson et al., 2013; Bayir et al., 2009; Biswas et al., 2002). There were no significant differences between groups in mortality rates (Adelson et al., 2005; Adelson et al., 2013) or outcomes such as arrhythmias, infection, or coagulopathy (Adelson et al., 2005; Adelson et al., 2013; Biswas et al., 2002). Compared to the normothermia group, ICP was significantly lower in the hypothermia group within 24 hours post-treatment (Adelson et al., 2005), however this improvement was not observed after 24 h (Adelson et al., 2005; Biswas et al., 2002). Total antioxidant reserve and glutathione levels in cerebrospinal fluid were significantly greater in the hypothermia group, highlighting the attenuated consumption of antioxidants with hypothermia treatment (Bayir et al., 2009). The biomarker for oxidative stress, cerebrospinal fluid F2-isoprostane, decreased during the monitoring period in both the hypothermia and normothermia groups, however there were no significant differences between groups. Both aforementioned findings indicate that cerebrospinal fluid markers may be beneficial tools to monitor effects of hypothermia on oxidative stress, a significant contributor to secondary damage post-TBI (Bayir et al., 2009).

The longest treatment time for hypothermia was 72 hours with an onset between 5-7 hours post-TBI (Beca et al., 2015; Li et al., 2009). There was no significant difference reported for infection, arrhythmias, bleeding (Beca et al., 2015) or blood pressure levels with these protocols compared to the normothermia groups (Li et al., 2009). A significant reduction in ICP was maintained at 72 hours when a cooling cap was used but no long-term follow-up was reported (Li et al., 2009). Levels of S-100 (Ca2+ binding protein), NSE (metabolic enzyme), and CK-BB (marker of brain damage) were all significantly lower in the hypothermia group, indicating that hypothermic treatment provided neuronal protection in children post-TBI (Li et al., 2009).

In one retrospective study, the effects of a hypothermia treatment protocol on an ABI inpatient unit were examined to determine associations between duration of hyperthermic state, acetaminophen administration, neurosurgical intervention, mortality, and length of stay (Lovett et al., 2017). The authors collected data from the patients at baseline, during the protocol change, maintenance phase, and second implementation of the protocol. They found that the median duration of hyperthermic state decreased throughout hypothermic protocol implementation (Lovett et al., 2017). This was achieved by varying the timing and duration of cooling blanket application to each patient's bed. Two cooling protocols were used, with protocol one initiating cooling blanket application when they were hyperthermic, and protocol two implementing cooling blanket application before the presence of hyperthermia. The authors found that there was a significant decrease in administration of acetaminophen from baseline to implementation of protocols one and two (Lovett et al., 2017).

In a secondary RCT analysis, the authors investigated mortality and unfavourable outcomes at 3-months post-TBI after hypothermic treatment (Rosario et al., 2018). Using a stepwise regression analysis, the authors found that spine injury severity and a midline shift on CT scan were significantly associated with mortality at 3 months post-TBI (Rosario et al., 2018). Using a bivariate analysis, the authors found that

fixed pupils, abdominal injury and presence of subarachnoid hemorrhage were significantly associated with unfavourable outcomes at 3 months post-TBI

Conclusions

There is level 1a evidence that therapeutic hypothermia delivered for 24 hours is no different than normothermia at increasing mortality and unfavourable outcomes in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 24 hours may decrease intracranial pressure during cooling compared to normothermia in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 24 hours may decrease heart rate (24 hr post treatment), cerebral perfusion pressure (25-72 hr post treatment), and blood pressure (25-72 hr post treatment) compared to normothermia in children post TBI.

There is level 1a evidence that decreases in cerebral perfusion pressure and blood pressure during treatment with therapeutic hypothermia (for 24 hr) are associated with development of unfavourable outcomes in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 48 hours is no different than normothermia with respect to mortality or complications (arrythmias, coagulopathies, infections) in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 48 hours may temporarily (<24 h) lower intracranial pressure in children post TBI compared to normothermia.

There is level 1b evidence that hypothermia treatment maintained for 48 hours may preserve antioxidant defenses in children following a severe TBI, when compared to normothermia.

There is level 1b evidence that therapeutic hypothermia delivered for 72 hours with a cooling cap may improve short-term intracranial pressure (<72 hr) and reduce biomarkers of brain damage (S-100, NSE, CK-BB), compared to normothermia therapy in children post TBI.

There is level 4 evidence that hypothermia induced through cooling blankets placed on the patient's bed may decrease the duration of hyperthermic state and acetaminophen administration upon arrival to the pediatric ABI inpatient unit.

There is level 1b evidence that spine injury severity and midline shift on CT scans, fixed pupils, abdominal injury, and subarachnoid hemorrhage are associated with mortality and unfavourable outcomes, respectively, at 3 months post-TBI in a pediatric population that underwent hypothermia treatment.

Therapeutic hypothermia delivered for 24, 48, or 72 hours can decrease intracranial pressure more than normothermia treatment for at least 24 hours in children post TBI, however, intracranial pressure may increase during the re-warming period.

Therapeutic hypothermia delivered for 24 or 48 hours is not different than normothermia in terms of mortality, unfavourable outcomes, or complications (arrythmias, coagulopathies, infections) in children post TBI.

Therapeutic hypothermia delivered for 24 hours can cause a decrease in heart rate, blood pressure, and cerebral perfusion pressure compared to normothermia treatment in children post TBI; further, decreases in blood pressure and cerebral perfusion pressure are associated with the development of unfavourable outcomes.

Therapeutic hypothermia delivered for 48 or 72 hours increases anti-oxidant markers, and decreases brain injury markers in the cerebrospinal fluid compared to normothermia treatment in children post TBI.

Enacting a protocol change to have cooling blankets placed on the patient's bed prior to arrival in the pediatric ABI inpatient unit may decrease duration of hyperthermic states and acetaminophen administration.

Spine injury severity, midline shift on CT scan, fixed pupils, abdominal injury, and subarachnoid hemorrhage are associated with mortality and unfavourable outcomes at 3 months post-TBI in a pediatric population that underwent hypothermia treatment.

14.1.2 Pharmacological Interventions

14.1.2.1 Hypertonic Saline

Mannitol is the most commonly used drug in the treatment of ICH in adults, however, research supporting its use in the pediatric population is lacking. In this sense, the use of mannitol in the treatment of pediatric ICH is neither supported or discouraged (Kochanek et al., 2012). Currently, hypertonic saline (HTS) is the most frequently used treatment for the acute management of ICP in children who have sustained a brain injury. 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 results in a reduction of cerebral water content, effectively lowering ICP (Khanna et al., 2000). Hypertonic saline is used more frequently in older children, children with intracranial hemorrhages and skull fractures, and children with severe TBI (Bennett et al., 2012). Although there is a move towards utilizing HTS, the appropriate concentration of NaCl remains elusive and a variety of different concentrations have been used in the literature, ranging from 0.1-23.4%. The methodological details and results from eight studies investigating HTS for the acute management of pediatric TBI are listed in Table 14.3.

Table 14.3 Hypertonic Saline for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcomes
Simma et al. (1998) Switzerland RCT	**Population:** TBI; *Lactated Ringer's Solution Group (LRS, n=17):* Mean Age=7.3yr; Gender: Male=9, Female=8; Time Post Injury=<3 d; Mean GCS=5.8. *Hypertonic Saline Group (HTS, n=15):* Mean	1. There was an inverse relationship between ICP and serum sodium concentration for both the LRS group ($p<0.030$) and the HS group ($p<0.001$) in the first 8hr of treatment.

Author Year Country Study Design Sample Size	Methods	Outcomes
PEDro=6 N=32	Age=7.3yr; Gender: Male=7, Female=8; Time Post Injury=<3d; Mean GCS=5.5. **Intervention:** Patients were randomly assigned to receive either LRS or HTS in addition to standard care over a period of 72 hr. Data was collected every 4 hr. **Outcome Measure:** Intracranial Pressure (ICP) , Cerebral Perfusion Pressure (CPP) , Serum Sodium Concentration, Length of Stay (LOS), Respiratory Distress Syndrome Rates, Complication Rates.	However, beyond this time point, only the hypertonic saline group maintained this significant relationship. 2. Correlations between CPP levels and serum sodium concentration only became significant for the HS patients after 8hr of treatment (p=0.002). 3. The LRS patients experienced a significantly longer LOS (p=0.040). LRS patients also experienced a greater frequency of respiratory distress syndrome, and more than two complications compared with the HS group; however, these did not reach statistical significance (p=0.100, p=0.090 respectively).
Fisher et al. (1992) USA RCT PEDro=6 N=18	**Population:** TBI; Mean Age=8.3 yr; Mean Time Post Injury=22.0 hr; Mean GSC=5.8. **Intervention:** Each patient received one saline bolus of 3% and 0.9% saline in a blinded, randomized crossover fashion. Doses ranged between 6.5-10 mL/kg in each patient. Intracranial pressure (ICP) was monitored for 2 hr post-administration. **Outcome Measure:** ICP, Central Venous Pressure (CVP), Renal Function.	1. Administration of 0.9% saline did not result in a change in ICP (p=0.320). 2. When participants received 3% saline, there was a significant within group difference in ICP from baseline to average ICP during the 2hr (p=0.003); serum sodium levels increased. 3. Significant difference in ICP between normal saline (0.9%) and 3% saline were noted post-intervention (p=0.002). 4. No significant change in CVP or renal function were seen within either group.
Rallis et al. (2017a) Greece Case Series N=29	**Population:** TBI; Mean Age=8.9 yr; Gender: Male=15, Female=14; Median GCS=6. **Intervention:** Patients with severe TBI who received hyperosmolar therapy (7.5% hypertonic saline) as a result of failure to lower ICP< 20 mmHg with standard therapy, were retrospectively reviewed. **Outcome Measure:** Intracranial Pressure (ICP), Cerebral Perfusion Pressure (CPP), Serum Sodium, Glasgow Outcome Scale Extended (GOSE), Adverse Effects.	1. Before receiving hypertonic saline, all patients first received therapy with mannitol. 2. Hypertonic saline dose started at 5 ml/kg/h and was adjusted accordingly thereafter (mean dose=3 ml/kg/h). Infusion was terminated when ICP fell below 20 mmHg. 3. Hypertonic saline was associated with significant reduction in ICP and CPP elevation at 30, 60 and 120 min post-infusion (all p<0.001). 4. Serum sodium was significantly elevated 120 min post-infusion (Median=142 mmol/L to 149 mmol/L; p<0.001). 5. One third of patients had severe neurological impairment (GOSE=3-4) at 6 mo post injury. 6. Five patients did not survive, 3 patients developed severe hypernatremia, 2 had acute respiratory distress syndrome and 1 patient developed an acute kidney injury.

Author Year Country Study Design Sample Size	Methods	Outcomes
Kannan et al. (2016) USA Case Control N=236	**Population:** Severe TBI; *Early Hypotension-No Treatment (n=5):* Mean Age=5.8yr; Gender: Male=3, Female=2. *Early Hypotension-Treatment (n=55):* Mean Age=10.6yr; Gender: Male=34, Female=21. *No Early Hypotension (n=174):* Mean Age=7.4yr; Gender: Male=125, Female=49. **Intervention:** Patient medical records were examined to compare outcomes of patients treated for early hypotension and those who received no hypotension treatment. **Outcome Measure:** In-hospital Mortality, Glasgow Outcome Scale (GOS).	1. Hypotension was associated with increased in-hospital mortality (23.3% versus 8.6%; p=0.010). Additionally, timely treatment of hypotension was associated with reduced in-hospital mortality when compared to non-early hypotension treatment (Adjusted relative risk=0.460). 2. Compared to those with hypotension not treated in a timely manner, those who received timely treatment had improved GOS at discharge (Adjusted relative risk=0.540).
O'Lynnger et al. (2016) USA PCT N=128	**Population:** TBI; *Pre-protocol (n=99):* Mean Age=6.54yr; Gender: Male=52, Female=47; Mean GCS=5.43. *Post-protocol (n=29):* Mean Age=5.89yr; Gender: Male=16, Female=13; Mean GCS=5.28. **Intervention:** Patients with severe TBI were retrospectively identified. Those treated before the implementation of a new treatment protocol (based on the Brain Trauma Foundation's 2012 guidelines) were compared with those treated after the new protocol was implemented. **Outcome Measure:** Protocol Adherence, Discharge Disposition, Glasgow Outcome Scale (GOS).	1. Use of 3% hypertonic saline (HTS) over mannitol was used as a surrogate measure of protocol adherence. After protocol implementation, HTS treatment was increased (22% to 41%; p=0.040) while mannitol use administration was decreased (48% to 14%; p=0.001). 2. Patients in the post-protocol group had more favourable discharge disposition than those in the pre-protocol group (69% versus 36%, respectively; p=0.002). 3. GOS scores were not significantly increased after protocol implementation (p=0.124).
Roumeliotis et al. (2016) Canada Case Series N=16	**Population:** TBI; Median Age=13; Gender: Male=12, Female=4; Median Time Post Injury=196 min; Median GCS=6. **Intervention:** Retrospective review of patients with severe TBI, admitted to a pediatric intensive care unit (ICU), who were treated with a hyperosmolar agent. **Outcome Measure:** Intracranial Pressure (ICP), Cerebral Perfusion Pressure (CPP), Serum Sodium.	1. All patients received 3% hypertonic saline (HTS,average dose=1.8 ml/kg), and all but 3 patients received mannitol (average dose=0.6 g/kg). 2. Both 3% HTS and mannitol were associated with a nonsignificant decrease in ICP (p=0.096 and p=0.055, respectively.) 3. No significant changes in CPP or serum sodium were observed.
Khanna et al. (2000) USA Case Series N=10	**Population:** TBI; Mean Age=5.7yr; Gender: Male=8, Female=2; Mean Time Post Injury=3.2 d; Mean Time Post Injury=3.2 d; Mean GCS=4.7. **Intervention:** Patients who had failed conventional therapy were treated with a continuous infusion of 3% hypertonic saline in order to achieve target serum sodium levels. Measurements were observed and recorded every 6 hr. Outcomes were assessed at 6mo follow-up. **Outcome Measure:** Glasgow Outcome Scale (GOS), Intracranial Pressure (ICP), Cerebral Perfusion Pressure (CPP) , Serum Osmolarity.	1. There was a significant decrease in ICP at 6, 12, 24, 48 and 72 hr time points compared to baseline (all p<0.01). 2. There was a significant decrease in ICP spike frequency and a significant increase in CPP at 6, 12, 24, 48 and 72 hr (all p<0.01). 3. A significant increase in serum osmolarity was reported at 12 hr (p<0.05) and at 24, 48 and 72 hr (all p<0.01). 4. Although one patient died, the remaining nine reported a median GOS score of 4 at 6 mo follow-up.

Author Year Country Study Design Sample Size	Methods	Outcomes
Peterson et al. (2000) USA Case Series N=68	**Population:** TBI; Mean Age=7.8yr; Gender: Male=47, Female=21; Mean GSC=5.5. **Intervention:** Children with intracranial hypertension (ICP >20 mmHg) were retrospectively analyzed. Patients were administered continuous hypertonic saline (3%) and intermittent mannitol to target serum sodium levels. Measurements were taken every 6 hr for 7 d. Mean dose of hypertonic saline was between 11-27 mL/kg per d over a 7 d period. **Outcome Measure:** ICP; serum sodium, osmolarity, and creatinine levels; renal function.	1. There were 3 patients (4%) that died of uncontrolled ICP. 2. Within 72hr, ICP was <20 mmHg 93% of the time, 21-30 mmHg 5% of the time, and >30 mmHg 2% of the time. 3. Patients with serum sodium levels >180 mEq/L, all had poor outcomes. 4. Serum creatinine levels increased with increased serum concentrations of sodium (p<.001) and with serum osmolarity (p<.001). 5. No development of renal failure or rebound of ICP.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Fluid resuscitation using hypotonic lactated Ringer's solution was compared to fluid resuscitation using HTS in children with a severe TBI during the first three days post-injury (Simma et al., 1998). There was an inverse relationship between sodium concentration and ICP and a direct relationship between sodium concentration and CPP (i.e., increased serum sodium concentration correlated with lower ICP and higher CPP). The children treated with HTS were reported to have a significantly lower frequency of acute respiratory distress syndrome (ARDS), a lower rate of occurrence of two or more complications and significantly shorter ICU stay in comparison to the lactated Ringer's solution group. (Simma et al., 1998).

A study investigating the efficacy of hyperosmolar therapy (3% HTS and mannitol) in children post TBI was analyzed (Roumeliotis et al., 2016). All patients received 3% HTS, while all but 3 received mannitol in addition. It was found that both 3% HTS and mannitol administration was not associated with any improvements in ICP, CPP or increases in serum osmolarity. While the previous study did not find any benefit to hyperosmolar therapy, 3 studies were analyzed evaluating the use of HTS in patients where standard therapy failed to lower ICP below 20 mmHg (Khanna et al., 2000; Peterson et al., 2000; Rallis et al., 2017a). Intracranial pressure was controlled acutely (within 30 min) after 7.5% HTS (Rallis et al., 2017a), and for as long as 72 h post treatment with 3% HTS (Khanna et al., 2000; Peterson et al., 2000). In addition, increases were found in both patient CPP (Peterson et al., 2000; Rallis et al., 2017a) as well as serum sodium and osmolarity (Khanna et al., 2000; Peterson et al., 2000). Treatment with HTS was not without its complications however, as studies noted kidney injury (Khanna et al., 2000; Rallis et al., 2017a), hypernatremia, ARDS, and severe neurological impairment (GOSE=3-4) in a third of the patient population (Rallis et al., 2017a).

While evidence continues to mount in favour of using HTS as a means of lowering ICP in children, adherence to new guidelines has been questioned. A group led by O'Lynnger (2016) implemented a new treatment protocol based on the guidelines proposed by the Brain Trauma Foundation, which center around the replacement of mannitol with HTS in the treatment of TBI in children. The researchers compared patients with TBI who received treatment before implementation of the new guidelines, to patients who were treated after the implementation of the new guidelines and noted an increase in favourable discharge disposition in the post-protocol group compared to the pre-protocol group. Despite the change in disposition, no inter-group differences were noted patients GOS scores.

Finally, HTS and osmotic agents were analyzed as a means of resuscitating hypotensive patients post TBI. A study by Kannan et al. (2016) discovered that early (<30 min post hypotensive episode) treatment of hypotension, by mainly using HTS, was associated with a reduction in mortality compared to non-early hypotension treatment (adjusted RR=0.46). Conclusions from this study support early hypotension treatment in ABI patients post TBI, however, further studies are required to determine which agent is best at reducing mortality, as patients also received blood products (28%) and vasopressors (13%).

Conclusions

There is level 1b evidence that serum sodium concentrations are inversely proportional to intracranial pressure, and directly proportional to cerebral perfusion pressure, after hypertonic saline or Lactated Ringer's solution therapy in children post TBI.

There is level 1b evidence that hypertonic saline is associated with a lower frequency of acute respiratory distress syndrome, shorter intensive-care unit stay, and lower rate of complications compared to treatment with Lactated Ringer's solution in children post TBI.

There is level 4 evidence that hyperosmolar therapy (3% hypertonic saline and mannitol) may not improve intracranial pressure or cerebral perfusion pressure, or increase serum osmolarity, in children post TBI.

There is level 4 evidence that intracranial pressure can be lowered acutely (within 30 minutes) after 7.5% hypertonic saline treatment, for as long as 72 hours, using 3% hypertonic saline treatment in children refractory to standard therapy (intracranial pressure >20 mmHg) post TBI.

There is level 4 evidence that hypertonic saline treatment (3 or 7.5%) may increase cerebral perfusion pressure, serum sodium, and serum osmolarity in children refractory to standard therapy (intracranial pressure>20 mmHg) post TBI.

There is level 4 evidence that 7.5% hypertonic saline treatment is associated with hypernatremia, kidney injury, acute respiratory distress syndrome, and low Glasgow Outcome Scale- Extended score (3-4) in children refractory to standard therapy (intracranial pressure>20 mmHg) post TBI.

There is level 2 evidence that treatment of children with TBI following a new hypertonic saline-based protocol may increase favourable discharge disposition, but not Glasgow Outcome Scale scores, compared to therapy without guidance of a strict protocol.

There is level 4 evidence that early (<30 minutes post episode) hypotension treatment may reduce mortality compared to non-early hypotensive treatment in children post TBI.

Treatment with hypertonic saline or Lactate Ringer's solution may decrease intracranial pressure and increase cerebral perfusion pressure proportional to the increase in serum sodium in children post ABI. However, hypertonic saline may cause lower rates of acute respiratory distress syndrome and a shorter hospital length of stay compared to Lactate Ringer's solution.

Hyperosmolar therapy (3% hypertonic saline and mannitol) may not improve intracranial pressure, cerebral perfusion pressure, or serum osmolarity in children post TBI.

Hypertonic saline treatment might lower intracranial pressure acutely (30 min, 7.5% hypertonic saline) and for up to 72 h (3% hypertonic saline) in children refractory to standard therapy (Intracranial pressure>20 mmHg) post TBI, however, both concentrations increase cerebral perfusion pressure, serum sodium, and serum osmolarity.

Hypertonic saline (7.5%) treatment might cause hypernatremia, kidney injury, acute respiratory distress syndrome, and severe neurological impairment in children post TBI refractory to standard therapy (Intracranial pressure>20 mmHg)

A hypertonic saline-based protocol could increase favourable discharge disposition, but not neurological outcomes compared to non-protocol guided therapy in children post TBI.

Early (<30 min post episode) hypotensive treatment may reduce mortality in pediatric patients post TBI.

14.1.2.2 Sedatives and Analgesics

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). These drugs are often used for the treatment of ICH in pediatric TBI, with 91% of practitioners reporting the use of sedatives as a first tier therapy for ICH (Welch et al., 2016). However, conflicting evidence suggests that such drugs may actually increase ICP (Welch et al., 2016). This mechanism is not fully understood, but may be due to changes in cerebral blood flow, altered systemic hemodynamics or autonomic reflexes (Welch et al., 2016).

The aim of this section is to summarize the effects of these pharmacological agents on secondary injury following TBI within the pediatric population. As such, the methodological details and results from three studies investigating the use of sedatives and analgesics for the acute management of pediatric TBI are listed in Table 14.4.

Table 14.4 Sedatives and Analgesics for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Shein et al. (2016) USA Pre-post N=16	**Population:** TBI; Mean Age=3.7yr; Gender: Male=12. Female=4; Mean GCS=5. **Intervention:** Patients who received doses of fentanyl, 3% hypertonic saline (HTS), and pentobarbital following intracranial hypertension episodes were analyzed. Mean bolus doses for each pharmacological treatment were: Fentanyl 2 µg/kg, HTS 3 mL/kg, and Pentobarbital 5 mg/kg. The patients received a median of 12 doses. Assessments were conducted at baseline and then	1. ICP levels were significantly decreased after administration of fentanyl, pentobarbital, or HTS within 15–25 min of initiation of the bolus (all p<0.050). 2. HTS was associated with a significant improvement in ICP within 5 min of initiation (mean change=-2.49 mmHg; p=0.004). 3. Both HTS and pentobarbital administration independently reduced ICP levels significantly after 5min (both p<0.001).

Author Year Country Study Design Sample Size	Methods	Outcome
	monitored every 5 min up to 120 min post-treatment. **Outcome Measure:** Intracranial Pressure (ICP) levels, Cerebral Perfusion Pressure (CPP).	4. CPP levels improved after HTS administration (p=0.001) but deteriorated after fentanyl treatment (p<0.001). 5. An adjusted model for ICP crisis resolution time revealed that HTS was found to be two-times faster than both pentobarbital and fentanyl (p=0.031) in reducing ICP.
Welch et al. (2016) USA Case Series N=31	**Population:** TBI; Mean Age=8yr; Gender: Male=20, Female=11; Mean GCS=5. **Intervention:** Data was collected from medical records of patients admitted to a children's Level 1 trauma hospital. All patients were intubated, mechanically ventilated, and received bolus doses of fentanyl and/or midazolam for treatment of intracranial hypertension. **Outcome Measure:** Intracranial Pressure (ICP) levels, Cerebral Perfusion Pressure (CPP).	1. There was a significant increase in mean area under the curve (AUC) for ICP (corresponding to an increase in ICP) following high-dose fentanyl (p=0.020), low-dose midazolam (p=0.006), high-dose fentanyl + low-dose midazolam (p=0.007). 2. AUC-ICP also increased for all other drug/dose combinations (ie. Low-dose fentanyl + high-dose midazolam) but these did not reach statistical significance. 3. There was no significant change in AUC-CPP after administration of fentanyl and/or midazolam.
Mellion et al. (2013) USA Case Series N=36	**Population:** TBI; *Controlled Refractory Intracranial Hypertension Group (RICH; n=10):* Mean Age=10.7yr; Gender: Male=2, Female=8; Mean Time Post Injury=3.0 hr. *Uncontrolled Refractory Intracranial Hypertension Group (URICH; n=26):* Mean Age=6.4yr; Gender: Male=13, Female=13; Mean Time Post Injury=1.5 hr. **Intervention:** Data on patients admitted between January 2001 and December 2010 and treated with barbiturate infusions for a minimum of 6 hr were extracted from electronic and paper medical records from a hospital trauma database. Patients who experienced Intracranial pressure (ICP) >20 mmHg despite first-tier therapies but treated successfully with barbiturates were classified as RICH and patients who still demonstrated ICP of >20 mmHg despite a minimum of 6 hr barbiturate therapy were classified as URICH. Assessments were conducted at discharge and 3 mo follow-up. **Outcome Measure:** ICP levels, Pediatric Cerebral Performance Category (PCPC).	1. Patients in the RICH group demonstrated significantly lower ICP levels immediately prior to loading dose of barbiturates compared to the URICH group (17 mmHg versus 25 mmHg, p=0.028). 2. PCPC scores at discharge and at 3 mo follow-up were significantly lower for the RICH group compared to the URICH group (p<0.050). 3. The amount of change in PCPC score from discharge to 3 mo follow-up did not differ significantly between groups. 4. The duration of barbiturate infusion was lower for the RICH group compared to the URICH group (median 56 hr versus 90 hr) but this did not reach statistical significance (p=0.433). 5. The RICH group received barbiturate therapy after a significantly greater amount of time had elapsed compared to the URICH group (median 76 hr versus 29hr, p=0.028).

Discussion

Within the sedatives and analgesics category, 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). This is critical due to the known detrimental effects of a transient period of ICH. Pentobarbital was shown to reduce ICP more gradually and without affecting CPP, whereas fentanyl decreased ICP but actually worsened CPP levels (Shein et al., 2016). In line with the previous studies, Welch et al (2016) found that fentanyl and midazolam were not effective treatments for episodic ICH when used alone or in

combination with each other, and even went to suggest that they in fact may even increase ICH. Furthermore, there was no effect on CPP levels following treatment with fentanyl and midazolam (Welch et al., 2016).

Pentobarbital administration in older children (mean age range 6-10 years) with refractory ICH was effective at reducing and controlling ICP in 28% of cases (Mellion et al., 2013). When refractory ICH was not controllable with pentobarbital, there was a reduction in time to death and increase in risk of death (Mellion et al., 2013). Of those children with severe TBI who received pentobarbital, 81% had at least one documented episode of decreased CPP. Almost all participants required vasoactive medications, and together with low CPP episodes, these results suggest that pentobarbital treatment can be associated with cardiovascular compromise (Mellion et al., 2013). The current pediatric guidelines suggest that pentobarbital therapy may be considered for children that are hemodynamically stable with refractory ICH, after other standard therapies and managements have been attempted (Kochanek et al., 2012). The data from these studies has not shown any evidence to suggest otherwise, especially because safer alternatives, such as HTS, exist and have been demonstrated to be more effective at lowering ICP.

Conclusions

There is level 4 evidence 3% hypertonic saline may decrease intracranial pressure and increase cerebral perfusion pressure faster than fentanyl (2µg/kg) and pentobarbital (5mg/kg) in pediatric patients post TBI.

There is level 4 evidence that high-dose fentanyl, low-dose midazolam, and high-dose fentanyl in combination with low-dose midazolam may increase intracranial pressure in pediatric patients post TBI.

There is conflicting (level 4) evidence regarding whether or not fentanyl reduces intracranial pressure and improves cerebral perfusion pressure in children following a severe TBI.

There is level 4 evidence that pentobarbital may lower intracranial pressure and cerebral perfusion pressure in pediatric patients with refractory intracranial pressure post TBI.

Compared to fentanyl (2µg/kg) and pentobarbital (5mg/kg), 3% hypertonic saline may reduce intracranial pressure and increase cerebral perfusion pressure more rapidly in pediatric patients post TBI.

The effect of fentanyl on intracranial pressure and cerebral perfusion pressure in pediatric patients post TBI is unclear, however, high-dose fentanyl and low-dose midazolam, used either alone or in combination, may increase intracranial pressure.

Pentobarbital administration may lower intracranial pressure and cerebral perfusion pressure in pediatric patients with refractory intracranial pressure post TBI.

14.1.2.3 Dopaminergic Agents

Disorders of consciousness are defined as a range of conditions where consciousness is either altered or absent, and includes comatose, vegetative, and minimally conscious states (Giacino & Whyte, 2005). In theory, promoting arousal in children with reduced consciousness in the acute phase can facilitate early participation in rehabilitation, thus improving outcomes post-TBI (Evanson et al., 2016; Suskauer & Trovato, 2013). Dopaminergic agents increase the amount of dopamine in the brain with the goal of facilitating arousal and responsiveness (McMahon et al., 2009). Potential dopaminergic agents utilized in the treatment of disorders of consciousness include pramipexole, bromocriptine, methylphenidate, and amantadine, which is the most commonly used (Suskauer & Trovato, 2013). Pramipexole and similar agents, such as bromocriptine are direct dopamine agonists that work on post-synaptic sites. While methylphenidate increases the stores of dopamine that are released from pre-synaptic vesicles and amantadine predominantly blocks re-uptake of dopamine, increasing dopamine levels (Patrick et al., 2003). Given that neurotransmitter systems are still developing in children, they may respond differently to dopaminethan adults (McMahon et al., 2009). As such, additional research investgating the use of dopaminergic agents in a pediatric population is necessary.

Table 14.5 Dopaminergic Agents for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcomes
McMahon et al. (2009) USA RCT PEDro=6 $N_{Initial}$=7, N_{Final}=6	**Population:** ABI: TBI=5, Stroke=1, Anoxia=1; Mean Age=12.7yr; Gender: Male=6, Female=1; Mean Time Post Injury=6.7wk; Mean GCS=4. **Intervention:** Patients were randomized to receive either 4 mg/kg body weight of amantadine for 1wk followed by 6 mg/kg body weight for 2wk or a placebo. After a 1wk washout period, the patients were crossed over and treated for another 3 wk. Assessments were conducted up to 3 x/wk. **Outcome Measure:** Coma/Near-Coma Scale (CNCS), Coma Recovery Scale Revised (CRS-R), Sleep Scale, Wee-FIM, Physician Evaluation, Parents' Evaluation.	1. There were no significant differences in recovery between amantadine and placebo according to CNCS, CRS-R or Wee-FIM scores (p=0.240, p=0.280, p=0.330 respectively). 2. Physician's evaluations revealed significantly greater improvements in consciousness (p=0.020) but not for changes in arousal (p=0.170). 3. Parent's evaluations did not reveal any significant differences in consciousness or arousal (p=0.500, p=0.120 respectively).
Vargus-Adams et al. (2010) USA *A secondary analysis of McMahon et al. (2009)*	**Population:** ABI: TBI=5, Stroke=1, Anoxia=1; Mean Age=12.7yr; Gender: Male=6, Female=1; Mean Time Post Injury=6.7wk; Mean GCS=4. **Intervention:** A secondary analysis to determine the pharmacokinetic properties of amantadine in children. **Outcome Measure:** Coma/Near-Coma Scale (CNCS), Coma Recovery Scale Revised (CRS-R), Sleep Scale.	1. A significant correlation was reported between CRS-R and maximum concentration of Amantadine (p=0.010), however, scatterplots did not reveal any observable relationship. 2. One significant association was found between CSR-R scores and average concentration of Amantadine (p=0.010). Other associations between CNCS (p=0.38, p=0.39, p=0.79) or CRS-R scores (p=0.06, p=0.11) and average concentration of Amantadine were not significant. However, the only significant CRS-R score did not reveal any relationship on the scatterplot. 3. Sleep Scale mean scores for nights on Amantadine and placebo were not found to be significantly different (p=0.20).
Patrick et al. (2003) USA Case Series N=10	**Population:** ABI: TBI=7, Encephalopathy=2, Stroke=1; Mean Age=13.7yr; Gender: Male=7, Female=3; Mean Time Post Injury=52.5 d; Mean GCS=3.1. **Intervention:** A retrospective review of patients who had been treated with dopamine agonists (amantadine, pramipexole, bromocriptine, levodopa,	1. Patients demonstrated significant improvement on WNSSP scores from baseline to final assessment (p=0.020) with overall mean score also significantly differing from baseline (p<0.010).

Author Year Country Study Design Sample Size	Methods	Outcomes
	methylphenidate) for a mean of 39d was conducted. Assessments were performed at 15, 26 and 43d on average following onset of treatment. **Outcome Measure:** Western NeuroSensory Stimulation Profile (WNSSP).	2. The rate of change for WNSSP scores was 1.11 points greater per day during the treatment phase compared to the pre-medication phase (p=0.020).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

The results of studies assessing the effects of dopaminergic agents on improvements in arousal and responsiveness post-ABI are conflicting and sparse. Patrick et al. (2003) initially conducted a retrospective review of children who received one of a variety of dopaminergic agents. Overall, there was an increase in responsiveness in these children, despite the difference in mechanism of action for each drug (Patrick et al., 2003). This study lacked a comparative control group and studied a variety of drugs but provided preliminary results for future Randomized Controlled Trials (RCT)s.

Further studies were then conducted regarding the effects of amantadine on disorders of consciousness (McMahon et al., 2009; Patrick et al., 2006). One RCT found that standardized measures of arousal and consciousness did not significantly improve in children treated with amantadine, however, blinded physicians' ratings of consciousness, but not arousal, improved significantly (McMahon et al., 2009). Authors hypothesize that the effectiveness of amantadine may be determined by etiology of brain injury, but lacked a separate analysis for TBI, stroke, and anoxic injury (McMahon et al., 2009).

Vargus-Adams et al. (2010) analyzed the pharmacokinetic properties of amantadine as a follow up to McMahon et al. (McMahon et al., 2009) and concluded that a dosage of 6 mg/kg per day was an effective and safe dose for a pediatric ABI population. At higher doses, amantadine caused nausea and vomiting. Therefore, the authors recommend beginning with a dose of 4 mg/kg per day and then increasing to 6 mg/kg per day after a week, to ensure minimal in side effects (Vargus-Adams et al., 2010).

Conclusions

There is level 1b evidence that amantadine may not improve level of consciousness (Coma/Near-Coma Scale, Coma Recovery Scale Revised, or Wee-FIM scores), but may improve blinded physicians' ratings of consciousness, compared to placebo in pediatric patients post ABI.

There is level 1b evidence that an amantadine administration consisting of 4 mg/kg/d for a week followed by 6 mg/kg may be a safe and effective protocol compared to placebo in pediatric patients post ABI.

There is level 4 evidence that dopaminergic agents may increase responsiveness (Western NeuroSensory Stimulation Profile scores) in pediatric patients post ABI.

It is unclear whether dopaminergic agents, including amantadine, improve emergence from disorders of consciousness post ABI, however, an amantadine protocol of 4mg/kg/d for a week followed by 6mg/kg may be a safe and effective regiment to follow.

14.1.2.4 Corticosteroids

Numerous corticosteroids have been used in adult brain injury care including dexamethasone, methylprednisolone, prednisolone, prednisone, betamethasone, cortisone, hydrocortisone, and triamcinolone (Alderson & Roberts, 2005). Using such a broad spectrum of agents within diverse patient groups has made understanding corticosteroid efficacy difficult. Adding to this difficulty is a lack of understanding regarding the mode of action of steroids. Laboratory studies have associated corticosteroid use with reductions in wet brain weight, 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) is thought to reduce vasogenic cerebral edema and thereby ICP (Fanconi et al., 1988), however there is a lack of evidence to support their use in pediatric brain injury. In addition, the most recent guidelines for the management of pediatric TBI do not suggest the use of corticosteroids to improve outcomes or reduce ICP (Kochanek et al., 2019).

Table 14.6 Corticosteroids for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Fanconi et al. (1988) Switzerland RCT PEDro=6 N=25	**Population:** TBI; *Dexamethasone Group (n=13):* Mean Age=7.5yr; Mean Time Post Injury=2 hr; Mean GCS=5.5. *Control Group (n=12):* Mean Age=7.4yr; Mean GCS=4.5. **Intervention:** Patients were randomized to receive either dexamethasone or a placebo over a period of 3 d before a 3 d washout phase. Patients receiving dexamethasone were administered 1 mg/kg dose once a day. Respiratory data was recorded every hour for 3 d and outcomes were assessed at 6 mo follow-up. **Outcome Measure:** Glasgow Outcome Scale (GOS), Cortisol Levels, Respiratory Complication Rates.	1. There was no significant difference between the two groups in GOS scores at 6mo follow-up (p>0.050). 2. Endogenous cortisol production was almost completely suppressed within 24 hr of administering dexamethasone and was still lower than controls during the washout phase. 3. Patients receiving dexamethasone experienced a greater frequency of bacterial pneumonia but there were no differences between groups regarding duration of mechanical ventilation, ICP, blood pressure, or peak inspiratory pressure.
Kloti et al. (1987) Switzerland RCT PEDro=6 N=24	**Population:** TBI; *Dexamethasone Group(n=12):* Mean Age=7.8yr; Mean GCS=5.5. *Control Group (n=12):* Mean Age=7.6yr; Mean GCS=4.5. **Intervention:** Patients were randomized to receive either dexamethasone or a placebo over a period of 3 d before a 3 d washout phase. Patients receiving dexamethasone were administered 1 mg/kg dose a day. Respiratory data was recorded every hour and outcomes were assessed at 6mo follow-up. **Outcome Measure:** Cortisol levels.	1. Endogenous cortisol production was almost completely suppressed within 24 hr of administering dexamethasone and was still significantly lower than in controls from day 2 to day 6 (all p<0.050). 2. Cortisol levels were up to 20 times higher in the control group compared with those who were treated with dexamethasone.

Author Year Country Study Design Sample Size	Methods	Outcome

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

The pediatric data highlights that dexamethasone suppresses endogenous production of glucocorticoids, compared to controls (Fanconi et al., 1988; Kloti et al., 1987) and that is does not provide any benefit for children with acute TBI. In addition to the suppression of endogenous glucocorticoids, excessive steroid present may lead to more severe side effects such as bacterial pneumonia (Fanconi et al., 1988; Kloti et al., 1987). Authors suggested that the lack of benefit with dexamethasone is due to the fact that the adrenal cortex can produce enough glucocorticoids on its own to elicit the maximum therapeutic effect on reduction of edema and membrane stabilization (Kloti et al., 1987). Therefore, dexamethasone is not superior compared to no steroid treatment at improving ICP, or neurological outcomes (GOS at 6 mo follow-up) and may even have detrimental side effects (Fanconi et al., 1988). The current pediatric guidelines recommend against dexamethasone administration for severe TBI (Kochanek et al., 2012; Kochanek et al., 2019).

Conclusions

There is level 1a evidence that administration of dexamethasone may inhibit endogenous production of glucocorticoids compared to placebo in pediatric patients post TBI.

There is level 1b evidence that dexamethasone administration may not improve Glasgow Outcome Scale (GOS) scores, intracranial pressure, or blood pressure, but may increase the risk of bacterial pneumonia, compared to placebo in pediatric patients post TBI.

Administration of dexamethasone can inhibit endogenous production of glucocorticoids in children post TBI.

Administration of dexamethasone likely increases the risk of bacterial pneumonia, but does not improve intracranial pressure, neurological outcomes, or blood pressure in pediatric patients post TBI.

14.1.2.5 Other medications

In addition to previously discussed pharmacological agents for the management of ABI/TBI in the pediatric population, a variety of other candidate therapeutic options have been reported in the literature including magnesium sulfate ($MgSO_4$), N-Acetylcysteine (NAC) and blood transfusions. Magnesium sulfate may act as a neuroprotective agent as it targets several pathophysiologic mechanisms that produce secondary brain injury (Natale et al., 2007). In particular, $MgSO_4$ has been shown to decrease cerebral vasoconstriction, attenuate reactive oxygen species and restore alterations within the cerebral

environment (Natale et al., 2007). In animal models, it was found that a decrease in intracellular magnesium resulted in worse neurological outcomes (Natale et al., 2007). However, there is limited evidence for the use of $MgSO_4$ in humans (Natale et al., 2007). In contrast, N-Acetylcysteine is an antioxidant and neuroprotective agent that has been used clinically for a wide array of conditions including major depression, neonatal asphyxia, and neurodegenerative diseases (Clark et al., 2017). NAC may prevent secondary brain injury by acting as an antioxidant directly via its thiol group or by aiding in the replenishment of glutathione under conditions of oxidative stress (Clark et al., 2017). Lastly, several studies have shown an association between blood transfusions and poorer outcomes in patients with severe TBI in adults (Salim et al., 2008; Sekhon et al., 2012). However, these results may not be generalizable to the pediatric population as significant differences in cerebral blood flow exist between the two populations (Yee et al., 2016). In contrast to adults, one group reported that 79% of pediatric patients with TBI that received a blood transfusion demonstrated substantial improvements in brain oxygenation (Zygun et al., 2009). Although evidence-based guidelines have been created to optimize the management of pediatric patients with TBI, there is no consensus on when to provide blood transfusions (Yee et al., 2016).

Table 14.7 Other medications for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Clark et al. (2017) USA RCT PEDro=10 N=14	**Population:** TBI; *Placebo (n=7)*: Mean Age=9.7yr; Median GCS=6. *Probenecid + N-Acetylcysteine (NAC;n=7)*: Mean Age=8.6yr; Median GCS=6. **Intervention**: Patients initially received comprehensive standard care with the aim of stabilization and mitigation of complications secondary to TBI injuries. Once stable, patients received probenecid (25 mg/kg load, then 10 mg/kg/dose every 6 h for 11 doses) and N-acetylcysteine (NAC) (140 mg/kg load, then 70 mg/kg/dose every 4 h for 17 doses) or placebo through a naso/orogastic tube. CSF and serum sample were collected over 4 days; prior and 1 hr after the first dose, and daily prior to drug administration) Outcome Measure: NAC CSF Concentration, Glasgow Outcome Scale (GOS), Length of Stay (LOS), Physiological Parameters.	1. NAC CSF concentrations were detectable 6 h after treatment, and continued to increase until they peaked at 72 hours. CSF NAC concentrations returned to baseline after 96h. 2. No difference between GOS scores were observed between groups after treatment or at 3 mo follow-up. 3. Median paediatric intensive care unit and hospital LOS were not significantly different between groups. 4. Temperature, mean arterial pressure, and ICP were not different between groups.
Natale et al. (2007) Canada RCT PEDro=5 N=6	**Population:** TBI; *Magnesium Sulfate Group ($MgSO_4$, n=4)*: Mean Age=8.9yr; Gender: Male=2, Female=2; Mean Time Post Injury=43.8 hr; Mean Highest GCS=4.5. *Placebo Group (n=2):* Mean Age=5.7yr; Gender: Male=0, Female=2; Mean Time Post Injury=21.5 hr; Mean Highest GCS=9. **Intervention:** Patients were randomized to receive either $MgSO_4$ or a placebo. A dosage of 50 mg/kg up to 4 g of $MgSO_4$ was administered in an appropriate volume of saline to create a concentration of 50 mg/ml. This was followed by a continuous intravenous $MgSO_4$ at a dosage of 8.3 mg/kg/hr for 24 hr. The placebo group received saline only, also for 24 hr. Intracranial Pressure (ICP) levels were	1. ICP and CPP levels did not significantly change during bolus dosage nor continuous infusion of $MgSO_4$ when compared to baseline. 2. MAP levels were significantly higher during the 14-24 hr infusion period for the $MgSO_4$ group compared to baseline (82 mmHg versus 93 mmHg, $p<0.050$). 3. CBFV among all patients with severe TBI did not reach the critically low level of 10 cm/sec and no deleterious effect of $MgSO_4$ on CBFV was detected.

Author Year Country Study Design Sample Size	Methods	Outcome
	measured every 5 min during the first 45 min of treatment, every 15 min after 90 min, every 30 min after 150 min then every 2 hr until the transfusion was complete. Assessments were conducted throughout the study period. **Outcome Measure:** ICP levels, Cerebral Perfusion Pressure (CPP) levels, Mean Arterial Pressure (MAP) levels, Cerebral Blood Flow Velocity (CBFV).	
Podolsky-Gondim et al. (2018) Brazil Retrospective N=66	**Population:** *TBI Group (N=66):* Mean Age=10.9y (3 – 17yr); Gender: Male=77.3%, Female=22.7%; Mean time post injury=acute; GCS=9.48 (4.39). **Intervention:** Retrospective chart review of a trauma centre investigating the effect of coagulopathy on neurological outcome post-TBI. Records examined inpatient stay, 1-month, and 6-month follow-up. **Outcomes:** ICP monitoring, coagulopathy rate, predictors of unfavorable Glasgow Outcomes Scale-Extended (GOS-E)	1. 32 of 66 (48.4%) received invasive ICP monitoring and in 16 of 66 (24.2%) ICP monitoring was the only neurosurgical intervention. 2. Four patients underwent consecutive decompressive craniectomy. 3. Coagulopathy was present in 34.8% of patients. 4. At 1-month follow-up, 71.2% of patients had favorable outcomes on the GOS-E, and 77.3% at 6-months. 5. Predictors of unfavorable GOS-E included: adolescence, low GCS, abnormal prothrombin time, fibrinogen levels, thrombocyte count, and neuroimaging findings of brain edema or bleeding ($p<0.05$).
Yee et al. (2016) Canada Case Control N=128	**Population:** TBI; *Patients Transfused (n=53):* Mean Age=3.5yr; Gender: Male=32, Female=21; Median GCS=3. *Patients not Transfused (n=67):* Mean Age=11.3yr; Gender: Male=47, Female=20; Median GCS=6. **Intervention:** Patients with severe TBI were retrospectively identified to investigate the association between blood transfusions, anemia and patient outcomes. **Outcome Measure:** Adverse Outcomes, Mortality.	1. For those who received transfusions, the mean number of transfusions received was 1.67. 2. Multivariable regression analysis did not reveal significant association between blood transfusion and anemia with adverse outcomes. However, non-accidental trauma suspected (Odds ratio=9.01; $p<0.050$) and Pediatric Risk of Mortality (PRISM) III score (Odds ratio=1.32; $p<0.050$) were significantly associated with mortality.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

A phase 1 clinical trial conducted by Clark et al. (2017) investigated the use of N-Acetylcysteine (NAC) and the adjuvant probenecid in pediatric patients with TBI with the goal of answering two specific questions: (1) can NAC be detected in the ECF after administration, and (2) are there any identifiable adverse effects that occur as a result of this treatment? The researchers found that NAC concentrations were elevated from baseline as early as 6 hrs after administration and did not return to baseline until the 96 hr mark. Furthermore, the treatment was not associated with any adverse events as GOS scores, hospital LOS, temperature, mean arterial pressure, and ICP was not different than controls. Given that NAC is an anti-oxidant and postulated to be neuroprotective, the results of this early study lay the foundation for further clinical trials evaluating the efficacy of the treatment at improving neurological outcomes post TBI.

Magnesium sulfate administration post-TBI was not found to compromise hemodynamics, such as mean arterial pressure, ICP, and CPP in children (Natale et al., 2007). The importance of these findings resides in the fact that magnesium sulfate may work to target the pathophysiologic mechanisms involved in secondary injuries, without compromising systemic hemodynamics in children (Natale et al., 2007). However, long-term neurological outcomes of magnesium were not reported. Future RCTs addressing the effects of magnesium sulfate on the pathophysiologic mechanisms of secondary injury in ABI/TBI are necessary.

One case control study investigated the effects of anemia and blood transfusions on pediatric patients post TBI (Yee et al., 2016). While the study did not report any association between anemia, blood transfusions and mortality, it was noted that factors such as presence of abusive head trauma, increasing PRISM III score, and low GCS after admission were associated with increased mortality. The study was conducted in light of the reported association between anemia, blood transfusions and adverse outcomes in the adult TBI population, however, the results of this retrospective study suggest this association may not be present in the pediatric population. Further studies are required to properly elucidate any potential association.

In a retrospective review of pediatric TBI cases at a trauma center, Podolsky-Gondim and colleagues investigated whether tests of coagulopathy had been performed and what the relative outcomes were (Podolsky-Gondim et al., 2018). The authors found that coagulation assessments like prothrombin time, fibrinogen levels, and thrombocyte count when performed at admission were potential prognostic indicators of favourable outcomes (Podolsky-Gondim et al., 2018).

Conclusions

There is level 1b evidence that N-Acetylcysteine in combination with probenecid may increase N-Acetylcysteine levels in cerebrospinal fluid, but may not be different from placebo in its effect on intracranial pressure, temperature, Glasgow Outcome Scale (GOS) scores, hospital length of stay, or mean arterial pressure, in pediatric patients post TBI.

There is level 2 evidence that magnesium sulfate may not affect hemodynamics (intracranial pressure, cerebral perfusion pressure, mean arterial pressure) compared to placebo in children post TBI.

There is level 3 evidence that the presence of abusive head trauma, high PRISM III score, and low post-admission Glasgow Coma Scale scores, but not anemia and blood transfusions, are associated with increased mortality in pediatric patients post TBI.

There is level 4 evidence that coagulation assessments performed upon admission to a pediatric inpatient unit may be potential prognostic indicators of favourable outcomes post TBI.

N-Acetylcysteine and probenecid administration likely increases N-Acetylcysteine cerebrospinal fluid levels and is not associated with adverse events or hospital length of stay, in pediatric patients post TBI.

Magnesium sulfate may not adversely affect intracranial pressure, cerebral perfusion pressure, or mean arterial pressure in children post TBI.

The presence of abusive head trauma, high PRISM III score, and low post-admission GCS score may be associated with mortality in pediatric patients post TBI, however, anemia and blood transfusions are not.

Coagulation assessments performed upon admission to the pediatric TBI inpatient unit may be prognostic indicators of favourable outcomes post TBI.

14.1.3 Surgical Interventions

14.1.3.1 Decompressive Craniectomy

The approach to management of individuals who sustain a severe TBI with refractory ICP and who have no evidence of a mass lesion, remains controversial (Kan et al., 2006). However, when interventions to manage elevated ICP fail, decompressive craniectomy (DC) may be a last resort to considered. (Kochanek et al., 2012; Ruf et al., 2003). The literature suggests that DCs are effective in reducing ICP and are associated with positive outcomes in children following a severe TBI (Jagannathan et al., 2007; Weintraub et al., 2012). Figaji et al. (2008) noted that in children who had sustained a severe TBI, DCs reduced diffuse brain swelling and improved ICP and cerebral oxygenation. Additionally, a systematic review revealed that favourable outcomes were observed after a DC regardless of the etiology of the ABI (Traumatic=60%, nontraumatic=69%), or whether it was performed within 24 hours compared to after 24 hours (61% versus 69% respectively) (Guresir et al., 2012). Based on a review of the literature from Weintraub et al. (2012) and the current pediatric guidelines (Kochanek et al., 2012), DCs are effective to manage ICP when ICP levels are hazardous to the child and cannot be alleviated non-surgically. However, the majority of studies are retrospectively conducted and further rigorous controlled trials are warranted to make definite conclusions regarding the effectiveness of DCs as an emergency treatment for ICP.

Table 14.8 Decompressive Craniectomy and Related Surgeries for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcomes
Taylor et al. (2001) Australia RCT PEDro=6 N=27	**Population:** TBI; Median Age=10.1yr; *Standard Management Group (n=14):* Median Time Post Injury=17.2 hr; Median GCS=5. *Standard Management + Craniectomy Group (n=13):* Median Time Post Injury=15.0 hr; Median GCS=6. **Intervention:** Patients were randomized to standard medical management (control group) or standard medical management plus decompressive craniectomy (treatment group). Outcome status was assessed at 6mo post-injury either by telephone interview or by chart review. **Outcome Measure:** Glasgow Outcome Scale (GOS), Health State Utility (HSU), Intracranial Pressure (ICP), Length of Stay (LOS).	1. Favourable outcomes on the GOS and HSU were more prevalent for the treatment group compared to the control group but no statistically significant difference was found. 2. Although the treatment group demonstrated a greater reduction in ICP from pre- to post-treatment, this difference between groups only approached significance (p=0.057). 3. The median LOS was 26.8 d for the treatment group and 47.7 d for the control group but this did not reach statistical significance (p=0.330).

Rallis et al. (2017a) Greece Case Series N=14	**Population:** TBI; Mean Age=7.7yr; Gender: Male=5, Female=9; Median Time Post Injury=19 h; Median GCS=6. **Intervention:** Patients with severe TBI who underwent decompressive craniectomy (DC) were retrospectively identified. **Outcome Measure:** Intracranial Pressure (ICP), Cerebral Perfusion Pressure (CPP), Mortality, Neurological Outcomes.	1. DC resulted in significantly reduced postoperative peak ICP (31 mmHg to 19 mmHg) and elevation of minimum CPP (41 mmHg to 58 mmHg) (both p<0.001). 2. Seventy-one percent of patients survived. 3. At 6 mo post-injury, 6 patients were in a vegetative state, and 2 suffered severe impairment.
Manfiotto et al. (2017) France Pre-Post Test N=150	**Population:** TBI; Mean Age=10.75yr; Gender: Male=103, Female=47. **Intervention:** Patients who underwent decompressive craniectomy (DC) were retrospectively analyzed. **Outcome Measure:** Complications.	1. Sixteen patients required the insertion of a CSF shunt device for CSF dynamics impairment. These patients were at increased risk of developing further complications and requiring additional treatment; particularly a cranioplasty infection (p=0.008). 2. Females were more likely to present post-DC CSF disorder (p=0.010). 3. The rate of overall complications was 42%.
Benifla et al. (2016) Israel Case Series N=14	**Population:** TBI; Age=5-16yr; Gender: Male=7, Female=7; GCS=7-14. **Intervention:** Anterior frontal space occupying lesions were treated with a supraciliary "keyhole" small craniotomy. Chart reviews were gathered and analyzed for pre- and post-operative statistics. **Outcome Measure:** Post-operative Outcomes, Complications	1. The operation was performed either on the left side of the brain (n=9) or on the right side (n=5). 2. With the exception of one patient who developed a recurring post-surgical epidural hematoma, there were no major operative or post-operative complications observed. . 3. At long-term follow-up, surgical scars were nearly invisible.
Matsuo et al. (2016) Japan Case Series N=25	**Population:** TBI; Mean Age=6.1mo; Gender: Male=21, Female=4. **Intervention:** Patients with chronic subdural hematoma and subdural hygroma (CSDH/SDHy) who underwent burr-hole craniotomy without continuous drainage were retrospectively identified. **Outcome Measure:** CSDH/SDHy reoccurrence, Complications.	1. Patients presented either with bilateral (n=17) or unilateral (n=8) CSDH/SDHy, resulting in a total of 42 burr-hole craniotomies. 2. CSDH/SDHy reoccurred in 5 patients (20%). These patients underwent a second operation at an average of 0.92 mo after the initial procedure. 3. No complications related to the surgical procedures were reported.
Pechmann et al. (2015) Germany Case Series N=12	**Population:** TBI; Mean Age=8.5yr; Gender: Male=8, Female=4; Mean GCS=4.5. **Intervention:** Data was collected retrospectively from records of patients who received a decompressive craniectomy from January 2005 to February 2013 at a university hospital. **Outcome Measure:** Glasgow Outcome Scale (GOS), Post-surgical Complications.	1. Patients achieved a mean GOS of 3.3 at follow-up (median 29.4mo). 2. Seven patients reached favourable outcomes, three required total care, and one was deceased. 3. Complications were observed in the majority of the patients with nine patients (75%) requiring additional surgery. 4. Long term complications included: hygroma (83%), aseptic bone resorption (50%), post-traumatic hydrocephalus (42%), secondary infection (25-33%), and epilepsy (33%).
Prasad et al. (2015) India Case Series N=71	**Population:** TBI; Mean Age=1.6yr; Gender: Male=43, Female=28; Mean Time Post Injury=11.5 hr; GCS Severity: Mild=9, Moderate=26, Severe=36. **Intervention:** A retrospective of young children who underwent a decompressive craniectomy (DC)	1. Mean pre-op ICP was 22.2 mmHg and the threshold for DC was 15 mmHg. 2. Primary DC occurred in 54% of patients and secondary DC occurred in 46%; DC was further broken down into unilateral (82%),

	for elevated intracranial pressure (ICP) was conducted. **Outcome Measure:** ICP Monitoring and Levels, Mortality, Type of Operation, Complications.	bilateral (6%), bifrontal (7%), and posterior fossa (5%). 3. DC performed within 2 hr of elevated ICP had survival rate of 58% compared to 42% after 2 hr. 4. Complications include: ventilator assisted pneumonia (31%), hydrocephalus (18%), subdural hygroma (15%), wound infection (10%), septicemia (8%), and late onset seizures (3%). 5. Perioperative mortality was overall 44%, where 50% with severe TBI and 58% of infants died. Mean pre-op ICP for patients who died was 27 mmHg, with 90% over 20 mmHg.
Khan et al. (2014) Pakistan Case Series N=25	**Population:** TBI; Mean Age=6.8yr; Gender: Male=21, Female=4; Mean GCS=6. **Intervention:** Data was collected retrospectively from records of patients who received a decompressive craniectomy (DC) from January 2000 to January 2010 at a university hospital. **Outcome Measure:** Glasgow Outcome Scale (GOS).	1. DC performed >4 hr after arrival to hospital was a significant predictor of worse GOS score (p=0.042). 2. Intraoperative blood loss exceeding 300 ml significantly predicted poor outcome on the GOS after a DC (p=0.001). 3. Single skull fractures also resulted in a worse GOS score than multiple fractures but this was not statistically significant (p=0.069).
Oluigbo et al. (2012) USA Case Control N=37	**Population:** TBI; *Non-Accidental Trauma Group (n=14):* Mean Age=2.2yr; Mean GCS=4.5. *Accidental Trauma Group (n=23):* Mean Age=8.4yr; Mean GCS=6.2. **Intervention:** Data was collected retrospectively from records of patients who received a decompressive craniectomy from January 2000 to December 2008 at a single children's hospital. **Outcome Measure:** Mortality rate, King's Outcome Scale for Closed Head Injury (KOSCHI), Visual Impairment.	1. Poor outcomes as measured by the KOSCHI were observed in 57% of non-accidental trauma patients compared to 30% of accidental trauma patients but this was not statistically significant (p=0.170). 2. The odds ratio for mortality in non-accidental trauma patients was 12.2 times greater than those with accidental trauma (p=0.020). 3. Surviving non-accidental trauma patients scored a mean of 3.7 on the KOSCHI but this was not significantly lower than accidental trauma patients who scored a mean of 4.0. 4. At discharge, 66.7% of non-accidental trauma patients were noted to have visual impairments, compared to 9.1% of accidental trauma patients (p<0.050).
Adamo et al. (2009) USA Case Control N=218	**Population:** TBI; Age Range=0-36mo; *Accidental Trauma Group(n=164):* Gender: Male=92, Female=72; Severity: Mild=142, Moderate=13, Severe=9. *Non-Accidental Trauma Group (n=54):* Gender: Male=32, Female=22; Severity: Mild=25, Moderate=20, Severe=8, Unknown=1. **Intervention:** A retrospective chart review of patients who were admitted between January 1st 2002 and December 31st 2008 and who had been entered into the New York State Trauma Registry was conducted. **Outcome Measure:** King's Outcome Scale for Childhood Head Injury (KOSCHI).	1. 18 patients (33%) in the non-accidental trauma group required a decompressive craniectomy or craniotomy compared to only 6 (<1%) patients in the accidental trauma group. 2. Patients who had sustained an accidental trauma were more likely to have a KOSCHI score of 5 (good recovery) at discharge and at follow-up (OR 6.48 and 4.58 respectively) compared with non-accidental patients. 3. KOSCHI scores of 3a, 3b, 4a and 4b (severe to moderate disability) at follow-up were more likely to be reported by non-accidental trauma patients (OR 6.48, 5.47, 2.44 and 3.62 respectively).

Josan & Sgouros (2006) United Kingdom Case Series N=12	**Population:** TBI; *Early Treatment Group (n=6):* Mean Age=13yr; Gender: Male=5, Female=1; Mean Time Post Injury=7.0 hr; Mean GCS=6.8. *Non-Operative Treatment Group (n=6):* Mean Age=11.5yr; Gender: Male=3, Female=3; Mean GCS=6. **Intervention:** A retrospective chart review of patients who were treated between 1999 and 2001 was conducted. Two groups of patients were compared, those who underwent decompressive craniectomy (DC) and those who received non-operative treatment. Outcomes at 1yr follow-up were also analyzed. **Outcome Measure:** Glasgow Outcome Scale (GOS), Intracranial Pressure (ICP) .	1. All patients who underwent a DC maintained a mean ICP of 12.3 mmHg post-operatively. 2. At follow-up amongst those treated with craniectomy, four patients scored a 5 (full recovery) and two patients scored 4 (required some psychological support) on the GOS (i.e., all patients have favourable outcomes). 3. Although three patients who did not receive operative surgery scored 5 on the GOS at follow-up (50%), two died and one scored a 3 (experiences memory and cognitive problems).
Rutigliano et al. (2006) USA Case Series N=6	**Population:** TBI; Mean Age=14.5yr; Time Post Injury=<24 hr; Mean GCS=8. **Intervention:** Data was extracted from the Brain Trauma Foundation TBI-trac online database for patients who had undergone decompressive craniectomy. **Outcome Measure:** Functional Independence Measurement (FIM).	1. All patients demonstrated improvements at discharge with GCS scores all between 12 and 15. 2. FIM ambulation scores revealed that four patients still required assistance one was dependent, and another was considered independent. 3. There were greater levels of independence on the FIM feeding measure with three considered independent, one dependent, and two requiring assistance.
Ruf et al. (2003) Germany Case Series N=6	**Population:** TBI; Mean Age=7.8yr; Gender: Male=2, Female=4; Mean Time Post Injury=2.5d; Mean GCS=4.3. **Intervention:** All patients underwent decompressive craniectomy after ICP levels exceeded 20 mmHg and did not respond to treatment for >30 min. Neurological outcomes were assessed at discharge and at 6mo follow-up. **Outcome Measure:** Intracranial Pressure (ICP), Somatosensory Evoked Potentials of Median Nerve (M-SEP), Complication Rate, Neurological Status.	1. ICP levels normalised to <12 mmHg immediately following surgery in 5 of the 6 patients. 2. M-SEP post-surgery results revealed that 2 patients were categorised as “normal”, one patient with mild impairment, one with moderate impairment, and 2 with severe impairment. 3. Neurological status was judged to be “normal” in 3 (50%) of the patients at 6mo follow-up. 4. Only 1 patient experienced complications post-surgery after developing aseptic necrosis of the replaced bone flap.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Refractory ICP levels normalized or improved significantly after a DC in children (mean age 7.7-14.5yr) who had sustained a severe TBI (Josan & Sgouros, 2006; Ruf et al., 2003; Rutigliano et al., 2006). ICP improved more in children (mean age 10.1 yr) who underwent a craniectomy compared to children who received “standard” ICP management, although this difference was not statistically significant (Taylor et al., 2001). Furthermore, a recent retrospective study suggested that a DC may also improve cerebral perfusion, as it was found that the minimum CPP observed was significantly higher after the procedure as compared to before (Rallis et al., 2017b). In younger children (mean age 1.6 yr), an early DC (< 2 hr after admission) had a survival advantage of 16% compared to a late DC (2 hr post admission) and the mean pre-op ICP for patients who died was 27 mmHg, with 90% of these patients having ICP over 20 mmHg (Prasad et al., 2015).

Although ICP appears to improve for most children following a DC, it is important to consider other complications that may arise. Two studies examined post-operative complications to highlight the potential detrimental effects of a DC (Pechmann et al., 2015; Prasad et al., 2015). The most common complications following DCs were insertion of a cerebrospinal fluid shunt (16%), cranioplasty infection (16%), ventilator associated pneumonia (31%), formation of hygroma (15-83%), and development of post-traumatic hydrocephalus (18-42%). Other potential complications included epilepsy, secondary infections from the surgery, requirement of additional treatment, and septicemia (Pechmann et al., 2015; Prasad et al., 2015). Seventy five percent of children required further surgery due to complications from the initial DC (Pechmann et al., 2015). When comparing those who received a DC to those who did not, it was found that 66% of patients undergoing a DC made a full recovery (GOS=5) and the other 33% had a GOS of 4, while only 50% of the non-DC patients made a full recovery, two died, and one has a GOS score of 3 (Josan & Sgouros, 2006).

Significant predictors of worse outcomes following DCs include surgical delay >4 hours after administration and intraoperative blood loss >300 mL (Khan et al., 2014). Additionally, young children with non-accidental head trauma had higher odds of mortality following a DC (Oluigbo et al., 2012) and poorer outcomes (Adamo et al., 2009) compared to those with accidental traumas. The authors suggest that either DCs are not likely to change fatal outcomes in this group or that the threshold requirement for decompression should be lower for children that have sustained a non-accidental head trauma (Oluigbo et al., 2012).

Anterior frontal space occupying lesions treated with a supraciliary “keyhole” small craniotomy were retrospectively analyzed (Benifla et al., 2016). The researchers noted that with the exception of one patient who developed a recurring post-surgical epidural hematoma, there were no major operative or post-operative complications. In a separate study by Matsuo and colleagues (2016), patients with a chronic subdural hematoma or a subdural hygroma underwent a burr-hole craniotomy without continuous drainage. It was reported that the majority of patients presented with bilateral chronic subdural hematoma or a subdural hygroma (17 out of 25), and with the exception of 5 patients where chronic subdural hematoma or subdural hygroma re-occurred, no complications were reported.

Conclusions

There is level 4 evidence that a decompressive craniectomy may improve intracranial pressure and cerebral perfusion pressure in pediatric patients post TBI.

There is level 1b evidence that a decompressive craniectomy is as effective as standard intracranial pressure management at reducing intracranial pressure in pediatric patients post TBI.

There is level 4 evidence that a late decompressive craniectomy (< 2hr post admission) and intraoperative blood loss (>300 mL) are associated with greater mortality and worse outcomes in pediatric patients undergoing this procedure post TBI.

There is level 4 evidence that children with a severe TBI are at risk of secondary complications following a decompressive craniectomy that may prolong rehabilitation.

There is level 4 evidence that patients who undergo a decompressive craniectomy have greater Glasgow Outcome Scale scores than pediatric patients with TBI who do not.

There is level 3 evidence that children who sustain a severe TBI from non-accidental trauma have poorer outcomes and higher odds of mortality following a decompressive craniectomy, when compared to accidental trauma victims.

There is level 4 evidence that supraciliary "keyhole" small craniotomies for the treatment of anterior frontal space occupying lesions are not associated with major operative or post-operative complications in pediatric patients post ABI.

There is level 4 evidence that a burr-hole craniotomy without continuous drainage for the treatment of either a chronic subdural hematoma or a subdural hygroma is not associated with complications in pediatric patients post ABI.

A decompressive craniectomy may improve intracranial pressure, cerebral perfusion pressure and be associated with improved GCS scores in children post TBI compared to those who do not receive the procedure.

A decompressive craniectomy may be just as effective as standard therapy at reducing intracranial pressure in pediatric patients post TBI.

A decompressive craniectomy may be associated with secondary complications such as infections, formation of hygroma, and insertion of a cerebrospinal fluid shunt, in children post TBI.

Predictors of poor outcomes after a decompressive craniectomy might include non-accidental head trauma, delay (>4 hours) in surgery following admission, and intraoperative bleeding that exceeds 300 mL, in children post TBI.

Supraciliary "keyhole" small craniotomies for the treatment of anterior frontal space occupying lesions may not be associated with major operative or post-operative complications in pediatric patients post ABI.

A burr-hole craniotomy without continuous drainage for the treatment of either a chronic subdural hematoma or a subdural hygroma may not be associated with complications in pediatric patients post ABI.

14.1.4. Pediatric Specific Care

Previous studies have reported conflicting evidence when comparing outcomes (i.e., mortality) of pediatric patients depending on whether they received treatment at an adult, or pediatric specific trauma center (Ochoa et al., 2007; Stelfox et al., 2010; Stylianos & Nathens, 2007). When compared to adult populations, pediatric patients vary greatly in their physiology and anatomy. As a result of this variability, pediatric patients who receive treatment from a pediatric-specific center may have better outcomes than those treated at adult trauma centres (Matsushima et al., 2012; Sathya et al., 2015; Walther et al., 2014). However, in remote communities adult trauma centers may be the only or easiest way to access care, given then urgent nature of TBIs (Miyata et al., 2017). To investigate this, one study examined outcome measures of pediatric patients in center-specific care for the acute management of pediatric TBI.

Table 14.9 Center-specific Care for the Acute Management of Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Miyata et al. (2017) USA Case Control N=26,276	**Population:** TBI; *Pediatric Trauma Center (n=3,737)*: Median Age=13yr; Gender: Male=2,571, Female=1,166. *Adult Trauma Center (n=22,539)*: Median Age=17yr; Gender: Male=19,430, Female=3,109. **Intervention:** Outcomes for pediatric patients with penetrating injuries who went to pediatric trauma centers versus adult trauma centers were compared. **Outcome Measure:** In-hospital Mortality, Discharge Location.	1. There was no significant difference in adjusted odds ratio for mortality between patients who went to pediatric trauma centers versus adult trauma centers 2. Children age≤12 yr (p<0.001), those with gunshot wounds (p<0.001), and those who underwent emergency operations at pediatric trauma centers (p<0.004) were more likely to be discharged home.

Discussion

A single study was reviewed analyzing the difference in outcomes for patients treated a pediatric trauma center compared to those treated at an adult trauma center (Miyata et al., 2017). After reviewing outcomes for close to 27,000 patients, the researchers found no significant difference in mortality between patients who were treated at an adult or pediatric trauma center. However, it was found that children who sustained gunshot wounds, were under 12 yr of age, and underwent emergency operations at pediatric trauma centers were more likely to be discharged home. Although this study draws from an extremely large sample, there is an uneven split between the two treatment groups. Future studies with a more even distribution between groups are required to further analyze outcomes in patients post TBI.

Conclusions

There is level 3 evidence that there may be no difference in mortality between pediatric patients post TBI who were treated either at an adult or pediatric trauma center.

There may be no difference in mortality between pediatric patients with TBI who sustained a penetrating injury and were treated at either an adult or pediatric trauma center.

14.2 Post Traumatic Seizures

Post traumatic seizures (PTS) are one the most common complications in adults and children following ABI (Rumalla et al., 2018). Risk factors for PTS include severe TBI, abusive head trauma, and younger age (<2 years) (Arndt et al., 2013; Liesemer et al., 2011; O'Neill et al., 2015). However, several observational studies have shown that PTS are associated with increased mortality and poorer functional outcomes in the pediatric population (Keret et al., 2017); (Pearl et al., 2013); (Ruzas et al., 2017). In addition, children differ from adults in terms of mechanism of injury and pathophysiology leading to the development of PTS. PTS are classified as occuring immediately (within 24 hours), early (within a week) or late (within a month). It is thought that PTS may contribute to secondary brain injury in children through severeal

mechanisms including increased metabolic demands, cerebral edema, neuronal excitotoxicity, impaired blood supply and elevated ICP (Chung & O'Brien, 2016); (Hale et al., 2018). However, pediatric ABI is associated with greater volumes of post traumatic edema as compared to adults (Aldrich et al., 1992). This may affect the development of PTS as intracerebral fluid deposition is thought to mediate pathogenesis of both early and late PTS (Willmore, 1990).

The incidence of early PTS in children has been reported to be between 12-18% (Liesemer et al., 2011; Rumalla et al., 2018; Thapa et al., 2010), although subclinical epileptiform activity has been detected with continuous EEG monitoring in up to 42.5% of children with head trauma (Arndt et al., 2013). The presence of PTS may be an early warning sign for developing post traumatic epilepsy (PTE). In one retrospective cohort study, children with moderate to severe TBI were found to have an increased risk of PTE (Keret et al., 2018). ProphylacticIn adults, prophylactic anticonvulsants have proved effective in reducing early PTS. Although, the existing evidence for the treatment of PTS in the pediatric population is relatively scarce and consists of a handful of studies. As such, prophylactic anticonvulsants are only administered to children at some institutions and the indications and protocols vary significantly (Rumalla et al., 2018). In this sense, further research is necessary to determine the safety and efficacy of pharmacological prophylaxis in the treatment of PTS.

Table 14.10 Pharmacological Prevention or Prophylaxis of Post Traumatic Seizures in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Young et al. (2004) RCT USA PEDro=6 $N_{Initial}$=102, N_{Final}=69	**Population:** TBI; *Phenytoin Group (n=46):* Median Age=6.4yr; Gender: Male=31, Female=15; Mean Time Post Injury=34 min; Median GCS=7. *Control Group (n=56):* Median Age=5. 9yr; Gender: Male=38, Female=18; Mean Time Post Injury=33 min; Median GCS=7. **Intervention:** Patients were randomized to receive either phenytoin or a placebo. Those in the phenytoin group received a loading dose of 18 mg/kg followed by 2 mg/kg every 8 hr for 48 hr. Phenytoin was prepared in a diluent of water, ethanol, and propylene glycol. Patients assigned to the placebo group received an equivalent volume of the diluent alone, at the same time points. All patients were kept under observation throughout the study. Median time to follow-up was 34.5 d. **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=0.900).
Young et al. (1983) USA RCT PEDro=6 N=41	**Population:** TBI; *Phenytoin (n=25):* Mean Age=9.3yr; Gender: Male=18, Female=7; Time Post Injury=<24 hr; Severity: Mild/Moderate=15, Severe=10. *Controls (n=16):* Mean Age=9.2yr; Gender: Male=15, Female=1; Time Post Injury=<24 hr; Severity: Mild/Moderate=6, Severe=10. **Intervention:** Patients were randomized to receive either phenytoin or a placebo. Phenytoin was administered intravenously at a dosage of 13 mg/kg with the aim of maintaining plasma phenytoin	1. Three patients receiving phenytoin, one patient receiving placebo and none of the patients that switched from phenytoin to phenobarbital experienced seizures. No significant difference was found between groups. 2. No patients with a phenytoin plasma concentration level above 10 ug/ml experienced a seizure. Of the three who experienced seizures, one patient was found

Author Year Country Study Design Sample Size	Methods	Outcome
	concentration of 10-20 ug/ml. Patients were switched to oral medication as soon as oral doses could be ingested. Any patients who became sensitive to phenytoin were switched to phenobarbital. Blood samples were taken every 24 hr. Follow-up was conducted 18mo post-treatment. **Outcome Measure:** Phenytoin Plasma Concentration , Occurrence of Seizure.	to be at a level of 0-5 ug/ml and two were at a level of 5-10 ug/ml.
Chung & O'Brien (2016) USA Post-Test 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 5-40 mg/kg day of levetiracetam as prophylaxis against post-traumatic seizures (PTS). Patients were monitored for up to 7 d 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=0.870).
Vaewpanich & Rice (2016) Thailand Case Series N=16	**Population:** TBI; Mean Age=3.1yr; Gender: Male=8, Female=8; Severity: Mild=5, Severe=11. **Intervention:** Data was collected from medical records of patients admitted to a Level 1 trauma center between December 2012 and June 2015. Outcomes measured at discharge and at 4-6wk follow-up. **Outcome Measure:** Incidence of PTS, Glasgow Outcome Scale Extended Pediatric (GOS-E Peds), Speech Pathology Neurocognitive/Functional Evaluations (SPNFE).	1. Fifteen of 16 patients received prophylactic levetiracetam with additional anti-seizure medications including phenobarbital (n=3), phenytoin (n=4), pentobarbital (n=3) and benzodiazepine (n=3). 2. Despite the administration of prophylactic levetiracetam, four patients (25%) experienced a PTS. All four had experienced non-accidental head trauma. 3. GOS-E Peds and SPNFE at discharge indicated severe disability for all four patients who experienced PTS.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Phenytoin prophylaxis was 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. However, there was an overall lower occurrence of PTS (6%) than what is reported in much of the PTS literature, according to the authors, which may have confounded the results (Young et al., 2004). 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). Although lacking a comparison group, Chung and O'Brien (2016) report that the prevalence of PTS (17.6%) post-levetiracetam administration is similar to prior studies without

any seizure prophylaxis. Due to the lack of randomization and a proper control population, further studies are suggested to fully investigate the effect of levetiracetam prophylaxis in preventing PTS.

Conclusions

There is level 1b evidence that phenytoin prophylaxis may not reduce the occurrence of early (<1 week post injury) or late (>1 week post injury) post traumatic seizures compared to placebo in children post TBI.

There is level 4 evidence that children who develop early post traumatic seizures while receiving levetiracetam prophylaxis are younger and have experienced abusive head trauma, compared to those that did not develop post traumatic seizures.

Prophylactic phenytoin likely does not reduce early (< 1 week post injury) or late (>1 week post injury) seizures in children post ABI.

Patients receiving prophylactic levetiracetam may be more likely to develop post traumatic seizures if they are younger and have experienced abusive head trauma.

14.3 Dysphagia, Feeding, and Nutrition

Similarly to adults, children post ABI are commonly affected by swallowing problems (dysphagia), with the incidence ranging from 68-76% after a severe TBI (Morgan, 2010); (Popernack et al., 2015; Redmond & Lipp, 2006). Impaired oral motor skills often compromise oral intake leading to nutritional deficiencies (Morgan, 2010);(Popernack et al., 2015). This is problematic as children already have difficulty meeting their metabolic demands (Morgan, 2010). In order to facilitate optimal nutrition, a multidisciplinary approach is essential (Mei et al., 2018). The expertise of dietitians, occupational therapists and speech-language pathologists, as well as medical staff should be implemented (Mei et al., 2018). Moreover, nutrient intake should focus on decreasing unnecessary losses of lean body mass and promoting strength/endurance for rehabilitation through optimal caloric and protein intake (Malakouti et al., 2012; Redmond & Lipp, 2006).

The first step in rehabilitation is to assess swallowing. The four stages of swallowing (oral prepaory, oral, pharyngeal and esophageal) must work together to properly transition a bolus of food without airway aspiration (Popernack et al., 2015). If aspiration occurs, a variety of pulmonary issues may arise, such as pneumonia or wheezing with respiratory compromise (Popernack et al., 2015). Evaluations should be completed once the child is alert enough to eat and if the initial bedside assessment identifies a need to proceed with further investigation, videoflouroscopy may be performed. Using this technique, pharyngeal or oral deficits in the transit of a food bolus or fluids may be identified (Morgan et al., 2002; Popernack et al., 2015).

The results of the initial assessment determine therapeutic approaches to facilitate feeding assistance. These approaches may include modifying diet consistencies, using adaptive feeding devices, meal scheduling and increasing endurance for self-feeding (Redmond & Lipp, 2006). In patients who cannot swallow independently, parenteral or enteral nutritional assistance may be provided. Several systematic

reviews have demonstrated that both feeding mechanisms increase survival rates when introduced early (<48 hours) rather than late (>48 hours) (Perel et al., 2006); (Hadley et al., 1986); (Taylor et al., 1999). In particular, one systematic review found earlier feeding was significantly associated with lower mortality rates (0.67 [0.41-1.07]) compared to late feeding (0.75 [0.50-1.11]) (Perel et al., 2006).

Table 14.11 Nutritional Management in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Meinert et al. (2018) USA Secondary RCT Analysis N=90	**Population:** *Group 1 (N=5):* Age=<18yr; Gender: Male=80%, Female=20%; Mean time post injury=acute; Mean GCS=5.6 (0.5). *Group 2 (N=32)*: Age=<18yr; Gender: Male=59.4%, Female=40.6%; Mean time post injury=acute; Mean GCS=5.5 (0.2). *Group 3 (N=36)*: Age=<18yr; Gender: Male=72.2%, Female=27.8%; Mean time post injury=acute; Mean GCS=6 (0.2). *Group 4 (N=17)*: Age=<18yr; Gender: Male=47.1%, Female=52.9%; Mean time post injury=acute; Mean GCS=6.3 (0.2). **Intervention:** Patients of a hypothermia RCT were stratified into 4 groups based on nutritional support: Group 1 had no nutritional support over the first 7 days; Group 2 had nutritional support initiated <48 hours after injury; Group 3 had nutritional support initiated between 48 and 72 hours after injury; Group 4 had nutritional support initiated 72 to 168 hours after injury. Assessed at 6m and 12m (for the GOS-E) **Outcomes:** mortality and Glasgow Outcomes Scale-Extended for pediatrics (GOS-E).	1. Significant main effect of group on mortality rates (p=0.01) indicating the earlier nutritional support had reduced mortality rates. 2. Significant main effect of group on GOS-E at 6 and 12 months (p=0.03 and p=0.04, respectively) showing earlier nutritional support had higher scores.
Briassoulis et al. (2006) Greece RCT PEDro=8 N=40	**Population:** TBI; Gender: Male=29, Female=11; Time Post Injury=<12 hr. *Immune Enhanced Formula (IEF; n=20):* Mean Age=10.6yr; Mean GCS=6.1. *Regular Formula (RF; n=20):* Mean Age=9.3yr; Mean GCS=6.3. **Intervention:** Patients that were mechanically ventilated were randomly assigned to receive either IEF or RF via enteral feeding. Patients were fed hourly over 5 d with increases made daily from 50% of predicted basal metabolic rate to 100%, 125%, 150% and 150% again on day five. **Outcome Measure:** Pediatric Risk of Mortality (PRISM), Length of Stay (LOS), Length of Mechanical Ventilation, Nitrogen Balance Levels, Gastric Culture Levels.	1. Severity of developed illnesses according to PRISM scores, LOS and length of mechanical ventilation did not differ significantly between groups (p>0.050) although IEF patients demonstrated a higher trend in illness severity. 2. Nitrogen balance was significantly higher in IEF patients after 24 hr of feeding (p<0.050) compared to RF patients. However, IEF patients did not change significantly over the course of treatment (p>0.050). 3. IEF patients exhibited significantly less gastric culture than RF patients (p<0.020) but bronchoalveolar lavage colonization and other nosocomial infections did not differ significantly between groups (p>0.050).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Early enteral administration of an immune enhanced formula (glutamine, arginine, antioxidants, and omega-3 fatty acids; Stresson) did not improve mean caloric and protein intake in children compared to modified regular feeding (Tentrini) (Briassoulis et al., 2006). Although not significant in the long-term, nitrogen balance, an important marker for metabolism, was greater for children receiving the immune enhanced formula within 24 hours. The authors attributed this increase to the presence of additional

nitrogen in arginine and endogenous nitrogen growth due to the presence of arginine and glutamine (Briassoulis et al., 2006). Overall, immunonutrition was only beneficial to reduce cytokines, specifically interleukin-8, and early gastric colonization (Briassoulis et al., 2006).

In a series of case studies, food texture was found to affect the amount of food consumed by children following a severe ABI (DeMatteo et al., 2002), which as mentioned earlier, is important to regulate in order to reach the enhanced metabolic demands. Soft textures were the most difficult to take in and swallowing efficacy between minced and pureed foods varied between children (N=3) (DeMatteo et al., 2002). Additionally, the person administering the food had a significant effect on the child's food intake, therefore the authors discussed the importance of individualized treatment plans for feeding in children following a severe ABI (DeMatteo et al., 2002).

In a secondary RCT analysis of a hypothermia treatment trial, Meinert and colleagues (2018) examined nutritional support in children post ABI. The authors stratified individuals into 4 groups corresponding to the onset of their nutritional support received: no support, nutritional support initiated <48 hours, between 48 and 72 hours, and support initiated 72 to 168 hours after injury (Meinert et al., 2018). The authors found a significant main effect of treatment group on mortality and Glasgow Extended Outcomes, with earlier nutritional support having better outcomes (Meinert et al., 2018).

Conclusions

There is level 1b evidence that the administration of enhanced immune formulas may not be superior to regular formulas in regards to increasing caloric and protein intake in children post TBI.

There is level 1b evidence that enhanced immune formulas may be superior to regular formulas at reducing markers of infection and inflammation (interleukin-8 concentrations and early gastric colonization) and improving 24 hour nitrogen balance in children post TBI.

There is level 1b evidence that initiating nutritional support earlier after ABI results in a decrease in mortality and better outcomes.

Enhanced immune enteral feeding formulas may not be superior to regular formulas in regards to improving caloric and protein intake, however, may have beneficial anti-inflammatory properties.

Initiating nutritional support earlier may result in a decrease in mortality and better outcomes in a pediatric population post ABI.

14.4 Rehabilitation

14.4.1 Behavioural Interventions

In adult and pediatric populations TBI can result in several negative outcomes including cognitive and behavioural impairments. In particular, one behavioural impairment commonly experienced is agitation, with 8-70% of patients recovering from severe TBI reporting having experienced it (Wolffbrandt et al.,

2013). Although agitation has not been defined consistently, it is commonly described as behavioural excess that occurs during altered states of consciousness (Nowicki et al., 2019). There are several common clinical characteristics that are reported across the literature including: aggression, restlessness, disinhibition and emotional lability (Gerring et al., 2009; Nowicki et al., 2019; Sohlberg, 2001). Additionally, following a TBI, children are at a greater risk for developing internalizing behaviours, such as anxiety, depression, and personality changes (Li & Liu, 2013). Often, these behaviours occur during the critical stages of rehabilitation, interrupting rehabilitation and education goals (Gurdin et al., 2005).

Despite what is known about the prevalence of agitation post TBI, the literature regarding methods to address the issue is limited. The behaviour therapies that have been evaluated in pediatric TBI populations can be grouped into five categories: cognitive and behavioural therapies, combinational or comparative studies examining behavioural therapies, family based behavioural therapy, community interventions for behavioural therapy, and social re-integration. These topics are explored below.

14.4.1.1 Cognitive and Behavioural Therapies

Behavioural therapies are directed at reducing or eliminating problematic behaviours through the application of behavioural and social learning principles. These treatments involve identifying behaviours and relevant stimulus cues to implement reinforcement strategies, which establish appropriate behaviours. Once adequate behavioural control is established, external “behavioural control” cues and contingencies can eventually be reduced or withdrawn with maintenance of the desired behaviours.

Different behavioural profiles are typically seen at different stages of 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; Sbordone, 1990). 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).

In their review of psychological interventions in children with ABI, Warschausky et al., (1999) indicated that most of the literature on behavioural therapies in children with ABI has focused on externalizing features (e.g., aggression, disruptive behaviours) but that few studies had involved rigorous evaluation of specific interventions. These authors concluded that behavioural therapies in this population appear promising but are in need of further empirical support. It appears that operant conditioning paradigms for decreasing aggressive behaviours have been successful, although there are inconsistent reports of maintenance of gains.

Table 14.10 Cognitive and Behavioral Therapies for the Treatment of Behavioural Disorders Post Pediatric ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Pastore et al. (2011) Italy PCT N=40	**Population:** TBI; *Cognitive Behavioural Therapy Group (CBT, n=28)*: Mean Age=10.9yr; Gender: Male=21, Female=7; Mean Time Post Injury=2.5yr; Mean GCS=5.5. *Control Group (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 4-8 mo in length with 2-3/wk lasting 45-60 min. 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 12 mo. **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, internalising, social problems, somatic complaints, and withdrawal (all p<0.050) compared to controls. 2. After removing patients who received adjunct pharmacotherapy from the analysis, the aforementioned CBCL subscale improvements remained significant, in addition to improvements in aggressive (p=0.002) and externalizing (p=0.004) behaviour. 3. The CBT group demonstrated significantly greater socialisation skills scores than controls (p<0.013) but no difference between groups was found regarding communication and daily living skills (p=0.392, p=0.436 respectively) according to VABS. 4. Patients who did not receive adjunct pharmacotherapy demonstrated greater improvement on all CBCL scales except thought problems, and significantly greater improvement on the VABS socialisation scale (p<0.050) compared with those who received drugs.
Selznick & Savage (2000) USA Pre-post N=3	**Population:** TBI; Mean Age=14.0yr; Gender: Male=3, Female=0; Mean Time Post Injury=5.7 yr. **Intervention:** Patients were trained to self-monitor their productivity, attention and accuracy in completing math assignments and then told to utilize their preferred methods of self-monitoring. A withdrawal phase followed with no audio cues and patients were asked to self-monitor if they chose to. Follow-up was collected after the first session following the withdrawal phase. **Outcome Measure:** Percentage of On-task Behavior, Accuracy Percentage, Duration of Task Engagement.	1. All three patients improved from a baseline of 64%, 55% and 71% of on-task behaviour to 92%, 98-100%, and 100% respectively. 2. Follow-up data was available for two patients, with both maintaining performance at 89-99% and 98% respectively. 3. Accuracy and task engagement remained variable throughout the study.
Slifer et al. (1997) USA Case Study N=3	**Population:** ABI; Mean Age=16.3yr; Gender: Male=0, Female=3; Mean Time Post Injury=31.3 d; Mean GCS=5. **Intervention:** Patients initially received compliance training during two phases, starting with minimal demands before entering a regular therapy phase. Compliance during therapy was reinforced through offering of preferred tasks and/or removing less-preferred tasks in addition to positive reinforcement for compliant behaviours, a low-stimulation environment, and a 24 hr behavioural assistant. Data was recorded daily. **Outcome Measure:** Agitation Rating Scale (ARS), Percentage of Therapy Sessions Attended, Percentage of Disruptive Behaviours.	1. ARS scores were maintained at low levels during therapy at the minimal demands phase and remained low during the regular therapy phase. 2. Mean attendances during the minimal demands phase were 51%, 66.3% and 46.1%. Attendance continued to improve at the regular therapy phase with mean attendances recorded at 85.5%, 100% and 100% respectively. 3. Mean number of disruptive behaviours during the minimal demands phase were 7.8%, 7.1% and 12.1%. An improvement at the regular therapy phase was recorded with mean percentages of 2.4%, 2.8%, and 7.3% respectively.

Author Year Country Study Design Sample Size	Methods	Outcome
Slifer et al. (1995) USA Case Series N=6	**Population:** ABI: TBI=5, Encephalopathy=1; Mean Age=11.5yr; Gender: Male=4, Female=2; Mean Time Post Injury=55.5 d; Mean GCS=5.2. **Intervention:** Patients participated in a behaviour management program with an emphasis on positive reinforcement for social and cooperative behaviour, planned ignoring for disruptive behaviour, and a loss of reward at the end of the session for aggressive behaviour. **Outcome Measure:** Occurrence of Target Problem Behaviours (Inattention, Disruption, Elopement, Crying, Noncompliance), Children's Orientation and Amnesia Test (COAT), Galveston Orientation and Amnesia Test (GOAT)	1. Negative behaviours ceased in four patients during the course of the program. 2. One patient continued to demonstrate negative behaviours but was still considered to be experiencing borderline Post-Traumatic Amnesia (PTA) by the end of the study with a GOAT score of 75. 3. The final patient demonstrated a reduction in negative behaviours during the program and behaviours reduced further after emerging from PTA (COAT z-score =-0.1).
Slifer et al. (1993) USA Case Study N=4	**Population:** TBI; Mean Age=12.8yr; Gender: Male=3, Female=1; Mean Time Post Injury=46.5 d; Mean GCS=8.3. **Intervention:** Patients participated in a behaviour management program with an emphasis on positive reinforcement for social and cooperative behaviour, planned ignoring for disruptive behaviour, and a loss of reward at the end of the session for aggressive behaviour. **Outcome Measure:** Percentage of Rules Followed, Percentage of Disruptive Behaviour in Staff Notes.	1. Two patients demonstrated an immediate reduction in negative behaviours after entering the program with a decrease from 80-100% to 33% and 0%. 2. One patient also reduced to 33% but did not do so until week 6 of the study. 3. One patient demonstrated an inconsistent trend in reducing negative behaviours but did not cease by the study end.
Pruneti et al. (1989) Italy Case Series N=20	**Population:** TBI; Mean Age=11.2yr; Gender: Male=14, Female=6; Severity: Severe=20. **Intervention:** Patients participated in a token economy program at home with parental emphasis on positive reinforcement. Patients also kept a diary and engaged in weekly sessions with a psychologist. Follow-up was conducted at 2yr post-intervention. **Outcome Measure:** Occurrence of Maladaptive Behaviours.	1. At the 20wk period following the introduction of the behavioral program, all Maladaptive behaviour was reduced or eliminated in every patiets. At 2yr follow-up, all 20 patients demonstrated positive outcomes. 2. Over 60% of patients demonstrated greater levels of autonomy after 2mo, rising to 81% after 14 wk. 3. Immature behaviour decreased after 4wk and was found to have ceased in 8-19 wk.

Discussion

Cognitive behavioral therapy improved adaptive behaviour and reduced dysfunctional behaviours such an anxiety, depression, and internalizing behaviours in children who sustained a severe TBI (Pastore et al., 2011). Furthermore, children with greater behavioural impairments at baseline improved the most in the "parental ratings of behaviour" section of the Child Behaviour Checklist. In children not receiving adjunct pharmacotherapy, CBT facilitated adequate social reintegration following a severe TBI. This group significantly improved on all Child Behaviour Checklist parameters, as well as the VABS socialization scale when compared to those receiving additional pharmacotherapy (Pastore et al., 2011).

An earlier method of evaluating a particular behavioural therapy was to compare pre- and post-intervention results for a small number of subjects (Pruneti et al., 1989; Slifer et al., 1993; Slifer et al., 1995; Slifer et al., 1997). One of these studies introduced patients to different self-monitoring techniques to monitor their own productivity, attention, and accuracy in completing math assignments (Selznick &

Savage, 2000). After a withdrawal period where patients were asked to self-monitor if they chose to, researchers found a significant increase in on-task behavior for all 3 subjects—improvements which were sustained on follow-up for the two patients whose data was available. It is important to note both accuracy in completing assignments and task engagement remained variable. The remaining studies implemented some form of compliance training protocol 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 (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 ranting scale scores (Slifer et al., 1997), occurrence of negative behaviours (Pruneti et al., 1989; Slifer et al., 1993; Slifer et al., 1995; Slifer et al., 1997), and greater level of autonomy (Pruneti et al., 1989). While all of the studies reviewed reported at least short-term gains in behaviour management following the interventions, the majority of these studies were uncontrolled multiple case reports. Moreover, in many of the multiple-case studies, subjects were not matched on many seemingly important variables, such as age, IQ, extent of cognitive deficits, or concurrent medication use.

An important variable that differs widely across studies is the time since injury. This is important because, as previously mentioned, different behavioural problems may appear at different stages of recovery. For example, Slifer and colleagues (1993; 1995; 1997) have focused on the very early stages of recovery, during the post-traumatic amnesia phase, whereas other researchers have studied children or adolescents years after a brain injury (Glang et al., 1997; Selznick & Savage, 2000).

Conclusions

There is level 2 evidence that cognitive behavioral therapy may reduce anxiety, depression, and internalizing behaviour compared to no therapy in pediatric patients post ABI.

There is level 2 evidence that cognitive behavioural therapy may be more effective at improving socialization and internalizing behaviour in children post ABI who are not receiving adjunct pharmacotherapy, compared to those who are.

There is level 4 evidence that self-monitoring training can improve on-task behaviour, but not accuracy in completing assignments or task engagement, in children post TBI.

There is level 4 evidence that behavioural therapies for children with ABI may be effective in reducing or eliminating problematic behaviours, lowering agitation, and increasing autonomy.

Cognitive behavioural therapy may reduce internalizing behaviour disorders and improve socialization in pediatric patients post ABI, especially in patients not receiving adjunct pharmacotherapy.

Self-monitoring training might improve on-task behaviour, but not accuracy in completing assignments or task engagement, in pediatric patients post TBI.

Behavioural therapies might reduce problematic behaviours, lower agitation, and increase autonomy in pediatric patients post ABI.

14.4.1.2 Combination or Comparative studies

The following studies investigate the effect of combinational behavioural therapies, or compare different behavioural therapies to examine their relative efficacy in treating behavioral disorders in pediatric patients post ABI.

Table 14.11 Combination or Comparative Behavioural Interventions for the Treatment of Behavioural Disorders Post Pediatric TBI)

Author Year Country Study Design Sample Size	Methods	Outcome
Tlustos et al. (2016) USA RCT PEDro=6 N=132	**Population:** TBI; *CAPS (n=65)*: Mean age=14.4yr; Gender: Male=44, Female=21. *IRC (n=67)*: Mean age=14.7yr; Gender: Male=42, Female=25. **Intervention:** Participants were randomly assigned to either a counselor-assisted problem-solving (CAPS) group that received online counselling or a internet resource comparison (IRC) group. Participants were measured at baseline, and at 6, 12, and 18 mo follow-up. **Outcome Measure:** Child Behavior Checklist (CBCL), Home and Community Social Behavior Scales (HCSBS), Behavioral and Emotional Rating Scale (BERS-2).	1. Results failed to reveal significant inter-group effects for any of the outcomes measured. However, the HCSBS test at follow-up indicated greater increases in social competence for the CAPS group compared to the IRC group in younger teens with moderate injuries and older teens with severe injuries ($p<0.010$). 2. Higher socioeconomic status was associated with higher scores on measures of social competence (HCSBS, CBCL, BERS-2) (all $p<0.050$).
Huebner et al. (2017) Secondary Analysis of Thustos et al. (2016)	**Population:** TBI; *CAPS (n=65)*: Mean age=14.4yr; Gender: Male=44, Female=21. *IRC (n=67)*: Mean age=14.7yr; Gender: Male=42, Female=25. **Intervention:** Participants were randomly assigned to either a counselor-assisted problem-solving (CAPS) group that received online counselling or a internet resource comparison (IRC) group. Participants were measured at baseline, and at 6, 12, and 18 mo follow-up. **Outcome Measure:** Mental Health Services Utilization, Index Of Impairment	1. Using the Services Assessment for Children and Adolescents (SACA), it was reported that between 22-31% of those studied utilized mental health services in the 2 yr post-TBI. 2. Using the Child and Adolescence Functional Assessment Scale (CAFAS), it was found that those with impairments were about 3x more likely to receive services compared to those without($p=0.001$). 3. Between 52-62% of primary caregivers reported having unmet healthcare needs over the duration of the 2 yr follow-up period. 4. Neither gender, race/ethnicity, nor socioeconomic status were predictors of 2 yr post-injury mental health service utilization. Although there were no differences in mental healthcare service use between the CAPS group and the IRC group, adolescents in the CAPS group had significantly lower rates of impairment at 18 months post baseline than those in the IRC group ($p<0.050$) 5. Although no statistically significant, increasing age at time of injury was associated with greater utilization of services at 2 yr post injury ($p=0.640$).

Wade et al. (2015b) USA RCT PEDro=8 N=132	**Population:** TBI; *Counsellor Assisted Problem Solving High School Group (CAPS-HS, n=32):* Mean Age=16.1yr; Gender: Male=15, Female=17; Severity: Moderate=15, Severe=17. *CAPS Middle School Group (CAPS-MS, n=33):* Mean Age=13.4yr; Gender: Male=29, Female=4; Severity: Moderate=25, Severe=8. *Internet Resource Comparison High School Group (IRC, n=40):* Mean Age=16.1yr; Gender: Male=21, Female=19; Severity: Moderate=25, Severe=15. *IRC Middle School Group (n=27):* Mean Age=13.3yr; Gender: Male=21, Female=6, Severity: Moderate=16, Severe=11. **Intervention:** Participants were randomly assigned to CAPS or IRC. In CAPS, participants received video-conferences with a therapist and completed weekly problem-solving skills training. The IRC group were given online access to resources and websites only. The interventions were provided for 6mo. Assessments were completed at post-treatment, 12 mo and 18 mo follow-up. **Outcome Measure:** Child Behavior Checklist (CBCL).	1. CAPS-HS had significantly lower internalizing behaviours on CBCL compared to IRC high school participants ($p<0.050$). 2. No significant interactions were observed for the CBCL Externalizing subscale. 3. CBCL Externalizing scores above the cut-off point was observed in 22% of the IRC patients compared to 17% of CAPS patients but this was not statistically significant ($p=0.500$). 4. However, patients with elevated externalizing behaviour problems in the CAPS group demonstrated significantly greater improvements than IRC group with lower levels of externalizing symptoms at 12mo ($p=0.010$) and 18mo ($p=0.003$) follow-ups.
Wade et al. (2014b) USA RCT PEDro=8 N=132	**Population:** TBI; *Counsellor Assisted Problem Solving Group (CAPS, n=65):* Mean Age=14.4yr; Mean Time Post Injury=0.3yr; Lowest GCS=10.1. *Internet Resource Comparison Group (IRC, n=67)*: Mean Age=14.7yr; Mean Time Post Injury=0.3yr; Lowest GCS=10.0. **Intervention:** Patients were randomly assigned to one of two groups; CAPS group where patients video-conferenced with a therapist and completed problem-solving skills training on the CAPS website, or the IRC group where patients were given online access to resources and websites only. The interventions were provided for 6mo. Assessments were completed at baseline and post-treatment. **Outcome Measure:** Child Behavior Checklist (CBCL).	1. Among older patients (grades 9-12), the CAPS group demonstrated significantly lower levels of externalizing, aggression, attention deficits, ADHD and conduct disorder symptoms (all $p<0.050$) on the CBCL compared to the IRC group. 2. No significant differences on the CBCL or any CBCL subscales were reported between groups among younger patients (grades 6-8). 3. Within the CAPS group, patients in middle school spent significantly more hours on the CAPS website ($p<0.050$) and rated CAPS helpful for anger management skills significantly higher than high school patients ($p<0.010$).

Wade et al. (2011) USA RCT PEDro=5 N=41	**Population:** TBI; *Teen Online Problem Solving Group (TOPS, n=20)*: Mean Age=14.0yr; Gender: Male=6, Female=14; Mean Time Post Injury=8.8mo; Mean GCS=9.5. *Internet Resource Comparison Group (IRC, n=21)*: Mean Age=14.5yr; Gender: Male=11, Female=10; Mean Time Post Injury=10.3mo; Mean GCS=10.5. **Intervention:** Patients were randomly assigned to either the TOPS or IRC group. The TOPS group received 10 internet sessions providing training in stress management, problem solving, planning, organization, communication and self-regulation, up to four supplemental sessions addressing the stressors and burden of individual families, and therapy via videoconferencing. The IRC group received access to online resources and were asked to spend at least 1 hr/wk accessing information. Assessments were conducted at baseline for both groups, at approximately 8mo follow-up. **Outcome Measure:** Child Behavior Checklist (CBCL), Interaction Behaviour Questionnaire (IBQ), Youth Self Report (YSR).	1. Parent ratings of conflict on the IBQ were significantly lower for the TOPS groups compared to the IRC group at follow-up (p=0.002), but not for adolescent ratings (p=0.900). 2. The TOPS and IRC groups did not differ on either parent or adolescent ratings of internalizing or externalizing symptoms at follow-up according to both the CBCL and YSR assessments. 3. Socioeconomic status was found to significantly moderate adolescent reports of externalizing and internalizing behavioural scores on the YSR (p=0.010 and p=0.040 respectively) and parent-reported adolescent externalizing behaviour scores on the CBCL (P=0.040). 4. Post-hoc analyses revealed that high-SES adolescents demonstrated significantly greater improvements in internalizing behaviour from baseline to follow-up according to the YSR (p=0.001).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Four studies compared the effects of an online problem solving intervention program (CAPS) to an internet resource intervention (IRC) administered to adolescents within the first year following a moderate TBI, in hopes of remediating refractory behavioural problems (Wade et al., 2014b; Wade et al., 2015b; Wade et al., 2011). The CAPS intervention was found to improve parental ratings of externalizing, but not internalizing behaviours (such as anxiety and depression) in children compared to the IRC group (Wade et al., 2014b). Different results were found by Tlustos and colleagues (2016), as they noted inter-group differences only in social behavioural (HCSBS scores) and in specific subpopulations: younger teens with moderate injuries and older teens with severe injuries. Conflict between parents and adolescents was significantly reduced following training in the CAPS group compared to the IRC group, which may lead to additional behavioural improvements over time (Wade et al., 2011). Adolescents with low socioeconomic status and greater injury severity were more susceptible to initial behavioural problems following injury, however, this subset of adolescents received the greatest benefit from the CAPS intervention (Wade et al., 2011). Interestingly, different results were reported by Tlustos et al. (2016) as it was found that patients with TBI of higher socioeconomic status had higher scores on measures of behavioural and social competence after treatment. Similarly, children who had more externalizing behaviours prior to the intervention reported significant reduction in externalizing behaviours post-intervention (Wade et al., 2015b).

A secondary analysis of the study by Tlustos et al. (2016) was recently conducted with the aim of analysing patient use of mental health services post injury (Huebner et al., 2017). While it was reported that only 30% of patients utilized mental health services in a 2-year period following TBI, there were no differences between treatment group (CAPS versus IRC), gender, race, age, or socioeconomic status in terms of service usage.

Problem solving training is important for teaching coping skills that will lead to situational adaptations and improvements in behavioural competence, which can reduce or prevent the negative effects of stress that are prominent following a TBI (Wade et al., 2014b).

Conclusions

There is conflicting (level 1b) evidence as to whether a counsellor-assisted problem-solving (CAPS) group is superior to an internet resource comparison intervention at improving management of externalizing, internalizing, and socialization behaviours in pediatric patients post TBI.

There is level 1b evidence that a counsellor-assisted problem-solving program may be superior to an internet resource comparison intervention at reducing conflict between parents and adolescents post TBI.

There is conflicting (level 1b) evidence as to whether lower or higher socioeconomic patients benefit most from a counsellor-assisted problem-solving intervention compared to an internet resource intervention post TBI.

There is level 1b evidence that treatment (counsellor-assisted problem-solving versus internet resource comparison), gender, race, age, or socioeconomic status do not affect use of mental health services in pediatric patients post TBI.

Counsellor-assisted problem-solving and internet resource interventions may be effective at mitigating behavioural problems in pediatric patients post TBI, however, conflicting evidence exists as to which is superior and who benefits the most.

Mental health services are commonly underutilized within the first two years of a TBI, regardless of treatment (counsellor-assisted problem-solving versus internet resource comparison), gender, race, age, or socioeconomic status.

14.4.1.3 Family-Supported Interventions

Familial support plays a critical role in a child's recovery and development following an ABI, as it has been demonstrated that family functioning is a significant moderator of outcomes following brain injury (Braga et al., 2005; Yeates & Taylor, 2005). This is particularly significant given that increases in family dysfunction following pediatric ABI have been well-documented (Cole et al., 2009). Families play a critical role throughout the acute and post-acute stages of recovery (Savage et al., 2005). It is thought that family-centered interventions help to improve parental, child and sibling adaptation following injury (Wade et al., 2006b). It has been noted that families take on four unique roles in a child's recovery from brain injury: (1) as observers of the child's care, (2) as experts with insightful pre- and post-injury information regarding the child's abilities, (3) as communicators with professional caregivers and (4) as advocates for the child (Savage et al., 2005).

Unfortunately, being the parent of a child with an ABI can be a demanding and stressful experience. For example, Brown et al. (2013) demonstrated that following a child's ABI, parents experience feelings of isolation, distress, relationship discord, anxiety, and engage in negative coping mechanisms such as

avoidance and disengagment behaviours. In addition, parental psychiatric symptoms can impact the childs recovery. One study showed that children of parents who demonstraetd internalizing issues were more likely to demonstrate internalizing issues of their own following an ABI (postitive correlation of 22-26%) (Peterson et al., 2013). 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 the reverse is also true (Taylor et al., 2001). Therefore it is important to target both child and parental outcomes for optimal recovery after a child has sustained a brain injury.

14.4.1.4 Web-Based Family-Supported Interventions

Family based interventions delivered online have gained popularity due to easier accessibility to treatment. Families can access online treatment programs from their homes and teleconference with a therapist over the phone/internet (Narad et al., 2015). Online programs address many frequently identified barriers to care and treatment, such as time, and proximity of knowledgeable providers (Wade et al., 2006b). Online family supported interventions aim to not only improve child outcomes, but also parental outcomes and communication between family members.

Table 14.12 Family-Supported, Web-based Interventions for the Treatment of Behavioural Disorders Post Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Counsellor Assisted Problem Solving Therapy		
Wade et al. (2018b) USA RCT PEDro=6 N=152	**Population:** *Teen Online Problem Solving (TOPS) with Family Group (N=49):* Mean Age=14.7y (2.1); Gender: Male=71%, Female=29%; Mean time post injury=5.3mo (3.9); GCS=N/A. *TOPS with teen only Group (N=51)*: Mean Age=14.8y (2.0); Gender: Male=69%, Female=31%; Mean time post injury=5.8mo (4.4); GCS=N/A. *Internet Resources Comparison (IRC) Group (N=52)*: Mean Age=15.1y (2.1); Gender: Male=71%, Female=29%; Mean time post injury=6.1mo (3.80); GCS=N/A. **Intervention:** The TOPS program is 10 core online modules providing training in stress management, problem-solving, self-regulation, communication, and social skills. The teen only content paralleled the family content but focused exclusively on the teen. The IRC group had access to a website with online resources. Assessments took place at baseline and 6-months later. **Outcomes:** Child Behaviour Checklist (CBCL), Behaviour Rating inventory of executive functions (BRIEF), and the self-report equivalents (Youth Self-Report [YSR] and BRIEF Self-report, respectively).	1. Group differed significantly on the parent-reported BRIEF ($p<0.05$) with children in the TOPS with family group showing significantly lower levels of executive dysfunction than TOPS with teen only. However, there was no significant difference between TOPS with family and the IRC group. 2. No significant group differences on the parent-reported CBCL ($p>0.05$). 3. No significant group differences on the YSR or the BRIEF self-report ($p>0.05$).
Narad et al. (2015) USA RCT PEDro=6 N=132	**Population:** TBI; *Counsellor Assisted Problem Solving (CAPS, n=65):* Mean Age=14.7yr; Mean GCS=10.1. *Internet Resource Comparison (IRC, n=67):* Mean Age=15.0yr; Mean GCS=10.0. **Intervention:** Participants were randomly assigned to the CAPS or IRC group. CAPS group underwent 6 45-60 min video conferencing sessions with a	1. All participants improved on FAD ($p=0.030$), however no significant between group effects were found. 2. Effective communication on IFIRS for participants with severe TBI decreased for both CAPS ($p<0.010$) and IRC ($p=0.030$) from baseline to 6 mo, signifying an improvement

Author Year Country Study Design Sample Size	Methods	Outcome
	counsellor for 6 mo, with both the adolescent and primary care giver. Participants received web-based problem-solving training with guidance from counsellor. Children and their families in the IRC group were given online access to resources and websites only. Assessments were completed at baseline, 6 mo, 12 mo and 18 mo. **Outcome Measure:** Family Assessment Device (FAD), Iowa Family Interaction Rating Scale (IFIRS), Problem-Solving Discussion Rating Scale (PSDRS).	in communication. This significant improvement was maintained for CAPS ($p<0.010$), but not IRC, at 12 mo. 3. Participants with severe TBI in the CAPS group had less severe conflicts on PSDRS at 18 mo relative to 12mo ($p=0.008$) and baseline ($p=0.040$). IRC participants with severe TBI demonstrated less severe conflict at 12 mo relative to 6mo only ($p=0.030$).
Wade et al. (2014a) USA RCT PEDro=8 N=132	**Population:** TBI; *Counsellor Assisted Problem Solving (CAPS, n=65):* Mean Age: Caregiver=41.9 yr, Child=14.6 yr; Mean Time Post-Injury Child=0.3 yr; Lowest GCS=10.1. *Internet Resource Comparison Caregiver Group (IRC, n=67):* Mean Age: Caregiver=42.8 yr, Child=15.0 yr; Mean Time Post-Injury Child=0.3 yr; Lowest GCS=10.0. **Intervention:** Participants were randomly assigned to CAPS or IRC. The CAPS group received video-conferences with a therapist and completed weekly problem-solving skills training as a family. The IRC group had online access to resources and websites only. The interventions were provided for 6 mo. Assessments for caregiver outcomes were completed post-treatment. **Outcome Measure:** Global Severity Index (GSI), Center for Epidemiologic Studies Depression Scale (CES-D), Caregiver Self-Efficacy Scale (CSES).	1. No significant difference in caregiver depression between groups according to CES-D ($p=0.055$). However, once removing CAPS participants who attended fewer than 4 sessions, a significant group effect was found ($p=0.030$) at 6 mo. 2. Caregivers in CAPS reported significantly higher self-efficacy on CSES than IRC for non-frequent computer users ($p=0.010$) but not for frequent users. 3. Both groups demonstrated a significant reduction in GSI distress (both $p=0.007$).
Petranovich et al. (2015) USA RCT PEDro=6 N=132 **follow-up to Wade et al. (2014 CAPS caregiver)*	**Intervention:** Assessments were completed 12 mo and 18 mo after initiation of treatment. **Outcome Measure:** Global Severity Index (GSI), Center for Epidemiologic Studies Depression Scale (CES-D), Caregiver Self-Efficacy Scale (CSES).	1. Significantly lower global distress levels on GSI for low-income parents in CAPS group relative to IRC group at 6 mo ($p=0.040$), 12 mo ($p=0.010$), and 18 mo ($p=0.004$). 2. All parents with high levels of depression on CES-D at baseline demonstrated a significant reduction over time ($p=0.002$), but no significant between group differences were found. 3. CAPS had significantly higher scores on CSES compared to IRC ($p=0.020$), but no significant group x time interaction was reported.
Wade et al. (2012) USA RCT PEDro=6 $N_I=41$, $N_F=35$	**Population:** TBI; *Teen Online Problem Solving Parents Group (TOPS, n=20)*: Mean Age=40.8 yr. *Internet Resource Comparison Parents Group (IRC, n=21):* Mean Age=41.6 yr. **Intervention:** Families were randomly assigned to receive either TOPS or IRC. TOPS included a visit from a therapist at the outset and 10 web-based sessions of 45-60 min each for adolescents and their family members. IRC group was given access to online resources only. The interventions were	1. Low income families in the TOPS group improved significantly from baseline to post-treatment in depressive symptoms on CES-D ($p=0.040$), and positive problem orientation and rational problem solving on SPSI ($p<0.050$). No significant difference found in the low income IRC group from baseline to post-treatment.

Author Year Country Study Design Sample Size	Methods	Outcome
	provided for 6 mo. Follow-up assessments were completed at a mean of 7.83mo (TOPS) and 7.92mo (IRC). **Outcome Measure:** Social Problem Solving Inventory-Revised Short Form (SPSI), Global Severity Index (GSI), Center for Epidemiologic Studies Depression Scale (CES-D).	2. High income families in the IRC group experienced significant reduction in depressive symptoms on CES-D (p=0.010) and positive problem orientation on SPSI (p<0.050) from baseline to post-treatment. No significant reductions were found for high income TOPS participants. 3. Upon regression analyses, change in overall problem solving explained 16% of variance in depression (CES-D, p=0.010) and 7% of variance in global distress (GSI, p=0.040).
Wade et al. (2008) USA RCT PEDro=5 N=9	**Population:** TBI; Mean Age=15.0yr; Gender: Male=5, Female=4; Mean Time Post Injury=9.3mo; Mean GCS=10.9. **Intervention:** Patients participating in the Teen Online Problem Solving (TOPS) program were randomly assigned to receive audio support (n=5) in the form of text being read aloud to them after clicking a "play" button or no audio support (n=4). The TOPS program consisted of 10 internet sessions providing training in stress management, problem solving, planning, organization, communication and self-regulation, six supplemental sessions addressing the stressors and burden of individual families, and therapy via videoconferencing. All sessions were provided every 1-2 wk. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** Child Behavior Checklist (CBCL), Conflict Behavior Questionnaire (CBQ), Center for Epidemiologic Studies Depression Scale (CES-D), Children's Depression Inventory (CDI), Number of Behavioural Issues, Severity of Behavioural Issues.	1. No significant differences were reported between groups on all measures. 2. Patients within the Audio Group improved significantly on the CBCL Internalizing scale (p=0.030), CES-D (p=0.020) and demonstrated a significant reduction in the number of behavioural issues (p=0.020) from baseline to post-treatment. 3. Patients within the Non-Audio Group improved significantly on the CBQ (p=0.040) and demonstrated a significant reduction in the severity of behavioural issues (p=0.050) from baseline to post-treatment. 4. Overall, all nine patients improved significantly on the CBCL Internalizing scale (p=0.030), CES-D (p=0.010), CDI (p=0.020), CBQ (p=0.040), number of behavioural issues (p=0.010) and the severity of behavioural issues (p=0.010) from baseline to post-treatment after participating in the TOPS program.
Wade et al. (2006b) USA RCT PEDro=7 N_I=46, N_F=40	**Population:** TBI: *Family Problem-Solving Group (FPS, n=20)*: Mean Age=10.9yr; Gender: Male=16, Female=4; Mean Time Post Injury=13.5mo; Mean Lowest GCS=12.2. *Internet Resource Comparison Group (IRC, n=20)*: Mean Age=11.0yr; Gender: Male=12, Female=8; Mean Time Post Injury=14.1mo; Mean Lowest GCS=10.5. **Intervention:** Patients were randomly assigned to either the FPS intervention or the IRC group. The FPS group received 14 online problem-solving sessions (8 core sessions), followed by an additional 6 individualized sessions to address unresolved stressors. Videoconferences with a therapist occurred every 1-2 wk. The IRC group received access to online brain injury resources only. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** Social Problem Solving Index (SPSI), Symptom Checklist-Revised Global Severity Index (SCL 90-GSI), Center for Epidemiologic	1. Parents in the FPS group reported less anxiety on the AI, less depression on the CES-D, and less psychiatric symptoms on the SCL 90-GSI compared to the IRC at post-treatment (p<0.050). 2. There we no significant between group differences in parental problem solving on SPSI (p=0.100). There was also no association between problem solving and parental outcomes on CES-D and SCL 90-GSI (p>0.050). 3. Six parents (30%) in FPS reported clinically significant depression on CES-D and two (10%) reported clinically significant distress on SCL 90-GSI compared to 12 (60) and 6 (31.6%) parents in the IRC. Neither of these reports were significant (p=0.057, p=0.950 respectively).

Author Year Country Study Design Sample Size	Methods	Outcome
	Studies Depression Scale (CES-D), Anxiety Inventory (AI).	
Wade et al . (2006a) USA RCT PEDro=6 N_I=46, N_F=40	**Population:** TBI: *Family Problem-Solving Group (FPS, n=20)*: Mean Age=10.9yr; Gender: Male=11, Female=9; Mean Time Post Injury=13.5mo; Mean Lowest GCS=12.2. *Internet Resource Comparison Group (IRC, n=20)*: Mean Age=11.0yr; Gender: Male=12, Female=8; Mean Time Post Injury=14.1mo; Mean Lowest GCS=10.5. **Intervention:** Patients were randomly assigned to either the FPS intervention or the IRC group. The FPS group received 14 online problem-solving sessions (8 core sessions) followed by an additional 6 individualized sessions to address unresolved stressors along with videoconferences every 1-2 wk. The IRC group received access to online brain injury resources and links but no access to the FPS content. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** Child Behavior Checklist (CBCL), Home and Community Social Behavior Scale (HCSBS).	1. The FPS group reported significantly higher HCSBS Self-Management/Compliance subscale scores at post-treatment compared to patients in the IRC group (p<0.050). 2. Greater improvement was noted for the FPS group on the HCSBS Social Competence subscale, CBCL Internalizing subscale, and CBCL Total score compared to the IRC group post-treatment but no significant between-group differences were reported. 3. Patients aged >11yr in the FPS group reported significantly higher HCSBS Self-Management/Compliance scores post-treatment compared to patients of the same age in the IRC group (p=0.030) but no significant difference was found between groups for patients aged <11 yr.
Wade et al. (2018a) USA Pre-Post N_I=12	**Population:** *TBI Group (N=8):* Mean Age=16.59yr (1.18); Gender: Male=50%, Female=50%; Age at injury=6.27y (5.5); GCS=N/A. Brain tumor (BT) group (N=4): Mean age=18.25yr (1.88); Gender: Male=25%, Female=75%; Age at injury=5.46yr (4.6); GCS=N/A. **Intervention:** ABI patients were nonrandomized to the intervention group. The intervention consisted of using an app-based coaching intervention (Social Participation and Navigation; SPAN) to help patients attain social goals. **Outcomes:** ease of use and satisfaction of intervention, Child Behaviour Checklist (CBC), Youth Self-Report (YSR).	1. Significant difference between-groups in self-reported ease of use of the app (p=0.04) with 100% of the BT Group stating it was easy to use (strongly agree/agree) versus 37.5% of the TBI group. 2. No significant group differences on whether the app was useful (both groups mostly agreed). 3. In an analysis of the full sample (N=12), on the CBC there was a significant increase pre to post on confidence in participation (p<0.01). No other significant results. 4. In an analysis of the full sample (N=12), on the YSR there was a significant increase pre to post on participation frequency (p=0.01) and decreases on total problems, internalizing problems, externalizing problems, and social problems (p<0.05).
Internet-Based Interacting Together Everyday: Recovery After Childhood Intervention		
Raj et al. (2018) USA RCT PEDro=6 N=113	**Population:** *InTERACT Group (N=39):* Mean Age=6.15yr (1.99); Gender: Male=66.7%, Female=33.3%; Mean time post injury=1.02yr (1.52); GCS=<12. *InTERACT express Group (N=36)*: Mean Age=6.16y (2.07); Gender: Male=58.3%, Female=41.7%; Mean time post injury=0.84yr (1.18); GCS=<12. IRC *Group (N=38)*: Mean Age=6.58y (1.83); Gender: Male=57.9%, Female=42.1%; Mean time post injury=0.90y (1.46); GCS=<12. **Intervention:** Caregivers of TBI children were randomized into one of three groups. The	1. No significant effect between-groups on the GSI, PSI, CSES, CES-D at follow-up at any time point.

Author Year Country Study Design Sample Size	Methods	Outcome
	InTERACT program combines features of Parent-Child interaction therapy with training in managing challenging child behaviours, TBI education, stress management, and communication. This group attended 10 sessions. Caregivers independently reviewed content and videoconferenced with a clinician. The InTERACT Express group had an abbreviated version including 7 sessions. The IRC group received access to a web site with links to various online resources on TBI and parenting. Assessed at baseline and 6 mo. **Outcomes:** Caregiver Depression (CES-D), caregiver psychological stress (GSI), Parenting Stress Index (PSI), Parenting Efficacy (CSES).	
Raj et al. (2015) USA RCT PEDro=5 N=37	**Population:** TBI; *Internet-Based Interacting Together Everyday (I-InTERACT, n=20)*: Mean Age=5.6yr; Gender: Male=14, Female=6; Mean Time Post-Injury=31.6 mo. *Internet Resource Comparison (IRC, n=17):* Mean Age=5.2yr; Gender: Male=11, Female=6; Mean Time Post-Injury=24.4 mo. **Intervention:** Parents and children were randomized to either I-InTERACT or IRC programs. The I-InTERACT program encouraged everyday interactions between child and parent, with 10 core sessions of videoconferencing with a therapist and self-guided online skill training. The IRC group was provided with online resources about TBI in children. The interventions were provided for 6 mo. Assessments were completed at baseline and post-treatment. **Outcome Measure:** Parenting Stress Index (PSI), Caregiver Self-Efficacy Scale (CSES), Global Severity Index (GSI), Center for Epidemiological Studies Depression Scale (CES-D).	1. Post-hoc analyses of GSI scores revealed that low-income parents in the I-InTERACT group demonstrated significant reductions in psychological distress from baseline to post-treatment (p=0.010) whereas low-income parents in the IRC group experienced a nonsignificant increase in distress. 2. There were no significant differences between groups for high-income parents. 3. No significant differences were observed between groups from baseline to post-treatment on the PSI (p=0.200), CES-D (p=0.580) and CSES (p=0.460). Further, no significant interactions with family income were observed.
Antonini et al. (2014) USA RCT PEDro=6 N=37	**Population:** TBI; *Internet-Based Interacting Together Everyday (I-InTERACT, n=20)*: Mean Age=5.6yr; Gender: Male=14, Female=6. *Internet Resource Comparison (IRC, n=17):* Mean Age=5.2yr; Gender: Male=11, Female=6. **Intervention:** Parents and children were randomly assigned to either I-InTERACT or IRC groups. The I-InTERACT program encouraged everyday interaction between child and parent, with 10 sessions of videoconferencing with a therapist and self-guided online skill training. The IRC received online resource for children following a TBI. Assessments were completed at baseline and post-treatment (6 mo). **Outcome Measure:** Dyadic Parent–Child Interaction Coding System (DPICS), Child Behavior Checklist (CBCL), Eyberg Child Behavior Inventory (ECBI).	1. Undesirable parenting behaviours on DPICS were significantly reduced in both groups (p=0.0002). 2. According to DPICS, parents in the I-InTERACT group were more likely to report positive parenting statements post-treatment compared to IRC group (p<0.0001). 3. Following intervention, parents in I-InTERACT group were recorded to administer a greater number of praises on DPICS following child compliance than were those in IRC (p<0.009). 4. Children in I-InTERACT in low income families improved on CBCL compared to those in IRC (p=0.001) whereas children in I-InTERACT with higher income had worse scores on CBCL than those in IRC (p=0.04).

Author Year Country Study Design Sample Size	Methods	Outcome
		5. No significant difference on ECBI between groups was identified.
Mast et al. (2014) USA RCT PEDro=4 N=7 *a subanalysis of Antonini et al. (2014)*	**Population:** TBI; *I-InTERACT (n=4)*: Age Range=3-9 yr. *IRC (n=3):* Age Range=3-9 yr. **Intervention:** Participants that sustained abusive head trauma were further analyzed. **Outcome Measure:** Dyadic Parent–Child Interaction Coding System (DPICS), Child Behavior Checklist (CBCL), Eyberg Child Behavior Inventory (ECBI).	1. According to the DPICS, parents in the I-InTERACT group were significantly more likely to provide praise (p=0.027) and reflective statements (p<0.0001), but less likely to ask their child questions (p<0.0001), than parents in the IRC group during child-lead interactions. 2. No difference was found between the I-InTERACT and IRC groups in the likelihood of giving commands to their children (p=0.150). 3. Children in the I-InTERACT group complied with 90% of parental demands compared to 50% in the IRC group (p=0.020). 4. The children of the parents in both groups did not differ on the CBCL but children of the I-InTERACT group scored significantly lower on the ECBI Total Intensity compared to children in the IRC group at follow-up (p=0.020).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Therapy provided with the assistance of a counsellor (CAPS) was examined for a population of children (mean age >10 yr) whose ABI had occurred within the last year (Narad et al., 2015). Counsellor assistance to complete psychoeducational modules did not significantly improve family function (i.e., communication and transactions between family members), when compared to an internet resource comparison group (IRC) (Narad et al., 2015). However, children improved in self-management and compliant behaviours from pre- to post-treatment in the CAPS group when compared to the IRC group (Wade et al., 2006c). Upon analyzing parental outcomes post-intervention, parents in the treatment group had a reduction in depressive symptoms, anxiety, and distress, but not problem solving compared to the IRC (Wade et al., 2006b). The reduction in depressive symptoms was particularly evident when participants completed more than four sessions (Wade et al., 2014a). However, long term analysis (18 months post-intervention) revealed that online counsellor assisted therapy only reduced caregiver psychological distress, not depression or self-efficacy (Petranovich et al., 2015).

Some benefits from counsellor assisted online therapy were evident only for a subset of individuals. For example, parental self-efficacy improved only in non-frequent computer users (Wade et al., 2015a) and self-management improved for older children (>11yr) in the treatment arm compared to older children in the IRC (Wade et al., 2006b). Other benefits were found for individuals with severe versus moderate TBI, however, the effect sizes were small and reports were inconsistent between parents and adolescents (Narad et al., 2015).

An important moderating variable that was found within the counsellor assisted online therapy group was socioeconomic status (Petranovich et al., 2015; Wade et al., 2012). Parental distress levels were reduced

for low income parents compared to those with high socioeconomic status, in the treatment group more so than for those in the IRC. Within both groups, low income parents reported significantly reduced depressive symptoms post-treatment. Among high income parents, the control group (IRC) reported reduced depressive symptoms post-treatment, whereas there was no significant difference observed in the online intervention group (Wade et al., 2012). Authors hypothesize that counsellor assisted therapy may be more beneficial for a subset of individual based on socioeconomic status and future research is warranted.

Online counsellor assisted therapy resulted in improved adolescent behavioural problems, parental depression and parent-child conflicts post-treatment (Wade et al., 2008). Additionally, there were improvements within intervention and IRC groups on several outcomes, such as the transactional family characteristics and effective communication (Narad et al., 2015), distress (Wade et al., 2014b), and depression (Petranovich et al., 2015). Although the differences between groups were not significant, the authors suggested that both interventions may be beneficial to reduce caregiver burden and family functioning post-ABI. Wade and colleagues (2018a) a follow-up study on the TOPS therapy intervention and found that the family group scored significantly lower on scores of executive dysfunction compared to the other two groups, however, no other significant between-groups differences were noted.

Wade and colleagues (2018a) launched a Social Participation and Navigation app that administers a coaching intervention. Using this app, they conducted a pilot study with 12 pediatric TBI and brain tumor individuals. They found both groups were satisfied with the app and it was easy to use. In addition, they found an increase pre to post-assessment in confidence scores and participation frequency (Wade et al., 2018a).

An online parenting skills program, Internet-Based Interacting Together Everyday (I-InTERACT), instructed parents on the management of children post-ABI. I-InTERACT was compared to an IRC to determine the effects on caregiver strain and parent-child interactions (Antonini et al., 2014; Mast et al., 2014; Raj et al., 2015). The I-InTERACT parenting skills program did not reduce depression or stress, nor did it improve self-efficacy and distress levels (Raj et al., 2015). However, within this population, 92% of caregivers were mothers and therefore the results may not be representative of what changes could be seen in other caregivers such as fathers or grandparents (Raj et al., 2015). I-InTERACT treatment increased the frequency of positive parental statements and praise compared to the IRC group (Antonini et al., 2014). This improvement was also present in a subset of children that who sustained abusive head trauma (Mast et al., 2014). The number of sessions completed by families positively correlated with the frequency of positive parenting skills (Antonini et al., 2014). Other significant differences were evident upon sub-analyses of parental income. Parental distress was significantly reduced in low-income, but not high income, families following the I-InTERACT program compared to pre-intervention (Raj et al., 2015). Additionally, parental income predicted child's behaviour following the intervention in that children from low-income families had a significant reduction in behavioural problems, which was not apparent in children from high-income families (Antonini et al., 2014). The authors performed a follow-up RCT on the I-InTERACT program, comparing it to an express model and a regular care group (Raj et al., 2018). The authors did not find any significant between-group differences from the regular program, the express model, and regular care on measures of caregiver depression, distress stress, and self-efficacy (Raj et al., 2018).

Conclusions

There is level 1b evidence that an online problem-solving program with therapist assistance may not be superior to an internet resource comparison group at improving parent-teen communications and conflict post ABI.

There is level 1a evidence that an online problem-solving program with therapist assistance may be superior to an internet resource comparison group at improving compliant behaviour and self-management in children post TBI.

There is level 1a evidence that an online problem-solving program with therapist assistance may be superior to an internet resource comparison group at acutely improving anxiety, depression, and distress in the parents of children post ABI; however, only improvements in distress may be present at 18 months.

There is level 1a evidence that lower socioeconomic status is associated with greater reductions in distress and depressive symptoms following counsellor-assisted online therapy when compared to higher socioeconomic status in parents of children post ABI.

There is level 2 evidence that online problem solving with audio support may not be superior to the same program without audio support with regards to improving adolescent behavioural issues and depression in children post TBI.

There is level 1b evidence that an online parenting skills workshops (I-InTERACT) may improve positive parental involvement with their child, when compared with an internet resource group, in children post TBI.

There is level 1b evidence that an online parenting skills program (I-InTERACT) may not be superior to an internet resource comparison group at improving caregiver stress, distress, depression, and self-efficacy in individuals caring for children post TBI.

There is level 4 evidence that an app-based coaching intervention may increase confidence and participation frequency in pediatric TBI and brain tumor individuals.

Online parenting skills workshops may be superior to internet resources in acutely reducing caregiver stress, depression, or self-efficacy. However, such workshops are likely not effective at improving parent-child communication post ABI.

An online problem-solving program with therapist assistance may be superior to an internet resource comparison group at improving compliant behaviour and self-management in children post TBI.

Web-based teen problem solving intervention programs are effective in reducing parental depression, anxiety, and distress compared to an internet resource comparison group, especially in families with lower socioeconomic status.

Family-based interventions benefit children, adolescents, and their families following brain injury.

An app-based coaching intervention may be effective in raising confidence and participation in activities following a pediatric TBI or brain tumor.

14.4.1.5 Alternative Family-Supported Interventions

A few non-web-based interventions have been evaluated for families of children that have sustained an ABI. Contrary to web-based programs, face to face interventions can provide social support for parents through the rehabilitation process (Brown & Whittingham, 2015). However, similarly to web-based interventions the main focus of therapy continues to be on family dynamics and improving long term outcomes in families with a child that has sustained an ABI.

Table 14.13 Alternative Family-Supported Interventions for the Treatment of Behavioural Disorders Post Pediatric ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Brown et al. (2015) Australia RCT PEDro=5 N=59	**Population:** ABI: TBI=34, Tumor=10, Encephalitis=9, Cardiovascular Accident=4, Hypoxia=2; *Acceptance and Commitment Therapy + Stepping Stones Triple P (ACT+SSTP, n=30)*: Mean Age=7.1yr; Gender: Male=17, Female=13; Mean Time Post Injury=3.1 yr. *Care As Usual (CAU, n=29):* Mean Age=6.9yr; Gender: Male=18, Female-11; Mean Time Post Injury=3.6yr. **Intervention:** Families were randomized to either the ACT+SSTP workshop or to CAU. SSTP involves 6 group sessions to educate on skills and 3 individual sessions to assist in refining learned skills. ACT aspect involves 2 sessions aimed to improve experiential avoidance and psychological flexibility. The interventions were both provided for 10wk lasting approximately 16hr in total. Assessments were conducted at baseline, post-intervention and 6mo follow-up. **Outcome Measure:** Parenting Tasks Checklist (PTC), Depression Anxiety and Stress Scale (DASS), Parenting Problem Checklist (PPC), McMaster Family Assessment Device (FAD), Relationship Quality Index (RQI), Acceptance and Action for ABI Questionnaire (AAABIQ).	1. Parents in the ACT+SSTP group demonstrated an increase in confidence in managing challenging behaviours on PTC ($p<0.001$), and a decrease in number of inter-parental disagreements on PPC ($p=0.021$) from baseline to post-intervention. The CAU group had no significant change on either ($p=0.340$ and $p=0.714$, respectively). 2. Family functioning on FAD and psychological flexibility on AAABIQ significantly improved for the ACT+SSTP group from baseline to post-intervention ($p<0.001$ for both), whereas the CAU group demonstrated no change ($p=0.440$ for both). 3. No significant differences between groups for parental distress or relationship satisfaction according to the DASS and RQI respectively were found.
Brown et al. (2014) Australia RCT PEDro=5 N=59	**Population:** ABI: TBI=34, Tumor=10, Encephalitis=9, Cardiovascular Accident=4, Hypoxia=2; *Acceptance and Commitment Therapy + Stepping Stones Triple P (ACT+SSTP, n=30)*: Mean Age=7.1 yr; Gender: Male=17, Female=13; Mean Time Post Injury=3.1 yr. *Care As Usual (CAU, n=29):* Mean Age=6.9 yr; Gender: Male=18, Female-11; Mean Time Post Injury=3.6 yr. **Intervention:** Families were randomized to either the ACT+SSTP workshop or to CAU. SSTP involves 6	1. The ACT+SSTP group demonstrated significant decreases in over-reactivity ($p=0.001$) and laxness ($p<0.001$) on the PS while the CAU group showed no change. 2. There was a large, significant decrease in problem behaviours amongst children in the ACT+SSP group from pre- to post-intervention ($p<0.001$) but no such change was reported in the CAU group. However, improvements for children in the ACT+SSP

Author Year Country Study Design Sample Size	Methods	Outcomes
	group sessions to educate on skills and 3 individual sessions to assist in refining learned skills. ACT aspect involves 2 sessions aimed to improve experiential avoidance and psychological flexibility. The interventions were both provided for 10wk and lasted approximately 16hr in total. Assessments were conducted at baseline, post-intervention and 6mo follow-up. **Outcome Measure:** The Parenting Scale (PS), Eyberg Child Behavior Inventory (ECBI), Strengths and Difficulties Questionnaire (SDQ).	group returned to baseline levels at follow-up. 3. There were significantly fewer ACT+SSTP participants in the clinical range on ECBI-Intensity (p=0.030), SDQ-Emotional (p=0.030), SDQ-Laxness (p=0.027) and SDQ-Over-reactivity (p=0.002) than CAU participants at follow-up.
Wade et al. (2006b) USA RCT PEDro=5 N_I=37, N_F=32	**Population:** TBI: *Family Problem-Solving Group (FPS, n=16)*: Mean Age=10.9yr; Gender: Male=10, Female=6; Mean Time Post Injury=8.7mo; Mean Lowest GCS=10.8. *Control Group (n=16)*: Mean Age=10.7yr; Gender: Male=11, Female=5; Mean Time Post Injury=8.8 mo; Mean Lowest GCS=11.1. **Intervention:** Patients were randomly assigned to receive either the FPS intervention or standard care. Those in the FPS group were provided with face-to-face problem-solving skills training with 7 biweekly sessions followed by an additional 4 individualized sessions to address unresolved stressors over a 6 mo period. Each session consisted of a didactic portion (30-40min) and a problem-solving portion (45-60min). The control group received standard medical care for TBI. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** Child Behavior Checklist (CBCL), Brief Symptom Inventory-Global Severity Index (BSI-GSI), Conflict Behavior Questionnaire (CBQ), satisfaction survey.	1. The FPS group demonstrated significantly greater reductions on the CBCL Internalizing, Anxious/Depressed, and Withdrawn subscales compared to the control group from baseline to post-treatment (all p<0.050). 2. No significant differences were found between the FPS group and the control group on the BSI-GSI or CBQ from baseline to post-treatment. 3. Patients and parents in the FPS group reported high levels of satisfaction with ratings of 9/10 and 8.8/10 respectively at post-treatment. 4. According to the satisfaction survey, more than 90% of parents in the FPS group reported that they now knew strategies for improving their child's attention and had developed a plan for handling future behavioural problems.
Braga et al. (2005) Brazil RCT PEDro=5 N_I=87, N_F=72	**Population:** TBI: *Indirect Family Support Group (IFS, n=38)*: Mean Age=8.1yr; Gender: Male=10, Female=6; Mean Time Post Injury=1.3yr; Mean GCS=6.7. *Direct Clinician Delivered Group (DCD, n=34)*: Mean Age=8.1yr; Gender: Male=19, Female=15; Mean Time Post Injury=1.1yr; Mean GCS=7.5. **Intervention:** Patients were randomly assigned to either the IFS or DCD group. The IFS group received an integrated support and intervention program consisting of simple home activities and visits from two case managers to educate and support the patient and their family. Patients in the DCD received conventional rehabilitation from health professionals for 2 hr/day, 5 day/wk. Both interventions were provided for 12 mo. Assessments were conducted at baseline, every 3 mo (IFS only), and post-treatment. **Outcome Measure:** SARAH Motor Functional Scale (SARAH), Wechsler Intelligence Scale for Children	1. The IFS group revealed significantly higher IQ on WISC-III (p=0.050) and motor development and functional independence on SARAH scores (p=0.0180) compared to the DCD group post-treatment. 2. Higher injury severity (based on GCS) was positively correlated with motor/functional improvements on SARAH classification (p=0.000), but not with IQ scores on WISC-III (p=0.757). 3. Parents of patients in the IFS group consistently learned the procedures and activities of the intervention over the course of the 12 mo study with no drop in performance despite the treatment changing as the patient demonstrated progress (p=0.999).

Author Year Country Study Design Sample Size	Methods	Outcomes
	Third Edition (WISC-III), number of activities performed by parents.	
Hickey et al. (2018a) Australia PCT N=47	**Population:** *Family Forward (FF) Group (N=25):* Mean Age of child=10.1yr (5.2); Gender: Male=56%, Female=44%; Mean time post injury=Acute; GCS=N/A. *Usual Care (UC) Group (N=22)*: Mean Age of child=8.5yr (5.6); Gender: Male=59.1%, Female=40.9%; Mean time post injury=Acute; GCS=N/A. **Intervention:** Families of children with ABI participated in either a UC or family forward (FF) social work program. Sessions for both occurred twice a week. The FF intervention consisted of a more tailored approach of monitoring the family for post-trauma symptoms in addition to regular social work. Measures taken at baseline, inpatient discharge, and at a 6-week follow-up. **Outcomes:** Impact of Events scale – revised (IES-R), parent experience of child illness (PECI), Brief Illness perception questionnaire (Brief IPQ).	1. No significant group differences were found at any time points on the outcome measures (p>0.05).
Hickey et al. (2018b) Australia PCT N=47	**Population:** *Family Forward (FF) Group (N=25):* Mean Age of child=10.1yr (5.2); Gender: Male=56%, Female=44%; Mean time post injury=Acute; GCS=N/A. *Usual Care (UC) Group (N=22)*: Mean Age of child=8.5yr (5.6); Gender: Male=59.1%, Female=40.9%; Mean time post injury=Acute; GCS=N/A. **Intervention:** Families of children with ABI participated in either a UC or family forward (FF) social work program. The cohorts were recruited sequentially from the inpatient ABI unit and sessions for both occurred twice a week. The FF intervention consisted of a more tailored approach of monitoring the family for post-trauma symptoms in addition to regular social work. Measures taken at baseline, inpatient discharge, and at a 6-week follow-up. **Outcomes:** Family Assessment Device-General Functioning (FAD-GF), Family Management Measure (FAMM), Psychosocial assessment tool (PAT2.0), Social work activity form (SWAF),	1. No significant difference between groups at any time point on the FAD-GF (p>0.05) 2. The condition management ability subscale of the FAMM was found to be significantly different between groups at 6-weeks post-discharge (p=0.029) showing higher scores in the FF group. No other subscales of the FAMM showed between-groups significance (p>0.05). 3. There were no significant between-group differences found on the PAT2.0 at any time points (p>0.05). 4. The three subscales of the SWAF (supportive counselling, family resources, and medical care issues) showed a significant between-groups difference at inpatient discharge (p<0.05) showing higher scores in the FF group.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

The Stepping Stone Triple P and Acceptance and Commitment Therapy (ACT+SST) combined programs aim to improve family outcomes and communication within families with a child who suffered an ABI (Karver et al., 2014; Narad et al., 2015). Behavioural problems were reduced in children who underwent the intervention, however, they were not maintained by the 6 month follow-up (Karver et al., 2014). Both cumulative and delayed deficits are possible following a brain injury, which may lead to long term clinical

deterioration post ABI. Thus, the authors hypothesize these children may have experienced such a phenomenon and perhaps maintaining interventions for longer time periods may be more beneficial (the presented study treatment lasted 10 weeks) (Karver et al., 2014). In terms of parental outcomes, confidence, disagreements between couples, and psychological distress were significantly improved following the ACT + SSTP intervention (Narad et al., 2015). Such improvements were not found in the usual care control group, therefore results cannot be attributed to spontaneous recovery (Narad et al., 2015). No significant changes were found for parental relationship satisfaction or depression as both control and intervention groups had improved post-treatment (Narad et al., 2015).

A family problem solving therapy that was delivered face to face was compared to usual care to determine its effects on behavioural problems and parental outcomes following a pediatric ABI (Wade et al., 2006b). Children within one-year post-injury improved in behavioural outcomes following the family problem solving intervention when compared to children in the usual care group. Particularly, improvements were reported for internalizing and withdrawal behaviours, as well as depression and anxiety. However, parental distress did improve following therapy, which is contrary to other studies (Wade et al., 2006b). Rather than changes in parental distress influencing the child's behaviour changes, the authors hypothesized that parental practices (which were reported in the satisfaction survey, such as better understanding of and relationship with their child) contributed to the magnitude of changes reported (Wade et al., 2006b).

Family rehabilitation consisting of home based activities improved both cognitive and physical abilities for children following a TBI, compared to standard clinician based therapy (Braga et al., 2005). Specifically, IQ, motor development, and functional independence were improved in children receiving the family rehabilitation. Parents were able to be effectively trained to deliver the intervention and this result was unrelated to parental education status. Therefore, children in the chronic phase of recovery (mean time post injury 1 year) can benefit from family driven rehabilitation at home that may be easily accepted and learned across families (Braga et al., 2005).

A study examining a dedicated 'family forward' social work program compared against a usual care population of children with TBI (Hickey et al., 2018b) looked specifically at the parents/caregivers experience (Hickey et al., 2018b). The authors first recruited for their usual care group, then recruited for the family forward program. This program involved family sessions each week that encouraged expression of grief responses to the child's injury and a counselling process. The usual care intervention consisted of a typical social work program (Hickey et al., 2018a). The study authors found both groups saw reductions in trauma and grief responses but were not significantly different from one another (Hickey et al., 2018a). In a separate paper, on the family forward program the authors found a significant difference between groups on supportive counselling, family resources, and medical care issue, with the family forward group showing higher scores at inpatient discharge. (Hickey et al., 2018b). At 6-weeks post discharge, the authors found that the family forward group scored higher on management of the TBI condition (Hickey et al., 2018b). The authors found no differences between groups on general family functioning and psychosocial measures (Hickey et al., 2018b).

Conclusions

There is level 2 evidence that the Stepping Stone Triple P program combined with Acceptance and Commitment Therapy may be superior to usual care at improving behavioural problems up to 6 months in children post ABI.

There is level 2 evidence that the Stepping Stone Triple P program combined with Acceptance and Commitment Therapy may improve parental distress, confidence, psychological flexibility, and conflict, but not depression, when compared to usual care in children post ABI.

There is level 2 evidence that face to face family problem solving therapy may be superior to usual care in terms of reducing internalizing problems (depression and anxiety) in children post TBI, but not parental distress or relationship satisfaction.

There is level 2 evidence that family-based therapy may be superior to standard clinician-directed care for improving intelligence, motor development, and functional independence in children post TBI.

There is level 4 evidence that a family focused inpatient social work program for parents/caregivers after their child's TBI may not significantly decrease feelings of trauma or grief any more than a usual care intervention.

There is level 4 evidence that a family focused inpatient social work program for parents/caregivers after their child's TBI may increase parent/caregiver confidence in managing the condition and feelings of more supportive counselling, increased family resources, and awareness of medical issues than a usual care intervention.

"Stepping Stone Triple P with Acceptance and Commitment Therapy" may improve parental outcomes and short-term behavioural problems in children post ABI.

Face to face family problem solving therapy may improve internalizing behavioural problems in children post TBI, however, it may not impact parental distress or relationship satisfaction.

Family based rehabilitation might be superior to clinician-directed care to improve cognitive and physical outcomes in children following a TBI.

A family focused inpatient social work program may be just as effective as a usual care intervention in reducing feelings of trauma and grief in parents/caregivers of children post-TBI. However, parents/caregivers undergoing an inpatient social work program may report increased confidence in managing pediatric TBI and feelings of more supportive counselling, increased family resources, and awareness of medical issues than a usual care intervention.

14.4.1.6 Community-Based Interventions

Rehabilitation efforts provided in the community are often proposed as an attractive and cost-effective alternative to residential or hospital-based rehabilitation programs. Following hospital discharge, the school setting can only provide so much re-integrative rehabilitation due to the restricted and planned environment at school. Participation in community based programming reflects real world skill development, such as interactions with others, and can foster more transferable and appropriate interactions for children post-ABI (Agnihotri et al., 2010).

Table 14.14 Community-Based Interventions for the Treatment of Behavioural Disorders Post Pediatric ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Carney et al. (2016) USA/Argentina RCT PEDro=8 N=308	**Population:** TBI; *Intervention (n=150):* Age Range=<18yr; Gender: Male=86, Female=64; Severity: Mild=65, Moderate=28, Severe=57. *Control (n=158):* Age Range=<18yr; Gender: Male=102, Female=56; Severity: Mild=72, Moderate=27, Severe=59. **Intervention:** Patients randomly assigned to the intervention group were provided with standard care in addition to a community resource coordinator who was in contact with the family 1 day/wk. The control group received standard care only. The intervention was provided for 6 mo. Assessments were conducted at baseline, 3mo and 6 mo. **Outcome Measure:** Family Impact Module of the Pediatric Quality of Life Inventory (Peds-QL), Pediatric Overall Performance Category (POPC), Pediatric Cerebral Performance Category (PCPC).	1. There were no significant differences between the two groups on the Peds-QL "Quality of Life" or "Cognition" subscales (p=0.342 and p=0.612 respectively) at 6 mo. 2. There were no significant differences between the two groups on the POPC (p=0.161) or the PCPC (p=0.454) at 6 mo. 3. A composite score made up of the Peds-QL Quality of Life and Cognition subscales, POPC and PCPC was significantly correlated with the Peds-QL Family Impact Module (p<0.0001). 4. There were no significant differences between the two groups on the composite score (p=0.2560) at 6 mo.
Emanuelson et al. (2003) Sweden/Finland Pre-Post N=10	**Population:** ABI: TBI=8, Tumor=1, Encephalitis=1; Mean Age=12.4yr; Time Post Injury=<6wk; Mean GCS=8.2. **Intervention:** Patients participated in a multidisciplinary community outreach intervention program consisting of one social worker, one physiotherapist, one occupational therapist, two neurologists, two neuropsychologists, and three special education teachers. Counselling was also provided by a special education teacher and/or a neuropsychologist. Assessments were conducted at 2 wk and 6 wk post-injury, and at 12 mo follow-up. **Outcome Measure:** Bruininks-Oseretsky Test of Motor Proficiency (BOTMP), Abilities Index (AI), Weschler Intelligence Scale for Children (WISC).	1. No significant improvements were reported on any of the WISC measures used from 6wk post injury to 12mo follow-up. 2. A significant improvement was found for BOTMP scores from 6 wk post injury to 12mo follow-up (p<0.050) with patients demonstrating greater motor functions. 3. Mild improvements were found on the AI for communication and behaviour but general health and extremity functioning declined slightly from 2 wk post injury to 12 mo follow-up. No significant improvements or decreases were found on any measures of the AI.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Two studies, one RCT and one pre-post, evaluated the effectiveness of community based therapy for children following an ABI. The RCT used an intervention group that received a Community Resource Coordinator (CRC) post-discharge to facilitate compliance with medications and attend follow-up visits (Carney et al., 2016). Children who were connected with this community resource coordinator did not improve on functional outcomes (PCPC, PCOC categories of the Peds-QL) compared to a usual care control group by 6 months post-injury. However, children with superior family functioning, as measured by scores on the family impact subscale of the pediatric quality of life, had better functional outcomes than those with lower family functioning (Carney et al., 2016). This relationship was correlative and future research is needed to determine causality.

A pre-post study examined the effectiveness of intervention by a multidisciplinary, community-based team on general areas of functioning early (<6 wk) after a child sustained an ABI (Emanuelson et al., 2003). Motor function and aspects of functional communication and behaviour, but not neuropsychological outcomes, significantly improved by the 12 month follow-up mark (Emanuelson et al., 2003). More research is required with this population, as community-based rehabilitation could provide a support network for children and their families dealing with the impact of brain injury.

Conclusions

There is level 1b evidence that the allocation of community resource coordinators to a family post discharge may not be superior to standard care at improving functional outcomes in children following a TBI.

There is level 4 evidence that a multidisciplinary outpatient program may improve functional communication and behaviour, but not neuropsychological outcomes, in children post ABI.

Use of community resource coordinators post discharge may not improve functional outcomes in children post TBI.

Multidisciplinary outpatient programs may improve functional outcomes for children following ABI.

14.4.1.7 Social Reintegration

Children with a physical disability or chronic condition may find it difficult to "fit in" with peers, as their care and needs are different than those of normally developing children of the same age. It has been suggested the children who have experienced head trauma may have even greater challenges, as they must often contend with dysfunctions of critical brain regions that enable normal social interaction (Lewis et al., 2000). Following a brain injury, the most detrimental long-lasting social consequences for children and adolescents are the loss of friends, the inability to participate in many social and leisure activities, and the absence of social support (Glang et al., 1997). Social networks are crucial to the psychological wellbeing of students, as those with social support are less likely to experience difficulties relating to depression, anxiety or other affective disorders. Returning to school can be a daunting prospect for a young student who has just recovered from TBI. Hawley (2012) reported that levels of self-esteem in children with a TBI at school were significantly lower than in controls and significantly lower than population based norms. Lower self-esteem in children with TBIs was also significantly associated with anxiety and depression.

A literature review by Mealings et al. (2012) on school re-entry revealed that students with a TBI found special accommodation/consideration, individual assistance, effective planning and a transition program as the most helpful methods of reintegrating back into school. Conversely, lack of understanding and awareness of TBI, and not receiving help that had been planned were regarded as the most detrimental issues. While these methods suit an educational setting, there may be different requirements in social environments.

Table 14.15 Social Building Interventions for the Treatment of Behavioural Disorders Post Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Glang et al. (2018) USA RCT PEDro=6 N=100	**Population:** *STEP Group (N=59):* Age range=6 to 21yr; Gender: Male=67.8%, Female=32.2%; Mean time post injury=N/A; GCS=mild=2, mod=30, severe=27. *Usual Care (N=41)*: Age Range=6 to 21yr; Gender: Male=75.6%, Female=24.4%; Mean time post injury=N/A; GCS=mild=1, mod=19, severe=21. **Intervention:** Families of children with TBI were randomly assigned to usual care or STEP (School Transition and Re-entry Programme) program. This program was implemented to facilitate a link from the hospital to the school for young patients with TBI returning requiring special education and behavioural adjustment. Measure taken at baseline and at 1 year later of being in either group. **Outcomes:** Achenbach child behavior checklist (CBCL); behavior rating inventory of executive function (BRIEF); Child and adolescent scale of participation (CASP); child and adolescent scales of environment (CASE).	1. There were no significant differences between groups on any measures (p>0.05).
Wade et al. (2015a) USA RCT PEDro=6 N=132	**Population:** TBI; *CAPS Group (n=65):* Mean Age=14.7yr; Gender: Male=44, Female=21; Severity: Moderate=40, Severe=25; Mean Time Post-Injury=3.7 mo. *IRC Group (n=67):* Mean Age=15.0yr; Gender: Male=43, Female=24; Severity: Moderate=41, Severe=26; Mean Time Post-Injury=3.5 mo. **Intervention:** Participants were randomly assigned to one of two groups; the Counsellor Assisted Problem-Solving (CAPS) group where participants received visits and eventually video-conferences with a therapist, and completed problem-solving skills training, or the Internet Resource Comparison (IRC) group where participants were given online access to resources and websites only. The interventions were provided for 6 mo. Assessments were completed at baseline, post-treatment, 12 mo and 18 mo follow-up. **Outcome Measure:** Child and Adolescent Functional Assessment Scale (CAFAS).	1. A significant Group x Visit interaction was observed for CAFAS Total score (p<0.010). Post hoc analyses revealed lower CAFAS scores (representing an improvement) at the final visit for the CAPS group compared to the IRC group. However, the groups did not differ at any other time. 2. A significant Group x Visit interaction was observed for CAFAS Community score (p=0.030). Post hoc analyses revealed the CAPS group was rated as having significantly better functioning in the community than the IRC group at 18 mo follow-up (p=0.040). 3. Total number of CAPS sessions completed was significantly correlated with CAFAS total score, indicating that families with more problems completed more sessions (p=0.040). 4. Premorbid history of learning, attention or behavior problems was significantly associated with poorer scores on the CAFAS Total (p=0.020), School (p=0.030), Community (p=0.030) and Behavior Toward Others (p=0.010) subscales.
Glang et al. (1997) USA Case Study N=3	**Population:** TBI; Mean Age=12.7yr; Gender: Male=3, Female=0; Mean Time Post Injury=5yr. **Intervention:** Patients participated in the Building Friendships process; a school-based, educator-mediated intervention designed to help patients expand their social networks. The patients, their family, existing friends, and school staff were consulted to identify a list of goals and implemented strategies to assist the patient in achieving these goals and prevent isolation. Assessments were	1. A significant intervention effect was reported with patients engaging in an average of 9.9 weekly social contacts compared to 2.1 at baseline (p<0.010). 2. Average parent ratings of satisfaction with the patients' level of social inclusion increased consistently from baseline to 12-18 wk assessment. 3. Patients' ratings of satisfaction also dropped between the 5-11 wk and 12-18 wk time-points.

	completed at baseline, 5-11wk and 12-18wk during the intervention. **Outcome Measure:** Number of Social Contacts Per Week, Parent and Facilitator Ratings of Social Inclusion and Satisfaction.	4. Follow-up investigation indicated that the increase in social contacts of the patients did not last beyond the remainder of the school year.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Glang and colleagues (2018) examined a hospital to school transition program for children with TBI that require special education or behavioural adjustments. This STEP program was designed to promote advocacy for TBI individuals and increase identification of a need for special education services (Glang et al., 2018). The authors did not find any significant difference between the STEP program participants and the usual care group on any of their measures, specifically the child behaviour checklist (CBCL) (Glang et al., 2018).

Wade et al. (2015b) utilized an online family program for problem solving therapy to elicit long-term improvements for adolescents an average of 3 months post-TBI. Adolescents in the intervention group improved in their everyday and community function at 12 months, but not in their home function, compared to a control group (Wade et al., 2015b). Such improvements were not apparent until 12 months and were not seen at the 18 moth follow up. The authors suggest that changes in problem solving and executive function resulting from the intervention may take time to translate to improvements in everyday functioning (Wade et al., 2015b). Improvements in school/work and community functioning were significant and are important for re-integration for a child post-discharge (Wade et al., 2015b).

Glang et al. (1997) investigated the results of a program designed to increase social networks for three children post TBI. The model appeared beneficial as social contacts increased after the intervention, however, no lasting changes in social functioning were reported. The ability to participate in social networking during childhood and adolescence is an important issue and should be investigated further. Indeed, social skills may be an important area for future focus given that social problems may be among the most significant and long-lasting sequelae of brain injury in children (Glang et al., 1997).

Conclusions

There is level 1b evidence that family based online problem-solving programs, when compared to an internet resource comparison group, may improve functioning in school and the community, but not at home, at 12 months in adolescents post TBI.

There is level 4 evidence that interventions directed at strengthening the social interactions of children with brain injury may be temporarily beneficial.

There is level 2 evidence that a dedicated transitional hospital to school program does not demonstrate any increased benefits than a usual care group for children post TBI.

Online family problem solving interventions likely improve everyday functioning, specifically in the school and community domains, but not at home, in adolescents who have sustained a TBI.

Interventions directed at improving social interactions might be beneficial in children post TBI.

A dedicated hospital to school transition program may not provide any more benefit than increasing special education and behavioural service access (usual care) in children post TBI.

14.4.1.8 Pharmacological Interventions

Pharmacological interventions are often used to treat aggressive or agitated behaviour post TBI in children and adults (Suskauer & Trovato, 2013). To date, no medication has proven to be effective in modifying outcomes in children with brain injury. However, investigators have studied the role of the psychostimulant methylphenidate and other dopamine enhancing medications, such as amantadine, for their effect on aggression and agitation post ABI.

As mentioned earlier in 'Promoting Emergence from the Unconscious State', amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist. Currently, it is used for the treatment of neurological diseases such as Parkinson's disease, neuroleptic side-effects (dystonia, akinthesia) and neuroleptic malignant syndrome (Schneider et al., 1999). It is also thought to work pre- and post-synaptically to increase the amount of dopamine available in the synaptic cleft (Napolitano et al., 2005). The methodologial details and results from two studies investigating the use of amantadine for the treatment of behavioural disorders post pediatric TBI are listed in Table 14.16.

Table 14.16 Amantadine for the Treatment of Behavioural Disorders Post Pediatric TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Beers et al. (2005) USA RCT PEDro=5 N_I=37, N_F=27	**Population:** TBI; Age Range=6-16yr; Gender: Male=24, Female=13; Mean Time Post Injury=0.9yr; Severity: Mild=11, Moderate=10, Severe=16. **Intervention:** Patients were randomized to receive amantadine or to a usual care control group. Amantadine was administered 2x/d for 12 wk. Dosages were determined by age and weight with those aged 6-9yr and weighing less than 40 kg receiving a maximum of 150 mg/d and those aged 10-16yr and more than 40 kg receiving a maximum of 200 mg/d. Patients were contacted daily for the first week then 1 day/wk for the remaining 11 wk. **Outcome Measure:** Behavior Rating Inventory of Executive Function - Global Executive Composite (BRIEF-GEC), BRIEF -Behavioral Regulation Index (BRIEF-BRI), BRIEF - Metacognition Index (BRIEF-MI), Tower of London Test (ToL), Wisconsin Card Sorting Test (WCST), Number of Side Effects.	1. BRIEF-BRI, BRIEF-GEC and BRIEF-MI scores for patients treated with amantadine all significantly improved from baseline to post-treatment compared to the control group (p=0.007, p<0.000, p<0.000 respectively). 2. No significant differences between groups on the ToL and WCST (both p>0.050). 3. Six patients experienced side effects including nausea, constipation and vomiting for <2 d. One patient experienced daily side effects for 1 wk and withdrew. No side effects were reported at 6-12 wk in the remaining participants.
Green et al. (2004) USA Case Control N=118	**Population:** TBI; *Amantadine Group (n=54):* Mean Age=11.8yr; Gender: Male=33, Female=21; Mean GCS=5.6. *Control Group (n=64)*: Mean Age=10.3yr, Gender: Male=47, Female=17; Mean GCS=7.4. **Intervention**: Participants that were admitted to the hospital for longer than 48 hr and administered amantadine were retrospectively analyzed. Patients who received amantadine were compared to a	1. Significant difference between groups for initial GCS and admission RLA scores (p<0.010). 2. Side effects from amantadine but not controls included: aggression, nausea/vomiting, hallucinations, and delusions. 3. Amantadine group had significantly greater increase in RLA during admission than controls

	control group which did not receive a neurostimulant. **Outcome Measure**: Glasgow Coma Scale (GCS), Length of Stay (LOS), Post-traumatic Amnesia (PTA) duration, Ranchos Los Amigos (RLA), Complications.	(p<0.010), but not LOS or PTA duration (p>0.050). 4. A subjective review of available charts (n=29) reveal improvement in alertness, initiation, verbalizations, and agitation.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Amantadine was determined 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 reduced the frequency of negative behaviours associated with frontal lobe injuries after 12 weeks of treatment (Beers et al., 2005). Subjective review of charts from observed behaviours in children (alertness, verbalizations, agitation) also improved, however, there were no comparator questions to help determine if such improvements were due to natural recovery or amantadine itself (Green et al., 2004). Although behaviours improved following amantadine treatment, cognitive function, post-traumatic amnesia, and hospital LOS did not (Beers et al., 2005). As such, the results must be interpreted with caution, due to lack of blinding between conditions and lack of comparators. Future placebo-controlled trials are warranted to determine the efficacy of amantadine to reduce negative behaviours in children following a TBI (Beers et al., 2005).

Conclusions

There is level 2 evidence that the use of amantadine can decrease the amount of aberrant behaviours, but may not improve cognitive functioning and problem solving, compared to usual care among children with a TBI.

There is level 3 evidence that amantadine is safe to administer in children following a TBI and facilitates rate of recovery, but not post-traumatic amnesia or hospital length of stay, post pediatric TBI.

Amantadine appears to be safe and efficacious in decreasing undesirable behaviours and improving the rate of recovery in children post TBI

14.4.2 Cognitive Therapies

In addition to behavioural problems, childhood ABI is associated with significant cognitive sequelae (Taylor et al., 2002; Yeates et al., 2002). Common cognitive consequences of childhood ABI include deficits in attention, memory, problem-solving, communication, decreased speed of information processing, and academic difficulties (Sohlberg, 2001).

Generally, communication skills in children with moderate to severe TBIs are more affected than those with a mild TBI (Rivara et al., 2011). For example, Rivara et al. (2011) found that children with mild cognitive impairments faired better when communication scores were measured at 3 and 9 months post

injury (Rivara et al., 2011). In terms of remediating communication skills, younger children benefit more from behaviour-based approaches whereas older adolescents benefit from reasoning strategies (Shaw, 2016). Compensatory assistance in an academic setting can reduce the cognitive demands of reading and writing. Examples of compensatory assistance tools include audiobooks, text-to-speech and speech-to-text software, educational assistants, and proof-reading programs. Interdisciplinary support such as ophthalmology, audiology, sleep management and pain management services can help to address cognitive-communicative disorders (Krause et al., 2015).

Cognitive therapies encompass a variety of interventions designed to help individuals with brain injury improve upon or compensate for cognitive deficits. There is a substantial body of research investigating the effectiveness of different rehabilitation techniques for remediating or compensating for cognitive deficits following brain injury in adults. However, research on the effectiveness of cognitive rehabilitation for the paediatric population is lacking.

14.4.2.1 Rehabilitation of Attentional Deficits

Following a brain injury, children often experience attentional deficits that require rehabilitation, however, determining the efficacy of rehabilitation is complicated by a number of factors. Firstly, there is no consensus regarding the definition of attention. In some cases, it is defined as a general construct, whereas in others it is defined as more specific sub-components of functioning (e.g. sustained, divided, focused or selective attention and, vigilance, or speed of information processing, etc). Secondly, interventions targeting attentional deficits have applied testing inconsistently, whereby the same tests are used to measure different aspects of attention. In addition, the same outcome measures are often used repeatedly, in turn confounding practice and treatment effects (e.g. if individuals are repeatedly exposed to PASAT performance testing, their scores improve significantly, biasing the results). Lastly, it appears as though many studies do not account for the rate of spontaneous recovery following brain injury, whereby the recovery of function occurs naturally in the absence of treatment (Welch-West et al., 2013).

14.4.2.1.1 Non-Pharmacological Interventions

Currently, there is a paucity of rehabilitation interventions targeting attentional deficits in children that have sustained an ABI. As previously discussed, attention is difficult to assess and is a multifaceted construct. However, attentional deficits in children have many negative implications and may lead to deficits in academic, social, and psychological function (Park et al., 2009). Therefore, it is imperative to determine effective interventions, which target attentional deficits.

14.4.2.1.1.1 Amsterdam Memory and Attention Training for Children

Despite the scarcity of interventions targeting the improvement of attention in children post ABI, one intervention has been established as a popular and reliable tool for improving attentional and memory deficits. The Amsterdam Memory and Attention Training for Children (AMAT-c), originally developed for the treatment of attention deficits in children after cancer treatment, is used for the rehabilitation of cognitive impairments in children post ABI (Catroppa et al., 2015; Dvorak & van Heugten, 2018; van't Hooft et al., 2003). 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) . After initial successes were reported in children post ABI, the AMAT-c gained

traction as one of the few interventions available that could improve cognitive outcomes in this vulnerable population. Studies evaluating the efficacy of AMAT-c on cognitive outcomes in a pediatric population post ABI are reviewed below.

Table 14.17 Amsterdam Memory and Attention Training for the Rehabilitation of Attention Deficits in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
van't Hooft et al. (2005) Sweden RCT PEDro=6 $N_{Initial}$=40, N_{Final}=38	**Population:** ABI: TBI=21, Brain Malignancies=14, Encephalitis=2, Anoxia=1; *Amsterdam Memory and Attention Training for Children Group (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. *Control Group (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 30 min, 6 day/wk over 17 wk using the AMAT-c program or to an interactive program chosen by the patient, teacher and parents. The AMAT-c was completed in three 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.	1. 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 post-treatment compared to baseline 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=0.020), and BCT number of correct answers (p=0.002) but not BCT reaction time (p=0.530). 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=0.390) but delayed recall on the test was significantly greater in the experimental group (p=0.020).
van't Hooft et al. (2007) **A follow-up to van't Hooft et al. (2005)*	**Population:** ABI: TBI=21, Brain Malignancies=14, Encephalitis=2, Anoxia=1; *Amsterdam Memory and Attention Training for Children Group (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. *Control Group (n=20)*: Mean Age=12.6yr; Gender: Male=10, Female=10; Mean Time Post Injury=2.6yr; Severity: Mild/Moderate=6, Severe=3. **Intervention:** A follow-up at 6 mo of children randomized to receive AMAT-c or an interactive program as described above. Outcome measures at 6 mo were compared to baseline and post-treatment. **Outcome Measure:** Wechsler Intelligence Scales for Children (WISC-III) Coding and Digit Span tests, Visual Reaction Time (VRT), Auditory Reaction Time (ART), Vigilance Test of the Gordon Diagnostic System (VGDS), Stroop Tests, Trail Making Tests A and B (TMT A and B), Rivermead Behavioural	1. At 6 mo follow-up, the AMAT-c group demonstrated significant attentional gains compared to the controls in VGDS correct answers (p<0.0003), VGDS commission errors (p<0.040); BCT correct answers (p<0.002) and TMT B (p=0.030) but not TMT A (p>0.050). 2. The AMAT-c group also showed significant memory improvements on the RBMT and ROCF (all p<0.0002), 15 Word Test immediate and delayed recall (p<0.005 and p=0.012 respectively) at follow-up. 3. No significant difference was found between groups in VRT, ART, and both WISC-III Coding and Digit Span tests. Importantly, two WISC-III factors, freedom of distractibility and verbal comprehension, were significantly greater in the AMAT-c group (p<0.050 and p<0.003 respectively) at 6 mo follow-up.

Author Year Country Study Design Sample Size	Methods	Outcome
	Memory Test (RBMT), Rey-Osterrieth Complex Figure (ROCF), Binary Choice Test (BCT), 15 Word Test.	
van't Hooft et al. (2003) Sweden Pre-Post N=3	**Population:** ABI: TBI=2, Intracerebral Bleeding=1; Mean Age=9.1yr; Gender: Male=2, Female=1; Mean Time Post Injury=3.5yr; Mean GCS=7. **Intervention:** Patients participated in the Amsterdam memory and attention training for children (AMAT-c) programme with exercises lasting 30 min/d for 20 wk. The AMAT-c was completed in three phases; sustained attention, selective attention, and mental tracking. Assessments were completed at baseline and within 2 wk of treatment completion. **Outcome Measure:** Deasey-Spinetta Behaviour rating scales (DSB), Trail Making Tests A and B (TMT A and B), Wechsler Intelligence Scales for Children (WISC-III) Digit Span test.	1. According to the neuropsychological test battery, all three patients demonstrated improvements in sustained and selective attention post-treatment. Memory improved slightly in all three patients. 2. The neuropsychological test battery revealed TMT A and B remained stable in two patients and improved one; an improvement in daily memory in all three patients; and WISC-III Digit Span improving in two patients but remaining stable in one. 3. Parents and teachers' DSB ratings revealed improvements on two of the patients with one patient demonstrating either no or minor improvement across the three scales (learning ability, social behaviour, emotional behaviour).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Four studies evaluated the effectiveness of the Amsterdam Memory and Training for children (AMAT-c) intervention in children post ABI (Catroppa et al., 2015); (van't Hooft et al., 2003); (Hooft et al., 2005). Three important aspects of cognitive function were evaluated in all four studies: sustained attention, selective attention, and memory. Several studies found no improvement in sustained attention among those children in the AMAT-c group when compared to baseline or to an interactive control group (Hooft et al., 2005; van 't Hooft et al., 2007). However, in a study with three participants, van't Hooft et al. (2003) reported that sustained attention improved in all participants following AMAT-c. The results of the intervention on patient's selective attention was conflicting. Three studies (2 RCTs and a case series) reported that selective attention improved in the AMAT-c intervention (Hooft et al., 2005; van't Hooft et al., 2003) and that this improvement was maintained at 6 month follow-up (van 't Hooft et al., 2007). While one pre-post study reported that selective attention did not improve following treatment (Catroppa et al., 2015). The third outcome measured by the AMAT-c, memory, was improved in all studies, with certain specific aspects of memory improving more than others.

Conclusions

There is level 1b evidence that the Amsterdam Memory and Training for children program may not improve sustained attention in pediatric patients post ABI compared an interactive program.

There is level 1b evidence that the Amsterdam Memory and Training for children may improve selective attention compared to an interactive program in pediatric patients post ABI.

The Amsterdam Memory and Training program may improve selective, but not sustained attention in pediatric patients post ABI.

14.4.2.1.1.2 Other Attention-Focused Interventions

While the AMAT-c program is the most commonly used intervention for improving cognitive deficiencies in children post ABI, other programs and interventions exist. The following studies analyzed the efficacy of non AMAT-c interventions on improving attention in children post ABI.

Table 14.18 Other Attention-Focused Interventions for the Rehabilitation of Attention Deficits in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Treble-Barna et al. (2016) USA PCT N=24	**Population:** TBI=13, Healthy Controls=11; *TBI Group*: Mean Age=13.11yr; Gender: Male=4, Female=9; Mean Time Post-Injury=5.2yr; Severity: Mild=5, Moderate=2, Severe=6. *Healthy Controls*: Mean Age=13.47yr; Gender: Male=4, Female=7. **Intervention:** TBI participants underwent the Attention Improvement and Management program (AIM) combining metacognitive strategy training and attention tasks for approximately 18 wk. Outcomes were assessed at pre and post intervention. **Outcome Measure:** The Test of Everyday Attention for Children (TEA-Ch), Delis–Kaplan Executive Function System (D-KEFS), The Behavior Rating Inventory of Executive Function (BRIEF).	1. There were no significant differences between groups from pre to post for Sky Search score and walk/don't walk (all p>0.050) of TEA-Ch; however, the TBI group improved significantly compared to the healthy controls on the TEA-Ch code transmission (p=0.014) from pre to post treatment. 2. There was no significant difference between groups from pre to post in all components of the D-KEFS (all p≥0.157) and child reported BRIEF (all p≥0.095). 3. All components of the parent reported BRIEF of the TBI group from pre to post improved significantly compared to healthy controls (all p≤0.001).
Galbiati et al. (2009) Italy PCT N=65	**Population:** TBI; *Experimental Group (n=40)*: Mean Age=13.9yr; Gender: Male=30, Female=10; Mean Time Post Injury=6.8mo; GCS Score=<8. *Controls (n=25)*: Mean Age=15.5yr; Gender: Male=16, Female=9; Mean Time Post Injury=9.7mo; GCS Score=<8. **Intervention:** Patients assigned to the experimental group received attention-specific neuropsychological training which included the use of picture and vignette interpretation, answering open and closed questions, providing suggestions for attention management and computer-based attention tasks. Controls did not receive any form of training. Each session lasted 45 min and took place 4/wk for 6 mo. Assessments were conducted at baseline, discharge, and 1 yr follow-up. **Outcome Measure:** Wechsler Intelligence Scale for Children-Revised (WISC–R), Wechsler Adult Intelligence Scale-Revised (WAIS–R), Continuous Performance Test II (CPT II), Vineland Adaptive Behavior Scales (VABS).	1. The experimental group demonstrated significantly greater improvements compared to controls on numerous CPT II scales including Omission, Standard Error, Risk-taking and on the Overall Index (all p<0.001), and Commission and Hit Reaction Time (both p<0.050). No differences were found on the Hit Block or Hit Reaction Time interstimulus intervals measure (p>0.050). 2. No significant differences were found between groups in Intelligence Quotient (IQ) (WISC-R & WAIS-R) from baseline to follow-up (p>0.050). 3. Parent reports in all three VABS domains (communication, daily living skills, social skills) improved significantly from baseline to follow-up compared to parents of control patients (all p<0.001). 4. Experimental group patients improved significantly in verbal IQ (VIQ) (p<0.001), performance IQ (PIQ) and full IQ (FIQ) at follow-up (both p<0.0001). Controls improved in FIQ

Author Year Country Study Design Sample Size	Methods	Outcome
		(p=0.005) and PIQ (p=0.002) but not in VIQ (p=0.068).

Discussion

Treble-Barna et al. (2016) used a computerized program to administer the Attention Improvement and Management (AIM) program in adolescents in the chronic phase of TBI recovery. Patients that received the intervention improved in sustained, but not selective attention compared to healthy controls. However, there was no follow-up to determine the long-term effects of such intervention on attention. Another intervention used attention and neurological training for adolescents an average of 7-9 months post-injury (Galbiati et al., 2009). Adolescents in the intervention significantly improved their cognitive performance, attention skills, and adaptive behavioural skills compared to patients in the control group. The authors concluded that improvements in attention positively influenced everyday adaptive behaviours (Galbiati et al., 2009). In a feasibility study of a computerized cognitive training (CCT) program (Lumosity™) the authors used a stepped wedge randomized design to administer 8 weeks of the CCT (Corti et al., 2018). The CCT program did not only focus on attention, but had tasks pertaining to memory and executive functioning as well (Corti et al., 2018). The authors had nearly full completion (31 out of 32 participants) of required training programs as well as completion of 8 other feasibility criteria, and found that their Lumosity Performance Index (LPI) increased significantly from baseline to post-therapy. The LPI should be taken with caution, as it is a non-standardized measure of cognitive performance being directly related to the CCT program and was found to have a minimally significant correlation to full scale IQ (Corti et al., 2018).

Conclusions

There is level 2 evidence that the Attention Improvement and Management (AIM) program may improve sustained, but not selective, attention compared to healthy controls in children post TBI.

There is level 2 evidence that attention-specific neuropsychological training may improve attention compared to no training in pediatric patients post TBI.

There is level 2 evidence that a cognitive computerized training (CCT) program is feasible for use within a pediatric TBI population.

The Attention Improvement and Management (AIM) program may improve sustained, but not selective, attention skills in pediatric patients with TBI compared to healthy controls.

Attention-specific neuropsychological training improves cognition, attention and behavioral skills in pediatric patients post TBI.

A cognitive computerized training (CCT) program may be feasible for pediatric patients post TBI.

14.4.2.1.2 Pharmacological Interventions

Methylphenidate

Pharmacotherapy is a viable treatment option for children with attention deficits post-ABI. Methylphenidate (Ritalin) is a psychomotor stimulant, often used in the treatment of attention deficit/hyperactivity disorder (ADHD) in children, however, it can also be used to improve attention in children who have sustained a brain injury. It is believed that children with ADHD share some similar characteristics to children with ABI including: attention deficits, hyperactivity and impulsivity (Leonard et al., 2004). Specifically, methylphenidate has been shown to improve memory and attention in those with ADHD (Kempton et al., 1999). As such, methylphenidate has been implicated for use in the treatment of attention deficit disorders as a result of ABI.

Table 14.19 Methylphenidate for the Rehabilitation of Attention Deficits in Children Post TBI

Author Year Country Study Design Sample Size	Methods	Outcome
Mahalick et al. (1998) USA RCT PEDro=8 N=14	**Population:** TBI; Mean Age=10.7yr; Gender: Male=11, Female=3; Mean Time Post Injury=14.1mo; Mean GCS=6.9. **Intervention:** Patients were randomly assigned to receive either methylphenidate or placebo (lactose) for 2 wk before crossing over conditions. Methylphenidate was administered in a dose of 0.3 mg/kg 2x/d at 8 am and 12 pm, for 14 d. Assessments were conducted 1wk into each phase. **Outcome Measure:** Gordon Diagnostic System (GDS), Woodcock-Johnson Psychoeducational Test Battery-Revised (WJPTB-R), Ruff 2 and 7 Cancellation Test (7 CT).	1. Patients significantly improved on GDS measures of delayed efficiency (impulsivity), vigilance and distractibility ($p<0.005$, $p<0.020$ and $p<0.020$ respectively) during the methylphenidate phase compared to the placebo phase. 2. Attentional processing performance on the WJPTB-R was also significantly improved during the methylphenidate phase ($p<0.040$) compared to the placebo phase. 3. Selective and sustained attention also significantly improved on both Ruff 2 and 7 CT subscales of letter and number processing during the methylphenidate phase compared to the placebo phase ($p<0.010$, $p<0.001$ respectively).
Williams et al. (1998) USA RCT PEDro=8 N=10	**Population:** TBI; Mean Age=10.4yr; Gender: Male=9, Female=1; Mean Time Post Injury=2.8 yr. **Intervention:** Patients were randomly assigned to receive either methylphenidate or placebo for 2wk before crossing over. Methylphenidate was administered 2x/d for 4 d, followed by a 3 d washout period. Dosage depended on patient weight with patients <20 kg receiving 5 mg, 21-29 kg receiving 7.5 mg and patients >30 kg receiving 10mg. Assessments were conducted at the start and end of each week. **Outcome Measure:** Conners Rrating Scale, Symbol Digit Modalities Test, Continuous Performance Test, Sternberg Memory and Reaction Time Task, Sentence Repetition Task, Rapid Automatized Naming Test, Developmental Test of Visual-Motor Integration, Finger Tapping Test, Purdue Pegboard.	1. No significant differences were found on any of the measures between groups ($p>0.050$).

Ekinci et al. (2017) Turkey Pre-Post Test N=40	**Population:** TBI=20, 1º ADHD=20; Mean Age=12.7yr; Gender: Male=27, Female=13. **Intervention:** Patients received immediate-release methylphenidate (IR-MPH). Dosage started at 5 mg 2x/d and was increased to 10 mg 2 x/day and 3 x/day at the first and second week, respectively. Measurements were taken at baseline and after 8 wk. **Outcome Measure:** Turgay DMS- IV Disruptive Behavior Disorders Rating Scale parent and teacher forms (T-DSM-IV-S), Conners' Parent Rating Scale (CPRS), Conners' Teacher Rating Scale-Revised (CTRS-R), The Clinical Global Impression-Severity and Improvement Scales (CGI-S), Adverse Effect Scale.	1. In children with TBI, most scores on T-DSM-IV-S, CPRS CGI-S, and CTRS-R improved significantly after IR-MPH treatment ($p<0.050$). 2. Ninety-five percent of patients reported no adverse effects, or mild adverse effects.
Nikles et al. (2014) Australia Pre-Post N=10	**Population:** TBI; Mean Age=12.9yr; Gender: Male=6, Female=4; Mean Time Post Injury=6.1yr; Mean GCS=8.3. **Intervention:** Patients were randomized to receive either a stimulant (methylphenidate or dexamphetamine) or a placebo for three cycles of 1wk each. The intervention was provided for 6wk in total. Assessments were conducted weekly after each 1wk trial. **Outcome Measure:** Conners' 3 Parent Rating Scales (C3PR), Conners' 3 Teacher Rating Scales (C3TR), Behaviour Rating Inventory of Executive Function (BRIEF), Eyberg Child Behaviour Inventory (ECBI).	1. A trend towards improved ADHD behaviour was noted on the C3TR in favour of the stimulant group, however this was not statistically significant. 2. A less pronounced difference was noted on the C3PR in favour of stimulants compared to placebo, however this was not statistically significant. 3. Teacher-reported intensity and parent-reported frequency of problem behaviours on the ECBI during stimulant cycles were reduced compared to placebo cycles, however this was not statistically significant. 4. Teacher-reported and parent-reported BRIEF scores revealed a mean score difference of 20.7 and 10.8 respectively in favour of the stimulant cycles but this did not reach statistical significance.
Hornyak et al. (1997) USA Case Series N=10	**Population:** TBI; Mean Age=10.11yr; Gender: Male=7, Female=3; Mean Time Post Injury=10mo; Mean GCS=6.2. **Intervention:** A retrospective review was conducted on medical records for patients who had been treated with methylphenidate. Qualitative assessments of behaviour pre- and post-treatment from parents, teachers, physicians and neuropsychologists were analyzed. **Outcome Measure:** Qualitative Observations of Behaviours, Ranchos Los Amigos (RLAS) scale.	1. Six patients at RLAS Level VII and one patient at RLAS Level IV demonstrated an improvement in attention. 2. Two patients at RLAS Level VII and one patient at RLAS Level IV demonstrated a decrease in impulsivity. 3. Two patients at RLAS Level III were found to demonstrate a slight increase in arousability and responsiveness. 4. No neuropsychometric changes in response to methylphenidate were reported in one patient (RLAS Level VII) but was noted to be more attentive and calmer in class.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

The literature regarding the effect of methylphenidate on the cognition of children post-TBI is conflicting. One RCT found improvement in all measures of cognition and attention (Mahalick et al., 1998), whereas another RCT found no improvements in behaviour, memory, speed of processing, or attention following methylphenidate treatment (Williams et al., 1998). Both RCTs utilized a placebo comparison group with a cross-over design, however, other methodological differences may have contributed to the conflicting

findings. Mahalick et al. (1998) administered methylphenidate for all children at a set dosage of 0.3mg/kg, whereas Williams et al. (1998) administered a standard dose based on body weight category (i.e., <20kg, 21-29kg, >30kg). Furthermore, Mahalick et al. (1998) administered methylphenidate for 2 weeks, whereas Williams et al. (1998) treated for only 4 days, with a 3 day washout period between weeks. Further, Williams et al. (1998) included children who varied greatly in time post injury. Six subjects were within the first two years post injury when rapid changes in cognition are more likely and four were more than two years post injury. Given the difficulties in determining the extent of injury (mild versus severe), the differences in the length of time since injury, and the small sample size, the results of this study should be interpreted with caution (Williams et al., 1998).

The findings of Hornyak et al., (1997), suggest that the introduction of methylphenidate (unreported dosing) resulted in improved cognitive and behavioural function in children post TBI. These improvements were associated with increased participation in therapy at school and improvements in behaviours at home (Hornyak et al., 1997). Further corroborating those findings, a recent 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 TBI and ADHD patients (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). Additionally, only children with ADHD-like behaviours were analyzed, which is a small subset of the overall TBI population, limiting generalizability. Future RCTs are needed to determine the effectiveness of methylphenidate on attention for pediatric TBI.

Conclusions

There is conflicting (level 1b) evidence regarding whether or not methylphenidate improves cognitive behavioural function compared to placebo in children following a TBI.

Evidence regarding the efficacy of methylphenidate in improving cognitive and behavioural function following pediatric TBI is conflicting.

14.4.2.2 Rehabilitation of Learning and Memory

Memory impairment is one of the most debilitating symptoms following brain injury. Additionally, it is estimated that the 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).

When evaluating intervention strategies to improve memory performance following brain injury, the literature indicates that there are two main approaches to rehabilitation (1) restoration/retraining of memory or (2) compensation. Compensation includes "*training strategies or techniques that aim to circumvent any difficulty that arises as a result of the memory impairment*." (McLean et al., 1991). Compensatory techniques include internal aids, for example "*mnemonic strategies that restructure information that is to be learned*" (McLean et al., 1991). Individuals with lower working memory capacity post-TBI are at a greater risk of encountering academic difficulties (Krause et al., 2015). Various interventions are designed to address this concern and support the literacy skills of adolescents with a

TBI. Reading interventions, such as flashcards and repeated oral readings, can improve word recognition in these patients. In addition, metacognitive strategies such as note-taking, focusing attention on new information, building referential relationships across texts, and ensuring that performance and goal attainment are monitored may also be associated with improvements in academic ability (Krause et al., 2015).

Table 14.20 Interventions for the Rehabilitation of Learning and Memory Impairment Post Pediatric ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Wilson et al. (2009) United Kingdom RCT PEDro=5 N=12	**Population:** ABI: TBI=6, Developmental Deficits=5, Anoxia=1; Mean Age=13.58yr; Gender: Male=10, Female=2. **Intervention:** Patients were randomised into two groups: One group received a pager (n=4), and the other was put on a waiting list (n=8). Patients with the pager received messages containing memory and planning cues for 7wk with self-report diaries completed for the last 2wk of the intervention. Cues included necessary items for school, homework reminders, hygiene, and medication. Waiting list patients completed diaries at the same time as the pager group. Groups crossed over at the end of the first phase. Assessments were completed at baseline, post-treatment, and post-treatment after crossover. **Outcome Measure:** Number of Target Behaviours Accomplished.	1. The pager group achieved 92% of their target behaviours at post-treatment indicating a significant gain from baseline ($p<0.001$). 2. After crossover, those in the pager group were still able to meet 81% of their target behaviours. Although this represented a significant decrease from during the intervention ($p<0.001$), this was still a significant improvement from baseline ($p=0.003$). 3. The waiting list group did not demonstrate any improvements from baseline to intervention ($p=0.260$) but after crossover, the waiting list group achieved 80% of their target behaviours with the pagers ($p<0.001$). 4. All participants demonstrated significant improvements in target behaviours completed over the entirety of the study ($p<0.050$).
Melchers et al. (1999) Germany RCT PEDro=2 N=45	**Population:** TBI; *Experimental Group (n=21)*: Median Age=11.5yr; Gender: Male=11, Female=10; GCS Score=<8. *Controls (n=19)*: Median Age=11yr; Gender: Male=14, Female=5; GCS Score=<8. *Escape (n=5)*: Median Age=13yr; Gender: Male=3, Female=2; GCS Score=<8. **Intervention:** Patients were randomized to receive stimulation during coma and neuropsychological rehabilitation upon awakening, or routine treatment. Stimulation included visual (coloured lights and objects), tactile (soft touches and massage), auditory, olfactoric (food and drink) and gustatory (salty, sour, sweet water) if not being ventilated. Stimulation was performed for 45 min, 2x/d during coma followed by neuropsychological rehabilitation for 9 wk. Follow-ups were conducted at 6 mo, 12 mo and 24 mo. **Outcome Measure:** Kaufman-Assessment Battery for Children (K-ABC), Intelligenz Struktur Test (IST-70), Enzephalopathie-Fragebogen (E-F).	1. After K-ABC and IST-70 scores were combined, preliminary results at 6mo follow-up revealed that the experimental group had regained average intellectual abilities while the control group were still at the same low level. 2. At 12 mo follow-up, K-ABC + IST-70 combined intelligence scores in the experimental group had returned to age-average levels but the controls demonstrated further decline. 3. Non-verbal learning scores improved in both groups at 6 mo follow-up, more so for controls. At 12 mo follow-up, the experimental group continued to improve but the controls declined slightly from their 6 mo scores. 4. Psychopathological changes according to the E-F were stable for the experimental group but were worse for the controls at 6mo and 12 mo follow-ups.
Ho et al. (2011) Australia Pre-Post	**Population:** ABI=12, Stroke=3; Mean Age=13.43 yr; Gender: Male=7, Female=8; Mean Time Post-Injury=5.79 yr; Mean GCS=9.33.	1. Significant increase in perceived memory (PMQ/CMQ) from pre to post-treatment ($p<.050$) but not at follow-up.

Author Year Country Study Design Sample Size	Methods	Outcome
N=15	**Intervention:** All participants underwent a memory rehabilitation program consisting of 6 1.5 hr sessions involving self-instruction and diary entry training. Outcome measures were completed at baseline, post-treatment, and 2 wk follow-up. **Outcome Measure:** Parent Memory Questionnaire (PMQ), Child Memory Questionnaire (CMQ), weekly diary entries, Creature Counting, Sky Search Divided Task, Sky Search, Child Behaviour Checklist (CBCL), Youth Self Report (YSR), Rey Auditory Verbal Learning Test (RAVLT).	2. Increased number of diary entries correlated with improved perceived memory (CMQ; p<.050). 3. PMQ significantly correlated with the number of correct answers on the Creature Counting (p<0.010) and the Sky Search Divided Task (p<0.050). 4. CMQ significantly correlated with time and attention on the Sky Search (all p<0.010) as well as the internalising problems on the CBCL and YSR (all p<0.050). 5. Weekly number of diary entries significantly correlated with the time portion of the Sky Search and Creature Counting (all p<0.050) as well as with the externalising problems of the YSR (p<0.050). 6. PMQ, CMQ and weekly diary entries did not correlate with RAVLT (p>0.050).
Brett & Laatsch (1998) USA Pre-Post N=10	**Population:** ABI: TBI=9, Viral Encephalopathy=1; Mean Age=16.2yr; Gender: Male=6, Female=4; Mean Time Post Injury=6.6 yr. **Intervention:** Patients received cognitive rehabilitation therapy biweekly with each session lasting approximately 40 min. The therapy focused on alertness, attention, concentration, perception, memory skills, and problem solving. Assessments were completed at baseline and post-treatment. **Outcome Measure:** Wide Range Assessment of Memory and Learning (WRAML), Test of Nonverbal Intelligence-2 (TONI-2), Benton Visual Form Discrimination Test (BVFDT), Tower of London (ToL), Wisconsin Card Sorting Test (WCST), Stroop Test, Wechsler Intelligence Scale for Children-III-Freedom from Distractibility Scale (WISC-III FDS), WISC-III Picture Completion Subtest (WISC-III PCS).	1. Of all the mental functioning measures, only WRAML memory scores significantly improved post-treatment (p=0.025). 2. Patients were observed utilising verbal memory skills during post-treatment testing. 3. No significant improvements were found on any of the other measures including TONI-2 (p=0.200), BVFDT (p=0.075), ToL (p=0.077), WCST (p=0.906), Stroop Test (p=0.137), WISC-III FDS (p=0.114), and WISC-III PCS (p=0.115).

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Several different interventions to rehabilitate memory and learning post TBI have been evaluated. Memory aids are one intervention tool that may be used to compensate for memory deficits in children post TBI. 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. Conversely, Ho et al. (2011) report that memory impairments are associated with internalizing behaviours such as depression and anxiety.

Using a different approach, Melchers et al. (1999) used sensory stimulation while children were in a coma followed by cognitive neuropsychological rehabilitation upon awakening to remediate learning deficits post-TBI. Although only reporting preliminary results, the authors report that children had greater improvements in intellectual development, approaching age appropriate levels, one-year post-injury as compared to controls who further declined from pre-treatment levels. However, due to lack of equal distribution of injury severity between groups, the results may not be generalizable (Melchers et al., 1999).

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).

Conclusions

There is level 2 evidence that the use of a pager system may improve memory and planning activities compared to having no pager system in adolescents post TBI.

There is level 4 evidence that rehabilitation focused around diary entries and self-instructional training may temporarily improve memory deficits in children post TBI.

There is level 2 evidence that sensory stimulation paired with cognitive neuropsychological rehabilitation may improve intellectual development in children with severe TBI compared to controls.

There is level 4 evidence that biweekly sessions of cognitive rehabilitation may improve memory skills in pediatric patients post TBI.

Utilization of a pager in adolescents post TBI may help improve memory.

Utilization of a diary in combination with self-instructional training might temporarily improve memory in children post TBI.

Cognitive rehabilitation can improve intellectual function for children following brain injury.

14.4.2.3 Rehabilitation of Executive Functioning

Executive function refers to higher-level cognitive functions that are primarily mediated by the frontal lobe. 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. The frontal lobe is frequently and bilaterally involved in TBI, in contrast to typically unilateral lesions following vascular injury (Greenwald et al., 2003). Direct contusions to the frontal and temporal lobes and diffuse axonal injury sustained as a result of TBI 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. Importantly, age when injured and injury severity were significantly associated with poorer outcomes in

children with TBI (Keenan et al., 2018). Thus, ongoing clinical surveillance is important for children severely injured at a young age.

14.4.2.3.1 Counsellor Assisted Problem Solving Therapy

Problem-solving therapies have shown promise for rehabilitating deficits post TBI in both adult and pediatric populations (Krasny-Pacini et al., 2014; Kurowski et al., 2014; Wade et al., 2014b). 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., 2014b; Wade et al., 2015b).

Linden et al. (2016) conducted a meta-analysis that confirmed that the CAPS intervention was beneficial in remediating executive functioning, however, only a small to medium effect size was found. A clinically important effect on the patients was deemed to be unlikely.

Table 14.21 Counsellor-Assisted Problem Solving for the Rehabilitation of Executive Functioning in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Karver et al. (2014) USA RCT PEDro=8 N=132	**Population:** TBI; *Counsellor Assisted Problem-Solving Group (CAPS; n=65):* Mean Age=14.4yr; Gender: Male=44, Female=21; Mean Time Post-Injury=0.3yr; Severity: Severe=40, Mild-Moderate=25. *Internet Resource Comparison Group (IRC; n=67):* Mean Age=14.7yr; Gender: Male=42, Female=25; Mean Time Post-Injury=0.3yr; Severity: Severe=41, Mild-Moderate=26. **Intervention:** Patients were randomly assigned to one of two groups: 1) CAPS, where patients received video-conference with a therapist and complete problem-solving skills training, or 2) IRC, where patients were given online access to resources and websites only. Follow-up was completed at 6 mo. **Outcome Measure:** Behavior Rating Inventory of Executive Function (BRIEF), Child Adolescent Functional Assessment Scale (CAFAS), Child Behavior Checklist (CBCL).	1. Patients with lower vocabulary scores benefitted significantly more in the CAPS program, but not in the IRC program, according to BRIEF Metacognition Index (MI) scores at follow-up (p=0.003). 2. There were no significant differences between groups on the BRIEF-MI among patients with higher vocabulary scores. Within-group analyses for patients with higher vocabulary scores did not demonstrate significant changes from baseline to follow-up for either of the CAPS and IRC groups. 3. There were no significant interactions or effects between vocabulary or group type on CAFAS scores or CBCL's Internalising and Externalising subscales.
Kurowski et al. (2014) USA RCT PEDro=8 N=132	**Population:** TBI; *Counsellor Assisted Problem-Solving Group (CAPS; n=65):* Mean Age=14.4yr; Gender: Male=44, Female=21, Mean Time Post-Injury=0.3yr; Severity: Severe=40, Mild-Moderate=25. *Internet Resource Comparison Group (IRC; n=67):* Mean Age=14.7yr; Gender: Male=42, Female=25; Mean Time Post-Injury=0.3yr; Severity: Severe=41, Mild-Moderate=26. **Intervention:** Patients were randomly assigned to one of two groups; the CAPS group where patients video-conferenced with a therapist and completed problem-solving skills training on the CAPS website,	1. Older patients (14-17yr) in the CAPS group demonstrated significant improvement on the BRIEF Global Executive Composite (GEC) at 6mo (p=0.050), 12mo (p=0.030) and 18mo follow-up (p=0.020). 2. Only older patients in the CAPS group reported significantly greater improvement on the BRIEF Behavioural Regulation Index (BRI) at 18mo follow-up (p=0.040). 3. Older patients in the CAPS group continued with improvements on the BRIEF Metacognition

Author Year Country Study Design Sample Size	Methods	Outcome
	or the IRC group where patients were given online access to resources and websites only. Follow-up was completed at 1yr and at 18 mo. **Outcome Measure:** Behavior Rating Inventory of Executive Function (BRIEF).	Index (MI) at 12mo (p=0.030) and 18mo follow-up (p=0.030). 4. No differences were observed between the CAPS and IRC groups for adolescent patients (12-14 yr) on the BRIEF GEC, BRI and MI.
Kurowski et al. (2013) USA RCT PEDro=8 N=132	**Population:** TBI; *Counsellor Assisted Problem-Solving Group (CAPS; n=65):* Mean Age=14.4yr; Gender: Male=44, Female=21, Mean Time Post-Injury=0.3yr; Severity: Severe=40, Mild-Moderate=25. *Internet Resource Comparison Group (IRC; n=67):* Mean Age=14.7yr; Gender: Male=42, Female=25; Mean Time Post-Injury=0.3yr; Severity: Severe=41, Mild-Moderate=26. **Intervention:** Patients were randomly assigned to one of two groups; the CAPS group where patients video-conferenced with a therapist and completed problem-solving skills training on the CAPS website, or the IRC group where patients were given online access to resources and websites only. Assessments were conducted post-treatment. **Outcome Measure:** Behavior Rating Inventory of Executive Function (BRIEF).	1. The amount of improvement on the BRIEF Global Executive Composite (GEC), Behavioural Regulation Index (BRI) and Metacognition Index did not differ between the two groups post-treatment (p=0.680, p=0.480, p=0.870 respectively). 2. When groups were stratified based on age, older patients (14-17yr) in the CAPS group demonstrated significantly greater improvement on the BRIEF GEC at post-treatment than older patients in the IRC group (p=0.010) but younger patients (12-14yr) did not differ (p=0.270). 3. Older patients in CAPS demonstrated significantly greater improvements on the Working Memory and Monitoring components of the BRIEF MI compared to older patients in the IRC group post-treatment (p=0.002, p=0.010 respectively). No differences were observed between groups for younger patients. 4. Improvement on the BRIEF BRI was significantly greater for older patients in the CAPS group compared to the IRC group (p=0.010) but no difference was observed between groups for younger patients.
Wade et al. (2010) USA RCT PEDro=5 N=41	**Population:** TBI; *Teen Online Problem Solving Group (TOPS; n=20)*: Mean Age=14.0yr; Gender: Male=6, Female=14; Mean Time Post Injury=8.8mo; Mean GCS=9.5. *Internet Resource Comparison Group (IRC; n=21)*: Mean Age=14.5yr; Gender: Male=11, Female=10; Mean Time Post Injury=10.3mo; Mean GCS=10.5. **Intervention:** Patients were randomly assigned to either the TOPS or IRC group. The TOPS group received 10 internet sessions providing training in stress management, problem solving, planning, organization, communication and self-regulation, six supplemental sessions addressing the stressors and burden of individual families, and therapy via videoconferencing. The IRC group received access to online resources and were asked to spend at least 1 hr/wk accessing information. Assessments were conducted at baseline for both groups, at 7.83mo follow-up for the TOPS group and at 7.92mo follow-up for the IRC group. **Outcome Measure:** Behavioral Rating Inventory of Executive Function (BRIEF), BRIEF-Metacognition Index (BRIEF-MI), BRIEF-Global Executive Composite (BRIEF-GEC).	1. At follow-up, patients with severe TBI in the IRC reported significantly greater levels of executive dysfunction than patients with severe TBI in the TOPS group and patients with moderate TBI in the IRC group (both p<0.050) according to the BRIEF-MI subscale. 2. Patients with severe TBI in the TOPS group reported significantly greater improvements on the BRIEF-GEC compared to patients with severe TBI in the IRC group (p<0.050) at follow-up. 3. No significant differences were reported between the TOPS and IRC groups for patients with moderate TBI. 4. No significant differences were reported between groups on parent-reported BRIEF scores at follow-up.

Discussion

Adolescents who underwent a counsellor assisted problem solving program (CAPS) were compared to a control group who were given standard internet resources. Older adolescents (≥14 yr) in the treatment group showed significant improvements in executive function, specifically behavioural regulation and metacognition compared to controls (Kurowski et al., 2013). Adolescents in grade 9-12 improved the most in executive function after the intervention according to primary caregiver's rating at 12 months post-injury. Upon further analyses, Kurowski et al. (2014) found that older adolescents maintain their improvement in executive functioning up to 18 months post-intervention. Interestingly, younger adolescents did not significantly improve in caregivers' ratings of executive function relative to the controls, even as they aged over the 18 month follow-up. Older adolescents may be more capable of using the training program than younger teens and as such the age of the patient at the time of the intervention may be important (Kurowski et al., 2013). Two other moderating variables were reported. Adolescents who sustained a severe, but not moderate, TBI had greater improvements in executive functioning post-intervention than the control group and. Adolescents with poor vocabulary improved in metacognitive abilities when in the CAPS group compared to the control group (Karver et al., 2014).

Conclusions

There is level 1a evidence that online counsellor-assisted problem solving programs may be superior to internet resource groups at improving executive function in adolescents post TBI.

There is level 1a evidence that older adolescents (14-17 years) benefit from counsellor-assisted problem solving programs more than younger (12-14 yr) adolescents in terms of improvements in executive functioning post TBI.

There is level 1b evidence that adolescents with a severe TBI, or poor vocabulary, benefit more from a counsellor-assisted problem solving program than adolescents with a moderate TBI, or adequate vocabulary, in terms of improvements in executive functioning post TBI.

Counsellor assisted problem solving programs may be effective in improving executive function in adolescents post TBI; especially older adolescents (14-17 years), adolescents who suffered a severe TBI, and those with poor speech.

14.4.2.3.2 Metacognitive Therapy

The following section reviews studies which investigated the efficacy of metacognitive therapy programs for improving executive function in pediatric patients post ABI. Some of the interventions/programs employed include the Strategic Memory Advanced Reasoning Training (SMART) program, Metacognitive Dimension Program, Attention Improvement Management program, and a multi-component cognitive-behavioural treatment programme.

Table 14.22 Metacognitive Therapy for the Rehabilitation of Executive Functioning in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Cook et al. (2014) USA RCT PEDro=7 N=20	**Population:** TBI; *Strategic Memory Advanced Reasoning Training (SMART, n=10):* Mean Age=15.4yr; Gender: Male=6, Female=4; Mean Time Post-Injury=4.9yr; Severity: Mild=6, Moderate=1, Severe=3. *Memory Group (n=10):* Mean Age=15.2yr; Gender: Male=7, Female=3; Mean Time Post-Injury=3.2yr; Severity: Mild=4, Moderate=2, Severe=4. **Intervention:** Participants were randomly assigned to one of two interventions; the SMART group which focused on gist (top-down) reasoning training, or the Memory group which was based on bottom-up memory training. Both training groups had 8 sessions of 45 min over 1 mo. **Outcome Measure**: Test of Strategic Learning (TOSL), Wechsler Abbreviated Scales of Intelligence (WASI), Behavior Rating Inventory of Executive Function (BRIEF), Digit Span subtest, Letter-Number Sequencing subtest.	1. There were no significant gains or differences between groups in working memory. However, upon closer inspection, SMART participants outperformed the Memory group on the Letter-Number Sequencing test (p=0.005). 2. The Memory group was rated as making a significant improvement according to parents' rating on the BRIEF test (p=0.008). 3. The SMART group significantly outperformed the Memory group on abstract meaning (TOSL) (p=0.006). 4. Furthermore, the SMART group demonstrated significant improvements on TOSL in interpretative statements from baseline (p=0.042) whilst the Memory group did not, but no significant difference was observed between the two groups.
Braga et al. (2012) Brazil RCT PEDro=6 N=29	**Population:** ABI; *Metacognitive Dimension Program (MCD; N=14):* Mean Age=10.3yr; Gender: Male=9, Female=5; Mean Time Post-Injury=5.5yr; Mean GCS=9.4. *Controls (N=15):* Mean Age=10.5yr; Gender: Male=12, Female=3; Mean Time Post-Injury=5.1yr; Mean GCS=9.1. **Intervention:** Patients randomized to the MCD were paired with psychology students and worked in pairs or small groups to plan and execute art, physical activities, and games utilizing mediational strategies and cooperative learning. The control group continued to be treated according to family-based treatment guidelines. The MCD was provided 2 days/wk for a total of 26 sessions over 3 mo. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** Self-Concept Scale for Children (SCSC), Behavioral Rating Inventory of Executive Functions (BRIEF), Evaluation Scale of Elementary School Learning Strategies (ESESLS).	1. The MCD group scored significantly higher on the SCSC and on the ESESLS post-treatment compared to the control group (p=0.043 and 0.033, respectively). 2. The ESESLS Metacognitive and Absence of Dysfunctional Strategies subscales were both significantly greater for the MDC group (both p=0.003) but no difference was found between the MDC and control group for the Cognitive Strategies subscale (p=0.660). 3. The MCD group performed better on parents' BRIEF scores at baseline and post-treatment but there were no significant difference between groups (no p-values given).
Chan & Fong (2011) Hong Kong RCT PEDro=5 N=32	**Population:** ABI: TBI=21, Tumour=6, Arteriovenous Malformation=5; *Experimental Group (n=16)*: Mean Age=12.0yr; Gender: Male=11, Female=5; Mean Time Post Injury=3.3yr; Severity: Moderate-Severe=16. *Controls (n=16)*: Mean Age=12.8yr; Gender: Male=9, Female=7; Mean Time Post Injury=3.9yr; Severity: Moderate-Severe=16. **Intervention:** Patients participated in a modified problem-solving skills program for 2 days/wk over 7 wk with each session lasting 3 hr. The program consisted of problem-solving heuristics such as thinking aloud, mind-maps, categorization, visual imagery, creative thinking, comparison techniques, and self-evaluation. Assessments were completed	1. The experimental group demonstrated a significantly greater improvement in BRIEF and TONI-3 scores (both p<0.000), and on all INSI and COPM measures (all p<0.000) scores at the end of treatment compared to the controls. 2. Patients in the experimental group also improved to a significantly greater degree on all MI components (all p<0.008) at the end of treatment compared to controls except for the average level of prompting for the Planning component (p=0.390).

Author Year Country Study Design Sample Size	Methods	Outcome
	at baseline and at post-intervention. **Outcome Measure:** Behavior Rating Inventory of Executive Function (BRIEF), Canadian Occupational Performance Measure (COPM), Test of Nonverbal Intelligence-3 (TONI-3), Metacomponential Interview (MI), Interpersonal Negotiation Strategies Interview (INSI).	
Treble-Barna et al. (2016) USA PCT N=24	**Population:** TBI=13, Healthy Controls=11; *TBI Group*: Mean Age=13.11yr; Gender: Male=4, Female=9; Mean Time Post-Injury=5.2yr; Severity: Mild=5, Moderate=2, Severe=6. *Healthy Controls*: Mean Age=13.37yr; Gender: Male=4, Female=7. **Intervention:** TBI participants underwent the Attention Improvement and Management program (AIM) combining metacognitive strategy training and attention tasks for approximately 18 wk. Outcomes were assessed at pre and post intervention. **Outcome Measure:** The Test of Everyday Attention for Children (TEA-Ch), Delis–Kaplan Executive Function System (D-KEFS), and The Behavior Rating Inventory of Executive Function (BRIEF).	1. There was no significant difference between groups from pre to post for Sky Search score or walk/don't walk subscales (all p>0.050) of TEA-Ch; however, the TBI group improved significantly from pre to post treatment compared to the healthy controls on the TEA-Ch code transmission (p=0.014). 2. There was no significant difference between groups from pre to post in any components of the D-KEFS (all p≥0.157) or in child reported BRIEF (all p≥0.095). 3. All components of the parent reported BRIEF of the TBI group from pre to post improved significantly compared to healthy controls (all p≤0.001).
Krasny-Pacini et al. (2014) France Pre-Post N_I=5, N_F=4	**Population:** TBI; Gender: Male=3, Female=2; Mean Age=4.8yr; Mean Time Post-Injury=6.8yr; Mean GCS=5.2. **Intervention:** Patients participated in a novel goal-management training intervention with emphasis on the patient's social network to assist in 'coaching'. Assessments were completed before and after intervention. **Outcome Measure:** Children's Cooking Task (CCT), Behavior Rating Inventory of Executive Function (BRIEF), Dysexecutive Questionnaire for Children (DEX-C).	1. 3 of the 4 children made improvements on the CCT with the remaining 1 child making more errors. 2. DEX-C scores decreased for 3 out of the 4 children indicating a reduction in executive dysfunction with continual reductions up to 6mo follow-up for 2 children (large effect sizes of 2.33 and 1.33 for each). 3. Parental BRIEF scores indicated a reduction in executive dysfunction in 3 children. However, teacher BRIEF scores were stable for 2 children and unreliable for the other 2.
Missiuna et al. (2010) Canada Pre-Post N=6	**Population:** TBI; Mean Age at Injury=10.53yr; Gender: Male=5, Female=1; Time Since Injury=10.5mo; Severity: Moderate. **Intervention:** All participants received the CO-OP intervention consisting of 10 individualized 1 hr sessions provided 1 x/wk by an occupational therapist focusing on executive function. Outcomes were assessed at baseline, post intervention and 4mo follow-up. **Outcome Measure:** Canadian Occupational Performance Measure (COPM), Performance Quality Rating Scale (PQRS), and Vineland Adaptive Behavior Scales (VABS).	1. There was a significant improvement in parent report COPM scores in all categories (performance, satisfaction, PQRS) from baseline to post intervention and 4mo follow-up (all p<0.010). 2. There was a significant improvement in all VABS scores, Composite (p<0.010), Communication (p<0.010), Activities of Daily Living (p<0.010) and Social (p<0.050) from baseline to post intervention and 4mo follow-up.
Catroppa et al. (2009) Australia Pre-Post N=3	**Population:** TBI; Mean Age at Injury=10.39yr; Gender: Male=2, Female=1; Time Since Injury=8.64yr; Mean GCS=8.33. **Intervention:** All participants underwent six 1 hr sessions 1 x/wk with content consisting of cognitive behavioural and psycho-educational approaches to develop executive functioning skills.	Case #1 1. Participant made 60% errors on the party planning task pre-intervention which reduced to 38% post-intervention (p<0.050). 2. Participant increased ABAS score from 88 to 101 from pre to post intervention and SPRS score from 54 to 68 (all p<0.050).

Author Year Country Study Design Sample Size	Methods	Outcome
	Outcome Measure: Color-Word Trial 4 time Taken, Color Word Total errors, Trails number-letter time taken, Rey Copy–organization, Tower Test–total achievement, Party Planning Task % total errors, Behaviour Rating Inventory of Executive Function (BRIEF), Sydney Psychosocial Reintegration Scale (SPRS), Adaptive Behaviour Assessment System (ABAS).	3. There was a significant reduction in BRIEF-Behavioural Regulation Index ($p<0.050$). 4. All other outcome measures were not significant ($p>0.050$). Case #2 1. There was a significant difference in colour word total errors from pre to post intervention ($p<0.050$). 2. All components of the BRIEF were significantly reduced ($p<0.050$). 3. All other outcome measures were not significant ($p>0.050$). Case #3 1. There was a significant difference in colour word total errors from pre to post intervention ($p<0.05$). 2. All other outcome measures were not significant ($p>0.050$).
Suzman et al. (1997) USA Pre-Post N=5	**Population:** ABI: TBI=4, Arteriovenous Malformation=1; Mean Age=8.2yr; Gender: Male=3, Female=2; Time Post Injury=3-9mo; Mean GCS=7.7. **Intervention:** Patients participated in a multi-component cognitive-behavioural treatment programme that included self-instruction and self-regulation, metacognition training, attribution training and reinforcement through a token economy. Each session lasted 40 min and was provided 3 days/wk. Patients were assessed at baseline and at post-treatment. **Outcome Measure:** Performance on computerised problem-solving task, Rey-Osterreith Complex Figure (ROCF), Porteus Maze Test (PMT), Wisconsin Card Sorting Test (WCST), Word Fluency Test (WFT), Social Validity 10-point Scale Questionnaire.	1. All patients demonstrated a decrease in errors performed on the computerised problem-solving task. Errors ranged from 75-100% at baseline and decreased to 11-56% at post-treatment. 2. Significant improvement was revealed from baseline to post-treatment on the ROCF and the WFT (both $p<0.040$) but not on the PMT ($p=0.340$) and WCST ($p=0.060$). 3. The average ratings for perceived improvement, enjoyment, continued use of problem solving skills, and recommendation of the program were 8.4, 8.9, 7.6 and 9.3 out of 10 respectively among patients, teachers and parents on the social validity questionnaire.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

Other interventions have been developed to target the development of metacognitive strategies for children post-TBI. In one intervention, children were paired with psychology students and given the opportunity to use their metacognitive strategies and cooperative learning in daily activities and games (Braga et al., 2012). Post-treatment, children decreased the use of ineffective metacognitive behaviours and increased in beneficial ones such as planning, regulating, and monitoring behaviours (Braga et al., 2012). Treble-Barna et al. (2016) had similar goals, but used a computerized program to deliver metacognitive instruction and attention tasks. Parent ratings of executive functioning improved significantly, suggesting that children may improve in everyday executive functioning tasks, metacognitive skills, and regulation of behaviours after metacognitive training. Krasny-Pacini et al. (2014) used a goal management intervention with metacognitive strategies and coaching guides. By the end of the study, all children decreased in cognitive executive impairments for assigned tasks and parental ratings of executive function improved overall (Krasny-Pacini et al., 2014). However, when a new task was introduced 6

months post-intervention, the children fell back to pre-treatment levels of performance, suggesting a lack of generalizability.

Catroppa et al. (2009) developed a pilot intervention program with three participants, requiring children to attend instructional sessions on cognitive behavioural and psychosocial skill developments post TBI. Preliminary results indicate that cognitive inflexibility was significantly improved in 2 participants, however, all other measures were not significant or only one participant had a significant effect (Catroppa et al., 2009). Future studies with an increased sample size are needed before conclusions can be drawn. Furthermore, Cook et al. (2014) used a "SMART" program for adolescents post-TBI. The SMART program focused on top-down executive function training whereas the control memory group focused on bottom-up processing. The SMART program was more effective in remediating deficits of high order cognition when compared to the memory group. Specifically, adolescents in their chronic phase of recovery were able to extract meaning from complex information. This improvement in top-down processing may in turn influence bottom-up processing, such as recall ability (Cook et al., 2014).

A few studies have targeted problem solving in order to improve executive functioning in children post-ABI. Chan and Fong (2011) examined a problem solving intervention that emphasized metacognition to improve executive function compared to usual care. Children with an ABI in the chronic recovery phase performed better in regards to abstract reasoning, metacognition function, and perceived themselves as having better performance in everyday tasks. Importantly, the problem solving intervention was targeted to relate to everyday skills and situations, thereby increasing generalizability and potential usefulness of the increased behaviours (Chan & Fong, 2011). In another case series 5 children, all under the age of 12, participated in a computer based training program to decrease undesirable behaviours, and improve positive cognitive behavioural outcomes. Results indicated that participants improved in their overall ability to problem solve (Suzman et al., 1997). Similarly, Missuina et al. (2012) used an individualized treatment program (CO-OP) to teach children cognitive strategies and problem solving skills that are necessary for successful occupational performance. Children overall improved in functional performance, with increased ability to perform their own identified goals. This improvement was maintained at the 4 month follow-up. Authors suggest that perhaps adaptation to the CO-OP program may be necessary to further enhance effects.

Conclusions

There is level 1b evidence that the Strategic Memory Advanced Reasoning Training (SMART) program may improve higher-order cognitive deficits compared to bottom-up processing training in children post TBI.

There is level 1b evidence that metacognitive therapy may improve learning strategies and executive function compared to usual care in children and adolescents with an ABI.

There is level 4 evidence that the use of goal management therapy may improve parental ratings of executive function in young children who have sustained a TBI.

There is level 2 evidence that metacognitive problem-solving skills training may improve executive function and metacognitive abilities compared to no intervention in children post ABI.

The Strategic Memory Advanced Reasoning Training (SMART) intervention may improve high-order cognitive functioning in adolescents post ABI.

Goal management therapy may reduce parental ratings of their child's executive dysfunction.

Therapist-assisted metacognitive treatment programs for pre-adolescents likely improve executive function and increase the use of metacognitive learning strategies post ABI.

Interventions that target problem solving may be effective at improving executive function and metacognitive abilities post ABI.

14.4.2.4 Rehabilitation of Communication Deficits

Communication has been described as the "*heart of learning, living adequately in society and developing one's unique personality*" (DePompei & Hotz, 2001). An ABI often results in several long-term consequences, potentially including an inability to communicate adequately (Savage et al., 2005). 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). For example, pragmatic language skills undergo development until at least the age of 12 years. When these skills are impaired and proper development does not occur, the child's ability to effectively interact with peers is affected, in turn impacting 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, while, '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 and 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, however, other therapies include targeting remediation and metacognitive strategies (Turkstra et al., 2015). The methodological details and results from two studies investigating these interventions for the rehabilitation of communication deficits in children post ABI are listed in Table 14.23.

Table 14.23 Interventions for the Rehabilitation of Communication Deficits in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Morgan et al. (2007) United Kingdom Pre-Post N=3	**Population:** TBI; Mean Age=15.0yr; Gender: Male=2, Female=1; Mean Time Post Injury=3.3yr; Mean GCS=4. **Intervention:** Patients received Electropalatography (EPG), a technique that requires the patient to wear a mould of the upper	1. Consonant imprecision was reduced from mild-moderate to mild, moderate to mild and marked to moderate across the three patients.

Author Year Country Study Design Sample Size	Methods	Outcome
	palate containing sensors that provide feedback to clinicians regarding tongue movement and the duration of phoneme production. Patients were treated 1/wk for 10 wk with each session lasting 45 min. Assessments were conducted at baseline and at post-treatment. **Outcome Measure:** Consonant imprecision, prolonged phoneme length, Children's Speech Intelligibility Measure (CSIM), Assessment of Intelligibility of Dysarthric Speech (ASSIDS).	2. Prolonged phoneme length was reduced from moderate to mild in two patients, and marked to moderate in one patient. 3. Single-word intelligibility, measured by the CSIM, was found to have improved in one patient from baseline to follow-up (76% to 92%), minor improvement in one patient (82% to 94%) and no improvement in the remaining patient (96% and 96%). 4. Sentence-level intelligibility, measured by the ASSIDS, improved by 10% in two patients (74% to 84%, and 80% to 90%) and by 8% in one patient (94% to 92%).
Wiseman-Hakes et al. (1998) Canada Case Series N=6	**Population:** ABI: TBI=5, Unspecified ABI=1; Mean Age=14.8yr; Gender: Male=3, Female=3; Mean Time Post Injury=3.1yr; Mean GCS=3.7. **Intervention:** Patients participated in a group program that taught patients how to give feedback and rate each other's communication abilities, how to cue each other to assist with self-monitoring, and practice conversations. Program sessions were conducted for 1 hr/day 4 days/wk with the program lasting for 6 wk. Assessments were performed at baseline, post-treatment and at 6 mo follow-up. **Outcome Measure:** Rehabilitation Institute of Chicago Rating Scale of Pragmatic Communication Skills (RICE-RSPCS), Communication Performance Scale (CPS), Vineland Adaptive Behaviour Scales-Socialization Domain (VABS-S).	1. The mean scores for the RICE-RSPCS increased by 44% with the Nonverbal Communication (p=0.010), Use of Linguistic Context (p=0.005), Organization of a Narrative (p=0.006) (all p=0.002) and Conversation Skills (p=0.001) from baseline to post-treatment. 2. Significant improvement was also reported on the RICE-RSPCS Nonverbal Communication, Use of Linguistic Context, Organization of a Narrative,(all p=0.002) and Conversation Skills (p=0.001) subscales when comparing scores at baseline to follow-up. 3. Patients significantly improved in CPS scores from baseline to post-treatment (p=0.001) and at baseline to follow-up (p=0.002). 4. Scores on the VABS-S did not reveal any significant changes at any time during the study. 5. No significant differences were reported from post-treatment to 6mo follow-up on any measures.

Discussion

Two different interventions examined the effects of speech and/or language therapy for children following an ABI. The first intervention evaluated the effectiveness of treating three teenagers with electropalatography (Morgan et al., 2007). Electropalatography "*is an instrumental treatment technique allowing visual feedback of tongue to palate movement during real time articulation".* All participants had improvement in the perceptual measure for articulation and speech intelligibility. Electropalatography treatment may be an effective rehabilitative tool to improve speech post TBI (in particular, phenome, word or sentence art) (Morgan et al., 2007). The second intervention examined the effectiveness of a peer-group training program aimed at improving pragmatic skills in adolescents with a brain injury (Wiseman-Hakes et al., 1998). Following the intervention, adolescents improved both in pragmatic language behaviours (i.e., intelligibility of speech, syntax, topic, etc.) and in a range of pragmatic communication abilities (i.e., conversational skills, emphasis of meaning, use of context to convey message, etc.).

Conclusions

There is level 4 evidence that electropalatography treatment may be effective at improving the articulatory component of dysarthria post TBI in children.

There is level 4 evidence that peer-group training of pragmatic language skills can improve pragmatic language behaviours and range of pragmatic communication abilities in children post ABI.

Speech therapy using electropalatography might improve articulation in children post TBI.

Peer-group training of pragmatic language skills might improve communication in children post ABI.

14.4.2.5 Rehabilitation of Self-Awareness

Children may have difficulties in understanding the extent of their brain injury (Krasny-Pacini et al., 2014; Wolfe et al., 2015). This can lead to a lack of awareness of any injury-related deficits, ultimately resulting in increased anxiety or poor self-esteem. Not only that, but lack of self-awareness regarding post ABI deficits may limit the ability of children to alter or compensate for inappropriate behaviour in social situations. Support for this theory has been garnered from studies that found imprecise self-ratings of skill are associated with lower social and academic proficiency (Gresham et al., 2000; Wolfe et al., 2015). Since parents are the major source of information for children, a child's understanding of his or her injuries likely depends upon his or her parents' level of understanding and knowledge about ABI. Thus, providing injury-related information to pediatric brain injury patients and their families should improve their awareness of injury-related deficits, which could indirectly improve cognitive processes and their social interactions.

Table 14.24 Injury-Related Information Interventions for the Rehabilitation of Self-Awareness in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
Beardmore et al. (1999) Australia RCT PEDro=6 N=21	**Population:** TBI; *Injury Group (n=11)*: Mean Age=13.3yr; Gender: Male=8, Female=3; Mean Time Post Injury=3.6 yr. *Study Group (n=10)*: Mean Age=13.3yr; Gender: Male=7, Female=3; Mean Time Post Injury=3.2 yr. **Intervention:** Patients were randomly assigned to either the Injury Group, where patients were received an injury-related information session, or the Study Group who received an attention-placebo information session which focused on coping at school. Each group received one session lasting 30 min. Assessments were conducted at baseline and at 1 mo post-treatment. **Outcome Measure:** Knowledge Interview for Children (KIC), Piers-Harris Children's Self-Concept	1. The Injury-related information intervention was not successful in improving children's knowledge or awareness of TBI as the Injury Group scored significantly lower on the KIC than the Study Group at post-intervention ($p<0.050$). 2. However, the Injury Group scored significantly lower RBMT scores than the Study Group ($p<0.010$) at pre-intervention, leading the authors to suggest that memory deficits may have led to difficulties in remembering newly acquired knowledge. 3. Parents of patients in the Injury Group reported a significant reduction in PSI scores in

	Scale (PH-CSCS), Child Behaviour Checklist-Problems Scale (CBCL-P), Parenting Stress Index (PSI), Rivermead Behavioural Memory Test (RBMT).	comparison with parents of children in the Study Group (p<0.050). 4. There were no significant differences between groups on the PH-CSCS and CBCL-P at post-treatment.

PEDro=Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

A single RCT evaluated the effect of injury-related information interventions for patients' self-awareness regarding their injury (Beardmore, 1999). Although the intervention was not effective in improving the children's knowledge or awareness of their deficits, self-esteem, or cognitive measures, it did significantly reduce the stress experienced by their parents. Additional studies using larger sample sizes should be conducted to elucidate the effects of injury-related information interventions upon children and their families.

Conclusions

There is level 1b evidence that injury-related information interventions may not improve knowledge or awareness of injury-related deficits compared to placebo information sessions in children post TBI.

Injury-related information provided to participants and parents may not have an effect upon deficit self-awareness in children post TBI.

14.4.3 Motor Rehabilitation

Motor capacity is another aspect of functioning that is often impaired following an ABI. 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). Therefore, despite improvements in overall function, residual impairments are common. Baque et al. (2016) report from a systematic review on motor rehabilitation that both physiotherapy and virtual reality result in favourable outcomes in the pediatric population. Other therapies that have had success within the adult ABI population for rehabilitation of motor abilities are bracing, botulin toxin, and constraint induced movement therapy (CIMT). However, there is lack of high-quality research investigating motor rehabilitation therapies post ABI in the pediatric population.

14.4.3.1 Bracing

In the growing child, bracing is often utilized to prevent contracture formation by providing regular stretching, or to improve functional gait and upper extremity use. Evidence from animal studies is often quoted in support of bracing children with spasticity, as there is data showing that stretching of muscles can negate the atrophic effects associated with spasticity, and thus promote muscle growth (Ziv et al., 1984). Unfortunately, data analyzing the impact of bracing children with a TBI is limited and the methodological details/results from one study are presented in Table 14.25.

Table 14.25 Bracing for Motor Rehabilitation in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Corn et al. (2003) United Kingdom Case Series N=4	**Population:** ABI=2, Cerebral Palsy=2; Mean Age=12yr; Gender: Male=2, Female=2. **Intervention:** Patients participated in a study testing the effect of an upper-limb, second skin lycra splint worn at school (6.5 hr/day) and its effect on upper limb movement. Both patients with an ABI were new users whilst the other two had been using splints for up to 12mo before the study. New users were assessed with the splint (intervention phase) then without the splint for a total of 17 wk. Long-term users did not wear their splint then resumed wearing the splint for a total of 14 wk. Assessments were conducted 2/wk. **Outcome Measure:** Melbourne Assessment of Unilateral Upper Limb Function (MAUULF).	1. One new user demonstrated significant improvements in MAUULF scores during the intervention phase of the splint ($p<0.050$) compared to the baseline phase. 2. One long-term splint user experienced a significant decrease in MAUULF scores ($p<0.050$) during the intervention phase compared to the baseline phase. 3. The remaining two users did not experience any significant increase or decrease in MAUULF scores during the intervention phase compared to the baseline phase.

Discussion

Corn et al. (2003) have studied the impact of utilizing second skin lycra splinting on the quality of upper limb movement in children. Due to low numbers (only 2 of 4 subjects being diagnosed with traumatic brain injury) and a single subject design, this data may not be generalizable to the broader TBI population. Lack of improvement in one child and significant improvement in another, as documented with the Melbourne Assessment of Upper Limb Function, highlights the need for goal focused use and careful measurement of outcomes when requesting a child and their family undertake a bracing protocol, which may be time consuming and uncomfortable.

Conclusions

There is inconclusive (level 4) evidence regarding whether or not upper limb lycra splints improve the quality of movement in children post TBI.

It is unclear whether upper limb lycra splints improve the quality of movement in children post TBI.

14.4.3.2 Constraint-Induced Movement Therapy

Constraint induced movement therapy (CIMT) has received increased attention in the literature as a possible treatment for cerebral palsy in children and stroke in adults. This treatment 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). This type of treatment has been shown to be effective in adults who have suffered a stroke, a TBI, or focal hand dystonia, however, little research has been conducted in children with ABI. The methodological

details and results from one study investigating constraint-induced movement therapy for motor rehabilitation in children post ABI are listed in Table 14.26.

Table 14.26 Constraint-Induced Movement Therapy for Motor Rehabilitation in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Cimolin et al. (2012) Italy PCT N=20	**Population:** TBI; *Hemiplegia TBI Group (n=10)*: Mean Age=9.8yr; GCS Range=4-8. *Healthy Controls (n=10)*: Age Range=7.3-13.6yr. **Intervention:** The Hemiplegia TBI Group was asked to wear a fabric glove with a built-in, stiff plastic volar splint on the unaffected hand, which prevented them from flexing their fingers and prevented their ability to grasp. The glove was worn 3 hr/day during which both groups participated in rehabilitation activities including playing cards, completing puzzles, using a spoon or fork, and dusting a surface. The Control group did not receive any type of treatment. The intervention was provided 7 days/wk for a total of 10 wk with rehabilitation activity sessions provided 3/wk. Assessments were completed at baseline and post-treatment. **Outcome Measure:** Quality of Upper Extremities Skills Test (QUEST), Gross Motor Function Measure (GMFM), Besta Scale (BS), Total Movement Duration (TMD), Mean Movement Velocity (MMV), Range of Motion (ROM), Average Jerk Index (AJ), Average Sway Index (AS).	1. All participants improved from baseline to post-treatment on the QUEST (A, B, C, and Total), GMFM, BS Grip, and BS Bilateral Manipulation with moderate to large Cohen D effect sizes (0.40 to 0.92). 2. TMD and MMV of the affected arm improved significantly from baseline to post-treatment (both $p<0.050$), in particular, during reaching and hand-to-mouth tasks. 3. ROM during reaching tasks improved significantly in shoulder flexion, shoulder abduction/adduction and elbow flexion/extensions in the hemiparetic arm (both $p<0.050$, $d=2.16$ and $d=1.52$ respectively) comparable to the Control group. 4. ROM during hand-to-mouth tasks improved significantly in shoulder and elbow joint excursion (both $p<0.050$). 5. AJ improved and AS reduced from baseline to post-treatment in the hemiplegic group, but were still unable to perform at the same level as controls.

Discussion

In a recent case control study looking at the effectiveness of CIMT with children post TBI, 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. Considerable debate exists regarding this last finding, as it is unclear whether motor improvements after CIMT are in fact due to the CIMT or the multiple hours of therapy the patient undergoes per week. Furthermore, 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). Therefore, future studies where controls, who are also patients with TBI, undergo the same amount of therapy without splinting of the less affected limb are required to determine whether the benefits of CIMT outweigh the risk when treating pediatric patients post TBI.

Conclusions

There is level 2 evidence that constraint-induced movement therapy (CIMT) may improve motor function of the hemiparetic limb compared to no care in children post TBI.

Constraint induced movement therapy may improve upper limb function in children post TBI, however, further research is required.

14.4.3.3 Technological Aids in Motor Rehabilitation

14.4.3.3.1 Virtual Reality and Videogame Therapy

Alternative methods for motor therapy have focused on the use of modern-day technology to remediate motor deficits post ABI. The use of the Nintendo Wii videogame console has been found to be a cost-effective and highly-motivating alternative to traditional physical and cognitive treatment, as both limb movement and social interactions are promoted at the same time (Loureiro et al., 2010). The use of the Nintendo Wii and Wii-Fit software has also been found to be successful amongst adult populations for remediation of balance (Gil-Gómez et al., 2011) and moderately successful for improving walking (McClanachan et al., 2013). Other systems have been used, including virtual reality simulators (Bart et al., 2011), to recreate a real-world environment. Specifically, Bart et al. (2011) used a virtual reality simulator that could distinguish between children with and without ABI. The results revealed that virtual reality game scores were correlated with self-care abilities and upper-extremity reaching. As a result, it is concluded that virtual reality and videogame therapy can both identify and improve motor deficits present in children post TBI.

Table 14.27 Virtual Reality and Videogame Therapy for Motor Rehabilitation in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Biffi et al. (2015) Italy Cohort N=14	**Population:** ABI: TBI=3, Tumor=1; *ABI Patients (n=4):* Gender: Male=1, Female=3; Mean Age=13.7yr; Mean Time Post Injury=8.5 mo. *Control Group (n=10):* Gender: Male=1, Female=9; Mean Age=26.0yr. **Intervention:** Patients performed a series of walking and balance exercises while engaging with a virtual reality (VR) environment. Kinematic and gait performance were compared with a reference control group of healthy adults who had participated in a prior study. The intervention consisted of 5 sessions, each 30 min over a 3 wk period. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** Ankle, Hip, Knee and Pelvic Kinematic Parameters on Instrumented Gait Analysis.	1. Left-side ankle plantar-flexion and peak dorsi-flexion improved significantly (both p<0.050) among ABI patients from baseline to post-treatment. 2. Left and right-side hip extension both improved significantly (p<0.050) from baseline to post-treatment among ABI patients. 3. Left and right-side mean pelvic tilt, pelvic tilt at initial contact and range of pelvic obliquity all improved significantly (all p<0.050) from baseline to post-treatment among ABI patients. 4. Left and right-side mean pelvic tilt, pelvic tilt at initial contact, right-side hip extension, and left-side ankle plantar-flexion and ankle dorsi-flexion all significantly differed compared to the control group at baseline but were no longer significantly different at post-treatment.
De Kloet et al. (2012) The Netherlands Pre-Post N_I=50, N_F=45	**Population:** ABI: TBI=27, Non-TBI=23; Gender: Male=26, Female=19. **Intervention:** Patients took part in two 1 hr training sessions 6wk apart with a Nintendo Wii and an assortment of games. Assessments were conducted at baseline and at 12wk follow-up. **Outcome Measure:** Children's Assessment of Participation and Enjoyment (CAPE), Amsterdamse	1. Patients reported a significant improvement in amount of physical activity (p=0.010) on the CAPE at follow-up. 2. CAPE scores revealed a significant increase in diversity of recreational activities (p=0.020), and intensity of physical activity (p=0.040) at follow-up. 3. ANT scores revealed significant improvements in dominant-hand reaction time (p=0.010),

Author Year Country Study Design Sample Size	Methods	Outcomes
	Neuropsychologische Taken (ANT), Goal Attainment Scaling.	feature identification (p=0.010), tracking speed (p=0.047), and discrepancy time (p=0.005). 4. 66% of patients reported an improvement in goals attained with 15 out of 19 reporting success for motor functioning goals but less than half reported success for information-processing goals.

Discussion

The literature demonstrates that use of a gaming console such as the Nintendo Wii has made positive contributions to motor therapy in pediatric ABI. De Kloet et al. (2012) reported that patients demonstrated significant increases in amount and intensity of physical activity, coordination of movement, and participation in a greater variety of recreational activities following 6 weeks of Nintendo Wii therapy. However it was conceded that quality of life was not measured so while motor functions improved, psychosocial issues may not have been addressed (De Kloet et al., 2012). Future pediatric research is required to assess the effectiveness of similar interfaces such as the Xbox Kinect system which operates without a controller and measures the player's own body movements.

Biffi et al. (2015) reported that paediatric patients with an ABI demonstrated significant improvements in multiple aspects of gait and walking ability, particularly in pelvic kinematics after performing walking and balance exercises in a virtual reality environment. However, certain parameters such as knee flexion did not improve. It is important to note that while left and right-side mean pelvic tilt, pelvic tilt at initial contact, right-side hip extension, left-side ankle plantar-flexion and ankle dorsi-flexion all significantly differed compared to the healthy control group at baseline, there were no longer any significant differences post-treatment. However, one major limitation was the lack of an age and condition-matched control group (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.

Conclusions

There is level 2 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.

There is level 4 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.

Virtual reality-based therapy focused on walking and balancing exercises may improve certain movements (pelvic and ankle kinematics) but not others (knee flexion) in pediatric patients post ABI.

Movement therapy using a Nintendo Wii console might improve motor coordination, as well as engagement and intensity of physical activity in pediatric patients post ABI.

14.4.3.3.2 Robot Mediated Therapy

Currently, there is a lack of studies addressing robot-assisted training among pediatric patients with an ABI (Fasoli et al., 2012). In a study of patients with an ABI (predominantly cerebral palsy and stroke), Keller et al. (2016) reported that use of the ChARMin exoskeleton for upper limb rehabilitation was feasible for all patients thereby highlighting the promise of this type of intervention. Robot-assisted therapy facilitated motor recovery within the cerebral palsy and stroke populations and may be beneficial for children who have sustained an ABI. Four studies have evaluated the use of robotic assistance for motor rehabilitation in the pediatric population.

Table 14.28 Robot Mediated Therapy for Motor Rehabilitation in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Beretta et al. (2018) Italy PCT N=41	**Population:** robotically-driven orthoses (RDO) *Group (N=29):* Mean Age=11.2yr; Gender: Male=62%, Female=38%; Mean time post injury=2.6yr; Median GCS=6. *Conventional therapy (CT) Group (N=12)*: Mean Age=11.92yr; Gender: Male=58%, Female=42%; Mean time post injury=2yr; Median GCS=5. **Intervention:** 2 cohorts of children with severe TBI were the RDO group or CT group. The RDO group underwent Lokomat (robotic assisted gait training) for 20 sessions and CT for 20 sessions, whereas the CT group received 40 sessions of CT. Sessions were 45 min/d and 5 days a week for 4 weeks. Evaluated pre and post-therapy. **Outcome Measures:** Gross motor function classification system (GMFCS), Disability rating scale (DRS), Functional Assessment questionnaire (FAQ), and the 6-min walk test (6MWT), 3-D gait analysis (including stance, cadence, step length, step symmetry, velocity, stride length, stride symmetry, step width).	1. GMFCS subscores of standing and walking (D & E) were significantly different between groups ($p<0.05$) showing higher scores in the RDO group. 2. Other measures were not significantly different between groups post-therapy ($p>0.05$) 3. All measures in both groups (except FAQ in CT group) showed significant improvement ($p<0.05$) from pre to post evaluation. 4. For the gait analysis, velocity was the only measure that showed significant between group difference ($p<0.05$) showing higher scores in the RDO group. However, scores for this measure did not significantly change within group. 5. Stance (% stride) in the unaffected side, step length in the unaffected side, and stride length in the unaffected side showed significant improvement within the RDO group ($p<0.05$). Only stride symmetry showed significant within-group improvement in the CT group.
Chen et al. (2018) USA Pre-Post N=10	**Population:** TBI Group (N=10): Mean Age=13yr (3.9); Gender: Male=30%, Female=70%; Mean time post injury=45.7 days. **Intervention**: A wearable ankle rehab robot with a computer game interface was used to aid acute rehab of TBI children. Therapy was conducted 3-5 times a week until 15 sessions had been complete, along with conventional therapy. Participants were evaluated pre and post-therapy, and at 6-weeks post (of which only 5 were able to attend). **Outcome Measures:** Modified Ashworth Scale (MAS) for spasticity, Pediatric Balance scale (PBS), Selective control assessment of the lower extremity (SCALE), Fugl-meyer lower extremity (FMLE), 6 min walk test (6MWT), timed up and go (TUG), and 10m walk test (10MWT). Biomechanical measured from the device were active range of motion (AROM), passive ROM	1. The MAS and PBS showed significant improvement pre to post evaluation ($p=0.004$ and $p=0.038$, respectively). 2. The plantarflexion MVC showed improvement from post-therapy to 6-week follow-up ($p=0.012$) 3. No other measures showed significant improvement ($p>0.05$)

Author Year Country Study Design Sample Size	Methods	Outcomes
	(PROM), and dorsiflexion & plantar flexion Maximal voluntary contraction (MVC)	
Beretta et al. (2015) Italy PCT N=23	**Population:** ABI: TBI=11, Tumor=7, Ictus=4, Anoxia=1; *Robotic-Aided Gait Training Group (RAGT; n=23):* Mean Age=11.8 yr; Gender: Male=12, Female=11. *Control Group (n=11):* Mean Age=10.4 yr; Gender: Male=7, Female=4. **Intervention:** Patients assigned to the RAGT group were provided with the use of an exoskeleton designed to perform a walking pattern on a treadmill, in addition to 20 sessions of physiotherapy. RAGT was performed for 45 min/d, 5 days/wk over 4 wk. The control group received physiotherapy only. Assessments were conducted at baseline and post-treatment. **Outcome Measure:** 6-Min 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). Specific improvements were found on the subscales of GMFM for lying/rolling and crawling/kneeling (both p<0.010) and standing and walking (both p<0.001). 2. There were significant improvements in walking ability on the FAQ in the RAGT group (p<0.010). 3. The control group improved significantly on the GMFM dimension C subscale (crawling and kneeling) only from baseline to post-treatment (p<0.010). 4. 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<0.050). 3D Gait Analysis of ambulant patients revealed that the RAGT group improved significantly in cadence, left-side step-length, velocity, ROM hip flex-extension during gait and swing, and maximum hip extension left-side stride length (all p<0.050) and right-side stride length (p<0.005) from baseline to post-treatment. The control group did not demonstrate any significant improvements.
Frascarelli et al. (2009) Italy Pre-Post N=12	**Population:** TBI=6, Stroke=4, Cerebral Palsy=2; Mean Age =11.7 yr; Gender: Male=9, Female=3; Mean Time Since Injury=3.5 yr. **Intervention:** Robot Mediated Therapy (RMT) for upper limb was combined with goal-oriented reaching tasks for 1 hr 3x/wk over a period of 6 wk. Outcome measures were assessed at baseline and 6 wk. **Outcome Measure:** Modified Ashworth Scale (MAS), Fugl-Meyer (FM), The Melbourne Assessment of Unilateral Upper Limb (Melbourne%), Reaching Performance Scale (RPS) close and far, Jerk Metric (JM), and Average Speed.	1. There was a significant improvement in MAS (p=0.001), FM (p=0.002), Melbourne% (p<0.001), JM (p=0.006) and average speed (p=0.010) from baseline to 6 wk. 2. There was a significant improvement from baseline to 6 wk follow-up in RPS at close and far distances (p=0.004 and p=0.032, respectively).

Discussion

Four robotic assisted therapies were examined, three for remediation of lower limb motor function (Biffi et al., 2015) with one focusing specifically on ankle remediation (Chen et al., 2018), and one for the upper limb (Frascarelli et al., 2009).

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. Specifically and perhaps more importantly, standing and walking abilities improved post-treatment (Beretta et al., 2015; Biffi et al., 2015), which is in line with findings from the adult TBI population (Wilson et al., 2006). Beretta and colleagues (2018) performed a follow-up study with additional participants. The authors found significant between-groups difference on gross motor function for standing and walking, showing improvement in the robotic assistance group. Both groups showed significant improvement on other measures, however, they were not significantly different from each other. Lastly, a study investigating a wearable robot for ankle remediation used a computer game interface and measured biomechanical forces of the ankle (Chen et al., 2018). In this pre-post study, the authors found a significant improvement in reduction of spasticity and increases in balance scores (Chen et al., 2018). This study does not include a control group and has a low sample size of 10 pediatric individuals. Further investigation is needed to make conclusions about it's use in rehabilitation.

Furthermore, Frascelli et al. (2009) report that upper limb motor function and spasticity are improved following short term robot mediated therapy on reaching tasks. Authors suggest that recovery in upper limb motor function can be influenced by repetitive training with a robotic arm, without negatively affecting muscle tone (Frascarelli et al., 2009).

Conclusions

There is level 2 evidence that exoskeleton, body-weight supported treadmill training paired with physiotherapy may be superior to physiotherapy alone at improving gait and motor function in pediatric patients post ABI.

There is level 4 evidence that an wearable ankle robot combined with a computer game interface may be beneficial in reducing spasticity and increasing balance in children post ABI.

There is level 4 evidence that Robot Mediated Therapy (RMT) combined with goal-oriented reaching tasks may improve upper limb motor function and spasticity in children post ABI.

Body-weight supported treadmill training with an exoskeleton combined with physiotherapy may be superior to physiotherapy alone at improving gait and motor function in pediatric patients post ABI.

A wearable ankle robot combined with a computer game interface might reduce spasticity and improve balance in pediatric patients post ABI.

Robot Mediated Therapy (RMT) combined with goal-oriented reaching tasks might improve upper limb motor function and spasticity in pediatric patients post ABI.

14.4.3.4 Pharmacological Treatment of Spasticity

Spasticity and elevated muscle tone are common complications that arise after an individual has experienced an ABI (Popernack et al., 2015). Spasticity has been broadly defined as "disordered sensorimotor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles" (Pattuwage et al., 2017). When damage occurs to the upper motor neurons of the corticoreticular pathway in the brain, an increase in muscle tone and exaggerated deep tendon reflexes may occur (Pattuwage et al., 2017). Muscle tone is defined as "velocity-dependent resistance of a muscle to stretching" (Pattuwage et al., 2017).

Within the pediatric population, spasticity has a range of implications from producing mild discomfort to extremely painful spasms, muscle contractures, pressure sores, and interfering with activities of daily living (Pérez-Arredondo et al., 2016). In order to prevent or delay long-term damages due to spasticity, several pharmacological and non-pharmacological approaches exist (Walter et al., 2015). Generally, clinicians begin with non-invasive/non-pharmacological approaches first, including physiotherapy, splinting and casting. If these treatments fail to work, they may gradually move to more invasive/pharmacological approaches using dantrolene, tizadine, botulinum toxin and baclofen (O'Brien, 2002; Pattuwage et al., 2017). These pharmacological agents reduce spasticity through a variety of different mechanisms:

a) Dantrolene reduces spasticity through inhibition of calcium release from the sarcoplasmic reticulum at the myoneural junction.
b) Tizadine inhibits the alpha-2 adrenergic system at the spinal and supra-spinal levels to reduce spasticity.
c) Local injections of botulinum toxin reduce spasticity through inhibition of intracellular acetylcholine secretion.
d) Balcofen inhibits the neurotransmitter gamma aminobutyric acid to prevent spinal reflexes from neurons that use it at the spinal interneuron level, in turn reducing spasticity.

A review of the literature on botulinum toxin suggests that injections are effective for lower limb functional improvements, however, future research is needed to determine the effects for the upper limb (Gordon & Di Maggio, 2012). This section reviews the administration and effectiveness of intrathecal baclofen and botulinum toxin in children post ABI.

Table 14.29 Pharmaceutical Agents for the Treatment of Spasticity in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcomes
Walter et al. (2015) Switzerland Case Series N=3	**Population:** ABI: Hypoxia=3; Mean Age=4.0 yr; Gender: Male=2, Female=1; Mean Time Post Injury=64.3 d. **Intervention:** Patients received intrathecal baclofen pump implants and were monitored for a mean of 2,315 d (approximately 6.3 yr). Dosage increased from 117 mcg at baseline to 660 mcg at the study end. Assessments were conducted at baseline and annually for at least 5 yrs.	1. Spasticity on MAS decreased from baseline to post-treatment in the upper and lower extremities. 2. Five occurrences of pump-related complications were observed including two cases of skin protrusion, one case of infection, one case of lumbar cerebrospinal fluid leak, and one case of intractable spasticity requiring a pump replacement.

Author Year Country Study Design Sample Size	Methods	Outcomes
	Outcome Measure: Modified Ashworth Scale (MAS), Complication Rate.	
Guettard et al. (2009) France Case Series N=25	**Population:** ABI: TBI=12, Stroke=6, Brain Tumour=5, Anoxia=2; Mean Age=9.3 yr, Gender: Male=14, Female=11; Mean Time Post Injury=3.0 yr. **Intervention:** Patients received botulinum toxin type A (BTX-A) to lower or upper limbs, or both. Doses were given in accordance with the patient's age and muscle size and did not exceed 10 U/kg or 300 U. All participants received physical therapy, occupational therapy and auto-exercises. Assessments were taken at baseline, 4 wk post-injection and 3 mo follow-up. **Outcome Measure:** Ashworth scale (AS), Zancolli Scale (ZS), Range of Motion (ROM).	1. Following the injections, spasticity was significantly reduced on the AS from baseline to 4 wk ($p<0.0001$). 2. Quality of opening hand improved significantly according to the ZS ($p<0.001$). 3. Mean ROM ($p=0.040$) improved from pre-injection to 4 wk. 4. Overall, 68.6% of treatment sessions led to positive results, whereas 23.6% did not have as good as expected functional outcomes.
Van Rhijn et al. (2005) Belgium PCT N=21	**Population:** TBI; Age Range=2.7 yr-19.8 yr; Gender: Male=15, Female=6. *Group 1 (n=4)*: Mean Time Post Injury=35.8 mo. *Group 2 (n=10):* Mean Time Post Injury=11.3 mo. *Group 3 (n=7):* Mean Time Post Injury=18.0 mo. **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 or 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, and at 1, 3 and 5 mo follow-ups. **Outcome Measure:** Modified Ashworth Scale (MAS), Range of Motion (ROM) Goniometry Assessment.	1. All groups demonstrated improvements in spasticity on MAS from baseline to 1 mo follow-up. 2. At 3 mo 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 3 mo follow-up. 3. At 5 mo 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 3 mo follow-up. 4. Group 2 exhibited the greatest level of improvement in ROM with mean increases of 23^o, 36^o and 53^o at 1 mo, 3 mo and 5 mo follow-ups compared to baseline. 5. ROM in Group 3 improved by a mean of 4^o from baseline to 1 mo follow-up but then experienced a -6^o decline at 3 mo follow-up and a -3^o decline at 5 mo follow-up compared to baseline ROM. 6. Group 1 exhibited moderate improvements in ROM with mean increases of 5^o, 7^o and 2^o at 1 mo, 3 mo and 5 mo follow-ups compared to baseline.

Discussion

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. However, 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. Future research should differentiate these groups to compare effectiveness (Guettard et al., 2009). 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 severely brain-injured children, and effective when used in combination with orthotic devices and specific functional exercise programs.

An intrathecal baclofen injection pump improved spasticity in three young children (Walter et al., 2015). However, unlike botulinum toxin, side effects were reported with the use of the intrathecal baclofen pump implant treatment. Two of the three patients had complications, with five of the complications being related to the device. Two of these complications were due to skin protrusions, as the pumps must be implanted under the skin and one child experienced problems with epifascial implantation. However these effects were minimized with modification of the protocol to a subfascial implantation, which has become the sole technique for intrathecal baclofen pump implantations for children (Walter et al., 2015). Other complications were due to wound infection, cerebrospinal fluid leakage, and intractable spasticity. All complications were reversed with treatment or relocation of the pump.

Conclusions

There is level 2 evidence that botulinum toxin type A (BTX-A) used in combination with adjunct therapy (physiotherapy, occupational therapy) may decrease upper and lower limb spasticity, as well as movement range of motion, in children and adolescents post ABI.

There is level 4 evidence that intrathecal baclofen pumps may be effective at reducing spasticity in the upper and lower limbs for children with ABI as a result of hypoxia.

Botulinum toxin type A, when used in combination with adjunct therapy (physiotherapy andoccupational therapy), may effectively reduce upper and lower limb spasticity to improve movement range of motion, in children and adolescents following ABI.

Intrathecal baclofen pumps may reduce upper and lower limb spasticity in children with hypoxic brain injuries, however, intrathecal pump implantation may be associated with complications such as infections and skin protrusions. Side effects may be mitigated by subfascial pump implantation.

14.5 Vestibular Recovery

Vestibular dysfunction is commonly overlooked in both the adult and 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), and therefore should not be overlooked. Unfortunately, the majority of research on vestibular dysfunction following brain injury is for sports-related mild TBIs. Two studies were conducted looking at treatment for balance deficits in children following a severe ABI (Katz-Leurer et al., 2008; Katz-Leurer et al., 2009). The results and methodological details from these studies are presented in Table 14.30.

Table 14.30 Vestibular Recovery in Children Post ABI

Author Year Country Study Design Sample Size	Methods	Outcome
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 or instructions to maintain regular daily activities. Home based exercise consisted of a series of exercises including sit-to-stand and step-up exercises with each leg forwards and sideways. All five exercises were completed 5 days/wk for 6 wk along with a diary to record number of repetitions and sets. Assessments were conducted at baseline, post-treatment and at 6 wk follow-up. **Outcome Measure:** Timed Up and Go Test (TUG), Functional Reach Test (FRT), Two-min Walk Test (2MWT), Walking Speed, Number of Repetitions for Sit-toSstand and Step-Up Exercises.	1. Patients in the exercise group demonstrated a significantly greater improvement in TUG scores, FRT forward, FRT preferred hand (p=0.010 for all) compared to controls from baseline to post-treatment. 2. No differences reported for FRT non-preferred hand subscore (p=0.100), 2MWT (p=0.780) or walking speed (p=0.840) from baseline to post-treatment. 3. The exercise group significantly increased their sit-to-stand (p=0.020), step-up sideways on preferred (p=0.050) and non-preferred leg (p=0.040) movements from baseline to post-treatment. Step-up exercises performed forwards, regardless of preferred or non-preferred leg (p=0.070 and p=0.090 respectively), did not yield significant improvements in number of repetitions performed when measured post-treatment. 4. No significant differences were found on any measures for the exercise group from post-treatment to 6 wk follow-up (controls not tested at 6 wk follow-up).

Discussion

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. However, there was no generalized effect for unpracticed motor skills (i.e. grasping action) (Katz-Leurer et al., 2008). In theory it would be beneficial for training programs to create positive transfer of practice tasks to everyday activities (Katz-Leurer et al., 2008), but this was not studied. Within this study population, there was variation in the number of training days each child received and spectrum of etiology of ABI (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). Results should be interpreted with caution as there appeared to be a high dropout rate for both studies (Katz-Leurer et al., 2008; Katz-Leurer et al., 2009). There also was a variation in children studied, as half of the participants had cerebral palsy and a subgroup analysis was not conducted to determine the effects of the exercise specifically on children with TBI (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 wk.

Conclusions

There is level 1b evidence that home based exercise programs may be superior to regular daily activities at improving balance, dexterity, and aerobic capacity short-term (<6 weeks) in children post ABI.

Home based exercise programs likely improve functional balance, aerobic capacity, and dexterity in children with an ABI, however, after 6 weeks, they have similar effects.

14.6 Shaken Baby Syndrome

The constellation of injuries associated with non-accidental trauma sustained during infancy, such as retinal hemorrhage, intracranial and musculoskeletal injuries are generally known as shaken baby syndrome (SBS) (Joyce & Huecker, 2019). Shaken baby syndrome has also been referred to as whiplash-shaken infant syndrome, shaken impact syndrome, infant shaken impact syndrome, non-accidental or abusive head injury (Dias et al., 2005). Regardless of what it is called the impact on a young infant can be quite severe and even fatal.

Shaken baby syndrome occurs when a child is taken by the torso, leg, or arm and vigorously shaken in an angular movement repeatedly (Joyce & Huecker, 2019). 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). There are several unique factors in infants that render their brains highly vulnerable to damage with shaking, including the relatively high weight of an infant's head, weak neck muscles, the thickness of the skull wall, the lack of myelination and the high water content of the infant brain (Lancon et al., 1998; Lewin, 2008; Showers, 1992). The force at which an infant is shaken causes blood vessels to rupture, resulting in bleeding within the brain and precipitation of further damage (Carbaugh, 2004; Macdonald & Helfrich, 2001). SBS is typically seen within the first year of life; however, cases have been reported up to the age of three (Duhaime et al., 1998; Lancon et al., 1998; Tsao et al., 2002).

14.6.1 Risk Factors & Incidence

Frustration with an infant's frequent and inconsolable crying is believed to the most common risk factor for SBS. An infant will typically cry 1.5 to 3 hours a day but an excessive amount of inconsolable crying can occur— a period known as "colic" or "purple crying". The frustration and anger felt by the caregivers during these periods of "colic" are often cited as the main trigger for shaking an infant (Carbaugh, 2004; Goulet et al., 2009; Lewin, 2008). Occurrences of SBS 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 undeveloped 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 Approximately 65% of SBS cases result in significant neruological disability and 13-50% all non-accidental pediatric deaths recorded are due to SBS (Dias et al., 2005; Goulet et al., 2009; Lancon et al., 1998). Additional risk factors for SBS include: male gender, behavioural health problems, history of domestic violence, lack of childcare experience, low education level, low socioeconomic status, single-parent families, difficult infant temperaments, prematurity, low-birth weight, special needs and medical fragility (Carbaugh, 2004; Lewin, 2008).

14.6.2 Diagnosis/Clinical Findings

As the clinical symptoms of SBS are non-specific, each case tends to vary in its presentation. Minor symptoms of SBS can be mistaken for other childhood illnesses, which leads to challenges in recognizing SBS. Common clinical signs include irritability, seizures, impaired consciousness, bulging fontanelle or forehead, lack of social smile, inability to focus the eyes, breathing abnormalities, vomiting, lethargy, constipation, poor feeding, apnea and muscle weakness (Altimier, 2008; Carbaugh, 2004; Duhaime et al., 1998; Lewin, 2008). Any Infant who has been the victim of SBS should undergo a complete assessment and receive immediate care/attention (Gutierrez et al., 2004).

Assessments such as neurologic and ophthalmologic examinations, skeletal survey, CT and MRI of the head are used to diagnose SBS (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). In infants where CT findings are not definitive, MRI has been shown to be useful in detecting extra axial hemorrhages (Duhaime et al., 1998).

A common finding in SBS, which has been reported in 65 to 95% of those affected, is retinal hemorrhage (RH) (Duhaime et al., 1998). The amount of force it takes to cause RH is unknown. Duhaime et al., (1998) noted that although RH is not specific to SBS, the appearance of "severe bilateral retinal hemorrhage with retinal folds or detachments" *is.*

Table 14.31 Diagnostic Findings in Shaken Baby Syndrome (Carbaugh, 2004) pg 110)

Test	Findings consistent with SBS
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 Metaphyseal fracture Shaft fracture Long bone bruising Skull fractures Rib fractures Fractures in various stage of healing
Ophthalmologic Examination	Retinal haemorrhages Vitreous haemorrhage Papilledema Retinal detachment Anisocoria (unequal pupils) Orbital and lid ecchymosis Subconjunctival haemorrhage Disconjugate eye movements Hyphema Sixth nerve palsy Disruptions of contents of the eye Optic nerve haemorrhage Optic nerve scleral junction haemorrhage Orbital fat haemorrhage
Other Findings	Bloody cerebrospinal fluid Mildly to moderate anemia Clotting dysfunction Elevated transaminase levels (indicates occult liver injury)

14.6.3 Treatment

Evidence regarding the types of treatment used specifically in the SBS population is scarce and requires more research. However, the type of treatment typically used parallels the treatment regimen of a TBI and is mostly supportive (Joyce & Huecker, 2019). The goal of treatment is to maintain normal blood and intracranial pressure to ensure adequate cerebral perfusion occurs (Joyce & Huecker, 2019).

The initial management of SBS is to maintain the patient's airway, breathing and circulation. If a child presents with no alterations of consciousness and normal blood pressure, they may be treated with supportive care (Joyce & Huecker, 2019). However, if a child presents with a Glasgow coma score of less than 9, respiratory distress or hemodynamic instability they may require intubation and mechanical ventilation to enhance oxygenation and prevent aspiration (Joyce & Huecker, 2019). An important consideration when performing advanced airway management is to maintain cervical spine stability (Joyce & Huecker, 2019). For the initial monitoring of ventilation, capnography is recommended to avoid hyperventilation and subsequent hypocapnia, which leads to vasoconstriction and decreased cerebral perfusion (Joyce & Huecker, 2019).

The treatment of immediate brain injury from the initial traumatic forces is equally important to the prevention of secondary brain injury that may occur (Joyce & Huecker, 2019). This includes preventing coagulation, hypoxemia, intracranial hypertension, hypercarbia, hyperglycemia or hypoglycemia, electrolyte abnormalities, hematomas, seizures and hyperthermia (Joyce & Huecker, 2019). Managing intracranial pressure is crucial in preventing secondary brain injury (Joyce & Huecker, 2019). Intracranial

pressure may be decreased by raising the patients head to 30 degrees (Joyce & Huecker, 2019). This optimizes CPP and improves venous drainage without affecting cerebral blood flow (Joyce & Huecker, 2019).

If intracranial hypertension is present, the patient will require sedation with barbiturates (Joyce & Huecker, 2019). Barbiturates work to lower intracranial pressure by decreasing cerebral metabolism and blood flow (Joyce & Huecker, 2019). In addition, therapeutic hypothermia may reduce cerebral metabolic demands and prevent secondary brain injury (Joyce & Huecker, 2019).

If a patient is not responding to supportive therapy or is demonstrating signs of herniation or neurologic deterioration a decompressive craniectomy may be necessary (Joyce & Huecker, 2019). This surgical procedure removes a portion of the skull to allow for swelling and limits secondary injury (see section 14.2.3.1). However, aggressive treatment of an infant with poor prognosis outcomes has been questioned since most cases result in death despite continuous management (Duhaime et al., 1998).

14.6.4 Long-Term Outcomes

SBS 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). Death occurs in approximately 5-35 percent of affected infants (Joyce & Huecker, 2019).

Eighty-four SBS cases were contacted to determine long term outcomes in a study conducted by Duhaime et al. (1998). Only 14 individuals completed the study and the mean duration of time elapsed since injury was 10 years. One patient died 5 years post injury but up until that time was in a vegetative state. Six patients were severely disabled, two patients were moderately disabled, and 5 patients presented with good outcomes. Associations were found between the severity of abnormalities in the acute stage of SBS and their long-term outcomes. Five patients who were unresponsive at acute care remained in a vegetative state or severely disabled long term. At acute care, six patients required intubation and all of these cases were described as having severe or moderate disabilities. Children who presented with bilateral or unilateral subdural hematoma on CT were found to have a severe disability at time of follow-up. Overall, children who were intubated, unresponsive, or who had a unilateral or bilateral subdural hematoma on CT while in acute care, had worse long term outcomes.

The cases of 404 children with SBS were reviewed by Bourgeois et al. (2008), to examine the prevalence of associated seizure disorder and how this related to SBS outcomes. Seventy-three percent of children (296 children) presented with seizures, with 50% of these patients displaying multiple seizure types. Behavioral problems were found to be closely associated with seizures, occurring in 96% of patients with chronic epilepsy. Seizure activity was found to be associated with worse outcomes for children with SBS.

In a case control study by Stipanicic et al. (2008), 11 SBS patients were compared to 11 healthy controls. It was found that SBS patients has significantly worse IQ scores (Stanford-Binet Intelligence Scale), comprehension of instructions and verbal fluency (NEPSY), time to complete an assignment (TMT-B, HRB-PF), and memory (digit-span backwards) compared to healthy controls.

King et al. (2003), reviewed the charts of 364 patients to determine the typical clinical characteristics of SBS, and related outcomes. Clinical features of SBS included seizures (45%), decreased consciousness (43%) and respiratory difficulties (34%). Retinal haemorrhages, which were found to be associated with

neurological deficits, subdural haemorrhages and death, were present in 76% of patients. Many patients (85%) were found to need ongoing multidisciplinary care for moderate to severe disability or were in a vegetative state.

14.6.5 Ophthalmological Outcomes

Retinal hemorrhages (RH) have been found in 65-95% of infants with SBS (Duhaime et al., 1998). Two theories exist regarding the etiology of RH in SBS. One suggests that the RH occurs due to retinal venous obstruction secondary to increased ICP, while the second postulates that when an infant's head is accelerating/decelerating, traction develops between the vitreous and the retina leading to RH (Kivlin et al., 2000). RH is a clinical presentation that should lead to clinician to pursue a CT scan of the head (Kivlin et al., 2000).

Kivlin et al. (2000) noted that RH was found in 79% of the entire study population (n=123). Of those, bilateral RH was found more frequently (68%) than unilateral RH (11%). Of the 36 patients who died, ophthalmologic examination revealed a lack of visual response in 35, poor pupillary response in 26, and RH in 34 patients. Study authors suggest the presence of these symptoms positively predicted fatal outcomes and severe neurological disability for those children with SBS (Kivlin et al., 2000). Furthermore, the researchers also noted that while patients who experienced seizures were less likely to die than those who didn't, seizures were associated with poor vision at follow-up.

Of the 30 cases reviewed by McCabe & Donahue (2000), subdural hemorrhages were detected in 21 patients and were more common than intracerebral (n=11) and subarachnoid (n=10) hemorrhages. Seizure activity occurred in 67% of the study population. All 8 patients who died had nonreactive pupils 6 of the patients who died had a midline shift detected on CT. It was determined that lack of visual response and a midline shift are predictors of fatal outcomes in SBS.

In a case series of 10 patients, Mills (1998) studied how ophthalmologic examinations of SBS individuals predicted future outcomes. Of note, intraretinal hemorrhages were found in all patients but were not found to be significantly associated with fatal outcomes. Further, a lack of visual response was found in 4 patients, 3 of which later died, and circular perimacular retinal folds and peripheral retinoschisis were also found in all 3 individuals who died. Moreover, in a case series of 14 children in Wilkinson et al. (2014), the severity of RH predicted the severity of acute neurological outcomes. Other predictors of severe neurological injury included vitreous or subhyaloid hemorrhages.

14.6.6 Education & Prevention

The "Don't Shake the Baby" project implemented by Showers (1992) provided a basis for future SBS educational programs to build upon. "Don't Shake the Baby" included an information card providing tips on how to calm a crying infant and a response card to be filled out by new parents. Evaluation of the program led to the conclusion that there needed to be more education provided to parents on the dangers of shaking infants and on how to properly care for a crying infant (Showers, 1992).

The prevention of SBS appears to be related to the education received by parents either prior to delivery at routine office visits, during prenatal visits, prenatal classes and/or post-delivery prior to discharge home (Walls, 2006).

Table 14.32 Educational Programs Designed to Reduce the Risk of Shaken Baby Syndrome

Author Year Country Study Design Sample Size	Methods	Outcomes
Period of PURPLE Crying Prevention Intervention		
Fujiwara et al. (2012) Japan RCT PEDro=7 $N_{Initial}$=230, N_{Final}=201	**Population:** *PURPLE (n=105)*: Gender: Male=0, Female=105. *Control Group (n=96)*: Gender: Male=0, Female=96. **Intervention:** Mothers of newborn infants were randomly assigned to receive the Period of PURPLE Crying prevention package consisting of a DVD and an 11-page booklet, or a DVD on injury prevention as part of a control group. All mothers completed a 4-day diary of the infant's behaviours at 6 wk post-birth followed by a telephone survey at 2 mo. Mothers' knowledge of crying and shaking, and their behavioural responses to stressful situations were assessed post treatment. **Outcome Measures:** Baby Day Diary (BDD), Telephone Survey.	1. Mothers who received the PURPLE intervention scored significantly higher on the Crying Knowledge scale of the telephone survey than the control group (p=0.004) but no significant differences were reported between groups for Shaking Knowledge (p=0.510). 2. Walking away from the infant during inconsolable crying was reported significantly more often within the PURPLE group compared to the control group (p=0.040). 3. The percentage of mothers who shared the advice of walking away during inconsolable crying with other caregivers was significantly higher for the PURPLE group compared to the control group (p=0.001) but sharing advice with other caregivers on the dangers of shaking a baby and infant crying did not differ significantly between groups (p=0.950 and p=0.870 respectively). 4. No significant differences were found between groups for duration of contact with child when distressed (p=0.280), picking-up the infant when distressed (p=0.380), and daily frustration scores (p=0.190) according to BDD entries.
Barr et al. (2009) 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 5 wk post-birth followed by a telephone survey at 2 mo. Mothers' knowledge of crying and shaking, and their behavioural responses to stressful situations were assessed post treatment. **Outcome Measures:** Baby Day Diary, 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. The percentage of mothers in the PURPLE group who shared advice with other caregivers about walking away during inconsolable crying (6.5%) and the dangers of shaking (5.6%) was greater than the control group but no between group difference was found for sharing advice on infant crying. 3. Responses to crying scores on the telephone survey were higher (improved) in the PURPLE group for crying, inconsolable crying, and self-talk compared to the control group but no significant difference was reported. 4. The PURPLE group documented significantly more infant distress in the BDD with a mean of 13.8min more time distressed compared to the control group (p<0.050).
Barr et al. (2009) Canada RCT PEDro=9 N=1833	**Population:** *PURPLE (n=649)*: Gender: Male=0, Female=649. *Control Group (n=630)*: Gender: Male=0, Female=630. **Intervention:** Mothers of newborn infants were randomly assigned to receive the Period of PURPLE Crying prevention material package consisting of a DVD	1. Mothers who received the PURPLE intervention scored significantly higher on the Crying Knowledge scale of the telephone survey than the control group (p<0.001) but no significant differences were reported between groups for Shaking Knowledge (p=0.200).

	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 5 wk post-birth followed by a telephone survey at 2 mo. Mothers' knowledge of crying and shaking, and behavioural responses to stressful situations were assessed post treatment. **Outcome Measures:** Baby Day Diary (BDD), Telephone Survey.	2. Mothers in the PURPLE group were significantly more likely to walk away during inconsolable crying than the control group (p=0.010). 3. The percentage of mothers who shared advice with other caregivers about walking away during inconsolable crying, the dangers of shaking (both p<0.001), and infant crying (p=0.010) was significantly higher for the PURPLE group compared to the control group. 4. No significant differences were found between groups for duration of contact with child when distressed (p=0.360), picking-up the infant when distressed (p=0.830), or daily frustration scores (p=0.260) according to BDD entries. 5. A significant positive association was found between Crying Knowledge and a greater level of interaction with the PURPLE package (p=0.020).
Reese et al. (2014) USA Post-Test $N_{Initial}$=211, N_{Final}=68	**Population:** Mean Age=28.1yr; Gender: Male=0, Female=211. **Intervention:** Mothers of newborn infants were provided with the Period of PURPLE Crying prevention education session from a nurse along with a 10-min DVD to take home and an 11-page booklet. Assessments were conducted at 2 mo follow-up. **Outcome Measures:** Custom Knowledge Scale on the Dangers of Shaking, Coping and Soothing Techniques, Crying.	1. On the crying subscale, 39 of 68 (57.4%) of mothers achieved a perfect score. 2. On the shaking subscale, 65 of 68 (95.6%) of mothers achieved a perfect score. 3. A total of 40 of 68 (58.8%) mothers attempted soothing behaviours and 35 of 68 (51.5%) were able to recall such behaviours. 4. A total of 18 of 68 (26.5%) mothers attempted coping behaviours and 28 of 68 (38.2%) were able to recall such behaviours. 5. Higher education was significantly associated with a perfect score on overall knowledge (p=0.020), knowledge of normal infant crying (p=0.007) and an increase in ability to recall one or more techniques for coping with infant crying (p=0.010).
Simonnet et al. (2014) France Pre-Post N=190	**Population:** *Mothers (n=186):* Mean Age=30.9yr. *Fathers (n=90)*: Mean Age=33.5yr. **Intervention:** Parents of newborn infants received a short informative talk from a maternity department pediatrician and a pamphlet on abusive head trauma. The intervention was approximately 3 min in length. Assessments were completed at baseline and at 6wk follow-up. **Outcome Measures:** Custom Multiple-Choice Questionnaire on Crying and Abusive Head Trauma.	1. Mothers provided significantly more correct answers post-intervention compared to baseline on four of five questions (all p<0.001). 2. Fathers also provided more correct answers post-intervention on four of five questions but statistical analyses were not completed due to a low number of fathers participating. 3. Fathers demonstrated greater improvement in knowledge than mothers with a mean knowledge improvement score of 1.58 compared to 1.19.
Altman et al. (2011) USA Case Series N=65,663	**Population:** 19 hospitals and 1 tertiary care center. **Intervention:** Participants were parents who had a baby at one of the included hospitals from 2000-2008. In 2005 the program was implemented, and after that participants received a brochure and an 8 min	1. Over the 8 yr study period a total of 16 infants in the region were treated for shaking injuries. 2. Of the 16 injuries, 14 were born in the 5 yr period prior to the introduction of the educational video and 2 were born in the 3 yr

	educational video with information on abusive head trauma and prevention. Rate of shaking injuries were examined in the 3 yr period following the educational video and compared to the 5 yr period prior to intervention. **Outcome Measure:** Rate of Injuries.	period after the educational video was introduced. 3. There was a significant reduction in injuries per year in the 3 yr period compared to the 5 yr period (p=0.030).
Bechtel et al. (2011) USA Case series N=222	**Population:** Caregiver's; *Take 5 Safety Plan for Crying (n=112)*: Mean Age=25.2yr; Gender: Male=8, Female=104. *Historical Control Group (n=110)*: Mean Age=25.7yr; Gender: Male=23, Female=87. **Intervention:** Researchers examined the effects of a previously implemented educational program, in which parents received a brochure on steps to take when an infant is crying. Follow-up interviews were conducted after the educational program was implemented and compared to interviews from the CG group prior to the educational program. **Outcome Measures:** Rate of Frustration, Infant Shaking, and Knowledge of Shaken Baby Syndrome (SBS).	1. Parents in the intervention group were more likely to take a break if frustrated with a crying infant (OR 3.10) and were more likely to state frustration caused infant shaking (OR 2.21). 2. Caregivers in the intervention group were more likely to state their knowledge of SBS was derived from hospital staff (OR 3.39).
Deyo et al. (2008) USA Pre-Post N=7051	**Population:** Mean Age=28yr; Gender: Male=0, Female=7051. **Intervention:** Mothers of newborn infants completed a pre-test of their knowledge of SBS before watching a short video and reviewing educational materials as part of the "Love me… Never shake me" program. After watching the video, the mothers completed a post-test. The intervention was provided only once and all mothers received a follow-up telephone call 3-4mo after participating in the program to test for retention. Assessments were conducted at baseline, post-treatment and 3-4mo follow-up. **Outcome Measure:** Custom Questionnaire Regarding SBS Knowledge.	1. A statistically significant increase in mothers' knowledge that it is okay to let an infant cry (p<0.050) was found of the post-test but no significant differences were found for any other questions. 2. At follow-up, 97% of mothers correctly defined SBS and the physiological consequences of shaking a baby, and 94% reported that they knew what to do when feeling stressed. 3. It was reported at follow-up that 62% of mothers did not receive any further information on SBS from their pediatricians.
Dias et al. (2005) USA Post-Test N=65,205	**Population:** TBI. **Intervention:** Parents of newborn infants were provided with a 1-page leaflet and watched an 11 min video about SBS before being asked to sign a commitment statement. The intervention was provided once only with a follow-up telephone call. Suspected cases of SBS were reviewed and cross-referenced with signed commitment statements. Assessments were conducted at 7 mo follow-up and annually by nursing managers. **Outcome Measures:** Incidence of SBS, Annual Nursing Managers' Survey.	1. In comparing incident rates of SBS in the 6 yr prior to the study and during the study period of 66 mo, a significant reduction was reported with 41.5 cases per 100,000 prior compared to 22.2 cases per 100,000 during the study (p=0.017). 2. When incidence rates were calculated based on year of birth instead of year of injury, a significant reduction for births during the study period was still found (p=0.022). 3. There was no significant difference for the incidence of SBS when comparing infants with and without a signed commitment statement (p=0.830). 4. At follow-up, only 27% of respondents discussed SBS in the annual survey completed by nursing managers, indicating that the 11 min videotape was not utilised frequently.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).

Discussion

A commonly used intervention for educating mothers about SBS and the strategies used to prevent such injuries is called PURPLE. Each letter in PURPLE represents a characteristic of crying in infants that is

troublesome for caregivers, potentially leading to SBS (Fujiwara et al., 2012). The PURPLE intervention has been shown to improve maternal knowledge of infant crying compared to an infant safety information control group (Barr et al., 2009; Fujiwara et al., 2012). Improvement in knowledge about infant shaking was not consistently identified, with two studies reporting no statistically significant improvement compared to the control group (Barr et al., 2009; Fujiwara et al., 2012) and one study reporting significant improvement (Barr et al., 2009). Overall, 95% of mothers post-intervention were reported to have a perfect score on knowledge of infant shaking following the PURPLE intervention, whereas only 57.4% scored perfectly on the crying knowledge subscale (Reese et al., 2014).

The improvement in knowledge of crying and shaking behaviours moderately translated into a change in behaviours following the PURPLE intervention. Mothers reported walking away from infant with inconsolable crying more than the control group (Barr et al., 2009; Fujiwara et al., 2012), and more mothers shared this information with other caregivers (Barr et al., 2009; Fujiwara et al., 2012). Two studies reported significant differences in caregivers who received PURPLE compared to controls in the sharing of information on the dangers of SBS with other caregivers (Barr et al., 2009) whereas another study reported no significant difference (Fujiwara et al., 2012). Overall, only 41% of mothers shared information that they had learned in the intervention with other care providers for their children (Reese et al., 2014). The most common reason for lack of sharing information was due to low perceived risk of infant shaking by the other caregiver. However, the majority of perpetrators of SBS are not mothers (Reese et al., 2014), and therefore the PURPLE intervention should be modified to increase the sharing of learned knowledge and to involve other caregivers.

Other educational programs have been evaluated for informing caregivers of the effects of SBS and its prevention. All of the programs that were implemented were short-term with little participant involvement. One program administered a brochure detailing on the steps to take when a child is crying inconsolably (Bechtel et al., 2011). Most programs used a brochure and short video (8-11min) combination (Altman et al., 2011; Deyo et al., 2008; Dias et al., 2005) and one used a talk from a pediatrician (Simonnet et al., 2014). These programs require minimal time to complete and are therefore attractive and relatively easily implemented. 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), helping parents change their behaviour, such as “taking a break if frustrated with a crying infant” (Bechtel et al., 2011), and were found to reduce the number of SBS cases post-implementation of the program (Altman et al., 2011; Dias et al., 2005).

Although all aforementioned studies improve caregiver knowledge on SBS, only a few evaluated the change in incidence of SBS following the educational interventions. Future research is warranted to determine the outcomes of educational interventions on rate of SBS.

Conclusions

There is level 1a evidence that the PURPLE intervention program may be effective for improving maternal knowledge of infant crying compared to an infant safety control group.

There is conflicting (level 1b) evidence regarding whether or not the PURPLE intervention program is effective at improving maternal knowledge of infant shaking, compared to an infant safety control group.

There is level 1a evidence that the PURPLE intervention program may be effective at improving maternal behaviours, such as walking away from an infant during inconsolable crying and sharing information on the dangers of shaken baby syndrome, compared to injury prevention educational materials.

There is level 4 evidence supporting the role of education programs for informing caregivers of children with shaken baby syndrome about its detrimental effects, helping parents change their behaviour, and reducing the number of shaken baby syndrome cases post intervention.

The PURPLE intervention for shaken baby syndrome may increase knowledge about crying and the effects of shaken baby syndrome among caregivers. It may also increase protective behaviours among caregivers, such as walking away during a period of inconsolable crying in their infant.

Education programs on infant crying and safety may be effective at informing parents about the dangers of shaken baby syndrome, helping change their behaviour, and reducing the number of shaken baby syndrome.

14.7 Conclusion

Overall the pediatric literature for ABI is sparse. It is imperative to determine preventative measures and interventions to reduce potential long-term effects of an ABI. Many of the interventions that were evaluated in this review have been studied and are effective in the adult ABI population. Children have different developmental trajectories compared to adults and there is also a developmental difference when comparing a young child to an adolescent. In children, a brain injury may affect the onset of a skill (i.e., skill acquisition may be delayed), the order of emergence of skills, the rate of skill development, and/or the degree to which complete development of a skill is attained. Therefore, health care professionals cannot generalize interventional studies conducted within the adult population to the pediatric ABI population. Further research is warranted in order to be able to make recommendations for the pediatric ABI population.

14.8 Summary

There is level 4 evidence that head elevation may reduce intracranial pressure, but not cerebral perfusion pressure, in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 24 hours is no different than normothermia at increasing mortality and unfavourable outcomes in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 24 hours may decrease intracranial pressure during cooling compared to normothermia in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 24 hours may decrease heart rate (24 hr post treatment), cerebral perfusion pressure (25-72 hr post treatment), and blood pressure (25-72 hr post treatment) compared to normothermia in children post TBI.

There is level 1a evidence that decreases in cerebral perfusion pressure and blood pressure during treatment with therapeutic hypothermia (for 24 hr) are associated with development of unfavourable outcomes in children post TBI.

There is level 1a evidence that therapeutic hypothermia delivered for 48 hours is no different than normothermia with respect to mortality or complications (arrythmias, coagulopathies, infections) in children post TBI.
There is level 1a evidence that therapeutic hypothermia delivered for 48 hours may temporarily (<24 h) lower intracranial pressure in children post TBI compared to normothermia.

There is level 1b evidence that hypothermia treatment maintained for 48 hours may preserve antioxidant defenses in children following a severe TBI, when compared to normothermia.

There is level 1b evidence that therapeutic hypothermia delivered for 72 hours with a cooling cap may improve short-term intracranial pressure (<72 hr) and reduce biomarkers of brain damage (S-100, NSE, CK-BB), compared to normothermia therapy in children post TBI.

There is level 4 evidence that hypothermia induced through cooling blankets placed on the patient's bed may decrease the duration of hyperthermic state and acetaminophen administration upon arrival to the pediatric ABI inpatient unit.

There is level 1b evidence that spine injury severity and midline shift on CT scans, fixed pupils, abdominal injury, and subarachnoid hemorrhage are associated with mortality and unfavourable outcomes, respectively, at 3 months post-TBI in a pediatric population that underwent hypothermia treatment.

There is level 1b evidence that serum sodium concentrations are inversely proportional to intracranial pressure, and directly proportional to cerebral perfusion pressure, after hypertonic saline or Lactated Ringer's solution therapy in children post TBI.

There is level 1b evidence that hypertonic saline is associated with a lower frequency of acute respiratory distress syndrome, shorter intensive-care unit stay, and lower rate of complications compared to treatment with Lactated Ringer's solution in children post TBI.

There is level 4 evidence that hyperosmolar therapy (3% hypertonic saline and mannitol) may not improve intracranial pressure or cerebral perfusion pressure, or increase serum osmolarity, in children post TBI.

There is level 4 evidence that intracranial pressure can be lowered acutely (within 30 minutes) after 7.5% hypertonic saline treatment, for as long as 72 hours, using 3% hypertonic saline treatment in children refractory to standard therapy (intracranial pressure >20 mmHg) post TBI.

There is level 4 evidence that hypertonic saline treatment (3 or 7.5%) may increase cerebral perfusion pressure, serum sodium, and serum osmolarity in children refractory to standard therapy (intracranial pressure>20 mmHg) post TBI.

There is level 4 evidence that 7.5% hypertonic saline treatment is associated with hypernatremia, kidney injury, acute respiratory distress syndrome, and low Glasgow Outcome Scale- Extended score (3-4) in children refractory to standard therapy (intracranial pressure>20 mmHg) post TBI.

There is level 2 evidence that treatment of children with TBI following a new hypertonic saline-based protocol may increase favourable discharge disposition, but not Glasgow Outcome Scale scores, compared to therapy without guidance of a strict protocol.

There is level 4 evidence that early (<30 minutes post episode) hypotension treatment may reduce mortality compared to non-early hypotensive treatment in children post TBI.

There is level 4 evidence 3% hypertonic saline may decrease intracranial pressure and increase cerebral perfusion pressure faster than fentanyl (2µg/kg) and pentobarbital (5mg/kg) in pediatric patients post TBI.

There is level 4 evidence that high-dose fentanyl, low-dose midazolam, and high-dose fentanyl in combination with low-dose midazolam may increase intracranial pressure in pediatric patients post TBI.

There is conflicting (level 4) evidence regarding whether or not fentanyl reduces intracranial pressure and improves cerebral perfusion pressure in children following a severe TBI.

There is level 4 evidence that pentobarbital may lower intracranial pressure and cerebral perfusion pressure in pediatric patients with refractory intracranial pressure post TBI.

There is level 1b evidence that amantadine may not improve level of consciousness (Coma/Near-Coma Scale, Coma Recovery Scale Revised, or Wee-FIM scores), but may improve blinded physicians' ratings of consciousness, compared to placebo in pediatric patients post ABI.

There is level 1b evidence that an amantadine administration consisting of 4 mg/kg/d for a week followed by 6 mg/kg may be a safe and effective protocol compared to placebo in pediatric patients post ABI.

There is level 4 evidence that dopaminergic agents may increase responsiveness (Western NeuroSensory Stimulation Profile scores) in pediatric patients post ABI.

There is level 1a evidence that administration of dexamethasone may inhibit endogenous production of glucocorticoids compared to placebo in pediatric patients post TBI.

There is level 1b evidence that dexamethasone administration may not improve Glasgow Outcome Scale (GOS) scores, intracranial pressure, or blood pressure, but may increase the risk of bacterial pneumonia, compared to placebo in pediatric patients post TBI.

There is level 1b evidence that N-Acetylcysteine in combination with probenecid may increase N-Acetylcysteine levels in cerebrospinal fluid, but may not be different from placebo in its effect on intracranial pressure, temperature, Glasgow Outcome Scale (GOS) scores, hospital length of stay, or mean arterial pressure, in pediatric patients post TBI.

There is level 2 evidence that magnesium sulfate may not affect hemodynamics (intracranial pressure, cerebral perfusion pressure, mean arterial pressure) compared to placebo in children post TBI.

There is level 3 evidence that the presence of abusive head trauma, high PRISM III score, and low post-admission Glasgow Coma Scale scores, but not anemia and blood transfusions, are associated with increased mortality in pediatric patients post TBI.

There is level 4 evidence that coagulation assessments performed upon admission to a pediatric inpatient unit may be potential prognostic indicators of favourable outcomes post TBI.

There is level 4 evidence that a decompressive craniectomy may improve intracranial pressure and cerebral perfusion pressure in pediatric patients post TBI.

There is level 1b evidence that a decompressive craniectomy is as effective as standard intracranial pressure management at reducing intracranial pressure in pediatric patients post TBI.

There is level 4 evidence that a late decompressive craniectomy (< 2hr post admission) and intraoperative blood loss (>300 mL) are associated with greater mortality and worse outcomes in pediatric patients undergoing this procedure post TBI.

There is level 4 evidence that children with a severe TBI are at risk of secondary complications following a decompressive craniectomy that may prolong rehabilitation.

There is level 4 evidence that patients who undergo a decompressive craniectomy have greater Glasgow Outcome Scale scores than pediatric patients with TBI who do not.

There is level 3 evidence that children who sustain a severe TBI from non-accidental trauma have poorer outcomes and higher odds of mortality following a decompressive craniectomy, when compared to accidental trauma victims.

There is level 4 evidence that supraciliary "keyhole" small craniotomies for the treatment of anterior frontal space occupying lesions are not associated with major operative or post-operative complications in pediatric patients post ABI.

There is level 4 evidence that a burr-hole craniotomy without continuous drainage for the treatment of either a chronic subdural hematoma or a subdural hygroma is not associated with complications in pediatric patients post ABI.

There is level 3 evidence that there may be no difference in mortality between pediatric patients post TBI who were treated either at an adult or pediatric trauma center.

There is level 1b evidence that phenytoin prophylaxis may not reduce the occurrence of early (<1 week post injury) or late (>1 week post injury) post traumatic seizures compared to placebo in children post TBI.

There is level 4 evidence that children who develop early post traumatic seizures while receiving levetiracetam prophylaxis are younger and have experienced abusive head trauma, compared to those that did not develop post traumatic seizures.

There is level 1b evidence that the administration of enhanced immune formulas may not be superior to regular formulas in regards to increasing caloric and protein intake in children post TBI.

There is level 1b evidence that enhanced immune formulas may be superior to regular formulas at reducing markers of infection and inflammation (interleukin-8 concentrations and early gastric colonization) and improving 24 hour nitrogen balance in children post TBI.

There is level 1b evidence that initiating nutritional support earlier after ABI results in a decrease in mortality and better outcomes.

There is level 2 evidence that cognitive behavioral therapy may reduce anxiety, depression, and internalizing behaviour compared to no therapy in pediatric patients post ABI.

There is level 2 evidence that cognitive behavioural therapy may be more effective at improving socialization and internalizing behaviour in children post ABI who are not receiving adjunct pharmacotherapy, compared to those who are.

There is level 4 evidence that self-monitoring training can improve on-task behaviour, but not accuracy in completing assignments or task engagement, in children post TBI.

There is level 4 evidence that behavioural therapies for children with ABI may be effective in reducing or eliminating problematic behaviours, lowering agitation, and increasing autonomy.

There is conflicting (level 1b) evidence as to whether a counsellor-assisted problem-solving (CAPS) group is superior to an internet resource comparison intervention at improving management of externalizing, internalizing, and socialization behaviours in pediatric patients post TBI.

There is level 1b evidence that a counsellor-assisted problem-solving program may be superior to an internet resource comparison intervention at reducing conflict between parents and adolescents post TBI.

There is conflicting (level 1b) evidence as to whether lower or higher socioeconomic patients benefit most from a counsellor-assisted problem-solving intervention compared to an internet resource intervention post TBI.

There is level 1b evidence that treatment (counsellor-assisted problem-solving versus internet resource comparison), gender, race, age, or socioeconomic status do not affect use of mental health services in pediatric patients post TBI.

There is level 1b evidence that an online problem-solving program with therapist assistance may not be superior to an internet resource comparison group at improving parent-teen communications and conflict post ABI.

There is level 1a evidence that an online problem-solving program with therapist assistance may be superior to an internet resource comparison group at improving compliant behaviour and self-management in children post TBI.

There is level 1a evidence that an online problem-solving program with therapist assistance may be superior to an internet resource comparison group at acutely improving anxiety, depression, and distress in the parents of children post ABI; however, only improvements in distress may be present at 18 months.

There is level 1a evidence that lower socioeconomic status is associated with greater reductions in distress and depressive symptoms following counsellor-assisted online therapy when compared to higher socioeconomic status in parents of children post ABI.

There is level 2 evidence that online problem solving with audio support may not be superior to the same program without audio support with regards to improving adolescent behavioural issues and depression in children post TBI.

There is level 1b evidence that an online parenting skills workshops (I-InTERACT) may improve positive parental involvement with their child, when compared with an internet resource group, in children post TBI.

There is level 1b evidence that an online parenting skills program (I-InTERACT) may not be superior to an internet resource comparison group at improving caregiver stress, distress, depression, and self-efficacy in individuals caring for children post TBI.

There is level 4 evidence that an app-based coaching intervention may increase confidence and participation frequency in pediatric TBI and brain tumor individuals.

There is level 2 evidence that the Stepping Stone Triple P program combined with Acceptance and Commitment Therapy may be superior to usual care at improving behavioural problems up to 6 months in children post ABI.

There is level 2 evidence that the Stepping Stone Triple P program combined with Acceptance and Commitment Therapy may improve parental distress, confidence, psychological flexibility, and conflict, but not depression, when compared to usual care in children post ABI.

There is level 2 evidence that face to face family problem solving therapy may be superior to usual care in terms of reducing internalizing problems (depression and anxiety) in children post TBI, but not parental distress or relationship satisfaction.

There is level 2 evidence that family-based therapy may be superior to standard clinician-directed care for improving intelligence, motor development, and functional independence in children post TBI.

There is level 4 evidence that a family focused inpatient social work program for parents/caregivers after their child's TBI may not significantly decrease feelings of trauma or grief any more than a usual care intervention.

There is level 4 evidence that a family focused inpatient social work program for parents/caregivers after their child's TBI may increase parent/caregiver confidence in managing the condition and feelings of more supportive counselling, increased family resources, and awareness of medical issues than a usual care intervention.

There is level 1b evidence that the allocation of community resource coordinators to a family post discharge may not be superior to standard care at improving functional outcomes in children following a TBI.

There is level 4 evidence that a multidisciplinary outpatient program may improve functional communication and behaviour, but not neuropsychological outcomes, in children post ABI.

There is level 1b evidence that family based online problem-solving programs, when compared to an internet resource comparison group, may improve functioning in school and the community, but not at home, at 12 months in adolescents post TBI.

There is level 4 evidence that interventions directed at strengthening the social interactions of children with brain injury may be temporarily beneficial.

There is level 2 evidence that a dedicated transitional hospital to school program does not demonstrate any increased benefits than a usual care group for children post TBI.

There is level 2 evidence that the use of amantadine can decrease the amount of aberrant behaviours, but may not improve cognitive functioning and problem solving, compared to usual care among children with a TBI.

There is level 3 evidence that amantadine is safe to administer in children following a TBI and facilitates rate of recovery, but not post-traumatic amnesia or hospital length of stay, post pediatric TBI.

There is level 1b evidence that the Amsterdam Memory and Training for children program may not improve sustained attention in pediatric patients post ABI compared an interactive program.

There is level 1b evidence that the Amsterdam Memory and Training for children may improve selective attention compared to an interactive program in pediatric patients post ABI.

There is level 2 evidence that the Attention Improvement and Management (AIM) program may improve sustained, but not selective, attention compared to healthy controls in children post TBI.

There is level 2 evidence that attention-specific neuropsychological training may improve attention compared to no training in pediatric patients post TBI.

There is level 2 evidence that a cognitive computerized training (CCT) program is feasible for use within a pediatric TBI population

There is conflicting (level 1b) evidence regarding whether or not methylphenidate improves cognitive behavioural function compared to placebo in children following a TBI.

There is level 2 evidence that the use of a pager system may improve memory and planning activities compared to having no pager system in adolescents post TBI.

There is level 4 evidence that rehabilitation focused around diary entries and self-instructional training may temporarily improve memory deficits in children post TBI.

There is level 2 evidence that sensory stimulation paired with cognitive neuropsychological rehabilitation may improve intellectual development in children with severe TBI compared to controls.

There is level 4 evidence that biweekly sessions of cognitive rehabilitation may improve memory skills in pediatric patients post TBI.

There is level 1a evidence that online counsellor-assisted problem solving programs may be superior to internet resource groups at improving executive function in adolescents post TBI.

There is level 1a evidence that older adolescents (14-17 years) benefit from counsellor-assisted problem solving programs more than younger (12-14 yr) adolescents in terms of improvements in executive functioning post TBI.

There is level 1b evidence that adolescents with a severe TBI, or poor vocabulary, benefit more from a counsellor-assisted problem solving program than adolescents with a moderate TBI, or adequate vocabulary, in terms of improvements in executive functioning post TBI.

There is level 1b evidence that the Strategic Memory Advanced Reasoning Training (SMART) program may improve higher-order cognitive deficits compared to bottom-up processing training in children post TBI.

There is level 1b evidence that metacognitive therapy may improve learning strategies and executive function compared to usual care in children and adolescents with an ABI.

There is level 4 evidence that the use of goal management therapy may improve parental ratings of executive function in young children who have sustained a TBI.

There is level 2 evidence that metacognitive problem-solving skills training may improve executive function and metacognitive abilities compared to no intervention in children post ABI.

There is level 4 evidence that electropalatography treatment may be effective at improving the articulatory component of dysarthria post TBI in children.

There is level 4 evidence that peer-group training of pragmatic language skills can improve pragmatic language behaviours and range of pragmatic communication abilities in children post ABI.

There is level 1b evidence that injury-related information interventions may not improve knowledge or awareness of injury-related deficits compared to placebo information sessions in children post TBI.

There is inconclusive (level 4) evidence regarding whether or not upper limb lycra splints improve the quality of movement in children post TBI.

There is level 2 evidence that constraint-induced movement therapy (CIMT) may improve motor function of the hemiparetic limb compared to no care in children post TBI.

There is level 2 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.

There is level 4 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.

There is level 2 evidence that exoskeleton, body-weight supported treadmill training paired with physiotherapy may be superior to physiotherapy alone at improving gait and motor function in pediatric patients post ABI.

There is level 4 evidence that an wearable ankle robot combined with a computer game interface may be beneficial in reducing spasticity and increasing balance in children post ABI.

There is level 4 evidence that Robot Mediated Therapy (RMT) combined with goal-oriented reaching tasks may improve upper limb motor function and spasticity in children post ABI.

There is level 2 evidence that botulinum toxin type A (BTX-A) used in combination with adjunct therapy (physiotherapy, occupational therapy) may decrease upper and lower limb spasticity, as well as movement range of motion, in children and adolescents post ABI.

There is level 4 evidence that intrathecal baclofen pumps may be effective at reducing spasticity in the upper and lower limbs for children with ABI as a result of hypoxia.

There is level 1b evidence that home based exercise programs may be superior to regular daily activities at improving balance, dexterity, and aerobic capacity short-term (<6 weeks) in children post ABI.

There is level 1a evidence that the PURPLE intervention program may be effective for improving maternal knowledge of infant crying compared to an infant safety control group.

There is conflicting (level 1b) evidence regarding whether or not the PURPLE intervention program is effective at improving maternal knowledge of infant shaking, compared to an infant safety control group.

There is level 1a evidence that the PURPLE intervention program may be effective at improving maternal behaviours, such as walking away from an infant during inconsolable crying and sharing information on the dangers of shaken baby syndrome, compared to injury prevention educational materials.

There is level 4 evidence supporting the role of education programs for informing caregivers of children with shaken baby syndrome about its detrimental effects, helping parents change their behaviour, and reducing the number of shaken baby syndrome cases post intervention.

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