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

8. Mental Health Issues Post Acquired Brain Injury

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Key Points

The effectiveness of sertraline in treating major depression post TBI is unclear due to conflicting findings.

Citalopram combined with carbamazepine may be an effective treatment for major depression post TBI.

Desipramine and methylphenidate may be effective treatments for major depression post TBI, although further research is required.

Cognitive behavioural therapy may be an effective treatment for depression following acquired brain injury.

Cognitive behavioral therapy may be effective when provided in groups or over the phone, although their relative effectiveness is unclear.

There may be no difference in the benefits between motivational interviewing and non-directive counselling when combined with cognitive behavioural therapy for the treatment of major depression in patients with TBI.

Mindfulness-based stress reduction may be an effective treatment for depression following traumatic brain injury.

Positive psychotherapy may increase happiness following TBI.

Neuro-systemic psychotherapy may be an effective treatment for depression following TBI.

Music therapy may be effective in reducing symptoms of depression following ABI.

Aerobic exercise and Tai Chi may improve mood following TBI, but aerobic exercise may not be effective in reducing symptoms of depression.

Psychosocial or cognitive rehabilitation may reduce depressive symptoms following TBI.

Community-based rehabilitation alone does not change depression and anxiety scores in patients after ABI.

Repetitive transcranial magnetic stimulation may improve cognition and depression.

Cognitive behavioural therapy may be an effective treatment for anxiety following ABI.

Cognitive behavioural therapy for anxiety may be similarly effective when delivered over the telephone as when delivered in a group.

It is unclear whether motivational interviewing is a more effective than non-directive counselling as an adjunct to cognitive behavioural therapy for anxiety.

Neurofeedback training may help reduce stress in patients recovering from ABI.

Group-based cognitive behavioural therapy may be an effective intervention for reducing feelings of hopelessness, a precursor of suicidal ideation, post TBI.

Problem-solving therapy may be a feasible intervention for reducing suicidal ideation post TBI; further research is required to determine its efficacy.

Sertraline may be an effective treatment for reducing aggression and irritability following brain injury, although additional research is needed.

Amitriptyline may be an effective treatment for reducing agitation following brain injury, although additional research is needed.

Amantadine requires further research before conclusions can be drawn regarding its effects on aggression and irritability following a TBI.

Methylphenidate may be effective in reducing anger following TBI.

Carbamazepine may be effective in reducing agitation and aggression following TBI.

Lamotrigine may be effective in reducing pathologic laughing and crying following a TBI. However, further research with larger sample sizes is needed to validate these findings.

Valproic acid may be effective in reducing aggression following a TBI, although additional research is needed.

Anticonvulsants may effective in reducing agitation following a TBI, although additional research is needed.

Quetiapine may be effective in reducing aggression following a TBI, although additional research is needed.

Ziprasidone may be effective in reducing agitation following a TBI, although additional research is needed.

Methotrimeprazine may be safe and effective for controlling agitation following an ABI, although additional research is required.

Droperidol may be effective in reducing agitation following TBI, although additional research is required.

Haloperidol appears to have no benefits, and possible negative effects on recovery, following a TBI.

Pindolol may be effective in reducing aggression following an ABI.

Propranolol may be effective in reducing the intensity of agitation and aggression following brain injury.

Lithium may reduce behavioural problems but is associated with a high risk of neurotoxicity.

Depo-Provera, in combination with directive counselling, may reduce sexual aggression following TBI, although additional research is needed.

Behavioural modification may be effective in improving behaviour following brain injury.

Cognitive behavioural therapy, self-management training, and antecedent interventions may be effective for anger management following TBI.

Social skills training may be effective in improving social behaviour following brain injury.

Music therapy may reduce post-coma agitation following a TBI, although additional research is needed.

Motivational interviewing and education may not be effective interventions for reducing substance abuse following TBI.

Financial incentives may increase signup, promote attendance, and attenuate dropout from substance abuse treatment programs following TBI; the impact of reducing logistical barriers is less considerable.

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Abbreviations

ABI   Acquired Brain Injury
BAC   Blood Alcohol Concentration
BAL   Blood Alcohol Level
CBT   Cognitive Behavioural Therapy
CSG   Coping Skills Group
GCS   Glasgow Coma Score
MBSR Mindfulness-Based Stress Reduction
OCD   Obsessive Compulsive Disorder
PCT   Prospective Controlled Trial
PEDro Physiotherapy Evidence Database rating scale
PTSD Post-Traumatic Stress Disorder
RCT   Randomized Control Trial
TBI   Traumatic Brain Injury

Mental Health Issues Post Acquired Brain Injury

8.0 Introduction

Mood is an internal subjective state, but it is often inferred from the way we behave and express ourselves. Following acquired brain injury (ABI), individuals may suffer from mood disorders such as major depression and various anxiety disorders. Challenging behaviours such as agitation and aggression, as well as addictive behaviours such as substance abuse, may also become a significant problem post ABI. These mental health issues are associated with worsening of other ABI sequela and poorer outcomes (Bedard et al., 2003; Berthier et al., 2001; Jorge, 2005). Among 361 individuals with severe ABI, Silver et al. (2001) found that the most prevalent issues were major substance abuse or dependence (34%) and depression (11.1%); these findings are similar to previous reports by other researchers (Deb et al., 1999; Hibbard et al., 1998; van Reekum et al., 1996).

Depression and *anxiety* post ABI are associated with individuals feeling tired, helpless, hopeless, socially withdrawn, and having difficulty concentrating. These disorders often arise once the implications of the injury become apparent, which may be a reaction to the injury or the result of the neurological changes that have taken place. For some, depression and anxiety will develop within months of the injury, but for others it will be a few years before clinical symptoms are diagnosed (Deb et al., 1999). Pharmacotherapy, counseling, and exercise have demonstrated some efficacy in treating depression and anxiety post ABI.

Suicidal ideation and attempts are also more frequent among the TBI population. Rates of suicidal ideation (23-28%) (Mackelprang et al., 2014; Simpson & Tate, 2002; Tsaousides et al., 2011) and attempts (26%) (Simpson & Tate, 2005) are high post TBI, but can be further augmented through the presence of emotional disturbance and substance abuse (Simpson & Tate, 2005). Counseling is a typical intervention for suicide prevention.

Challenging behaviour following ABI occurs with a relatively high frequency (25-50%) (Baguley et al., 2006). Challenging behaviours include agitation, anger, aggression, non-compliance with treatment, and difficulties with emotional regulation. The emergence of these behaviours likely arises from injury to the frontal lobes, resulting in disinhibited behaviour and lack of recognition of the associated consequences. Behavioural management and pharmacological treatment are often used to address these challenges, each with varying levels of success.

Addictive behaviours can be a serious problem for some individuals post ABI. In TBI populations, pre-injury substance use disorders are more common than the general population (Alway et al., 2016; Hibbard et al., 1998). Pre-injury substance use is a significant predictor of abuse after TBI (Alway et al., 2016). Alcohol abuse has also been linked to major depression both before (Dikmen et al., 2004; Seel et al., 2010) and after injury (Jorge, 2005), although it remains unclear as to which problem evolved first. Educational and interventional programs have been implemented to address addictive behaviours post ABI.

Affective symptoms such as depression and anxiety along with aggression, agitation, and addictive behaviours appear to be important determinants of functional and quality of life outcomes. They frequently cause significant distress for individuals with ABI and their family members, and may result in diminished access to services. This module will review the available evidence for both pharmacological and non-pharmacological treatments for each. Issues regarding the use of restraints will also be discussed.

8.1 Depression

In Canada, approximately 11% of adults experience depression at some point during their lives, and women are almost twice as likely as men to experience depression (Knoll & MacLennan, 2017). For those who sustain an ABI, depression is the most common mood disorder diagnosed (Jean-Bay, 2000; Jorge, 2005; Osborn et al., 2018; Seel et al., 2010; Underhill et al., 2003). Studies have suggested the development of depression may be related to the location of injury, a pre-existing mental health condition, TBI severity (Scholten et al., 2016; Singh et al., 2018), personality type, family support, social support, psychological stressors, and/or neurochemical imbalances (Bay & Covassin, 2012; Bombardier et al., 2016; Cnossen et al., 2016; Jorge, 2005; Ownsworth & Oei, 1998; Rosenthal et al., 1998; Sigurdardottir et al., 2013). Moreover, depression has been associated with poorer functional recovery and quality of life following ABI (Anke et al., 2015; Grauwmeijer et al., 2018; Hudak et al., 2012; Kumar et al., 2018).

It is often difficult to diagnose depression post ABI due to the complexities of the injury itself (Underhill et al., 2003). Distinguishing between depression and the behaviours resulting from the injury can prove to be challenging as there is overlap between symptoms. For example, the gradual decline in the ability to perform everyday tasks and cope with everyday stressors, as well as an increase in irritability and behavioural issues may be symptoms of either depression or brain injury (Fleminger et al., 2003).

8.1.1 Incidence and Prevalence of Depression

Depression is the most common psychiatric condition following ABI, with incidence rates higher than the general population (Gould et al., 2011; Osborn et al., 2014; Osborn et al., 2018; Ouellet et al., 2018; Singh et al., 2018). Often, depression presents within the first-year post ABI (Alway et al., 2016; Scholten et al., 2016). In patients one-year post ABI reports of prevalence are variable, ranging from 13% to 61% (Alway et al., 2016; Fleminger et al., 2003; Gordon et al., 1998; Grauwmeijer et al., 2018; Osborn et al., 2014; Sigurdardottir et al., 2013). Accurate estimations of prevalence is challenging given mixed populations, risk factors that are not completely understood, and variable methods of diagnosis (Osborn et al., 2018). A meta-analysis conducted by Osborn et al. (2014) reported that 21% to 43% of individuals have depression within the first five years of TBI, which then stabilizes to approximately 22% after five years. A systematic review and meta-analysis by Scholten et al. (2016) reported pooled prevalence rates in TBI patients increased over time with long-term rates of depression estimated at 43%. Another meta-analysis by Osborn et al. (2018) estimated rates at 30%. However, these reviews, along with the majority of the literature, are specific to TBI, and reports rates of depression in populations of mixed injury severity. In two long-term prospective cohorts of patient with moderate to severe TBI, rates of depression were 4-6 times higher than the general population (Alway et al., 2016) and prevalence was 20% 10 years after TBI (Grauwmeijer et al., 2018). Overall, the risk for depression is high post ABI, and unlike many mood disorders, remains this way for years following injury (Alway et al., 2016; Grauwmeijer et al., 2018; Hoffman et al., 2010; Ponsford et al., 2018; Scholten et al., 2016).

8.1.2 Pharmacological Interventions for Depression

Following ABI, depression can be treated pharmacologically. Among these interventions are various antidepressants: selective serotonin reuptake inhibitors such as paroxetine, fluoxetine, sertraline, or citalopram; serotonin norepinephrine reuptake inhibitors such as duloxetine, milnacipran, and venlafaxine; and tricyclic antidepressants such as amitriptyline and nortriptyline. Anticonvulsants such as carbamazepine have also been used to treat depression post ABI. Various pharmacological interventions for post-ABI depression are summarized in Table 8.1.

Table 8.1 Pharmacological Interventions for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Sertraline		
Ashman et al. (2009) USA RCT PEDro=10 N=41	**Population:** TBI; Mean Age=49.1yr; Gender: Male=24, Female=17; Mean Time Post Injury=17.7mo; Injury Severity: Mild=15, Moderate=16, Severe=10. **Intervention:** Patients were diagnosed with major depression. The treatment group (n=22) received sertraline (25mg adjusted every 2wk, up to 100 mg) and the control (n=19) received a placebo, both for 10wk. **Outcome Measure:** Diagnostic and Statistical Manual of Mental Disorders (DSM), Hamilton Rating Scale for Depression (HAM-D), Beck Anxiety Inventory (BAI), Life-3 Scale (QOL).	1. Treatment responders, based on HAM-D (score <10 or decreased by 50%), were 59% in the treatment group and 32% in the control (p=0.08). Changes in scores on the HAM-D, BAI, and QOL scales showed improvement (p<0.001) but no group effects were found.
Desipramine		
Wroblewski et al. (1996) USA RCT PEDro=4 N=10	**Population:** TBI; Mean Age=32.2yr; Gender: Male=7, Female=3; Mean Time Post Injury=1.5yr; Injury Severity=Severe. **Intervention:** Patients were diagnosed with major depression. The treatment group (n=6) received desipramine (150 mg/d for 30day, 150-300 mg/day after) and the control group (n=4) received a placebo. The control group crossed over and received desipramine after day 30. **Outcome Measure:** Diagnostic and Statistical Manual of Mental Disorders (DSM), Affect/Mood Scale (AMS).	1. Three individuals from each group had nearly complete resolution of depression (DSM) on desipramine. 2. Seventy percent of subjects showed improvement over time on the AMS. 3. There were different rates of improvement over time in those started on the desipramine rather than placebo, with the treatment group making more rapid and greater improvements (p=0.001).
Multiple Medications Evaluated		
Lee et al. (2005) Korea RCT PEDro=8 N=30	**Population:** TBI; Gender: Male=24, Female=6. *Group A (n=10):* Mean Age=35.3yr; Mean Time Post Injury=34.8d. *Group B (n=10):* Mean Age=33.6yr; Mean Time Post Injury=31.9d. *Group C (n=10)*: Mean Age=35.5yr; Time Post Injury=30d. **Intervention:** Patients diagnosed with major depression were assigned to one of three groups for 4wk: Group A received methylphenidate (5mg/d increased to 20mg/d); Group B received sertraline (25mg/d increased to 100mg/d); or Group C received placebo. **Outcome Measure:** Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HAM-D).	1. In all 3 groups, scores on the HAM-D and BDI improved from the baseline and week 4 (Group A, p<0.001 on both measures; Group B, p<0.01, for both; Group C, p<0.05 BDI and p<0.01 for HAM-D). 2. Groups A (p=0.005) and B (p=0.05) were significantly superior to Group C on the HAM-D. 3. The number of adverse events was significantly higher in Group B than Group A (13 versus 6, p=0.010).
Perino et al. (2001) Italy Pre-Post N=20	**Population:** TBI; Gender: Male=11, Female=9. *Group A (n=11)*: Mean Age=26.9yr; Mean GCS Score=5.5; Mean Time Post Injury=4.7 mo. *Group B (n=9)*: Mean Age=31.3yr; Mean GCS Score=6.1; Mean Time Post Injury=34.6 mo. **Intervention:** Patients diagnosed with major depression received citalopram (20 mg/day) and carbamazepine (600 mg/day), and were divided	1. Total sample significantly improved from baseline to 12wk on the BPRS (62.3±17.6 versus 51.7±12.8, p≤0.05) and CGI (4.4±1.1 versus 3.4±0.8, p≤0.005). 2. When comparing groups, Group B had higher global scores on the BPRS at baseline and 12wk than Group A.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	into subgroups based on time post injury (Group A, <6mo; Group B, 24-36mo). **Outcome Measure:** Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI).	

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

Discussion

A single, small crossover randomized control trial (RCT) found that desipramine, a tricyclic antidepressant, was effective in treating chronic depression (Wroblewski et al., 1996). Three individuals in the treatment group, and three in the control group following crossover, had near complete resolution of depression. However, additional studies are necessary before conclusions can be made regarding this medication.

Two RCTs examined the effects of sertraline on depression following TBI (Ashman et al., 2009; Lee et al., 2005). One RCT randomized participants with major depression to a sertraline or placebo group (Ashman et al., 2009). The authors found improvements over time for both groups in terms of depression, anxiety, and quality of life. While no statistically significant differences were found between the two groups, the sertraline group had a significantly greater proportion of treatment responders than the placebo group. Another RCT randomized participants to a sertraline, methylphenidate, or placebo group (Lee et al., 2005). Similar to the previous study, all participants improved on measures of depression; however, the study results indicated that those assigned to the sertraline and methylphenidate groups had significantly lower depression scores than the placebo group at the end of the study (Lee et al., 2005). As well, fewer adverse events were reported for individuals receiving methylphenidate than those receiving sertraline.

The remaining study examined the effects citalopram and carbamazepine on depression post TBI (Perino et al., 2001). The study found that a combination of citalopram and carbamazepine significantly reduced depressive symptoms in patients diagnosed with depression after 12 weeks (Perino et al., 2001).

Conclusions

There is level 1b evidence that methylphenidate may be an effective treatment for major depression post TBI compared to placebo.

There is level 2 evidence that desipramine may be an effective treatment for major depression post TBI compared to placebo.

There is level 4 evidence that a combination of citalopram and carbamazepine may be an effective treatment for major depression post TBI.

There is conflicting (level 1b) evidence as to whether sertraline is a more effective treatment than placebo for major depression post TBI.

> **The effectiveness of sertraline in treating major depression post TBI is unclear due to conflicting findings.**
>
> **Citalopram combined with carbamazepine may be an effective treatment for major depression post TBI.**
>
> **Desipramine and methylphenidate may be effective treatments for major depression post TBI, although further research is required.**

8.1.3 Non-Pharmacological Interventions for Depression

Several non-pharmacological Interventions have been used to treat depression post ABI including: cognitive behavioural therapy (CBT), mindfulness-based stress reduction (MBSR), other forms of psychotherapy, exercise, music therapy, and transcranial stimulation. There is preliminary evidence for multiple non-pharmacological interventions for mood, and the treatment of depression in particular; however, non-pharmacological interventions are often considered as adjunct interventions to pharmacological treatment.

8.1.3.1 Cognitive Behavioural Therapy

CBT is the primary psychotherapy for anxiety and depression in the general population (Butler et al., 2006). CBT focuses on teaching cognitive skills, such as challenging unhelpful thoughts, and behavioural skills, such as coping, relaxation, graded exposure, and activity scheduling. In a meta-analysis of CBT for the treatment of depression following ABI, Waldron et al. (2013) found a large treatment effect when CBT was focused on the treatment of depression. Of note, Waldron et al. (2013) included all brain injury severities (including mild brain injury) and cerebrovascular accidents within the ABI population examined.

Table 8.2 Cognitive Behavioural Therapy for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Ponsford et al. (2016) Australia RCT PEDro=7 N_{Start}=75, N_{End}=51	**Population:** TBI. *CBT+MI Group (n=26):* Mean Age=46.69yr; Gender: Male=18, Female=8; Mean Time Post Injury=4.88yr; Mean GCS=10.43. *CBT+NDC Group (n=26):* Mean Age=39.88yr; Gender: Male=20, Female=6; Mean Time Post Injury=3.58yr; Mean GCS=10.48. *WC Group (n=23):* Mean Age=39.87yr; Gender: Male=17, Female=6; Mean Time Post Injury=2.61yr; Mean GCS=8.23. **Intervention:** Participants diagnosed with depression and/or anxiety were allocated to receive cognitive behavioural therapy (CBT) with either motivational interviewing (CBT+MI) or non-directive counseling (CBT+NDC), or to a waitlist control (WC). MI and NDC were each delivered for 3wk, followed by 9wk of CBT, with	1. All groups demonstrated significant improvements on the DASS-Depression, HADS-Anxiety, and SPRS-2 over time. 2. On the DASS-Depression, there was a significantly greater reduction in score over time in CBT+MI versus WC (p<0.005) but not CBT+NDC versus WC; there was no significant difference between CBT+MI and CBT+NDC. 3. On the HADS-Anxiety, there was a significantly greater reduction in score over time in CBT+NDC versus WC (p<0.05) but not CBT+MI versus WC; there was no significant difference between CBT+MI and CBT+NDC.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	three CBT booster sessions 21-30wk from baseline. Assessments were conducted at baseline, 3wk, 12wk, 21wk, and 30wk. **Outcome Measure:** Depression, Anxiety & Stress Scale (DASS), Hospital & Anxiety Depression Scale (HADS), Sydney Psychosocial Reintegration Scale 2 (SPRS-2).	4. On the SPRS-2, there was no significant difference in improvement between groups over time. 5. Higher baseline DASS-Depression and HADS-Anxiety scores were significantly associated with greater response to treatment (r=0.34, $p < 0.05$ and r=0.37, $p < 0.05$, respectively). 6. When combining CBT+MI and CBT+NDC groups, there were significantly greater improvements on HADS-Anxiety ($p < 0.05$), DASS-Depression ($p < 0.005$), and SPRS-2 ($p < 0.05$) in the combined group versus WC.
Ashman et al. (2014) USA RCT PEDro=7 $N_{Initial}$=54, N_{Final}=43	**Population:** TBI. *CBT Group (n=28)*: Mean Age=47.5yr; Gender: Male=10, Female=18; Mean Time Post Injury=7.8yr; Severity: Mild=10, Moderate/Severe=17. *SPT (n=26)*: Mean Age=47.1yr; Gender: Male=12, Female=14; Mean Time Post Injury=13.2yr; Severity: Mild=9, Moderate/Severe=12. **Intervention:** Participants diagnosed with depression were randomized to receive cognitive behavioural therapy (CBT) or supportive psychotherapy (SPT). The CBT group received treatment based on standard techniques with focus on cognitive restructuring and reshaping automatic thoughts. The SPT group received client-centered treatment to improve ability to deal with daily problems effectively. Both groups had 90min sessions 2 day/wk for the first week, followed by 50min sessions 1 day/wk for 3mo. Assessments were conducted before and after each treatment session. **Outcome Measure:** Beck Depression Inventory-Second Edition (BDI-II), State-Trait Anxiety Inventory (STAI), Life-3.	1. Rate of remission of depression between groups was not statistically significant (p=0.16), but 35% in CBT group were no longer depressed at end of treatment compared to 17% in SPT group. 2. Within groups, there was a significant improvement on BDI-II scores in the CBT group (p=0.03) and a marginal improvement in the SPT group(p=0.06). 3. No significant differences in anxiety between groups were found at the end of treatment (p=0.12). 4. No significant differences in quality of life as measured by Life-3 were found at the end of treatment ($p > 0.05$).
D'Antonio et al. (2013) USA RCT PEDro=6 N=44	**Population:** TBI; Mean Age=48.8yr; Gender: Male=19, Female=25; Mean Time Post Injury=7.7yr. **Treatment:** Participants diagnosed with depression were randomized to receive 16 sessions of cognitive behavioural therapy (CBT) or supportive psychotherapy (SPT) for over 3mo. For both groups, the first session lasted 90min and each subsequent session was 50min. Assessments were conducted at baseline and 3mo. **Outcome Measure:** Beck Depression Inventory-II (BDI-II).	1. The CBT group reported significant decreases in sadness, loss of interest, and loss of interest in sex ($p < 0.05$). 2. The SPT reported decreases in agitation ($p < 0.05$), irritability ($p < 0.01$), and the somatic factor of the BDI-II ($p < 0.05$). 3. Overall BDI-II scores significantly decreased compared to baseline for both groups ($p < 0.05$). 4. No significant differences were found for individual items or total score of the BDI-II between groups after treatment.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Anson & Ponsford (2006) Australia RCT PEDro=5 N=31	**Population:** TBI; Gender: Male=26, Female=5. *Group A (n=15)*: Mean Age=38.9yr; Mean Time Post Injury=755.8d. *Group B (n=16)*: Mean Age=37.8yr; Mean Time Post Injury=340.8d. **Intervention:** For Group A (n=15), baseline phase was 5wk, followed by 5wk of intervention, and a 5wk follow-up phase. For Group B (n=16), baseline was 10wk, followed by 5wk of intervention and a 10wk follow-up phase. The CSG consisted of 10 group sessions and ran for 900min 2×/wk. **Outcome Measure:** Coping Scale for Adults, Hospital Anxiety and Depression Scale, Rosenberg Self Esteem scale.	1. No significant changes in anxiety or self-esteem scores were noted following the CSG (p>0.05). 2. Although levels of depression and psychosocial dysfunction were significantly different between the two groups (p<0.05) participation in the CSG did not have an effect on their scores. 3. Both groups significantly increased their adaptive coping skills following the CSG (p<0.01).
Hodgson et al. (2005) Australia RCT PEDro=5 N=12	**Population:** ABI; Gender: Male=7, Female=5. *Treatment Group (n=6)*: Mean Age=44.2yr; Mean Time Post Injury=96.7mo. *Waitlist Group (n=6)*: Mean Age=33.8yr; Mean Time Post Injury=150.5mo. **Intervention:** Participants were randomized to receive cognitive behavioural therapy (CBT) or waitlist control. The CBT treatment program consisted of relaxation training, cognitive strategies, graded exposure, and assertiveness skills training. CBT was delivered in 1hr sessions 1 day/wk for 9-14wk. Assessments were conducted before and after treatment, and at 1mo follow-up. **Outcome Measure:** Hospital Anxiety and Depression Scale (HADS), Social Phobia and Anxiety Inventory (SPAI), Coppersmith Self Esteem Inventory.	1. After treatment, the CBT group had significantly lower scores on HADS-Depression, HADS-Anxiety, and SPAI than the control group (p<0.05). 2. At follow-up, the treatment group maintained improvement relative to the control group.
Fann et al. (2015) USA PCT $N_{Initial}$=100, N_{Final}=72	**Population:** TBI; Mean Age=45.8yr; Gender: Male=63, Female=37; Mean Time Post Injury=3.33yr; Severity: Moderate=69, Severe=31. **Intervention:** Participants diagnosed with depression received cognitive behavioural therapy (CBT) on telephone (CBT-T), CBT in person (CBT-IP), or usual care (UC). Both CBT treatments consisted of 30-60 min weekly sessions for 12wk, where in-session work and inter-session homework was assigned. UC group received a phone call encouraging them to continue rehabilitation and directing them towards community resources. Assessments were conducted at baseline, 8wk, 16wk, and 24wk. **Outcome Measure**: Structured Clinical Interview for DSM (SCID), Hamilton Rating Scale for Depression (HAM-D), Symptom Checklist-20 (SCL-20), Patient Global Impression (PGI), Satisfaction with Depression Care (SDC).	1. On SCID, there were no significant differences in rate of depression diagnosis for CBT-T versus UC, CBT-IP versus UC, or combined CBT versus UC at 16wk or 24wk (p>0.05). 2. On HAM-D, there were no significant differences for CBT-T versus UC, CBT-IP versus UC, or combined CBT versus UC at baseline, 8wk, 16wk, or 24wk (p>0.05). 3. On SCL-20, CBT-T showed significantly greater improvement than UC at 8wk (p=0.002) and 16wk (p=0.043), but not 24wk (p=0.065). 4. On SCL-20, there were no significant differences between CBT-IP and UC at baseline, 8wk, 16wk, or 24wk (p>0.05). 5. On SCL-20, combined CBT showed significantly greater improvement than UC at 8wk (p=0.001), but not at 16wk (p=0.074) or 24wk (p=0.250).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
		6. On PGI at 16wk, there was significantly greater satisfaction with combined CBT (p=0.010) and CBT-T (p=0.012), but not CBT-IP (p=0.133), than UC. 7. On PGI at 24wk, there was significantly greater satisfaction with combined CBT (p=0.040) and CBT-T (p=0.026), but not CBT-IP (p=0.633), than UC. 8. On SDC at 16wk, there was significantly greater satisfaction with combined CBT (p<0.001), CBT-T (p<0.001), and CBT-IP (p=0.007) than UC. 9. Participants without pre-TBI depression had a significantly larger decrease in HAM-D score (p=0.036) and SCL-20 score (p=0.008) when randomized to CBT than UC, whereas those with prior depression did not show a difference.
Ashworth et al. (2015) UK Pre-Post N=12	**Population:** TBI=7, Stroke=3, ABI=2; Mean Age=40.9yr; Gender: Male=7, Female=5. **Intervention:** Participants received two phases of compassion-focused therapy (CFT) 1 day/wk for 18wk. Group sessions focused on identifying emotions that encompass ABI and strategies to manage them. Individual sessions addressed content from mood groups and in-depth development of CFT skills. Inter-session homework was encouraged. Assessments were conducted at baseline, 18wk, and 3mo follow-up. **Outcome Measure**: Hospital Depression and Anxiety Scale (HADS), Forms of Self-Criticism/Self-Attacking and Self-Reassuring Scale (FSCRS).	1. Significant decreases in depression and anxiety on the HADS from baseline to post treatment and baseline to follow-up (p<0.05). 2. Significant increase in reassured self and reductions in hatred and inadequate self, according to FSCRS, from baseline to post-treatment and baseline to follow-up (p<0.05).
Arundine et al. (2012) Canada PCT N$_{Initial}$=20, N$_{Final}$=17 Follow up to Bradbury et al. (2008)	**Population:** TBI=10, ABI=10, Severity: Moderate-Severe. *CBT Group (n=10):* Mean age=39.8yr; Gender: Male=5, Female=5; Mean Time Post Injury=7.00yr. *EC Group (n=10):* Mean age=42.5yr; Gender: Male=5, Female=5; Mean Time Post Injury=11.4yr. **Intervention:** Participants with psychological distress were randomized to receive cognitive behavioural therapy (CBT) or education control (EC). CBT involved one individual introductory session, and then 10 sessions either in a group (CBT-G) or individually by telephone (CBT-T). EC group received CBT after initial group. Assessments were conducted at baseline, post treatment, 1mo follow-up, and 6mo follow-up. **Outcome Measure:** Depression Anxiety Stress Scales 21 (DASS-21), Symptom Checklist 90 Revised (SCL-90-R).	1. At 6mo follow-up, all participants showed significant improvements from baseline on DASS-21 (p<0.01) and SCL-90-R (p<0.01); CBT-G and CBT-T were comparable.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Bradbury et al. (2008) Canada PCT N=20	**Population:** TBI=10, ABI=10, Severity: Moderate-Severe. *CBT Group (n=10):* Mean age=39.8yr; Gender: Male=5, Female=5; Mean Time Post Injury=7.00yr. *EC Group (n=10):* Mean age=42.5yr; Gender: Male=5, Female=5; Mean Time Post Injury=11.4yr. **Intervention:** Participants with psychological distress received cognitive behavioural therapy (CBT) or education control (EC). CBT involved one individual introductory session, and then 10 sessions either in a group (CBT-G) or individually by telephone (CBT-T). Assessments were conducted at baseline, post treatment, and 1mo follow-up. **Outcome Measure:** Depression Anxiety Stress Scales 21 (DASS-21), Symptom Checklist 90 Revised (SCL-90-R).	1. At post treatment and 1mo follow-up, combined CBT showed significantly greater improvement from baseline than EC on DASS-21 ($p<0.001$) and SCL-90-R ($p<0.01$). 2. On DASS-21 and SCL-90-R, there were significant improvements from baseline to post treatment and to 1mo follow-up for CBT-G ($p<0.01$) and CBT-T ($p<0.05$), but there were no there were no significant improvements from post treatment to 1mo follow-up ($p>0.05$). 3. There were no significant differences between CBT-G and CBT-T at any time point on DASS-21 or SCL-90-R ($p>0.05$).

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

Discussion

In an early trial, Hodgson and colleagues (2005) found that CBT significantly reduced symptoms of depression and anxiety post ABI compared to a waitlist control. Similarly, Anson and Ponsford (2006) compared a CBT program to a waitlist control in individuals post TBI. While participants in CBT increased their adaptive coping skills, there were no significant improvements in depressive symptoms, anxiety, or self-esteem. Follow-up analysis revealed that participants who had greater self-awareness and self-esteem, as well as fewer depressive symptoms, demonstrated better outcomes with the program (Anson & Ponsford, 2006). It should be noted that participants in these studies were not diagnosed with a depressive disorder, and so conclusions cannot be drawn regarding CBT as a formal treatment for depression.

In patients with a diagnosis of depression post TBI, CBT was compared to a waitlist control in three trials. Two trials delivered CBT either in a group or by telephone (Bradbury et al., 2008; Fann et al., 2015), and one trial combined CBT with motivational interviewing or non-directive counselling (Ponsford et al., 2016). In the first trial, the authors reported significantly greater reductions in depression, anxiety, stress, and psychological impairment with CBT than control for up to six months after treatment (Arundine et al., 2012; Bradbury et al., 2008). As well, the authors found no significant differences between group CBT and telephone CBT in terms of efficacy. In the second trial, CBT did not demonstrate significant reductions in depression when compared to controls, whether in person, by phone, or combined (Fann et al., 2015). The telephone CBT significantly reduced psychological impairment relative to the control, but in-person CBT and combined CBT were not superior. Patients' subjective response to telephone CBT and combined CBT were more favourable than the control, and all forms of CBT had greater levels of satisfaction with depression care than the control. In the third trial, CBT demonstrated significant reductions in depression compared to the control when combined with motivational interviewing, but not non-directive counselling; there were no significant differences between the CBT groups (Ponsford et al., 2016). The

authors also noted that participants with greater baseline depression had significantly greater response to CBT.

Supportive psychotherapy was compared to CBT in two RCTs; both trials only included patients diagnosed with depression following ABI (Ashman et al., 2014; D'Antonio et al., 2013). In both trials, overall depression scores decreased from baseline following treatment. However, there were no significant differences in effectiveness between the two treatments (Ashman et al., 2014; D'Antonio et al., 2013). Compassion-focused therapy is a form of CBT that incorporates compassionate mind training (Gilbert, 2018). One small pre-post study found that this form of CBT led to a reduction in symptoms of depression and anxiety post ABI, although the participants did not have a depression and/or anxiety diagnosis (Ashworth et al., 2015). Moreover, participants demonstrated greater self-reassurance and self-adequacy, as well as less self-hatred after the treatment.

Conclusions

There is level 1a evidence that cognitive behavioural therapy may be an effective treatment for depression compared to waitlist controls post TBI.

There is level 1a evidence that cognitive behavioural therapy may be no more effective than supportive psychotherapy as a treatment for depression post TBI.

There is level 1b evidence that cognitive behavioural therapy combined with motivational interviewing or non-directive counselling may be equally effective treatments for depression post TBI.

There is level 2 evidence that cognitive behavioural therapy, compared to controls, may improve adaptive coping but may not reduce depressive symptoms post TBI.

There is level 4 evidence that compassion-focused therapy reduces depressive symptoms post ABI.

There is level 1b evidence that cognitive behavioural therapy is effective when delivered over the phone or in person.

Cognitive behavioural therapy may be an effective treatment for depression following acquired brain injury.

Cognitive behavioral therapy may be effective when provided in groups or over the phone, although their relative effectiveness is unclear.

There may be no difference in the benefits between motivational interviewing and non-directive counselling when combined with cognitive behavioural therapy for the treatment of major depression in patients with TBI.

8.1.3.2 Mindfulness-Based Stress Reduction

MBSR is a program that incorporates mindful meditation, body awareness, and yoga to promote relaxation and stress management (Shapiro et al., 1998). It has been evaluated as a potential intervention for depression in individuals with ABI (Table 8.3).

Table 8.3 Mindfulness-Based Stress Reduction for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Bedard et al. (2014) Canada RCT PEDro=6 N=76	**Population:** TBI; Gender: Male=42, Female=34; Mean Age=46.5yr; Mean Time Post Injury=4.25yr. **Intervention:** Participants were diagnosed with depression. The treatment group (n=38) received 1.5hr weekly sessions of mindfulness-based cognitive therapy for 10wk. The control group (n=38) received usual care. Assessments were conducted at baseline, 10wk, and 3mo follow-up. **Outcome Measure:** Beck Depression Inventory II (BDI-II), Patient Health Questionnaire 9 (PHQ-9), Symptom Checklist 90 Revised (SCL-90-R). Philadelphia Mindfulness Scale (PHLMS), Toronto Mindfulness Scale (TMS).	1. The treatment group showed significantly greater reduction in BDI-II scores than the control group (p=0.029), which was maintained at the 3mo follow-up. 2. No significant between-group differences on PHQ-9 and SCL-90-R were found (p>0.05). 3. Neither PHLMS nor TMS reached significance in demonstrating increases in mindfulness for the treatment group (p>0.05).
Combs et al. (2018) United States Pre-Post N$_{Initial}$=29, N$_{Final}$=19	**Population:** TBI=15, ABI=4; Mean Age=32.8yr; Gender: Male=17, Female=2; Severity of Injury: Mild=3, Severe=12, ABI patients not specified. **Intervention:** Inpatients at a Veterans Affairs Polytrauma Rehabilitation Program (PTRP) participated in mandatory mindfulness-based group interventions. Participants beliefs were evaluated with a questionnaire before starting and when leaving PTRP. **Outcome Measures:** Questionnaires about current pain, TBI symptoms, sleep, psychological function, and beliefs about mindfulness and yoga. Format based on Beliefs About Yoga Scale (BAYS)	1. Participants generally perceived some benefit from attending the mindfulness-based group interventions. 2. The number of mindfulness-based group session showed significant positive correlations on participants self-reported beliefs about the benefits of mindfulness and yoga for overall health (p<0.001), mood (p<0.001), physical health (p<0.05), focus (p<0.05) and self-awareness (p<0.05). Self reported beliefs about sleep and cause of pain were not significantly correlated with number of sessions attended (p>0.05). 3. The only significant overall change from pre to post intervention beliefs was participants beliefs of the benefits mindfulness and yoga can have on sleep. All other beliefs were not significantly changed.
Bedard et al. (2012) Canada Pre-Post N=20	**Population:** TBI; Mean Age=47.1yr; Gender: Male=9, Female=11; Time Post Injury ≥1yr. **Treatment:** Participants with a diagnosis of depression received 90min sessions of mindfulness-based stress reduction 1 day/wk for 8wk. Sessions included topics such as acceptance, staying in the present, and improving awareness of thoughts and feelings. Homework assignments were given after each	1. After treatment, there were significant changes in scores on the BDI (p=0.001), PHQ-9 (p=0.003), and HADS-Depression (p=0.023). 2. There was no significant improvement on HADS-Anxiety after treatment (p=0.116).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	session. Assessments were conducted at baseline and 8wk. **Outcome Measure:** Beck Depression Inventory-II (BDI-II), Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire-9 (PHQ-9).	
[Bedard et al.](#) (2003) Canada Pre-Post N=13	**Population:** TBI; *MBSR Group (n=10)*: Mean Age=43yr; Gender: Male=3, Female=7. *Control Group (n=3)*: Mean Age=39yr; Gender: Male=3, Female=0. **Intervention:** Participants received 12 weekly group sessions of mindfulness-based stress reduction (MBSR). Dropouts served as controls. Assessments were conducted at baseline and 12wk. **Outcome Measure:** Beck Depression Inventory (BDI-II), Short Form Health Survey (SF-36), Global Severity Index (GSI), Positive Symptom Distress Index (PSDI), Perceived Stress Scale (PSS).	1. After treatment, the MBSR group showed significant improvements on BDI-II (p=0.006), GSI (p=0.004), PSDI (p=0.002), and PSS (p=0.026). 2. Compared to controls, the MBSR group showed no significant differences after treatment on BDI-II, GSI, PSDI, or PSS (p>0.05). 3. MBSR group showed significant improvements on SF-36 Mental Health over time (p=0.001) and compared to controls (p=0.036).

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

Discussion

Four studies examined the efficacy of MBSR post TBI, three of which were conducted by Bedard and colleagues (Bedard et al., 2003; Bedard et al., 2012; Bedard et al., 2014; Combs et al., 2018). A small pilot study found that MBSR was associated with a significant reduction in symptoms of depression, distress, and stress (Bedard et al., 2003). A later pre-post study examined MBSR in patients with a depression diagnosis, which significantly reduced depression but not anxiety (Bedard et al., 2012). Combs et al. (2018) conducted another pre-post study examining the impact MBSR had on the beliefs of patients with a history of TBI. Patient's were more likely to believe MBSR could benefit physical health, focus, self-awareness and overall health with the more sessions they attended. However, the only belief that was significantly changed pre to post MBSR program was patient's beliefs of the benefit of MBSR could have on sleep.

In the only RCT conducted, Bedard (2014) investigated an MBSR program with aspects of CBT for patients with diagnosed depression, in comparison with usual care. The program consisted of 10 weeks of therapy designed to encourage new ways of thinking about life and disability. The authors found that the intervention group showed a significantly greater reduction on the Beck Depression Inventory, but not on the Patient Health Questionnaire, compared to the control group; these findings were maintained at follow-up.

Conclusions

There is level 1b evidence that mindfulness-based stress reduction may be an effective treatment for depression post TBI compared to usual care.

<div style="border: 1px solid black; padding: 10px;">

Mindfulness-based stress reduction may be an effective treatment for depression following traumatic brain injury.

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8.1.3.3 Psychotherapy

Psychotherapy aims to improve individual's thoughts, behaviours, beliefs or emotions to benefit their social skills, relationships, mental health and well-being. Specific forms of psychotherapy have been discussed in previous sections (CBT, MBSR). Stalder-Lüthy et al. (2013) conducted a systematic review that found psychotherapy to be an effective treatment for depression in individuals who have experienced an ABI. In addition to CBT and MBSR, other forms of psychotherapy have been examined for mood and affective disorders following ABI (Table 8.4).

Table 8.4 Psychotherapy for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Brenner et al. (2017) United States RCT PEDro=6 $N_{Initial}$=44, N_{Final}=35	**Population:** TBI**;** Gender: Male=32, Female=2, Transgender=1. *Experimental Group (n=15)*: Mean Age=47.7yr *Control Group (n=20):* Mean Age=54.6yr. **Intervention:** Participants were randomized to receive a manualized, small-group cognitive behavioural intervention focused on alleviating hopelessness or to a waitlist. The intervention was 2hr and delivered weekly for 10 wk. Participants were crossed over to the alternate intervention after 10wk. Assessments occurred at baseline, 10wk, and 20wk. **Outcome Measure:** Beck Hopelessness Scale (BHS), Beck Depression Inventory (BDI), Beck Scale for Suicide Ideation (BSSI).	1. After controlling for baseline BHS scores, the intervention group had significantly lower hopelessness post intervention compared to those on the waitlist (p=0.03); these reductions were maintained at follow-up. 2. The waitlist group demonstrated significant reductions on the BHS (p=0.01) and depression (p=0.003) after completing the intervention. 3. There were no significant between-group differences for the BDI or BSSI.
Andrewes et al. (2014) UK RCT Pedro=5 $N_{Initial}$=10, N_{Final}=9	**Population:** TBI; Mean Age=42.2yr; Gender: Male=9, Female=1; Mean Time Post Injury=4.8yr. **Intervention:** In-patients being treated for substance mis-use and challenging behavior were randomized to 12wk Positive Psychology group (intervention group) or control. Positive Psychology consisted of "Three Good Things" and "Signature Strengths" interventions. **Outcome Measure:** Seligman's Authentic Happiness Index (AHI), Head Injury Semantic Differential Scale (HISDS), The Hospital Anxiety and Depression Scale and Brief Strengths Test.	1. After the "three good things" intervention, the intervention group scored significantly higher on the AHI measurement of happiness than the control group (p=0.02). 2. No significant between group differences for the AHI scores from pre-test compared to at the end of the 12wk program. 3. No significant between group or pre-post intervention differences were found for HISDS scores.
Holleman et al. (2018) Netherlands PCT N=75	**Population:** TBI=33, Stroke=14, Other=28**;** Gender: Male=47, Female=28. *Experimental Group (n=42)*: Mean Age=43.3yr; Mean Time Post Injury=7.9yr. *Control Group (n=33):* Mean Age=40.7yr; Mean Time Post Injury=6.9yr. **Intervention:** Participants received Intensive	1. The INR treatment group had significantly greater mean change from baseline compared to the WC group for psychological well-being (p<0.001), Depression (p<0.001), Anxiety (p<0.001), and Quality of Life (p=0.001).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	NeuroRehabilitation programme (INR; 16wk, with 2wk break) or were placed in a waitlist control group (WC). The INR sessions focused on orientation, cognitive training, relaxation and physical activities, and group discussion to help patients cope with cognitive, emotional and behavioral changes. Outcome measures for the experimental group were evaluated pre and post-INR. Control group baseline was 15 weeks prior to their INR start date and follow-up at their start date. **Outcome Measure:** Dutch Symptom Check-list-90 (SCL-90), Beck Depression Inventory II (BDI-II), Hospital Anxiety Depression Scale (HADS), Quality of Life in Brain Injury questionnaire (QOLIBRI), and neuropsychological tests.	2. At follow-up, the INR group scored significantly better than WC for psychological well-being (SCL-90, p=0.005), depression (BDI-II, p=0.001; HADS, p=0.009), anxiety (HADS, p=0.003), and quality of life (QOLIBRI, p=0.008). 3. There were no significant between group differences at baseline or follow-up for neuropsychological tests scores.
Wiart et al. (2012) France Case Series N= 47	**Population:** TBI; Mean Age=33.4yr; Gender: Male=35, Female=12; Mean Time Post Injury=11.1yr. **Intervention:** Retrospective review of patients with mood disorders referred to a single physician for at least 1yr of neuro-systemic psychotherapy. **Outcome Measure:** Diagnostic and Statistical Manual of Mental Disorders (DSM), Glasgow Outcome Scale.	1. Significant improvement of affective disorders was found: depression (p<0.001), anxiety (p<0.001), and hostility (p<0.01). 2. No improvements were seen in apathy, bipolar symptomatology, loss of control, or addictive disorders. 3. GOS classification was 50% as very good or good, 21% average, and 27% poor.

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

Discussion

A retrospective study examined a series of patients with mood disorders post TBI who received neuro-systemic psychotherapy (Wiart et al., 2012). The study found that patients had significant reductions in depression, as well as anxiety and hostility, after one year of treatment. Further, half of patients had a good outcome according to the Glasgow Outcome Scale. Holleman et al. (2018) examined cognition and mood symptoms in an intensive neurorehabilitation program. After the program participants had significantly improved scores for depression, anxiety, physical well-being and quality of life. The neurophysiological test scores remained unchanged.

In a pilot RCT, patients with TBI were randomly assigned to a control group or positive psychology intervention, consisting of "Three Good Things" or "Signature Strengths" interventions (Andrewes et al., 2014). The intervention group demonstrated significant improvements in happiness after the "three goods things" intervention when compared to control, although the improvements were not sustained at the end of the 12-week program. The strength of the conclusions was limited by the small sample size in the study (Andrewes et al., 2014). Another RCT used a randomized waitlist-controlled crossover design to examine the effects of the Window to Hope program on depression in veterans with TBI. The program was designed from a CBT framework and focused on behavioural activation, cognitive restructuring, problem-solving and relapse prevention. Participants in the treatment and control groups did not differ significantly on depression scores post intervention. Of note, the initial intervention group had

significantly lower depression scores compared to pre-intervention, and the improvements were maintained 3mo after the program. The waitlist group had significantly improved depression scores after the treatment period compared to the waitlist period.

Conclusions

There is level 4 evidence that long-term, neuro-systemic psychotherapy is an effective treatment for depression post TBI.

There is level 2 evidence that neurorehabilitation programs focused on cognitive training, relaxation and physical activity may improve depression and anxiety.

Positive psychotherapy may increase happiness following TBI.

Neuro-systemic psychotherapy may be an effective treatment for depression following TBI.

8.1.3.4 Music Therapy

Music therapy is based upon the hypothesis that music encourages more harmonious cerebral activity given the involvement of both hemispheres in processing musical stimuli (Besson & Schon, 2001). As guided by a music therapist, the therapy can involve a combination of listening, singing, and playing instruments. While music therapy is often employed in cognitive rehabilitation, it has also been explored as an intervention for disorders of mood (Table 8.5).

Table 8.5 Music Therapy for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Guetin et al. (2009) France Pre-Post N=13	**Population:** TBI; Mean Age=31yr; Gender: Male=3, Female=10; Mean Time Post Injury=8yr. **Treatment:** Participants received music therapy (1 hr/wk for 20wk). Each session was divided into two segments: receptive music therapy (e.g. listening) and active music therapy (e.g. playing an instrument). Assessments were conducted at baseline, 1wk, 5wk, 10wk, 15wk, and 20wk. **Outcome Measure:** Hospital Anxiety and Depression Scale (HADS).	1. Following each music therapy session, significant improvements in mood were noted on the HADS (p<0.05). 2. Anxiety scores significantly decreased from baseline to 10wk, 15wk, and 20wk (p<0.05). 3. Depression scores significantly decreased from baseline to 10wk and 15wk (p<0.05).
Thaut et al. (2009) USA PCT N=54	**Population:** TBI=24, Stroke=5, Other=4; Mean Age=31yr; Gender: Male=3, Female=10. **Intervention:** Participants were assigned to a treatment group (n=31) or a control group (n=23). The treatment group received four different sessions of neurologic music therapy (30 min) focused on emotional adjustment, executive function, attention, and memory. The control group were sent to a quiet room to rest for 30 min over four sessions.	1. On the MAACL, Depression and Anxiety improved significantly in the treatment group (p<0.05) but did not change in the control group (p>0.05). 2. On the MAACL, Positive Affect did not change in the treatment group (p=0.039) but significantly worsened in the control group (p=0.04).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	Outcome Measure: Multiple Affect Adjective Checklist (MAACL), Brief Symptom Inventory 18 (BSI-18).	3. On the MAACL, Hostility significantly improved in the control group (p=0.02) but not the treatment group (p=0.06). 4. On the MAACL, Sensation Seeking significantly improved in the treatment group (p<0.01) and significantly worsened in the control group (p=0.04). 5. On the BSI-18, both groups showed significant improvement after four sessions (treatment group, p<0.01; control, p=0.010).
[Nayak et al.](#) (2000) USA PCT N=18	**Population:** TBI and Stroke; Mean Age=59.89yr; Gender: Male=6, Female=12. **Intervention:** Participants were assigned to either a control group who received standard rehabilitation alone (n=8) or a treatment group (n=10) who received standard rehabilitation plus music therapy. The treatment group received music therapy 2-3 days/wk for up to 10 wk. **Outcome Measure:** Mood (Self-Report, Family-Rated, Staff-Rated), Social Interaction (Family-Rated), Participation (Staff-Rated).	1. The treatment group was associated with greater improvements in mood according to self-report (p<0.10), family (p<0.10), and staff (p<0.10) than control. 2. The treatment group was more motivated to participate (p=0.06) and more involved in therapy (p<0.01) than the control. 3. The treatment group had higher levels of social interaction than the control (p<0.02). 4. There was a significant, positive correlation between social behaviour at baseline and benefit from the therapy (p<0.02).

Discussion

Studies investigating music therapy as an intervention post ABI have demonstrated positive results related to mood; none of the participants were explicitly diagnosed with a depressive disorder. In an early study, patients who received music therapy had greater improvements in reported mood compared to patients who received only standard rehabilitation, although the results were not statistically significant (Nayak et al., 2000). A later study examined the effect of both receptive (i.e., listening to music) and active (e.g., singing, writing a song, playing an instrument) music therapy (Guétin et al., 2009). The study found significant improvements in mood (i.e., symptoms of anxiety and depression) immediately after sessions and over time. In a comparative study, a treatment group participated in four sessions of music therapy focusing on attention, memory, executive function, and emotional adjustment, while the control group received no treatment (Thaut et al., 2009). Although there were no improvements on cognitive measures, the treatment group showed reductions in symptoms of depression and anxiety, whereas the cognitive showed no improvement. The control group also showed significant reduction in positive affect, while the treatment group did not change. Unfortunately, the study did not perform statistical analysis for between-group comparisons.

Conclusions

There is level 2 evidence that music therapy reduces symptoms of depression post ABI compared to standard rehabilitation.

Music therapy may be effective in reducing symptoms of depression following ABI.

8.1.3.5 Physical Activity

The positive impact of physical activity on mood has been well-established in the general population (Byrne & Byrne, 1993). There is evidence that exercise is an effective therapy for depression in patients without ABI (Kvam et al., 2016; Schuch et al., 2016). A variety of physical activity interventions have been explored as treatments for mood-related issues in individuals following ABI (Table 8.6).

Table 8.6 Physical Activity for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	Aerobic Exercise	
Bellon et al. (2015) USA RCT PEDro=6 N$_{Initial}$=123, N$_{Final}$=69	**Population:** TBI; Mean Age=43.7yr; Gender: Male=41, Female=28; Mean Time Post Injury=100.5mo; Severity: Mild=10, Moderate=10, Severe=35. **Intervention:** Participants were randomized into a walking group (treatment) or nutrition group (control). The home-based walking group was administered a pedometer to track steps taken weekly for 12wk, with a coaching call 3 days/wk to encourage increase in weekly step count. The home-based nutrition group learned about healthy eating habits through coaching calls 3 days/wk for 12 wk. After 12wk, participants crossed over. Measures were assessed at baseline, 12wk, and 24wk. **Outcome Measure:** Centre for Epidemiological Studies-Depression (CES-D), Perceived Stress Scale (PSS).	1. Depression on the CES-D decreased significantly from baseline to 12wk and 24wk for all participants (p=0.007), but there was no significant difference between groups at 12wk or 24wk. 2. Stress on the PSS decreased overall from baseline to post-treatment for all participants (p=0.006), with a greater decrease in the walking group (p=0.006).
Wise et al. (2012) USA RCT PEDro=5 N$_{Initial}$=84, N$_{Final}$=40 Follow-up to Hoffman et al. (2010)	**Population:** TBI. *Treatment Group (n=40):* Mean Age=39.7yr; Gender: Male=15, Females=25. *Control Group (n=40):* Mean Age=37.1yr; Gender: Male=20, Female=20. **Intervention:** The treatment group received a 10wk exercise program with 15min education session, 15min of warm-up exercises, 30 min of aerobics, and 15min of cool-down exercises. Each participant was asked to perform 30min sessions for 4d/wk. The control group was given the opportunity to participate in the exercise	1. At 6mo, there was a reduction in the number of participants able to exercise >90min per week (77% versus 52%).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	program at the end of the trial. Measures were assessed at baseline, 10wk, and 6mo. **Outcome Measure:** Beck Depression Inventory (BDI), Perceived Quality of Life Scale (PQOL), Short Form Health Survey (SF-12).	
Hoffman et al. (2010) USA RCT PEDRo=5 $N_{Initial}$=84, N_{Final}=76	**Population:** TBI. *Treatment Group (n=40)*: Mean Age=39.7yr; Gender: Male=15, Females=25. *Control Group (n=40)*: Mean Age=37.1yr; Gender: Male=20, Female=20. **Intervention:** The treatment group received a 10wk exercise program with 15min education session, 15min of warm-up exercises, 30min of aerobics, and 15min of cool-down exercises. Each participant was asked to perform 30min sessions for 4d/wk. The control group was given the opportunity to participate in the exercise program at the end of the trial. Measures were assessed at baseline, 10wk. **Outcome Measure:** Beck Depression Inventory (BDI), Perceived Quality of Life Scale (PQOL), Short Form Health Survey (SF-12).	1. At 10wk, there were no significant differences between the exercise and control groups on the BDI (p=0.250). 2. Participants exercising >90 min/wk were found to have lower depression scores than those exercising <90 min/wk (p=0.033). 3. Those who exercised >90min per week, compared to those exercising <90min had lower BDI scores (p=0.037) and higher scores on PQOL (p=0.014) and SF-12 (p=0.014).
Driver & Ede (2009) USA RCT PEDro=5 N=16	**Population:** TBI; *Treatment Group (n=8)*: Mean Age=38.78yr; Mean Time Post Injury=40.75mo. *Control Group (n=8)*: Mean Age=37.62yr; Mean Time Post Injury=36.25mo. **Intervention:** Participants were randomised to aquatic exercise (treatment) or a vocational rehabilitation class (control) for 3 days/wk over 8wk. Measures were assessed at baseline and 8wk. **Outcome Measure:** Profile of Mood States (POMS).	1. At 8wk, significant differences in total POMS scores were noted between the groups in favour of treatment (p<0.05). 2. Within-group scores for the treatment group showed significant differences on each of the POMS subscales (all p<0.05). 3. No significant differences were noted on each of the sub-scales for the control group (p>0.05).
Damiano et al. (2016) USA Pre-Post N=12	**Population:** TBI; Mean Age=31.3yr; Gender: Male=7, Female=5. **Intervention:** Participants completed a home-based, aerobic exercise program for 5 days/wk over 8wk. Training included exercise of moderate intensity for 30 min on the elliptical machine. Measures were assessed at baseline, 8wk, and 16 wk. **Outcome Measure:** Hamilton Rating Scale for Depression (HAM-D), Beck Anxiety Inventory (BAI), Pittsburgh Sleep Quality Index (PSQI).	1. No significant changes in HAM-D or BAI scores from baseline to 8wk or 16wk were found. 2. Walking on the elliptical at a slower speed was associated with higher scores on HAM-D (p=0.03), whereas large excursion movements to the right was associated with lower scores (p=0.04). 3. Better sleep scores on PSQI post exercise were associated with decrease in depressive symptoms (p=0.04). 4. Larger gain in excursion was associated with decreased scores on BAI (p=0.02) and HAM-D (p<0.01).
Weinstein et al. (2017) USA Pre-Post $N_{Initial}$=12, N_{Final}=10	**Population:** TBI; Mean Age=32.9yr; Gender: Male=4, Female=6; Mean Time Post Injury=6.6yr; Severity: Mild=5, Moderate=4, Severe=1. **Intervention:** Participants completed one-on-one supervised aerobic exercise sessions (3 days/wk for 12wk) where they reached 70-80% of maximum heart rate. Assessments were	1. Significant improvement from baseline to 12wk were found, as 80% of participants reported less mood disturbance on POMS-SF (p=0.04); there was a 9% reduction in POMS-SF scores (p=0.04).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	conducted before and after sessions at baseline, 4wk, 8wk, and 12wk. **Outcome Measure:** Profile of Mood States - Short Form (POMS-SF).	2. There were significant short-term changes in POMS-SF scores in response to singular exercise sessions, with the most substantial changes in fatigue inertia (p=0.01) and anger hostility (p=0.09).
Gordon et al. (1998) USA Case Control N=240	**Population:** TBI. *Non-Exercise Group (n=176)*: Mean Age=37.1yr; Mean Time Post Injury=9.1yr. *Exercise Group (n=64)*: Mean Age=37.8yr; Mean Time Post Injury=11.2yr. **Intervention:** Retrospective comparison of exercisers and non-exercisers. **Outcome Measure:** Beck Depression Inventory (BDI), The Institute for Rehabilitation Research (TIRR) Symptom Checklist.	1. Individuals who exercised had less depressed mood (BDI) than those who did not exercise (p<0.01). 2. Individuals who exercised reported significantly fewer symptoms on the TIRR checklist compared to those who did not exercise (p<0.0004).
Tai Chi		
Blake & Batson (2009) UK RCT PEDro=6 N=20	**Population:** TBI; Gender: Male=15, Female=5; Injury Severity: Mild=7, Moderate=8, Severe=5. *Treatment Group (n=10)*: Mean Age=44.5yr; Mean Time Post Injury=16.4 yr. *Control Group (n=10)*: Mean Age=46.2yr; Mean Time Post Injury=13.62 yr. **Intervention:** The treatment group performed tai chi (qigong) for 1 hr/wk over 8wk. The control group attended non-exercise social and leisure activities for 1 hr/wk over 8wk. Measures were assessed at baseline and 8wk. **Outcome Measure:** General Health Questionnaire-12 (GHQ-12), Physical Self-Description Questionnaire.	1. At 8wk, GHQ-12 showed a significant improvement in mood scores for those in the treatment group compared to the control group (p=0.026). 2. Physical self-esteem was found to improve significantly from baseline to 8wk for those in the treatment group (p=0.017).
Gemmell & Leathem (2006) New Zealand RCT PEDro=6 N=18	**Population:** TBI; Mean Age: Males=51.2yr, Females=40.2yr; Gender: Male=9, Female=9; Mean Time Post Injury=8.7yr. **Intervention:** The treatment group (n=9) performed tai chi (chuan) for 6wk. The control group (n=9) was waitlisted for tai chi. Measures were assessed at baseline, 6wk, and 9wk. **Outcome Measure:** Visual Analog Mood Scale (VAMS), Medical Outcome Scale Short Form 26 (MOS SF-36), Rosenberg Self-Esteem Scale (RSES).	1. At 6wk, the treatment group reported significant improvements on VAMS (fear, confusion, sadness, anger, tiredness, tension, happiness, energy; not fatigue) compared to the control group. 2. When compared to the control group, the differences on the MOS SF-36 and the RSES were not significant. 3. At 9wk, the treatment group reported feeling less impaired due to emotional problems (RSES, p=0.007).

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

Discussion

Several studies examined the effectiveness of aerobic exercise in improving mood and related symptoms post TBI; none of the studies explicitly included participants with a depression diagnosis. Mood was significantly improved following 8 weeks of aquatic exercise (Driver & Ede, 2009) and 12 weeks of high-intensity aerobic training (Weinstein et al., 2017); the latter study reported significantly greater improvements in mood than conventional rehabilitation (Weinstein et al., 2017). Conversely, three

studies reported that depressive symptoms were not significantly changed following aerobic exercise. One pre-post study reported that eight weeks of elliptical training did not reduce symptoms of depression or anxiety immediately after treatment or at follow-up (Damiano et al., 2016). The authors noted that lower self-selected speeds on the elliptical were associated with greater depressive symptoms. When compared to non-exercise controls, individuals participating in exercise programs demonstrated similar changes in depressive symptoms in two RCTs (Bellon et al., 2015; Hoffman et al., 2010). Further analysis of one RCT found that participants who exercised for more than 90 minutes per week had significantly lower depressive symptoms than those who exercised for less time (Wise et al., 2012). A meta-analysis examining exercise for the treatment of depression in patients with TBI, including all injury severities (mild, moderate, severe), reported a small to moderate positive effect (Perry et al., 2018).

Two studies investigated the benefits of the Chinese exercise Tai Chi in those who had sustained a TBI: Tai Chi Qigong (Blake & Batson, 2009) and Tai Chi Chaun (Gemmell & Leathem, 2006). Results from both studies found significant improvement in mood compared to the control group.

Conclusions

There is level 1a evidence that Tai Chi may improve mood compared to wait-list controls following TBI.

There is level 1a evidence that aerobic exercise, compared to waitlist controls, does not reduce symptoms of depression following TBI.

There is level 1b evidence that aerobic exercise, compared to waitlist controls, improves mood following TBI.

Aerobic exercise and Tai Chi may improve mood following TBI, but aerobic exercise may not be effective in reducing symptoms of depression.

8.1.3.6 Rehabilitation Programs

Despite not incorporating psychotherapy or focusing on psychological outcomes, rehabilitation programs may improve mood following ABI (Table 8.7).

Table 8.7 Rehabilitation Programs for the Treatment of Depression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
[Schonberger et al.](#) (2014) Australia Pre-Post N=42	**Population:** TBI; Mean Age=32yr; Gender: Male=37, Female=5; Mean Time Post Injury=81d. **Intervention:** Community Based Rehabilitation Program with a multi-disciplinary team (3-4×/wk). **Outcome Measure:** Hospital Anxiety and Depression Scale (HADS), Self-Awareness of Deficits Interview (SADI), Sydney Psychosocial	1. Based on RIDI, no significant differences between the start and end of therapy occurred. 2. Good RIDI adjustment was predicted by a good functional status as rated by SPRS total and positive SADI score. 3. RIDI adjustment was predicted by: SPRS- Therapist, SADI, and SPRS-Therapist interaction (p<0.05).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	Reintegration Scale-2 (SPRS) and Reactions to Impairment and Disability Inventory (RIDI).	4. There was a significant association between positive RIDI and low levels of self-reported depression on the HADS (p<0.001).
[Ruff & Niemann](#) (1990) USA RCT PEDro=7 N=24	**Population:** TBI; Gender: Male=17, Female=7. *Group 1 (n=12)*: Mean Age=28.3 yr; Mean Time Post Injury=44.3mo. *Group 2 (n=12)*: Mean Age=31.1 yr; Mean Time Post Injury=52.2 mo. **Intervention:** Group 1 participated in an intensive cognitive retraining program, which was comprised of 4 modules and ran for 12 wk. The control group participated in a day treatment rehabilitation program focused on psychosocial functioning and activities of daily living. **Outcome Measure:** Katz Adjustment Scale (KAS).	1. Individuals in both groups experienced a decrease in depressed mood, as measured by the KAS.

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

Discussion

Ruff and Niemann (1990) compared participants in an eight-week cognitive remediation program with those attending a functional rehabilitation program. As measured by the Katz Adjustment Scale, both groups experienced significant decreases in depressed mood after treatment. The community-based rehabilitation program examined by Schonberger et al. (2014) consisted of a multidisciplinary team, and focused on helping patients return to pre-injury functional status and roles. After completing the program there were no significant psychological changes detected in the patients; good psychological adjustment was more closely related to good functional status.

Conclusions

There is level 4 evidence that rehabilitation programs, whether focused on cognitive or psychosocial remediation, may reduce depressive symptoms post TBI.

There is level 4 evidence that community-based rehabilitation programs alone do not change the psychological status of patients with ABI.

Psychosocial or cognitive rehabilitation may reduce depressive symptoms following TBI.

Community-based rehabilitation alone does not change depression and anxiety scores in patients after ABI.

8.1.3.7 Transcranial Magnetic Stimulation

Transcranial Magnetic Stimulation is a fairly novel technique for the treatment of mood disorders. It has shown promising results in populations without TBI, but the effectiveness is not entirely clear (Brunoni et al., 2017). There is limited literature evaluating its role in patients with ABI (Table 8.8).

Table 8.8 Transcranial Magnetic Stimulation for Mood Disorders post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Lee & Kim (2018) South Korea RCT PEDro=8 N=13	**Population:** TBI; Male=9, Female=4. *Experimental Group (n=7)*: Mean Age=42.42yr; Mean Time Post Injury= 3.85mo; Mean GCS=13.71. *Control Group (n=6)*: Mean Age=41.33yr; Mean Time Post Injury= 3.88mo; Mean GCS=13.66. **Intervention:** Participants received neurodevelopmental therapy for muscle strengthening/movement followed by repetitive transcranial magnetic stimulation (rTMS; experimental group) or sham rTMS (control). Interventions were performed for 30min/d for 5d on, 2d rest, 5d on. **Outcome Measure:** Montgomery-Asberg Depression Rating Scale (MARDS); Trail Making Test (TMT); Stroop Color Word Test (SCWT)	1. Between pre and post intervention, the experimental group showed a significant improvement in MARDS, TMT, and SCWT (p<0.05); no significant differences were shown in the control group. 2. There was a significant between group difference found for all outcome measures favouring the experimental group.

Discussion

Lee & Kim (2018) evaluated the effect of repetitive transcranial magnetic stimulation depression and cognition in patients with TBI. The intervention group showed significant improvements compared to the control group in both depression and cognition scores.

Conclusions

There is level 1b evidence that repetitive transcranial magnetic stimulation improves cognition and depression in patients with TBI.

> **Repetitive transcranial magnetic stimulation may improve cognition and depression.**

8.2 Anxiety Disorders

Anxiety is a subjective sensation of apprehension that may be accompanied by signs that are part of the fight or flight response (e.g., restlessness, tension, tachycardia, shortness of breath). Anxiety disorders are common following ABI and can be disabling whether they are generalized or include a specific phobia to a certain stimulus. Anxiety can be related to cognitive impairment resulting from injury or may be related to the psychological trauma of the injury itself.

8.2.1 Incidence and Prevalence of Anxiety

Following ABI, anxiety or anxiety disorders have been reported to occur in 4% to 34% of individuals (Alway et al., 2016; Alway et al., 2012; Anke et al., 2015; Deb et al., 1999; Fann et al., 1995; Gould et al., 2014; Hart et al., 2016; O'Donnell et al., 2008; Osborn et al., 2016; van Reekum et al., 1996). An older study by Hibbard et al. (1998) examined various anxiety disorders post ABI and found that 19% of the study population was diagnosed with post-traumatic stress disorder (PTSD), 15% with Obsessive Compulsive Disorder, and 14% with panic disorder. These findings were confirmed in a later study, where the most frequently reported disorders post TBI were anxiety disorders otherwise not specified, followed by PTSD (Gould et al., 2014). In a more recent meta-analysis of 32 studies, self-reported rates of anxiety in the TBI population were approximately 37% (Osborn et al., 2016). Post-ABI anxiety has demonstrated a positive correlation with depression (Sigurdardottir et al., 2013), as well as non-productive coping strategies (Spitz et al., 2013). Moreover, individuals with anxiety disorders post ABI have reported lower life satisfaction and functional recovery at one-year post injury (Anke et al., 2015).

8.2.2 Non-Pharmacological Interventions for Anxiety

8.2.2.1 Cognitive Behavioural Therapy for Anxiety

While anxiety disorders appear to be well recognized post ABI, there is minimal literature regarding the use of non-pharmacological interventions specific to anxiety. In the non-brain injured population, a CBT program directed at managing and reducing the disabling symptoms that cause avoidance of the stimulus may effectively treat anxiety. In a meta-analysis of CBT for the treatment of depression following ABI, Waldron et al. (2013) found a large treatment effect when CBT was focused on the treatment of depression. As stated earlier, Waldron et al. (2013) included all brain injury severities and cerebrovascular accidents in their sample.

Table 8.9 Cognitive Behavioural Therapy for the Treatment of Anxiety Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Ponsford et al. (2016) Australia RCT PEDro=7 N$_{Start}$=75, N$_{End}$=51	**Population:** TBI. *CBT+MI Group (n=26):* Mean Age=46.69yr; Gender: Male=18, Female=8; Mean Time Post Injury=4.88yr; Mean GCS=10.43. *CBT+NDC Group (n=26):* Mean Age=39.88yr; Gender: Male=20, Female=6; Mean Time Post Injury=3.58yr; Mean GCS=10.48. *WC Group (n=23):* Mean Age=39.87yr; Gender: Male=17, Female=6; Mean Time Post Injury=2.61yr; Mean GCS=8.23. **Intervention:** Participants diagnosed with depression and/or anxiety were allocated to receive cognitive behavioural therapy (CBT) with either motivational interviewing (CBT+MI) or non-directive counseling (CBT+NDC), or to a waitlist control (WC). MI and NDC were each delivered for 3wk, followed by 9wk of CBT, with three CBT booster sessions 21-30wk from baseline. Assessments were conducted at	1. All groups demonstrated significant improvements on the DASS-Depression, HADS-Anxiety, and SPRS-2 over time. 2. On the DASS-Depression, there was a significantly greater reduction in score over time in CBT+MI versus WC (p<0.005) but not CBT+NDC versus WC; there was no significant difference between CBT+MI and CBT+NDC. 3. On the HADS-Anxiety, there was a significantly greater reduction in score over time in CBT+NDC versus WC (p<0.05) but not CBT+MI versus WC; there was no significant difference between CBT+MI and CBT+NDC. 4. On the SPRS-2, there was no significant difference in improvement between groups over time.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	baseline, 3wk, 12wk, 21wk, and 30wk. **Outcome Measure:** Depression, Anxiety & Stress Scale (DASS), Hospital & Anxiety Depression Scale (HADS), Sydney Psychosocial Reintegration Scale 2 (SPRS-2).	5. Higher baseline DASS-Depression and HADS-Anxiety scores were significantly associated with greater response to treatment (r=0.34, p<0.05 and r=0.37, p<0.05, respectively). 6. When combining CBT+MI and CBT+NDC groups, there were significantly greater improvements on HADS-Anxiety (p<0.05), DASS-Depression (p<0.005), and SPRS-2 (p<0.05) in the combined group versus WC.
[Hsieh et al.](#) (2012a) Australia RCT PEDro=6 N$_{Initial}$=27, N$_{Final}$=24	**Population:** TBI; Mean Age=38yr; Gender: Male=21, Female=6; Mean Time Post Injury=37.9 mo. **Intervention:** Participants diagnosed with anxiety received motivational interviewing followed by cognitive behavioural therapy (CBT+MI; n=9), non-directive counselling followed by CBT (CBT+NDC; n=10), or standard care (control; n=8) for 12 wk. Assessments were conducted at baseline, 3wk,12 wk, and 21wk. **Outcome Measure:** Hospital Anxiety and Depression Scale (HADS), Depression Anxiety Stress Scale (DASS), Coping Style for Adults (CSA), Sydney Psychosocial Reintegration Scale (SPRS-2)	1. CBT+MI and CBT+NDC had significantly greater reductions on HADS-Anxiety than control (both p=0.03), but not on DASS-Anxiety. 2. CBT+NDC had significantly greater reduction on DASS-Stress than control (p=0.03), but CBT-MI did not. 3. CBT+MI had significantly greater reduction on CSA-Non-productive than control (p=0.001), but CBT+NDC did not. 4. There were no significant differences between CBT+MI or CBT+NDC versus control on HADS-Depression, DASS-Depression, CSA-Adaptive, or SPRS-2. 5. CBT+MI showed significantly greater reductions on HADS-Anxiety (p=0.001), DASS-Anxiety (p=0.026), and DASS-Stress (p=0.005) than CBT+NDC; there were no significant differences on HADS-Depression or DASS-Depression. 6.
[Hsieh et al.](#) (2012b) Australia RCT PEDro=6 N$_{Initial}$=27	**Population:** TBI; Mean Age=38yr; Gender: Male=21, Female=6; Mean Time Post Injury=37.9 mo. **Intervention:** Participants diagnosed with anxiety received motivational interviewing followed by cognitive behavioural therapy (CBT+MI; n=9), non-directive counselling followed by CBT (CBT+NDC; n=10), or standard care (control; n=8) for 12 wk. Assessments were conducted at baseline, 3wk,12 wk, and 21wk. **Outcome Measure:** Anxiety Change Expectancy Scale (ACES).	1. CBT+MI showed a significantly greater increase in ACES than CBT+NDC after CBT (p=0.04) and at 9wk follow-up (p=0.015), but not immediately after MI (p=0.22). 2. There was a moderate, non-significant correlation between posttraumatic amnesia and ACES (r=0.485, p=0.067), suggesting that greater reduction in anxiety is associated with less severe injury.
[Anson & Ponsford](#) (2006) Australia RCT PEDro=5 N=31	**Population:** TBI; Gender: Male=26, Female=5. *Group A (n=15)*: Mean Age=38.9yr; Mean Time Post Injury=755.8d. *Group B (n=16)*: Mean Age=37.8yr; Mean Time Post Injury=340.8d. **Intervention:** For Group A (n=15), baseline phase was 5wk, followed by 5wk of intervention, and a 5wk follow-up phase. For Group B (n=16), baseline was 10wk, followed by 5wk of intervention and a 10wk follow-up phase. The	4. No significant changes in anxiety or self-esteem scores were noted following the CSG (p>0.05). 5. Although levels of depression and psychosocial dysfunction were significantly different between the two groups (p<0.05) participation in the CSG did not have an effect on their scores.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	CSG consisted of 10 group sessions and ran for 900min 2×/wk. **Outcome Measure:** Coping Scale for Adults, Hospital Anxiety and Depression Scale, Rosenberg Self Esteem scale.	1. Both groups significantly increased their adaptive coping skills following the CSG ($p<0.01$).
Hodgson et al. (2005) Australia RCT PEDro=5 N=12	**Population:** ABI; Gender: Male=7, Female=5. *Treatment Group* (n=6): Mean Age=44.2yr; Mean Time Post Injury=96.7mo. *Waitlist Group* (n=6): Mean Age=33.8yr; Mean Time Post Injury=150.5mo. **Intervention:** Participants were randomized to receive cognitive behavioural therapy (CBT) or waitlist control. The CBT treatment program consisted of relaxation training, cognitive strategies, graded exposure, and assertiveness skills training. CBT was delivered in 1hr sessions 1 day/wk for 9-14 wk. Assessments were conducted before and after treatment, and at 1mo follow-up. **Outcome Measure:** Hospital Anxiety and Depression Scale (HADS), Social Phobia and Anxiety Inventory (SPAI), Coppersmith Self Esteem Inventory.	1. After treatment, the CBT group had significantly lower scores on HADS-Depression, HADS-Anxiety, and SPAI than the control group ($p<0.05$). 2. At follow-up, the treatment group maintained improvement relative to the control group. 2.
Arundine et al. (2012) Canada PCT N$_{Initial}$=20, N$_{Final}$=17 Follow up to Bradbury et al. (2008)	**Population:** TBI=10, ABI=10, Severity: Moderate-Severe. *CBT Group (n=10):* Mean age=39.8yr; Gender: Male=5, Female=5; Mean Time Post Injury=7.00yr. *EC Group (n=10):* Mean age=42.5yr; Gender: Male=5, Female=5; Mean Time Post Injury=11.4yr. **Intervention:** Participants with psychological distress were randomized to receive cognitive behavioural therapy (CBT) or education control (EC). CBT involved one individual introductory session, and then 10 sessions either in a group (CBT-G) or individually by telephone (CBT-T). EC group received CBT after initial group. Assessments were conducted at baseline, post treatment, 1mo follow-up, and 6mo follow-up. **Outcome Measure:** Depression Anxiety Stress Scales 21 (DASS-21), Symptom Checklist 90 Revised (SCL-90-R).	3. At 6mo follow-up, all participants showed significant improvements from baseline on DASS-21 ($p<0.01$) and SCL-90-R ($p<0.01$); CBT-G and CBT-T were comparable.
Bradbury et al. (2008) Canada PCT N=20	**Population:** TBI=10, ABI=10, Severity: Moderate-Severe. *CBT Group (n=10):* Mean age=39.8yr; Gender: Male=5, Female=5; Mean Time Post Injury=7.00yr. *EC Group (n=10):* Mean age=42.5yr; Gender: Male=5, Female=5; Mean Time Post Injury=11.4yr. **Intervention:** Participants with psychological distress received cognitive behavioural therapy (CBT) or education control (EC). CBT involved one individual introductory session, and then 10 sessions either in a group (CBT-G) or individually by telephone (CBT-T). Assessments were	1. At post treatment and 1mo follow-up, combined CBT showed significantly greater improvement from baseline than EC on DASS-21 ($p<0.001$) and SCL-90-R ($p<0.01$). 2. On DASS-21 and SCL-90-R, there were significant improvements from baseline to post treatment and to 1mo follow-up for CBT-G ($p<0.01$) and CBT-T ($p<0.05$), but there were no there were no significant improvements from post treatment to 1mo follow-up ($p>0.05$).

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
	conducted at baseline, post treatment, and 1mo follow-up. **Outcome Measure:** Depression Anxiety Stress Scales 21 (DASS-21), Symptom Checklist 90 Revised (SCL-90-R).	3. There were no significant differences between CBT-G and CBT-T at any time point on DASS-21 or SCL-90-R (p>0.05).

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

Discussion

Three trials compared the effectiveness of CBT to a non-interventional control group. A non-randomized trial reported that CBT significantly reduced symptoms anxiety, depression, and stress for up to six months, whether delivered in a group or over the phone (Arundine et al., 2012; Bradbury et al., 2008). A small, low-quality RCT found a significant reduction in symptoms of anxiety and depression following 9 to 14 sessions of CBT for addressing social anxiety (Hodgson et al., 2005). However, a larger RCT of similar quality found that 10 sessions of CBT did not reduce symptoms of anxiety, depression, or low self-esteem, despite increases in adaptive coping skills (Anson & Ponsford, 2006).

Two trials examined the efficacy of CBT in combination with either motivational interviewing (MI) or non-directive counselling (NDC), and compared both to a control group. Both trials hypothesized that MI would enhance the treatment response to CBT over NDC (Hsieh et al., 2012b; Ponsford et al., 2016). The first trial found that both CBT groups had significantly greater reductions in anxiety than controls on the Hospital Anxiety Depression Scale (HADS), but not on the Depression Anxiety Stress Scale (DASS)(Hsieh et al., 2012a; Hsieh et al., 2012b). The CBT+MI group also showed significantly greater reductions in anxiety on HADS and DASS than the CBT+NDC group. As well, there were no significant differences between any of the groups on measures of depression. In the second trial, a combined CBT group (both CBT+MI and CBT+NDC) demonstrated significantly greater reductions in anxiety on HADS than the control group (Ponsford et al., 2016). However, unlike the previous trial, the study did not find a significant difference in anxiety reduction between the two CBT groups. The authors also noted that greater HADS anxiety scores at baseline were associated with a greater response to CBT.

Conclusions

There is level 1a evidence that cognitive behavioural therapy combined with motivational interviewing may be an effective treatment for anxiety post ABI, compared to waitlist controls.

There is level 2 evidence that group cognitive behavioural therapy and telephone cognitive behavioural therapy are similarly effective in reducing anxiety following ABI.

There is conflicting (level 1b) evidence as to whether motivational interviewing is more effective than non-directive counselling as an adjunct to cognitive behavioural therapy for anxiety post ABI.

Cognitive behavioural therapy may be an effective treatment for anxiety following ABI.

Cognitive behavioural therapy for anxiety may be similarly effective when delivered over the telephone as when delivered in a group.

It is unclear whether motivational interviewing is a more effective than non-directive counselling as an adjunct to cognitive behavioural therapy for anxiety.

8.2.2.2 Neurofeedback training

Neurofeedback has been used for the treatment of depression and anxiety in non-TBI populations (Hammond, 2005). There is limited information evaluating the role for neurofeedback training in patients with ABI (Table 8.10).

Table 8.10 Neurofeedback Training for Mood Disorders Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Bennet et al. (2018) India PCT N=60	**Population:** TBI; Mean Time Post Injury= <6mo(n=30), 12-18mo(n=30) **Intervention:** Participants received EEG neurofeedback training (NFT) or treatment as usual (control group). 3 NFT sessions/wk on alternate days were completed for a total of 16-20 sessions. NFT and control groups were further divided into <6mo and 12-18mo time post-injury (n=30/group). Participants were evaluated pre and post intervention. The NFT group was evaluated an additional time at 3mo follow-up with Glasgow Outcome Scale-Extended (GOS-E). **Outcome Measure:** Visual Analogue Scale (VAS) for symptom severity, Perceived Stress Scale (PSS), serum cortisol and GOS-E.	1. At baseline, NFT group had significantly higher VAS and PSS scores (p<0.001). Further comparisons were converted to pre-post intervention change to accommodate initial differences between groups. 2. Compared to baseline, post intervention VAS and PSS scores were significantly lower for both <6mo and 12-18mo NFT groups (p<0.001). There were no significant changes in control group scores. 3. Pre-post intervention change in VAS and PSS scores were significantly greater for NFT group than controls in both <6mo and 12-18mo groups. (p<0.001). 4. Pre-post intervention change in VAS and PSS were not significantly different between the <6mo and 12-18mo groups in NFT or control groups. 5. Compared to baseline, post intervention cortisol was significantly higher for the <6mo control group. There were no other significant between group differences in cortisol. 6. 28 of 30 NFT participants completed 3mo follow-up GOS-E. 22 showed good recovery and 6 moderate recovery.

Discussion

One trial compared neurofeedback training to usual care in two groups at different stages of recovery from ABI (Bennett et al., 2018). The training consisted of relaxation techniques administered by a trained

neuropsychologist with immediate electroencephalogram feedback. Intervention participants less than six months and 12-18 months after injury had lower self perceived stress levels compared to the usual care group.

Conclusions

There is level 2 evidence that neurofeedback training may improve stress in patients with ABI.

Neurofeedback training may help reduce stress in patients recovering from ABI.

8.2.3 Obsessive Compulsive Disorder

Rates of Obsessive Compulsive Disorder (OCD) in patients after ABI are similar to rates in the general population. Two prospective studies in patients after TBI reported similar incidence rates; Gould et al. (2011) found rates of 1% in the first year following injury in a population with mixed severity, and Alway et al. (2016) found incidences between 0-2.6% in the first five years following injury in patients with moderate to severe TBI. Retrospective studies have mixed results, reporting rates from 1 to 15% (Hibbard et al., 1998; Koponen et al., 2011; van Reekum et al., 1996; Whelan-Goodinson et al., 2009). Ponsford et al. (2018) suggested one possible reason for high reported rates of OCD is that behaviours related to TBI are similar to symptoms of OCD, such as frequent checking due to memory problems. Treatments for OCD include psychotherapy and antidepressant medications. No clinical trials for the treatment of OCD in patients after ABI have been identified.

8.2.4 Post-Traumatic Stress Disorder

Early PTSD literature focused on patients with mild TBI; this was based on the belief that PTSD could not develop in the presence of amnesia following a traumatic event (Bryant et al., 2001; Mayou et al., 1993; Warden et al., 1997; Zatzick et al., 2010). Since then, research has found the PTSD can occur in individuals with moderate and severe TBI as well (Al-Ozairi et al., 2014). A population-based sample of individuals with TBI found that nearly 18% met criteria for PTSD, which included patients across the spectrum TBI severity (Barker-Collo et al., 2013). Individuals with comorbid PTSD and TBI may experience cognitive impairment and sleep disruptions, along with anxiety and depressive symptoms (Balba et al., 2018; Bosma et al., 2018). Additional research is necessary to confirm factors that correlate with PTSD in moderate to severe TBI, and to implement treatment programs involving interventions to target PTSD symptoms.

8.3 Suicidal Ideation

Suicidal ideations are the thoughts or considerations of suicide that when left unattended can lead to distress and attempted suicide. Risk factors for suicide overlap with characteristics present after a TBI which explains, in part, why there is an increased risk of suicide following a TBI (Ahmedani et al., 2017; Bahraini et al., 2013; Simpson & Tate, 2007). Unfortunately, the risk for suicidal ideation and attempt remains high even 20 years post injury (Fisher et al., 2016).

8.3.1 Incidence and Prevalence of Suicidal Ideation

The prevalence of suicide is much greater than the general population. A large retrospective cohort estimated an incidence rate ratio of 2.38 in patients with severe TBI compared to controls (Madsen et al., 2018). Within other TBI populations, 23-28% of individuals report suicidal ideation post injury (Mackelprang et al., 2014; Simpson & Tate, 2002; Tsaousides et al., 2011). Males are more likely to have suicidal ideation compared to females (Wisco et al., 2014), while age at time of injury was not associated with suicidal ideation (Mackelprang et al., 2014; Simpson & Tate, 2002). Risk of suicidal ideation can be further augmented with comorbid diagnosis of depression, anxiety, or PTSD (Tsaousides et al., 2011) and the number of sustained TBIs (Shura et al., 2018; Wisco et al., 2014). Furthermore, elevated suicidal ideation at one year post TBI is associated with continual elevation of ideation at five years (Fisher et al., 2016), demonstrating the necessity for therapies targeting such ideations.

If suicide ideation is not minimized, the risk of suicide attempts is high (Simpson & Tate, 2007) and is further increased when emotional distress is present (Gutierrez et al., 2008; Simpson & Tate, 2002). Within their lifetime, 26% of individuals post TBI attempt suicide, with half of these individuals making more than one attempt (Simpson & Tate, 2002, 2005). Moreover, emotional disturbance and substance abuse history increase the risk for attempted suicide by a factor of 21, compared to individuals with no history (Simpson & Tate, 2005).

8.3.2 Non-Pharmacological Interventions for Suicide Prevention

Specific interventions have been developed, primarily psychotherapy, in order to address suicidal ideation in individuals following ABI.

Table 8.11 Non-Pharmacological Interventions for Suicide Prevention Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Brenner et al. (2017) Australia RCT PEDro=6 N$_{Start}$=44, N$_{End}$=35	**Population:** TBI. *Intervention Group (n=15)*: Mean Age=47.7yr; Gender: Male=13, Female=1, Transgender=1. *Waitlist Group (n=20)*: Mean Age=54.6yr; Gender: Male=19, Female=1, Transgender=0. **Intervention:** Participants were randomized to receive a manualized, small-group cognitive behavioural intervention focused on alleviating hopelessness or to a waitlist. The intervention was 2hr and delivered weekly for 10 wk. Participants were crossed over to the alternate intervention after 10 wk. Assessments occurred at baseline, 10wk, and 20 wk. **Outcome Measure:** Beck Hopelessness Scale (BHS), Beck Depression Inventory (BDI), Beck Scale for Suicide Ideation (BSSI).	1. After controlling for baseline BHS scores, the intervention group had significantly lower hopelessness post intervention compared to those on the waitlist (p=0.03); these reductions were maintained at follow-up. 2. The waitlist group demonstrated significant reductions on the BHS (p=0.01) and depression (p=0.003) after completing the intervention. 3. There were no significant between-group differences for the BDI or BSSI.
Simpson et al. (2011) Australia RCT PEDro=8	**Population:** TBI; Severity: Severe. *Treatment Group (n=8)*: Mean Age=39.4yr; Mean Time Post Injury=6.3 yr. *Control Group (n=9)*: Mean Age=44.1yr; Mean Time Post Injury=7.6 yr.	1. Significant group-by-time interaction on BHS (p=0.002) but no significant main effects for either group or time.

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
N=17	**Intervention:** Participants were randomized to receive a manualized, small-group cognitive behavioural intervention focused on alleviating hopelessness or to a waitlist. The intervention was 2 hr and delivered weekly for 10 wk. Participants were crossed over to the alternate intervention after 10 wk. Assessments occurred at baseline, 10wk, and 20 wk. **Outcome Measure:** Beck Hopelessness Scale (BHS), Beck Scale for Suicide Ideation (BSSI), Hospital Anxiety and Depression Scale (HADS), Herth Hope Index (HHI), Rosenberg Self-Esteem (RSE), Social Problem Solving Inventory-Revised (SPSI-R).	2. Individuals receiving treatment had larger improvements in hopelessness (BHS scores) at 10wk; 75% reduced hopelessness by 1 severity band and 50% maintained/reduced severity by 20 wk. 3. Hopelessness on BHS improved significantly from pre to post treatment for all participants (p=0.008), a clinical improvement from moderate to mild severity. 4. Suicidal ideation according to mean BSSI scores was stable in the treatment group, but increased in the control group. 5. No significant change on BSSI, HADS, HHI, RSE, and SPSI-R were found.
Barnes et al. (2017) USA Post-Test N$_{Start}$=17, N$_{End}$=13	**Population:** TBI; Median Age=54.5 yr; Gender: Male=12, Female=2; Severity: Moderate=4, Severe=10. **Intervention:** Participants received 10 sessions of problem-solving therapy for suicide prevention. Assessments occurred after the intervention. **Outcome Measure:** Client Satisfaction Questionnaire-8 (CSQ-8), Narrative Evaluation of Intervention Interview (NEII).	1. On the CSQ-8, participants reported high satisfaction with the program (mean score=27.8). 2. On the NEII, participants reported that they found the intervention valuable, beneficial, and without negative effects.

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

Discussion

Hopelessness is a precursor to suicidal ideation, which in turn increases the risk of suicide. Two RCTs found that feelings of hopelessness after severe TBI may be reduced through group-based therapy that targets associated psychological problems. Hopelessness decreased in the treatment group, but suicidal ideation increased in the control group who did not receive treatment, underlining the risk of leaving suicidal distress untreated (Brenner et al., 2017; Simpson et al., 2011). While only half of the individuals were able to maintain the reduction in hopelessness by study end in the earlier RCT (Simpson et al., 2011), the subsequent RCT found that reductions remained significant at follow-up (Brenner et al., 2017). Both RCTs noted significant reductions in depressive symptoms and suicidal ideation following treatment, although these reductions were not significant when compared to the control group over time (Brenner et al., 2017; Simpson et al., 2011). The authors argued that hopelessness and depression can manifest independently, and therefore it is important to develop therapies focused on all precursors of suicidal ideation (Simpson et al., 2011).

Due to impaired executive function and other cognitive processes, problem-solving deficits are a common issue following TBI. These issues have been associated with suicidal ideation and attempts in other populations, and so problem-solving therapy (PST) has been proposed as a potential intervention for suicide prevention. Barnes et al. (2017) provided ten sessions of PST to individuals with moderate to severe TBI. The authors found that the participants were highly satisfied with the program and found it to

be valuable and beneficial (Barnes et al., 2017). However, the study did not measure symptoms of suicidal ideation, hopelessness, or depression, and so the efficacy of the program is unknown.

Conclusions

There is level 1a evidence that a group-based cognitive behavioural intervention, compared to a waitlist control, may be effective in reducing hopelessness post TBI.

There is level 4 evidence that problem-solving therapy may decrease suicidal ideation post TBI.

Group-based cognitive behavioural therapy may be an effective intervention for reducing feelings of hopelessness, a precursor of suicidal ideation, post TBI.

Problem-solving therapy may be a feasible intervention for reducing suicidal ideation post TBI; further research is required to determine its efficacy.

8.4 Challenging Behaviours

Behaviour can be defined as any interaction between an organism and their environment. Behavioural issues are often defined as antisocial, uncooperative, or negative interactions associated with interpersonal problems. Challenging behaviour following ABI occurs with a relatively high frequency (25-50%), which often includes anger, agitation, aggression, and non-compliance with treatment. The emergence of these behaviours likely arises from injury to the frontal lobes, which results in disinhibited behaviour and a lack of recognition for the consequences (Kim, 2002). Individuals found to have poorer social functioning often engage in a variety of aggressive or agitated behaviours including refusing participation, hitting, kicking, throwing objects, verbal abuse, and self-harm (McNett et al., 2012; Rao et al., 2009). Typically, behavioural management techniques and pharmacological interventions are used to alleviate these challenges with varying degrees of success.

8.4.1 Prevalence and Predictors of Agitation and Aggression

Agitation and aggression occur in approximately 33% to 70% of patients with TBI (Janzen et al., 2014; Nott et al., 2006; Sabaz et al., 2014; Singh et al., 2014). Agitation is generally defined as restlessness, impulsiveness, edginess, distractibility, wandering, and/or non-compliance, while aggression is defined as physical or verbal violence that may put the individual and others at risk for injury (Eisenberg et al., 2009). These behaviours have been associated with several clinical factors in individuals with ABI, including younger age (Baguley et al., 2006; Jean-Bay, 2000; Wolffbrandt et al., 2013), frontal lobe sessions (Tateno et al., 2003; Warriner & Velikonja, 2006), premorbid major depression (Baguley et al., 2006; Bakchine et al., 1989; Jean-Bay, 2000; Kim & Humaran, 2002; Sabaz et al., 2014; Tateno et al., 2003), and premorbid substance abuse (Sabaz et al., 2014; Tateno et al., 2003). During rehabilitation, the severity and duration of these challenging behaviours can have a negative impact on functional outcomes (Jean-Bay, 2000; Singh et al., 2014).

8.4.2 Pharmacological Interventions for Agitation and Aggression

Agitation is often a recovery-limiting factor, as it creates both a disruptive and unsafe environment for rehabilitation (Rosati, 2002). An ideal medication should have "a rapid onset of action, achieve maximal effect with a single dose, cause minimal adverse effects, and allow the patient to resume normal daily activities as quickly as possible without causing protracted sedation or cognitive impairments" (Stanislav & Childs, 2000). Pharmacological interventions used to treat agitation include a variety of medications such as: antidepressants, stimulants, anticonvulsants, antipsychotics, and beta-blockers. Ideally, the safety and efficacy of pharmacological interventions for agitation and aggression would be studied using a RCT design; however, few of these trials have been conducted in ABI (Levy et al., 2005; Williamson et al., 2018)(Williamson 2018). Moreover, due to the lack of consistency in measuring agitation and aggression (Baguley et al., 2006), comparing studies is challenging. A systematic review by Williamson et al. (2018) examined controlled trials of pharmacological interventions for agitated behaviours in patients with mixed severity of TBI. The authors concluded that propranolol, methylphenidate, valproic acid and olanzapine may offer some benefit, where as sertraline, lisdexamfetamine and dextroamphetamine were not supported. Additionally, antipsychotics could increase the length of post traumatic amnesia and decrease cognitive function. Another systematic review that included case-series and case-report studies also reported weak support for the use of propranolol and antiepileptics (Nash et al., 2018). The review by Nash et al. (2018) concluded amantadine was among the best supported medication in acute management of behavioral and emotional dysregulation. Williamson et al. (2018) reported mixed findings for the use of amantadine, and cautioned that it may increase agitation in acutely ill patients. Overall, both reviews commented on the paucity of high-quality primary research, expressing a need for more tailored trials, in various stages of recovery, and standardized assessments of agitated behaviours (Nash et al., 2018; Williamson et al., 2018).

8.4.2.1 Antidepressants

Depression is a common correlate of agitation and aggression following ABI, which may be linked to serotonergic , dopaminergic, and noradrenergic dysfunction resulting from injury (Jorge, 2005). Studies have examined the effect of antidepressants on reducing these challenging behaviours in patients with ABI.

Table 8.12 Effects of Sertraline and Amitriptyline on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Kant et al. (1998) USA Pre-Post N=13	**Population:** TBI; Mean Age=37.6yr; Gender: Male=10, Female=3; Injury Severity: Mild=5, Moderate=6, Severe=6; Mean Time Post Injury=2yr. **Intervention:** Participants with aggression received sertraline (50-200 mg/day) for 8 wk. Assessments were conducted at 4wk and 8wk. **Outcome Measure:** Overt Aggression Scale-Modified (OAS-M), Anger Irritability Assault Questionnaire (AIAQ), Beck Depression Inventory (BDI).	1. Significant improvement on OAS-M (p<0.001) and AIAQ (p<0.01) found at 4wk and 8wk. 2. Significant improvement on BDI found at 4wk (p=0.04) but not 8wk (p=0.14).
Mysiw et al. (1988) USA	**Population:** TBI; Mean Age=29.4yr; Gender: Male=18, Female=2.	1. Thirteen patients experienced significantly reduced levels of agitation

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Pre-Post N=20	**Intervention:** Participants with persistent agitation failing to respond to conventional behavioural techniques received amitriptyline (25-150 mg/day). Assessments were conducted at 1wk and follow-up. **Outcome Measure:** Orientation Group Monitoring Scale (OGMS).	after 1wk (p<0.001), which was maintained in the ensuing weeks (p<0.001) but did not significantly decrease from 1wk (p>0.6). 2. Thirty percent of patients (n=6) experienced no significant change in agitation levels, despite increasing the dose at 1wk (p>0.7) and beyond (p>0.3).

Discussion

Two studies demonstrated the potential of antidepressants to improve aggressive and agitated behaviour in patients with brain injuries. Kant et al. (1998) examined the effect of sertraline, a selective serotonin selective reuptake inhibitor, whereas Mysiw et al. (1988) examined the effect of amitriptyline, a tricyclic antidepressant with both serotonergic and noradrenergic reuptake inhibition. For sertraline, Kant et al. (1998) found that patients responded positively at both four and eight week follow-ups, showing significant reductions in aggressive and irritable behaviour; patients also had reductions in depression at four weeks. For amitriptyline, Mysiw et al. (1988) found that 65% of patients displayed significant reductions agitation within the first week of treatment (Mysiw et al., 1988).

Conclusions

There is level 4 evidence that sertraline may reduce aggression and irritability post TBI.

There is level 4 evidence that amitriptyline reduces agitation post TBI.

Sertraline may be an effective treatment for reducing aggression and irritability following brain injury, although additional research is needed.

Amitriptyline may be an effective treatment for reducing agitation following brain injury, although additional research is needed.

8.4.2.2 Stimulants

Stimulants have been utilized as interventions for improving cognitive function and reducing psychiatric symptoms following brain injury (Maksimowski & Tampi, 2016). A limited amount of research has explored the use of stimulants for challenging behaviours that emerge post ABI.

8.4.2.2.1 Amantadine

Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist that decreases glutamate levels, which may improve learning, memory, and behaviour deficits (Hammond et al., 2014). Amantadine can also indirectly facilitate dopamine release pre-synaptically and directly inhibit dopamine reuptake at

the post-synapse (Hammond et al., 2014). Amantadine was initially used as an antiviral medication for influenza A but later gained popularity as an anti-Parkinsonian treatment. For the ABI population, the effects of amantadine on reducing agitation and aggression have yet to be established.

Table 8.13 Effects of Amantadine on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Hammond et al. (2015) USA RCT PEDro=10 N$_{Initial}$=168, N$_{Final}$=157	**Population:** TBI. *Amantadine Group (n=82)*: Mean Age=40.2yr; Gender: Male=66, Female=16; Severity: Mild=20, Moderate=3, Severe=59. *Placebo Group (n=86)*: Mean Age=38.2yr; Gender: Male=64, Female=22; Severity: Mild=22, Moderate=1, Severe=63. **Intervention:** Participants were randomized to receive either placebo or 100 mg of amantadine 2x/day for 60 days. Assessments were conducted at baseline, 28 days, and 60 days. **Outcome Measure:** Neuropsychiatric Inventory Irritability (NPI-I).	1. Observer-rated NPI-I scores showed no significant differences between groups at 28d or 60d, but both groups showed improvement in irritability. 2. Participant-rated NPI-I Most Problematic (p=0.0353) and Distress (p=0.0362) scores were significantly different between amantadine and placebo at 60d, but there was no significant difference after adjustment for multiple comparisons.
Hammond et al. (2014) USA RCT PEDro=9 N$_{Initial}$=76, N$_{Final}$=72	**Population:** TBI. *Amantadine Group (n=38)*: Mean Age=34.7yr; Gender: Male=25, Female=13; Mean Time Post Injury=5.3yr; Mean GCS=9.5. *Placebo Group (n=38)*: Mean Age=42.1yr; Gender: Male=22, Female=16; Mean Time Post Injury=4.7yr; Mean GCS=7.5. **Intervention:** Participants were randomized to receive placebo or 100 mg of amantadine 2x/day for 28 days. Assessments were conducted at baseline and 28 days. **Outcome Measure:** Neuropsychiatric Inventory (NPI) Irritability (NPI-I), NPI Agitation/ Aggression (NPI-A), NPI Distress (NPI-D), Beck Depression Inventory-II (BDI-II), Brief Symptom Inventory (BSI), Global Mental Health Scale (GMHS).	1. Eighty-one percent of the amantadine group had improved irritability by at least 3 points on NPI-I, compared to 44% of placebo (p=0.0016). 2. Significant difference in frequency and severity of irritability on NPI-I between amantadine and placebo groups (p=.0085). 3. No significant differences between amantadine and placebo groups on NPI-D, BDI-II, BSI-Anxiety, or GMHS. 4. Only individuals with moderate to severe aggression at baseline on NPI-A had significant reduction in aggression after amantadine treatment compared to placebo (p=0.046).

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

Discussion

Two RCTs compared the effects of amantadine and placebo on irritability and aggression post TBI. Hammond and colleagues (2014) found that the frequency and severity of irritability were reduced when individuals received amantadine for 28 days compared to placebo. However, amantadine only significantly reduced aggression in individuals who had moderate to severe aggression at baseline (Hammond et al., 2014). A subsequent trial by Hammond and colleagues (2015) found that amantadine produced a non-significant reduction in irritability compared to placebo at 28 and 60 days, according to the most problematic and aberrant items on the neuropsychiatric inventory (Hammond et al., 2015).

Conclusions

There is level 1b evidence that amantadine compared to placebo may reduce aggression post TBI in individuals with moderate to severe aggression.

There is conflicting (level 1b) evidence as to whether amantadine reduces irritability compared to placebo post TBI.

Amantadine requires further research before conclusions can be drawn regarding its effects on aggression and irritability following a TBI.

8.4.2.2.2 Methylphenidate

Methylphenidate is a catecholamine inhibitor that reduces the concentration of dopamine and norepinephrine in the synaptic cleft (Hodgkins et al., 2012). As well, it has been demonstrated that methylphenidates acts as a weak agonist of the serotonin 1A receptor (Markowitz et al., 2009). Methylphenidate is typically used as a treatment for attention deficit hyperactivity disorder and narcolepsy (Hodgkins et al., 2012), but it has been explored as a potential intervention for agitation and aggression in individuals with ABI.

Table 8.14 Effects of Methylphenidate on Agitation and Attention Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Mooney & Haas (1993) USA RCT PEDro=5 N=38	**Population:** TBI; Mean Age=29.45yr; Gender: Male=38, Female=0; Mean Time Post Injury=27.08mo. **Intervention:** Patients received methylphenidate (30 mg/day; n=19) or placebo (n=19) for 6 wk. **Outcome Measure:** State-Trait Anger Scale, Katz Adjustment Scale - Belligerence, Profile of Mood States - Anger-Hostility.	1. After controlling for differences in baseline anger scores, there was a significant main effect for the drug treatment (p<0.001). 2. For all of the anger outcome measures, a significant drug by time interaction effect was noted (p=0.002).

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

Discussion

In a RCT, Mooney and Haas (1993) demonstrated that methylphenidate significantly reduced anger following brain injury using several anger outcome measures. Despite the differences between the groups on one measure at baseline, a significant treatment effect was demonstrated.

Conclusions

There is level 2 evidence that methylphenidate compared to placebo reduces anger post TBI.

Methylphenidate may be effective in reducing anger following TBI.

8.4.2.3 Anticonvulsants

Post TBI, there is typically diffuse injury with primary involvement of the frontal-subcortical and temporal-limbic regions. As a result, seizure disorders are not uncommon and may result in episodic lack of control. For the use of any medication, a balance must be struck between managing behaviour and maintaining cognitive functioning. Thus, some anticonvulsants have been found to be a good alternative to antipsychotics and/or benzodiazepines in managing aggression, as they tend to have fewer cognitive side effects (e.g., sedation, confusion, memory impairment).

8.4.2.3.1 Carbamazepine

Carbamazepine, an antiepileptic, has been shown to successfully treat various seizure disorders as well as schizophrenia and bipolar disorder (Alrashood, 2016). It has been suggested that carbamazepine may be effective in treating aggressive behaviour post TBI, offering an effective alternative to lithium (Azouvi et al., 1999).

Table 8.15 Effects of Carbamazepine on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Azouvi et al. (1999) France Pre-Post N=10	**Population:** TBI; Mean Age=33.7yr; Gender: Male=8, Female=2; Mean GCS Score=5.3; Mean Time Post Injury=58 wk. **Intervention:** Patients received carbamazepine (mean dose=9.47±2.9 mg/kg/day) for 8 wk. **Outcome Measure:** Neurobehavioural Rating Scale (NRS), Agitated Behaviour Scale (ABS), Katz Adjustment Scale (KAS), Mini-Mental Status Examination (MMSE).	1. Total NRS-R and ABS scores showed significant improvement (p=0.02); improvements plateaued after 2 wk. 2. At follow-up, significant improvements were shown for only the irritability (p<0.01) and disinhibition (p<0.05) portions of NRS-R. 3. Global NRS-R significantly decreased from baseline (p=0.01). 4. No significant changes on MMSE were observed (p>0.01).

Discussion

In an 8-week trial, Azouvi et al. (1999) administered carbamazepine to 10 individuals with severe brain injury who had significant behavioural challenges that were interfering with care and/or family integration. After two weeks, results indicated improvement on behavioural scales but only the improvements in irritability and disinhibition were maintained by the end of the trial. Overall neurobehavioural and social functioning had improved. It should be noted that drowsiness was a frequent adverse event which limited a dosage increase in 40% of the participants.

Conclusions

There is level 4 evidence that carbamazepine may reduce agitation and aggression post TBI.

Carbamazepine may be effective in reducing agitation and aggression following TBI.

8.4.2.3.2 Lamotrigine

Lamotrigine has demonstrated effectiveness as an antiepileptic (Brandt & May, 2018) and mood stabilizer (Baldessarini et al., 2018). Among individuals with ABI, however, its effectiveness as a mood stabilizer has yet to be established (Gao & Calabrese, 2005; Tidwell & Swims, 2003).

Table 8.16 Effects of Lamotrigine on Inappropriate Behaviour Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Results
Chahine & Chemali (2006) Lebanon Case Series N=4	**Population:** TBI; Mean Age=26 yr; Gender: Male=4, Female=0. **Intervention:** Lamotrigine (range 125 to 300mg/d) to reduce inappropriate behaviours (e.g. laughing, impulsivity or verbal aggression)**. Outcome Measure:** Frequency of crying, pathological laughing, behaviours of impulsivity, and seizures. Also, notes of depression.	1. All behaviours decreased once the patient was placed on lamotrigine. 2. Crying decreased and inappropriate laughing ceased. 3. Impulsivity did not cease.

Discussion

Results from a single study indicate that lamotrigine helps to reduce unwanted behaviours such as pathologic laughter and crying but did not address impulsivity (Chahine & Chemali, 2006). All four participants were on other medications to control for additional behaviours, but these medications were eventually eliminated once lamotrigine was introduced. No formal outcome assessments were conducted, which makes it difficult to draw conclusions from this study.

Conclusions

There is level 4 evidence that lamotrigine may reduce inappropriate behaviours post TBI.

> **Lamotrigine may be effective in reducing pathologic laughing and crying following a TBI. However, further research with larger sample sizes is needed to validate these findings.**

8.4.2.3.3 Valproic Acid

Valproic acid, an antiepileptic, has been used to treat seizure disorders in both adults and children. It has also been used to treat mania, bipolar disorder, and PTSD (McElroy et al., 1987). A case study of an individual with TBI showed a reduction in episodic explosiveness (Geracioti Jr, 1994), and so it has been explored as an intervention for challenging behaviours post ABI.

Table 8.17 Effects of Valproic Acid on Agitation and Aggression Post TBI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Wroblewski et al. (1997) USA Case Series N=5	**Population:** TBI; Mean Age=38.2yr; Gender: Male=4, Female=1. **Intervention:** Patients received valproic acid for destructive and aggressive behaviours. **Outcome Measure:** Aberrant Behaviour Checklist.	1. All patient showed a substantial reduction in target behaviours.

Discussion

Wroblewski and colleagues (1997) examined the effects of valproic acid on reducing aggressive behaviour in a case series of five patients. The study reported that all patients showed a substantial reduction in challenging behaviour (i.e., outbursts, agitation, and anger) within one to two weeks, even when other medications were not successful. No statistical analyses were conducted, making it difficult to draw conclusions from these findings. As well, patients were also part of a specialized neurobehavioural unit, which may have contributed to the positive results.

> **Valproic acid may be effective in reducing aggression following a TBI, although additional research is needed.**

8.4.2.3.4 Divalproex

Divalproex, a compound of valproic acid and sodium valproate, has been used to control seizures, treat bipolar disorder, and prevent migraines. It has been explored an intervention for reducing challenging behaviours in individuals post TBI.

Table 8.18 Effects of Divalproex on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Chatham Showalter & Kimmel (2000) USA Case Series N=29	**Population:** TBI; Mean Age=48.2yr; Mean Time Post Injury=28.6d. **Intervention:** A retrospective chart review of patients receiving divalproex treatment in an attempt to reduce symptoms of agitation following injury. Symptoms of agitations included easily aggravated, escalating temper, biting, punching, restless, etc. **Outcome Measure:** Agitated Behaviour Scale (ABS).	1. Eight patients had treatment with divalproex (mean 714 mg) that led to rapid resolution of symptoms and near total recovery. 2. For a second subgroup of patients(n=18), progress notes prior to and during treatment demonstrated decreased and significant improvement in symptoms within 7d of receiving divalproex (mean dose 1,257 mg). 3. Most patients were discharged to their homes (n=23) or to other community sites (n=4).

Discussion

Divalproex was used to treat symptoms of agitation in 29 patients post injury (Chatham Showalter & Kimmel, 2000). Symptoms decreased in the majority of patients, with a portion showing near total resolution of symptoms. Due to a lack of statistical analysis, it is difficult make firm conclusions based on these results.

Anticonvulsants may effective in reducing agitation following a TBI, although additional research is needed.

8.4.2.4 Antipsychotics

Treatment with antipsychotic medication following brain injury remains controversial. Clinical research of typical and atypical antipsychotics is often limited to a single case series for each medication. Due to lack of evidence for antipsychotic effectiveness, prolonged post-traumatic amnesia and decreased cognitive function (Bogner et al., 2015; McKay et al., 2018; Mysiw et al., 2006), current recommendations and reviews advise against the use of antipsychotics to manage behaviour (Plantier & Luaute, 2016; Ponsford et al., 2014; Williamson et al., 2018). However, observational studies suggest that antipsychotics are frequently used for agitated behaviours (Bogner et al., 2015; Perreault et al., 2017; Pisa et al., 2015; Williamson et al., 2019).

8.4.2.4.1 Quetiapine

Quetiapine is an atypical antipsychotic that has been used to reduce aggressive behaviour among those diagnosed with schizophrenia and Alzheimer's disease (Volavka et al., 2004; Webb & Glueckauf, 1994). However, there is limited examination of its impact within a brain injury population.

Table 8.19 Effects of Quetiapine on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Kim & Bijlani (2006) USA Case Series N=7	**Population:** TBI; Mean Age=48.9 yr; Gender: Male=4, Female=3; Mean Time Post Injury=23.1 mo. **Intervention:** Patients received quetiapine (25-300 mg/day; mean=110.7 mg/day) for 6 wk. **Outcome Measure:** Overt Aggression Scale-Modified (OAS-M), Clinical Global Impression (CGI), Neurobehavioural Functioning Inventory (NFI), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).	1. After treatment, OAS scores were significantly reduced (p=0.002). 2. After treatment, CGI scores were significantly improved (p=0.002). 3. After treatment, significant improvements were noted on the aggression subscale of NFI (p=0.036). 4. RBANS scores indicated a mean improvement of 8.02% (p=0.027).

Discussion

In one case series, quetiapine was associated with a reduction in aggressive behaviour in seven individuals (Kim & Bijlani, 2006). The study also noted significant improvements in neuropsychological status and

clinical impression. The authors suggested that it could be considered as an alternative to typical antipsychotics, such as haloperidol or chlorpromazine, if additional research finds it to be as effective and with fewer side effects (Kim & Bijlani, 2006).

Conclusions

There is level 4 evidence that quetiapine may reduce aggression post TBI.

Quetiapine may be effective in reducing aggression following a TBI, although additional research is needed.

8.4.2.4.2 Ziprasidone

Ziprasidone is an atypical antipsychotic has been approved for the treatment of acute agitation in schizophrenia as well as acute mania associated with bipolar disorder. Following a TBI, ziprasidone may be similarly effective in reducing agitation.

Table 8.20 Effects of Ziprasidone on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Noe et al. (2007) USA Case Series N=5	**Population:** TBI; Mean Age=26.8yr; Gender: Male=3, Female=2; Mean Time Post Injury=54.6 days; Mean GCS Score=6. **Intervention:** Ziprasidone (30-80 mg/day for 35-68 days) was given to participants. **Outcome Measure:** Agitation Behaviour Scale (ABS).	1. Mean dose of the drug was 52.8 mg/day. 2. Scores on the ABS decreased within the first 14 days (27.3 to 18). 3. Scores on the disinhibition portion of the ABS decreased from 28.6 to 17.1, while scores on the aggressiveness subsection of the scale decreased from 26.1 to 20.4. 4. No side effects were noted.

Discussion

The period of post traumatic amnesia has been defined as a period where the individual is disorientated and may suffer from behaviour alterations (Brooke et al., 1992). Researchers have suggested that these changes in behaviour result from a lack of self-awareness, which may be associated with memory alterations that appear after injury (Noé et al., 2007). One study examined individuals who were still suffering from post-traumatic amnesia upon admission to rehabilitation. These patients showed a decrease in agitation during the first two weeks of ziprasidone administration. As well, it was noted that all patients tolerated the medication, with no clinical side effects observed (Noe et al. 2007).

Conclusions

There is level 4 evidence that ziprasidone may reduce agitation post TBI.

> **Ziprasidone may be effective in reducing agitation following a TBI, although additional research is needed.**

8.4.2.4.4 Methotrimeprazine

Methotrimeprazine is a psychotropic medication that has antipsychotic properties, as mediated by dopamine blocking. It also has tranquilizing and analgesic properties, and appears to have an effect on opiate (pain) receptors (Maryniak et al., 2001). Its effect on challenging behaviours post ABI has received limited investigation.

Table 8.21 Effects of Methotrimeprazine on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Maryniak et al. (2001) Canada Case Series N=120	**Population:** TBI=95, ABI=25; Mean Age=37.8yr; Gender: Male=89, Female=31. **Intervention:** Retrospective review of patients attending an inpatient ABI rehabilitation unit, and some received methotrimeprazine (MTZ). **Outcome Measure:** Agitated Behaviour Scale.	1. Fifty-eight percent had agitation but 56 patients were treated with MTZ (10-25 mg, 4x/day) with a mean length of treatment of 41.9 days. 2. MTZ, was both safe and effective for controlling agitation in 96% of patients.

Discussion

The oral administration of methotrimeprazine for agitation was evaluated in a retrospective review of 56 patients during inpatient rehabilitation (Maryniak et al., 2001). The authors found that methotrimeprazine was both safe and effective for controlling agitation in nearly all cases. However, the study did not utilize standardized outcome measures, include a control group, or perform statistical analysis. Therefore, a more rigorous study examining the safety and efficacy of methotrimeprazine within an ABI population is necessary before a firm conclusion can be determined.

Conclusions

There is level 4 evidence that methotrimeprazine may be effective for controlling agitation post ABI.

> **Methotrimeprazine may be safe and effective for controlling agitation following an ABI, although additional research is required.**

8.4.2.4.5 Droperidol

Droperidol is a butyrophenone antipsychotic agent that acts as a potent dopamine receptor antagonist. It is a typical antipsychotic that has been used for the treatment of psychosis in Europe (Stanislav & Childs, 2000). There is limited research regarding its use as an intervention for post-ABI agitation.

Table 8.22 Effects of Droperidol on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Stanislav & Childs (2000) USA Case Series N=27	**Population:** TBI; Gender: Male=21, Female=6. **Intervention:** Patients received intramuscular injection of droperidol as needed to relieve agitation. **Outcome Measure:** Episodes of agitation.	1. Mean dose was 3.25 mg; a single dose reduced agitation in 96% of patients. 2. Time to achieve calming following episodes of agitation was significantly shortened with droperidol compared to haloperidol, lorazepam, or diphenhydramine (p=0.02).

Discussion

One study found that a single dose of droperidol effectively calmed patients displaying agitated behaviour (Stanislav & Childs, 2000). The study also found that droperidol calmed individuals more quickly than haloperidol, lorazepam, and diphenhydramine, without heavily sedating the patients like the comparative medications. It is worth noting that a standardized outcome measure was not utilized, and that a large proportion of the sample had psychiatric co-morbidities.

> **Droperidol may be effective in reducing agitation following TBI, although additional research is required.**

8.4.2.4.6 Haloperidol

Haloperidol is a butyrophenone antipsychotic agent that acts as a dopamine receptor antagonist. It is a typical antipsychotic that is used to treat schizophrenia, bipolar disorder, delirium, and agitation. Haloperidol does have several known side effects, adverse events, and contraindications. Given the former, there is concern that it may impede recovery post ABI.

Table 8.23 Effects of Haloperidol on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcomes
Rao et al. (1985) USA Case Series N=26	**Population:** TBI; Age Range=16-48yr; Injury Severity: Severe. **Intervention:** Retrospective review of patients attending an inpatient ABI rehabilitation unit whose agitation was treated with haloperidol (n=11; 2-15 mg/day) and those who were not (n=15). **Outcome Measure:** Patient Evaluation Conference Systems.	1. Those treated had a longer length of post-traumatic amnesia (p<0.03). 2. No statistically significant differences were shown between those who were and were not treated in terms of independent living at discharge (64% versus 60%) or independence in managing behaviour (40% versus 60%). 3. Three untreated patients obtained independence in intellectual skills but none of the treated patients achieved it.

Discussion

In a retrospective chart review, agitation was managed during inpatient rehabilitation in eleven patients with haloperidol and in fifteen patients without haloperidol (Rao et al., 1985). No significant differences were found between the two groups with regards to success of rehabilitation, although none of the treated patients obtained independence in intellectual skills (Rao et al., 1985).

Conclusions

There is level 4 evidence that haloperidol may not be effective in treating behavioral disorders post TBI.

> **Haloperidol appears to have no benefits, and possible negative effects on recovery, following a TBI.**

8.4.2.5 Beta-Blockers

Beta-blockers are a class of medications that act as competitive antagonists of the catecholamine receptors. It has been suggested that these medications may reduce restlessness, anxiety, agitation, and aggression following brain injury. Given that dosage is often high, patients may be vulnerable to adverse effects such as lethargy, sedation, and depression; although, motor recovery post injury does not seem to be negatively affected (Levy et al., 2005).

8.4.2.5.1 Pindolol

Pindolol is an atypical beta-blocker in that it exerts a partial agonist effect on the serotonin 1A receptor which provides a slight stimulation of the blocked receptor and helps maintain a better resting sympathetic tone. The use of pindolol in individuals with aggressive behaviour following ABI was investigated in a clinical trial.

Table 8.24 Effects of Pindolol on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Greendyke & Kanter (1986) USA RCT PEDro=7 N$_{Initial}$=11, N$_{Final}$=9	**Population:** ABI; Mean Age=52yr; Gender: Male=9, Female=0; Mean Time Post Injury=7.8yr. **Intervention:** Patients received pindolol (60-100 mg/day) or placebo for 10 days. Groups were then crossed over and received the alternate treatment for 10 days. Supplemental psychotropic medication was given as needed. **Outcome Measure:** Frequency of assaultive behaviour.	1. Significant reduction of assaultive episodes, need for supplemental medication, and hostility were demonstrated during pindolol treatment (p<0.05). 2. Significant improvements in willingness to communicate and cooperate (p<0.025) and significant reduction of stereotyped behaviours (p<0.01) were demonstrated during pindolol treatment.

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

Discussion

Greendyke and Kantor (1986) investigated the effectiveness of pindolol in improving behavioural disturbances post ABI. A significant reduction in behaviours that lead to assaults was demonstrated during treatment with pindolol, as well as improved communication and cooperation. The authors noted that the optimal dose, in terms of maximizing therapeutic efficacy and minimizing adverse events, ranged between 40-60 mg per day. The frequency of supplemented psychotropic medications was reduced with pindolol treatment, although these medications were still administered and may have contributed to the reduction in assaultive episodes.

Conclusions

There is level 1b evidence that pindolol may reduce aggression compared to placebo post ABI.

Pindolol may be effective in reducing aggression following an ABI.

8.4.2.5.2 Propranolol

Propranolol is a non-selective beta-blocker that has been used for the reduction of aggressive behaviours associated with compromised brain function. It appears to lack the serious cognitive and affective side effects associated with other medications used to treat agitation post injury (Levy et al., 2005). The use of propranolol in individuals with post-TBI aggression was investigated in two clinical trials.

Table 8.24 Effects of Propranolol on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Brooke et al. (1992) USA RCT PEDro=7 N=21	**Population:** TBI; Severity of Injury: GCS <8. **Intervention:** Patients were randomized to receive either propranolol (n=11; 60 mg/day, max 420mg) or placebo (n=10). **Outcome Measure:** Overt Aggression Scale.	1. No significant differences between the two treatments in terms of agitation episodes per wk. 2. More intense episodes of agitation with placebo than propranolol ($p<0.05$). 3. More participants were placed in restraints with placebo than propranolol ($p<0.05$). 4. No differences between the two treatments in the proportion receiving sedating drugs or drugs for agitation.
Greendyke et al. (1986) USA RCT PEDro=7 N=10	**Population:** Mean Age=52yr; Gender: Male=9, Female=0; Mean Time Post Injury=7.8yr. **Intervention:** Patients were randomized to receive either propranolol (520 mg/day) or placebo for 11wk. Groups were then crossed over and received the alternate treatment for 11wk. **Outcome Measure:** Assaultive behaviour, Supplemental medication, Nurses Observation Scale for Inpatient Evaluation.	1. Significantly fewer assaults and attempted assaults occurred during propranolol treatment when compared to placebo ($p<0.05$). 2. No significant changes in irritability, social interests, or psychomotor retardation were noted. 3. No abnormalities were noted on laboratory measures.

Discussion

Greendyke et al. (1986) investigated the effectiveness of propranolol for the improvement of behavioural issues associated with brain disease. Significantly fewer assaults and attempted assaults occurred during the 11-week propranolol treatment as compared to placebo. Of the nine patients in the trial, five showed marked improvement, two showed moderate improvement, and two showed little or no improvement. It should be noted that the patients also had severe dementia, and so this study cannot be used to draw conclusions for the ABI population as a whole. A later study by Brooke et al. (1992) found that propranolol was effective in reducing the intensity of the agitation and use of restraints when compared to placebo. However, propranolol was not more effective than placebo in reducing the frequency of agitation episodes or the number of adjunctive medications for agitation and sedation.

Conclusions

There is level 1b evidence that propranolol compared to placebo reduces the intensity of agitated symptoms post ABI.

There is conflicting evidence (level 1b) that propranolol compared to placebo reduces the frequency of aggressive behaviour post ABI.

> **Propranolol may be effective in reducing the intensity of agitation and aggression following brain injury.**

8.4.2.5.3 Lithium Carbonate

Lithium carbonate has been used for many years in the treatment of mania and bipolar disorder (Kim, 2002). It has been suggested that mood disorders occurring post TBI may contribute to the development of aggression (Kim, 2002; Wroblewski et al., 1997). In the search for a pharmacological agent that reduces post-TBI aggression with limited side effects, the use of lithium has been explored.

Table 8.25 Effects of Lithium Carbonate on Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Glenn et al. (1989) USA Case Series N=10	**Population:** TBI=8, CVA=2; Mean Age=31.6yr; Gender: Male=5, Female=5. **Intervention:** Patients showing mood disorders and unstable, aggressive, combative, or self-destructive behaviour were administered lithium. **Outcome Measure:** Observed improvement.	1. Five participants showed a significant improvement with no decrease in motor or cognitive performance, one showed moderate response, and one improved dramatically but regressed after 7wk. 2. Four participants regressed after medications stopped. 3. Three participants had neurotoxic side effects.

Discussion

Lithium carbonate was studied in a case series of ten individuals with either TBI or stroke (Glenn et al., 1989). The authors reported favourable outcomes for the majority of patients, meaning a decrease in observed unstable, aggressive, combative, or self-destructive behaviour. The study highlighted the high risk of potential neurotoxicity among individuals with brain injuries, specifically in combination with neuroleptic drugs.

Conclusions

There is level 4 evidence to suggest that lithium carbonate may reduce aggressive/agitated behaviour following a brain injury.

Lithium may reduce behavioural problems but is associated with a high risk of neurotoxicity.

8.4.3 Sexually Disinhibited Behaviour

Sexual dysfunction following TBI has been reported to occur in at least 50% of patients (Emory et al., 1995). Hypersexuality is less common than hyposexuality, but results in a greater negative effect for the individual and a greater burden of care. Hypersexual behaviour can encompass a range of behaviours, from promiscuity, exhibitionism, and indiscriminate sexual advances, to assault and/or rape (Mania et al., 2006). A study revealed inappropriate sexual talk to be the most common inappropriate sexual behaviour in a sample of patients with TBI (Simpson et al., 2013).

8.4.3.1 Interventions for Sexually Disinhibited Behaviour

Treatment for sexual offenders without brain injuries often involves pharmacological intervention, counselling, and education. Typically, medication is used to reduce the sexual drive, but it is unclear if it has effect on cognitive processing. A review by Clay et al. (2018) concluded there was insufficient evidence to consider any specific treatment effective for decreasing inappropriate sexual behaviour in individuals with ABI. However, Clay et al. (2018) comment that some behavior analytic approaches have been effective.

Table 8.26 Effects of Depo-Provera and Counselling on Sexually Disinhibited Behaviour Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Emory et al. (1995) USA Case Series N=8	**Population:** TBI; Mean Age=25.5yr; Gender: Male=8, Female=0. **Intervention:** Patients received weekly intramuscular injections of Depo-Provera (400 mg) in conjunction with directive, individual-specific counseling for 6 mo. **Outcome Measure:** Incidence of hypersexual behaviour.	1. Family members reported all subjects stopped aberrant behaviour while taking medication. 2. Three subjects returned to previous patterns after stopping medication, due to inconsistent family support. 3. Three subjects dramatically improved and did not stop medication.

Discussion

Depo-Provera, an anti-androgen drug, was evaluated in terms of its efficacy for controlling sexual aggression in eight male patients with TBI experiencing onset of sexual aggression three years post injury (Emory et al., 1995). Weekly intramuscular injections of Depo-Provera (400 mg) in conjunction with monthly psychoeducational counseling resulted in a cessation of hypersexual behaviour and reduced testosterone levels. Three patients reoffended after they stopped taking the medication, two stopped taking it and maintained cessation of hypersexual behaviour, and three remained on it.

Conclusions

There is level 4 evidence that Depo-Provera, in combination with counselling, may reduce sexually aggressive behaviour post TBI.

Depo-Provera, in combination with directive counselling, may reduce sexual aggression following TBI, although additional research is needed.

8.4.4 Behavioural Management Following ABI

Common sequelae to brain injury are behavioural disturbances that impact relationships and recovery. In some cases, individuals with brain injury develop behavioural difficulties that impact their compliance with rehabilitation, which can result in limited participation in activities and/or early discharge (Alderman, 1991; Alderman et al., 2013). When challenging behaviours take the form of aggressive acts, this may prevent or decrease functional gains in neurorehabilitation (Alderman et al., 1999). In a cross-sectional study of patients admitted to a brain injury unit, Lequerica et al. (2007) found an inverse relationship between agitation and engagement in physical and occupational therapy. Behavioural analysis examines the relationship between events and behaviour with the goal of increasing social interactions and independence (Ashley MJ et al., 1995).

Behavioural techniques have been used for many years to treat an array of disorders, including brain injury. Techniques are often used to teach new skills, instil socially appropriate behaviour, and improve independent functioning. In the past, the alternative to behavioural techniques has been sedation, restraint, and/or institutionalisation. Teaching behavioural techniques encourages positive behaviours through an individualized approach rather than coercive management of behaviours. These techniques are not only applicable in a variety of settings and with a variety of behaviours, but they also address the main goal of rehabilitation – the development of functional life skills (Jacobs, 1993).

8.4.4.1 General Behavioural Modification

Broad programs for the modification of various challenging behaviours have been evaluated in individuals with brain injury.

Table 8.27 General Behavioural Modification Interventions for the Treatment of Behavioral Disorders Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Carnevale et al. (2006) USA RCT PEDro=5 N=37	**Population:** TBI=24, ABI=13; Mean Age=40.5yr; Gender: Male=28, Female=7; Mean Time Post Injury=7.6yr. **Intervention:** Participants were randomized to a control group (n=12) that received no treatment, an education group (n=13) that received education only, and a Natural Setting Behaviour Management (NSBM) group (n=12) that received both education and an individualized behaviour modification program. **Outcome Measure:** Neurobehavioural Functioning Inventory Revised (NFI-R).	1. NSBM had more improvement in behaviour than the other two groups at 30wk (p<0.002). 2. A significant difference was noted between the education group and the NSBM group (p<0.04).
Schlund & Pace (1999) USA Pre-Post N=3	**Population:** TBI; Mean Age=36yr; Gender: Male=3, Female=0; Mean Time Post Injury=5.7yr. **Intervention:** Patients received behavioural modification using systematic feedback based on frequency of maladaptive behaviour. **Outcome Measure:** Maladaptive behaviour.	1. Variability and frequency of maladaptive behaviour generally decreased from baseline (2.0-5.1/wk) to completion (0.18-1.8/wk).
Eames & Wood (1985) UK Pre-Post N=24	**Population:** ABI=22, Stroke=1, Other=1; Mean Age=26.8yr; Gender: Male=18, Female=6; Mean GCS Score=7.8; Mean Time Post Injury=44.7mo. **Intervention:** Patients were on a specialized TBI unit that used a wide range of physical, occupational, social, cognitive, and behavioural techniques based token economy. **Outcome Measure:** Patient placement.	1. More than 2/3 of patients had improved placements after treatment; only one person had a substantial improvement. 2. Fewer than 1/3 of patients made no change, and no one was demoted to a worse setting.

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

Discussion

Different behavioural interventions have demonstrated efficacy in modifying negative behaviours post ABI. An RCT by Carnevale et al. (2006) found significant improvements in behaviour for participants who received an individualized education and behaviour modification program in the natural community setting compared to those who only received education. Schlund and Pace (1999) showed that a behaviour modification program based on delivering feedback about the frequency of maladaptive behaviours was able to reduce the occurrence of such behaviours. However, the study consisted of only three individuals with mild cognitive impairment attending a medical rehabilitation program five days a week. An earlier study by Eames and Wood (1985) reported that a behaviour modification program based on token economy reduced some negative behaviours in participants. As well, improved relationships and living arrangements were demonstrated in two thirds of participants.

Conclusions

There is level 2 evidence that behavioural modification incorporating reinforcement compared to education alone may improve negative behaviours post brain injury.

8.4.4.2 Behavioural Interventions for Anger and Aggression

Specific interventions have been developed to manage anger and aggression in individuals following brain injury. A recent meta-analysis of various psychological interventions found a substantial reduction in aggressive behaviours for single and group-based therapy (Byrne & Coetzer, 2016).

Table 8.28 Behavioural Interventions for the Treatment of Anger Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Hart et al. (2017) USA RCT PEDro=7 N_{Start}=90, N_{End}=84	**Population:** TBI; Severity: Severe. *Treatment Group (n=60):* Mean Age=30.4yr; Gender: Male=49, Female=11; Median Time Post Injury=69mo. *Control Group (n=30):* Mean Age=36.2yr; Gender: Male=24, Female=6; Median Time Post Injury=72mo. **Intervention:** Participants were randomized to receive anger self-management training (treatment) or personal readjustment and education (control) in 90min weekly sessions for 8wk. Assessments were conducted at baseline, 4wk, 8wk, and 16wk. **Outcome Measure:** State-Trait Anger Expression Inventory 2 (STAXI-2); Brief Anger-Aggression Questionnaire (BAAQ).	1. At 8wk, the proportion of responders on self-reported STAXI-2 Trait Anger was significantly greater in the treatment group than control group for intention-to-treat analysis (68.3% versus 46.7%, p=0.047) and per protocol analysis (71.9% versus 51.9%, p=0.031); these improvements were maintained at 16wk. 2. There were no significant differences in response rates between groups on self-reported STAXI-2 Anger Expression-Out or BAAQ at 8wk or 16wk. 3. There were no significant differences in response rates between groups on STAXI-2 or BAAQ as rated by a significant other at 8wk or 16wk. 4. There were no significant differences between groups in mean scores on STAXI-2 or BAAQ by self-report over time.
Aboulafia-Brakha et al. (2016) Switzerland RCT $N_{Initial}$=24, N_{Final}=19	**Population:** ABI: TBI=15, Stroke=4; Gender: Male=16, Female=3; Mean GCS=7.8; *Intervention Group* (N=8): Mean Age=46.1yr; Mean Time Post Injury=12.7mo; *Control Group* (N=11): Mean Age=39.3yr; Mean Time Post Injury=19.45mo **Intervention:** Patients self-reporting increased anger were randomized to one of two groups (AB or BA). The AB group received an 8-wk anger management programme (60 min, 1x/wk), followed by a 4wk psycho-educational programme. For group BA, the order was reversed. Outcomes were assessed at baseline: 6–12wk prior intervention (T0), second baseline: first session (T1), 4wk after beginning the intervention (T2), 8wk after beginning the intervention (T3), 12wk after the intervention, the final assessment (T4). **Outcome Measures:** The Aggression	1. AQ-12 scores significantly improved from TI to T4 (p = 0.01). 2. All STAXI-2 subscales showed significant improvement from T1 to T4 (p < 0.01). 3. MARS subscales of rumination and venting showed significant improvement from T1 to T4 (p = 0.01; p = 0.04). Other subscales were non-significant (p > 0.05).

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
	Questionnaire (AQ-12), State-Trait Anger and Expression Inventory (STAXI-2), Multidimensional Anger Reaction Scale (MARS).	
Medd & Tate (2000) Australia RCT PEDro=5 N=16	**Population:** TBI; Gender: Male=14, Female=2. *Treatment Group (n=8)*: Mean Age=35.88yr; Mean Time Post Injury=37.25mo; *Waitlist Group (n=8)*: Mean Age=34yr; Mean Time Post Injury=74.25mo. **Intervention:** Participants were randomly allocated to either the treatment group or the waitlist group. The treatment group received 5-8 individualized sessions of cognitive behavioural therapy based on the Commonwealth Rehabilitation Service Anger Management Program. **Outcome Measure:** State-Trait Anger Expression Inventory (STAXI), Hospital Anxiety and Depression Scale (HADS), Self-Esteem Inventories (SEI), Patient Competency Rating Scale (PCRS).	1. The treatment group had significantly higher pre-intervention levels of Anger Expression-Out (AX-O) on the STAXI than the waitlist group (p=0.004). 2. The treatment group showed a greater improvement in AX-O (p=0.006) and trait anger (p=0.054) from pre to post treatment when compared to the waitlist group. 3. No significant differences were found on HADS, SEI, or PCRS between groups.
Aboulafia-Brakha et al. (2013) Switzerland Pre-Post N$_{Initial}$=10, N$_{Final}$=9	**Population:** TBI; Median Age=47yr; Gender: Male=8, Female=2; Median Time Post Injury=27.5mo; Median GCS=5. **Intervention:** Participants completed a semi-structured group treatment program for the management of anger and aggressiveness (1 hr, 1 day/wk for 8wk). The program was based on a cognitive behavioural therapy framework as led by a therapist. Inter-session homework was encouraged to apply new strategies. Outcomes were assessed at baseline, immediately after treatment, and at 4-5mo follow-up. **Outcome Measure**: Buss and Perry Aggression Questionnaire (AQ-12), UPPS Impulsive Behaviour Scale (UPPS-P), Frontal System Behavioural Scale (FrSBe), Cambridge Behaviour Scale (EQ), Hospital Anxiety Depression Scale (HADS), Quality of Life Assessment (SF-36).	1. Significant improvement in feelings of aggression on AQ-12 was found from baseline to follow-up (p=0.02). 2. No significant improvement on AQ-12 was found from baseline to post treatment (p=0.84) or from post treatment to follow-up (p=0.57). 3. No significant improvements were found for UPPS-P, FrSBe, EQ, HADS, or SF-36 between baseline and post treatment (p>0.05).
Hart et al. (2012) USA Pre-Post N=10	**Population:** TBI; Mean Age=43.3yr; Gender: Male=8, Female=2; Range of Time Post Injury=6-243mo; Range of Injury Severity: Moderate to Severe. **Intervention:** 8 sessions that consisted of self-monitoring training to build awareness of anger problem and training of specific problem solving skills (anger self-management training). **Outcome Measure:** State Trait Anger Expression Inventory 2 (STAXI-2), Brief Anger-Aggression Questionnaire (BAAQ).	1. Following the intervention, there were significant reductions on self-reported STAXI-2 Trait Anger (p=0.02), STAXI-2 Anger Expression-Out (p=0.002), and BAAQ (p=0.01). 2. There were no significant improvements on STAXI-2 or BAAQ as rated by a significant other.
Walker et al. (2010) Australia Pre-Post	**Population:** TBI; Mean Age=32.3yr; Gender: Male=40, Female=12; Mean Time Post Injury=4.1yr; Injury Severity: Severe.	1. At post treatment, there were significant reductions in trait anger (p=0.002), anger expression-out

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
N=52	**Intervention:** Participants received 2hr sessions of group-based CBT focused on anger management, 1 x/wk for 12wk. Assessments were conducted at baseline, 12wk, and 3-16mo follow-up. **Outcome Measure:** State-Trait Anger Expression Inventory (STAXI).	(p=0.003), and anger control (p=0.005), but not in state anger or anger expression-in. 2. At follow-up (n=31), the improvements from baseline were maintained, but there were no further improvements from post treatment.
O'Leary (2000) USA Pre-Post N=5	**Population:** ABI; Age Range=21-42yr; Gender: Male=5, Female=0; Time Post Injury Range=4 mo-5 yr. **Intervention:** Patients attended a 10wk training cognitive behavioural therapy program for anger management and coping skills through the use of written materials, audiotapes, lectures, role-play, and group discussions. **Outcome Measure:** Frequency of aggression.	1. Training reduced the number of incidents of both verbal and physical aggression for all participants.
Feeney & Ylvisaker (1995) USA Case Series N=3	**Population:** TBI; Mean Age=18.3yr; Injury Severity: Severe. **Intervention:** Patients received antecedent interventions, comprised of photographic and written cues, for managing aggression. **Outcome Measure:** Aberrant Behaviour Checklist (ABC).	1. All three patients showed a decrease in aggressive behaviours and ABC ratings indicated decreased intensity. 2. Two patients showed a mild increase in aggressive behaviours with written cues, which decreased when substituted with photographic cues.
Burke et al. (1988) USA Pre-Post N=5	**Population:** TBI; Mean Age=23.2yr; Gender: Male=5, Female=0. **Intervention:** Patients received behaviour therapy, with emphasis on reinforcement and antecedent conditions, for managing aggression. **Outcome Measure:** Frequency of aggression.	1. Measurements showed a 97% decrease in aggressive behaviour from baseline levels at 1wk and 100% at 3 wk. 2. There was a significant reduction in behaviour at all time-points compared to baseline (p<0.001). 3. No incidents of aggression were recorded during a 6mo follow-up.

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

Discussion

CBT was investigated as an intervention for anger and aggression post TBI in several studies. A small study by O'Leary (2000) reported that a 10-week CBT program focusing on anger management and coping skills reduced the frequency of verbal and physical aggression in all participants. Aboulafia et al. (2013) provided an eight-week, group-based CBT program with emphasis on reduction of aggression and found that self-reported aggressive behaviours were significantly reduced at follow-up. An RCT by Medd and Tate (2000) reported that six sessions of an individualized CBT program significantly reduced trait anger and outward anger expression when compared to no treatment. Similarly, a study by Walker et al. (2010) found that 12 sessions of group-based CBT significantly reduced trait anger, anger expression-out, and anger control. These findings align with a review by Waldron and colleagues (2013) that found CBT to be efficacious in reducing symptomology when it is targeted for a specific problem (e.g. aggression). However, a meta-analysis evaluating the effectiveness of CBT interventions for aggression in patients with moderate to severe ABI by Iruthayarajah et al. (2018) found that CBT was effective at improving external behaviours, but not internal anger.

A psychoeducational treatment program called Anger Self-Management Training was evaluated in three studies. The eight-session program was designed to help the individual identify anger and aggression through self-monitoring, and to learn specific problem-solving skills for managing these issues. The first study found that all measures of self-reported anger and aggression significantly improved following treatment; there were no improvements on outcomes as reported by a significant other (Hart et al., 2012). The second study compared the anger management program to a personal readjustment and education program (Hart et al., 2017). The authors reported that there was significantly greater improvement on self-reported trait anger with self-management training than with the control program. These improvements were maintained at follow-up. However, there was no significant improvement in outward anger expression with treatment compared to control. Similar to the previous study, outcomes as reported by a significant other were not improved. The third study compared an eight week anger management programme to a psycho-educational program in a cross-over design (Aboulafia-Brakha & Ptak, 2016). There were no differences in anger between the treatment programs, but both groups showed significant improvements in anger scores after completing both programs.

Antecedent interventions involve environmental modifications that prompt individuals to engage with interfering behaviours. A study of three patients with severe TBI found that an antecedent behavioural intervention, which structured the environment with high support and then reduced it, was able to significantly reduce aggressive behaviour (Feeney & Ylvisaker, 1995). An earlier study found that a program incorporating self-management, antecedent interventions, and positive reinforcement significantly reduced aggressive behaviours (Burke et al., 1988).

Conclusions

There is level 1b evidence that self-management training reduces anger and aggression compared to education post TBI.

There is level 2 evidence that cognitive behavioural therapy, compared to waitlist control, reduces anger and aggression post TBI.

There is level 4 evidence that antecedent interventions reduce anger and aggression post TBI.

Cognitive behavioural therapy, self-management training, and antecedent interventions may be effective for anger management following TBI.

8.4.4.3 Social Skills Training

Social skills training aims to minimize socially unacceptable behaviours and help reintegrate individuals into the community following brain injury (Table 8.28).

Table 8.29 Social Skills Training for the Treatment of Maladaptive Behaviors Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
McDonald et al. (2008) Australia RCT PEDro=6 N=39	**Population:** TBI; Gender: Male=28, Female=11. *Treatment Group (n=13)*: Mean Age=35.5yr; Mean Time Post Injury=4.0yr. *Social Group (n=13)*: Mean Age=34.3yr; Mean Time Post Injury=4.3yr. *Waitlist Group (n=13)*: Mean Age=35.3yr; Mean Time Post Injury=3.5yr. **Intervention:** Participants were randomly allocated to waitlist (deferred treatment group; n=13), control (non-therapeutic social group; n=13), or the social skills group (treatment group; n=13). Participants in the skills training group attended 12wk program of group and individual sessions totaling 4 hr/wk. Control group received 4 hr/wk of social activities only for 12wk. **Outcome Measure:** Partner Directed Behaviour Scale (PDBS), Personal Conversational Style Scale, Depression Anxiety and Stress Scale, Awareness of Social Inference Test.	1. The social skills training group made significant improvement on the PDBS compared to the placebo and waitlist group (p<0.004). 2. Results indicate no effects for the social group relative to the waitlist group. 3. Changes were not noted for any group when looking at social functioning and social participation post treatment. 4. Treatment effects were found to be modest at best and limited to direct measures of social behaviour.
Brotherton et al. (1988) USA Case Series N=4	**Population:** TBI; Mean Age=23.5yr; Gender: Male=3, Female=1; Mean Time Post Injury=5.75yr. **Intervention:** Social skills training program comprised of education, instruction, manipulation, feedback, and reinforcement. **Outcome Measure:** Behavioural changes.	1. Intervention was effective in 3 of 4 patients treated, but not all behaviours were equally amenable to treatment. 2. Behaviours showing clear training effects also showed good maintenance 1yr after training.

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

Discussion

A multicenter RCT conducted by McDonald et al. (2008) compared social skills training, social activity, and a waitlist control group. The social skills group showed a significant, positive improvement in behaviour compared to the other interventions, but there was only a modest treatment effect. In an earlier study, social skills training demonstrated effectiveness for improving some behaviours in three out of four participants; some of these improvements were maintained up to one year after treatment (Brotherton et al., 1988).

Conclusions

There is level 1b evidence that a social skills training programs, compared to controls, may improve social behaviour post ABI.

Social skills training may be effective in improving social behaviour following brain injury.

8.4.4.4 Music Therapy

Music therapy is an approach that involves *"using music therapeutically to address physical, psychological, cognitive and/or social functioning for patients of all ages"* (AMTA, 2004). It was first used with World War I veterans in hospital and was formally recognized as a therapeutic tool in 1950. Music therapy has been used to treat a variety of disorders (e.g., neurological, psychiatric, medical, developmental), and it has been found to result in physiological changes (e.g., respiration, blood pressure, heart rate, endorphins, cortisol levels) and increased wellbeing. In more recent years, music therapy has been used in patients with TBI to decrease agitation.

Table 8.30 Music Therapy for Agitation and Aggression Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Outcome
Formisano et al. (2001) Italy Case Series N=34	**Population:** TBI=18, Other=16; Mean Age=35.9yr; Gender: Male=17, Female=17; GCS Score<8. **Intervention**: Patients received music therapy treatment based on Nordoff & Robbins, 20-40 min for 3x/wk during rehabilitation. Evaluation occurred at six different time points. **Outcome Measure:** Undesired behaviours, Glasgow Outcome Scale, Disability Rating Scale (DRS), Coma Recovery Scale (CRS).	1. During music therapy, patients showed a reduction in undesired behaviours. 2. Positive effects were reported in 27 of 34 patients 1mo after starting treatment and at follow-up. 3. No improved interaction with the environment was recorded (DRS, CRS).

Discussion

Formisano et al. (2001) reported that music therapy had a beneficial effect in reducing post-coma agitation and inertia in 62% of slow-to-recover subjects after one month of treatment. Given the study's lack of both prospective data and statistical analysis, further research is required to determine the efficacy of music therapy in reducing challenging behaviours post ABI.

Conclusions

There is level 4 evidence that music therapy may reduce post-coma agitation in slow-to-recover patients after severe TBI.

Music therapy may reduce post-coma agitation following a TBI, although additional research is needed.

8.5 Addictive Behaviours

8.5.1 Incidence and Prevalence of Substance Abuse

Rates of pre-injury substance abuse in those who have sustained a TBI are high. Substance use disorders and TBI are most common in young males and substance intoxication is a leading contributor to accident-

related injury (Kraus et al., 1989; Ponsford et al., 2018). Studies differ in the criteria used to determine if an individual has an issue with addiction, dependence, or abuse. Studies that only include subjects with a positive Blood Alcohol Concentration (BAC) at time of admission will report an inflated incidence compared to patient reported substance use disorders. Additionally, prevalence rates are variable between populations. Rates of pre-injury alcohol abuse in Australian and North American populations have been recorded at 20-40%, where as rates in Finland are reported at 8%, which likely reflects cultural differences in alcohol consumption (Alway et al., 2016; Gould et al., 2011; Hibbard et al., 1998; Koponen et al., 2002).

Among those who sustain their injury in a motor vehicle collision, which is one of the leading causes of TBI, almost half were found to be intoxicated (DeLambo et al., 2008; Wehman et al., 2000; West et al., 2009). Studies suggest that alcohol and substance abuse decline within the first year of injury (Bombardier et al., 2003; Jorge, 2005; Kelly et al., 1997; Ponsford et al., 2007), but those who returned to drinking two years post injury are likely to consume more than before the injury (Bombardier et al., 2002; Ponsford et al., 2007). In fact, individuals who abused alcohol pre-injury were ten times more likely to demonstrate problematic alcohol use post injury (Bombardier et al., 2003). Individuals who drink excessively and have large negative consequences associated with their drinking are more likely to report alcohol as the cause of their TBI and are more likely to report pre-injury substance abuse (Turner et al., 2003). Moreover, the correlation between mood disorders and substance abuse has also been shown to be quite strong both before and after injury (Jorge, 2005).

8.5.2 Effect of Intoxication on Initial Assessments

Several issues have been raised about assessing the severity of injury, particularly with the use of the GCS. It has been suggested that the GCS is unreliable when used to establish functioning level at time of injury for those who have been drinking and/or using other substances (Jagger et al., 1984). Some studies have reported a negative correlation between GCS score and BAC among individuals admitted to hospital post TBI (Alexander et al., 2004; Berry et al., 2010; O'Phelan et al., 2008; Schutte & Hanks, 2010; Shahin et al., 2010); a positive correlation has been noted between BAC and Injury Severity Scale score (Salim et al., 2009a; Salim et al., 2009b). Andelic and colleagues (2010) noted that patients diagnosed with a less severe TBI more frequently reported substance use at the time of injury, while those diagnosed with a more severe injury frequently report pre-injury substance abuse. Of note, other studies did not find a correlation between the two variables (Kelly et al., 1997; Sperry et al., 2006; Stuke et al., 2007). To date, there is conflicting evidence regarding the effects of alcohol on injury severity.

8.5.3 Effect of Intoxication on Mortality

The protective role of elevated levels of serum ethanol levels and TBI is a controversial topic. It has been suggested that alcohol acts as a neuroprotective agent and plays a role in survival post injury (Berry et al., 2010). Several studies reported lower mortality rates among individuals who were intoxicated at time of injury than those who were not intoxicated (Berry et al., 2010; O'Phelan et al., 2008; Salim et al., 2009a; Salim et al., 2009b; Tien et al., 2006). A retrospective study reported that BAC was higher for survivors than non-survivors of TBI (Salim et al., 2009a), while a prospective study found that low to moderate BAC was associated with lower risk of mortality in those who had sustained a severe TBI (Tien et al., 2006). While these studies primarily focus on alcohol intoxication, their findings can also apply to illicit drug intoxication at time of injury (O'Phelan et al., 2008; Salim et al., 2009b). Overall, further research needs

to be conducted to conclusively determine the effects of alcohol and other substances on survival following ABI.

8.5.4 Effect of Intoxication and Substance Abuse on Recovery

Recovery following ABI will likely be negatively impacted if individuals continue to abuse alcohol or other substances. Many of these individuals have been found to spend more time in rehabilitation programs due to accentuated deficits of sensory, motor, cognitive, and communication functions (Wehman et al., 2000). As well, continued abuse of alcohol and other substances increases the risk of developing medical complications (Salim et al., 2009a). Involvement in rehabilitation deters or prevents individuals from using various substances, as patients are monitored rather closely (Bjork & Grant, 2009). However, once patients are discharged from inpatient rehabilitation, no monitoring exists and patients may return to their previous behaviours as a coping strategy. Addictions to alcohol and other substance may lead to a failure to survive independently in the community (Burke et al., 1988).

During acute recovery, high BAC was found to be predictive of poorer performance on a variety of neuropsychological measures, including orientation, concentration, reasoning, and memory (Bombardier & Thurber, 1998; Kelly et al., 1997; Tate et al., 1999; Wilde et al., 2004). Wilde and colleagues (2004) also noted that high BAC was associated with increased brain atrophy post injury. In terms of long-term recovery, the impact of BAC and substance abuse is unclear. One study reported that acute BAC was not associated with outcome on the Glasgow Outcome Scale up to one year post injury (Alexander et al., 2004). Another study found that acute BAC was correlated with Functional Independence Measure (FIM) score upon admission to rehabilitation, but not with FIM at discharge or one year post injury (Schutte & Hanks, 2010). The authors also reported that acute BAC was not predictive of long-term cognitive outcomes as well (Schutte & Hanks, 2010). Comparatively, a smaller study found that many cognitive measures were negatively impacted by hazardous drinking both before and after injury (Ponsford et al., 2013).Vickery and colleagues (2008) demonstrated that acute BAC and a history of hazardous drinking were associated with outcome on the Disability Rating Scale (DRS) but not the FIM. Interestingly, while high acute BAC was associated with lower score on the DRS, a history of hazardous drinking was associated with a higher score (Vickery et al., 2008).

8.5.5 Substance Abuse Treatment Post ABI

Several programs have been proposed and developed in order to reduce substance abuse in the TBI population. In a systematic review, Corrigan and colleagues (2010) identified 28 studies of screening and/or interventions for substance abuse, but noted that most research specifically excluded participants with severe TBI. The authors suggested that researchers and clinicians should address barriers to routine use of screening and interventions, as well as develop systematic accommodations for individuals with neurobehavioural impairments post injury.

Table 8.31 Programs for the Treatment of Substance Abuse Post ABI

Author Year Country Research Design PEDro Sample Size	Methods	Results
Sander et al. (2012) USA RCT PEDro=5 N=104	**Population:** TBI. *Intervention Group (n=54)*: Mean Age=36.1yr; Gender: Male=44, Female=10; Median GCS Score=14. *Control Group (n=50)*: Mean Age=35.4yr; Gender: Male=41, Female=9; Median GCS Score=12. **Intervention:** Participants were randomly assigned to receive intervention or control. The intervention group received a motivational interview and education: they watched a 10min educational video about potential negative effects of substance abuse after TBI, and were then asked to consider pros/cons of substance abuse. The control group received standard care: information and referrals typically given to those with substance issues. Assessments were conducted at 3mo follow-up. **Outcome Measure:** CAGE Alcohol Questionnaire (CAGE-AQ), Alcohol Expectancy Questionnaire-III (AEQ), Readiness to Change Question (RTC).	1. There was no treatment effect on CAGE-AQ, AEQ, or RTC. 2. After treatment, individuals with severe injury indicated alcohol use could result in physical and cognitive impairment 3. Individuals who attributed their TBI to alcohol use indicated alcohol use could result in physical and cognitive impairment.
Tweedly et al. (2012) USA RCT PEDro=5 N=60	**Population:** TBI; *ID Group (n=20)*: Mean Age=36.5yr; Gender: Male=15, Female=5; Mean Time Post Injury=8 mo. *INFO Group (n=20)*: Mean Age=35.1yr; Gender: Male=14, Female=6; Mean Time Post Injury=7.95 mo. *MI Group (n=20)*: Mean Age=33.9yr; Gender: Male=16, Female=4; Mean Time Post Injury=7.79mo. **Intervention:** Participants were randomly assigned to one of three conditions: Informal Discussion (ID), a general 30min discussion about changes that had occurred since injury; Information (INFO), a package outlining cognitive, physiological, and behavioural changes that can occur following injury, plus ID; or Motivational Interviewing (MI), plus ID and INFO. Assessments were conducted at baseline and 6mo follow-up. **Outcome Measure:** Alcohol Use Disorders Identification Test (AUDIT), Timeline Follow-Back (TLFB), Readiness to Change Questionnaire (RTCQ), Hospital and Anxiety and Depression Scale (HADS).	1. Both MI and INFO groups were drinking less frequently and consuming fewer drinks than ID at follow-up, but the differences were not significant.
Corrigan & Bogner (2007) USA RCT PEDro=5 N=74	**Population:** TBI; Mean Age=42.5yr; Gender: Male=46, Female=28. **Intervention:** Participants were randomly assigned to one of three conditions: financial incentive (FI, n=24), barrier reduction (BR, n=26), or attention control (AC, n=24).	1. FI resulted in significantly fewer missed appointments and less premature termination ($p<0.05$). 2. BR did not result in fewer missed appointments or prevent premature termination.

Author Year Country Research Design PEDro Sample Size	Methods	Results
	Participants then participated in a treatment program. Assessments were conducted at follow-up. **Outcome Measure:** Treatment attendance, Premature termination, Perceived therapeutic alliance.	3. There were no significant differences within or between groups in perceived therapeutic alliance between participant and counsellor.
Corrigan et al. (2005) USA RCT PEDro=5 N=195	**Population:** TBI; Mean Age: 36.6yr; Gender: Male=138, Female=57. **Intervention:** Participants were randomly assigned one of four groups: motivational interviewing (MI), barrier reduction (BR), financial incentive (FI), or attention control (AC). Participants were then asked to sign up for an Individualized Service Plan (ISP). Assessments were conducted at 30d, 3mo, and 6 mo. **Outcome Measure:** ISP signup, ISP compliance, ISP attrition, Addiction Severity Index (ASI).	1. The proportion of participants who signed the ISP within 30d differed among conditions ($p<0.001$): FI (83%) and BR (74%) had greater signing than MI (45%) and AC (45%). 2. The mean number of days to sign the ISP differed among conditions ($p=0.01$): FI had quicker signing than MI (22.8d versus 44.0d, $p<0.001$). There were no significant differences with BR (32.1d) or AC (34.8d). 3. ISP compliance (missed appointments) did not differ between FI (40%), BR (42%), MI (57%), or AC (64%). 4. ISP attrition at 3mo (premature termination) did not differ between FI (4%), BR (6%), MI (9%), or AC (15%). 5. ISP attrition at 6mo significantly differed among conditions ($p<0.05$): FI (21%) and BR (16%) had lower attrition than AC (47%), but not MI (34%). 6. ASI was a significant, negative predictor of ISP signing ($p<0.05$), time to ISP signing ($p<0.05$), and ISP attrition ($p<0.05$).
Cox et al. (2003) USA PCT N=94	**Population:** TBI; *Treatment Group (n=40)*: Mean Age=32.5yr; Gender: Male=33, Female=7; Mean Time Post Injury=4.4 yr. *Comparison Group (n=54)*: Mean Age=35.6yr; Gender: Male=38, Female=16; Mean Time Post Injury=4.4yr. **Intervention:** The treatment group received 12 sessions of individual systematic motivational interviewing for substance abuse. The control group received no counselling. Assessments were conducted at baseline, after treatment, and at follow-up. **Outcome Measure:** Substance use, Motivational Structure Questionnaire (MSQ), Positive Affect Negative Affect Scale (PANAS).	1. Substance use significantly decreased in the treatment group across all time points ($p=0.02$), but was not significant when compared to the control group ($p=0.056$). 2. The proportion of participants who were abstinent in the treatment group after treatment was greater than in the control group (50% versus 21%, $p=0.057$). 3. The proportion of participants who 'improved' in terms of substance use over time was greater in the treatment group than in the control group (47% versus 18%, $p=0.040$). 4. There were no significant differences in the number of each substance used over time within or between groups. 5. On PANAS, the treatment group experienced a significant reduction in negative affect over time ($p=0.02$), but there were no significant differences when compared with the control group ($p>0.10$). 6. On MSQ, the treatment group experienced a significant improvement in motivational

Author Year Country Research Design PEDro Sample Size	Methods	Results
		structure over time (p<0.05) over time, which was significantly greater than the control group (p<0.05). 7. Substance use was correlated with joy, commitment, sorrow, and success on MSQ.
[Bogner et al.](#) (1997) USA Case Series N=72	**Population:** TBI; Mean Age=26yr; Gender: Male=56, Female=16; Mean Time Post Injury=44.3mo. **Intervention:** Subjects received a substance abuse treatment plan and were monitored for 1yr. Some subjects had support of a community team. **Outcome Measure:** Quantity-Frequency-Variability Index, General Health and History Questionnaire, Addiction Severity Index.	1. A positive substance abuse outcome was found in 75% of subjects: 18% maintained abstinence, 32% attained abstinence, and 25% reduced alcohol use. 2. A significant difference in abstinence was found between initial assessment and 1yr follow-up (p<0.05). 3. Subjects with a community team had more positive substance abuse outcomes than those without (p<0.05). 4. A greater proportion of subjects with community teams attained abstinence, but a greater proportion of those without teams maintained it.

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

Discussion

In an early study, a substance abuse treatment program for individuals with TBI was found to be effective (Bogner et al., 1997). After one year of treatment, abstinence from substances was significantly lower and three quarters of participants reported a positive outcome (i.e. maintained abstinence, attained abstinence, or reduced consumption). As well, the study found that individuals who had support from a community team had better outcome than those without such support. A subsequent study provided a treatment group with 12 one-on-one sessions of systematic motivational interviewing, while a control group received standard care (Cox et al., 2003). Substance use significantly decreased in the treatment group over time, but was not significantly different when compared to the control group. However, the proportion of individuals who were abstinent or improved was significantly greater in the treatment group than among controls.

Two studies examined the effect of a brief motivational interviewing intervention for alcohol abuse post TBI. In one of these studies, participants were randomly assigned to receive an informal discussion alone, with educational information, or with both educational information and motivational interviewing (Ponsford et al., 2012; Ponsford et al., 2013; Tweedly et al., 2012). Frequency and intensity of drinking were higher in the informal discussion group than in enhanced intervention groups, but the differences were not statistically significant. Follow-up analysis revealed that readiness to change was associated with better treatment outcomes, while depression was associated with poorer outcomes (Ponsford et al., 2012). Similarly, Sander and colleagues (2012) reported that a combination of motivational interviewing and educational information did not reduce excessive drinking; positive expectancies and readiness to change were not improved after treatment. However, participants demonstrated awareness regarding the negative impact of their substance abuse on their physical and cognitive impairments.

In two other studies, researchers compared brief interventions for attracting participants, maintaining attendance, and reducing attrition for a substance abuse program (Corrigan & Bogner, 2007; Corrigan et al., 2005). Corrigan and colleagues (2005) found that providing financial incentives and reducing logistic barriers led to a greater number of individuals signing up for the program than motivational interviewing or an attention control. While program attendance was similar between interventions, financial incentives and barrier reduction had fewer dropouts from the program than the attention control at six months. A subsequent study by Corrigan and Bogner (2007) found that financial incentives resulted in fewer missed appointments and premature dropouts than barrier reduction or attention control. However, the perceived therapeutic alliance between the counselor and participant was similar among the three groups.

Conclusions

There is level 2 evidence that motivational interviewing and education do not reduce frequency or intensity of substance consumption post TBI.

There is level 2 evidence that motivational interviewing does not increase signup, promote attendance, or reduce premature dropouts in a substance abuse treatment program post TBI when compared to barrier reduction, financial incentive, or attention control.

There is level 2 evidence that providing financial incentives increases signup, promotes attendance, and reduces premature dropouts in a substance abuse treatment program post TBI compared to attentional controls.

There is level 2 evidence that reducing logistical barriers increases signup for a substance abuse treatment program post TBI, but the evidence is conflicting as to whether it promotes attendance and reduces premature dropouts compared to controls.

There is level 4 evidence that a long-term substance abuse program reduces consumptions and increases abstinence post TBI.

Motivational interviewing and education may not be effective interventions for reducing substance abuse following TBI.

Financial incentives may increase signup, promote attendance, and attenuate dropout from substance abuse treatment programs following TBI; the impact of reducing logistical barriers is less considerable.

8.6 Restraints

8.6.1 Use of Restraints

Due to the continued concern regarding the safety of both patients and staff in hospitals and long-term care facilities, the use of restraints continues to be part of clinical practice; however, their use remains

controversial. Studies have found as many as 13%-32% of survivors may be restrained while undergoing care in either an acute or rehabilitative hospital (Gregory Jr & Bonfiglio, 1995; McNett et al., 2012; Morrison et al., 1987; Stubbs & Alderman, 2008). Due to the broad definition of agitation, the reported numbers of agitated patients may be misleading, and thus questions are being raised about how many individuals actually need to be restrained (Eisenberg et al., 2009).

The term *"restraint"* includes the use of either chemical (medications) or physical (mechanical) restraints, or a combination of both (Marks, 1992). Chemical restraints used to assist in controlling behaviours that occur during agitated states include many pharmaceutical agents with primary or secondary psychotropic effects, including beta blockers, antidepressants, anticonvulsants, psychostimulants, and anti-Parkinson's agents (Gregory Jr & Bonfiglio, 1995; McNett et al., 2012). Medications used in non-emergent situations to reduce the need for physical restraints include propranolol, neuroleptics, and valproic acid (Busch & Shore, 2000). Physical restraints have been defined as any manual method that immobilizes or reduces the ability of individuals to move their arms, legs, trunk, or head freely (Busch & Shore, 2000; Stevens, 2012). Physical restraints include the use of bed rails, feeding trays, hand tying, chest straps, seat belts, ankle/wrist restraints, and jacket restraints (Busch & Shore, 2000; Gregory Jr & Bonfiglio, 1995; Marks, 1992; Morrison et al., 1987). Typically, these restraints are not meant to be a part of the standard practice of care (Amato et al., 2006).

Policies related to the application of restraints often state that the use of restraints should meet the following criteria: (1) be individualized and offer as much dignity to the individual as the situation allows; (2) be humanely and professionally administered; (3) have safety protocols in place; (4) patient must be monitored; (5) careful documentation of the type of restraint, the reason for it, and the means for observation while in the restraint; (6) the method or choice of restraint must be the least restrictive option available (American Nurses Association, 2012; College of Nurses of Ontario, 2009; Ministry of Health and Long Term Care for the Province of Ontario, 2001; St. Joseph's Health Care, 2012). In accordance with provincial legislation, the College of Nurses for Ontario suggests that the following information is to be recorded when using restraints: type used, alternatives considered and used, date and time of application, reason given to patient, significant patient behaviours, and patient response.

The decision to use restraints is generally made by physicians and/or nurses on the unit. In a survey, hospital physicians were asked to review a series of vignettes and to comment on the likelihood of ordering restraints (Sandhu et al., 2010). Those most likely to order restraints were family physicians and surgeons, while geriatricians were least likely to do so. Further, male doctors were more likely to order restraints than female doctors and they were more likely to order them for male patients. The use of restraints must be accompanied by a consent form signed by the family or caregiver indicating they are in agreement; this form may not be required in emergency situations.

8.6.2 Reasons for Restraints

A great deal of research has been conducted investigating the use of physical restraints in nursing homes or in acute care hospitals (Evans & FitzGerald, 2002; Ludwick et al., 2008). Nursing literature indicates that the use of restraints is influenced by the values, education, and beliefs of the nurses themselves, as well as the behaviours and demographic characteristics of the patients (Ludwick et al., 2008). Reasons often cited for the use of a restraint include impulsiveness, pulling at devices, or removing endotracheal tubes, central venous lines, and other life support measures (McNett et al., 2012). Additional reasons for restraint used are controlling agitation, aggression, and behaviour related to confusion and altered mental status;

increasing patient safety related to impaired mobility; supporting patient posture or sitting balance; preventing disruption of therapy; and protecting the safety of family and staff (Evans & FitzGerald, 2002; Kow & Hogan, 2000; Minnick et al., 2007; Mion et al., 1996; Sandhu et al., 2010).

Many care professionals indicate that the use of restraints prevents the individual from falling and further injuring themselves (Kow & Hogan, 2000; Minnick et al., 2007; Mion et al., 1996; Sandhu et al., 2010; Schleenbaker et al., 1994; Suen et al., 2006). Despite the use of restraints to prevent falls, there is no evidence to suggest this procedure is effective. On the contrary, there is some evidence to suggest that restraints put patients at a greater risk of injury (Busch & Shore, 2000; Evans & FitzGerald, 2002; Mion et al., 1996; Sandhu et al., 2010). While legitimate reasons exist for using restraints, some reasons are not justified; one study found that over 70% of nurses felt restraints enabled them to spend less time on nursing care (Suen et al., 2006). Alternative strategies to restraint use were not known to many of these nurses, including manipulating the environment, reviewing prescribed medications, and supervision (Suen et al., 2006).

Patients in physical restraints have been found to have higher rates of clinical agitation, as did patients who require constant supervision (McNett et al., 2012; Minnick et al., 2007; Morrison et al., 1987; Visscher et al., 2011). Visscher and colleagues (2011) found that 42% of the study population, which included patients with ABI, had engaged in one or more aggressive acts prior to being restrained; three or more aggressive acts were dealt with daily. Using the Staff Observation Aggression Scale, 67% of the aggressive incidents were judged to be mild in severity and 33% were severe. These incidents were triggered by asking the individual to engage in an activity or take medications, or when the individual required help with their activities of daily living (Visscher et al., 2011). As well, a higher level of aggression was also related to an increase length of stay and lower scores on the Functional Independence Measure and Mini Mental State Examination (Visscher et al., 2011). Another study noted that reorientation, redirection, constant supervision, environment modification, benzodiazepines, and/or restraints were common methods of managing agitation post TBI (McNett et al., 2012).

8.6.3 Effectiveness of Restraints

Many hospitals use physical restraints to ensure the safety of patients, staff, and family members. The use of restraints is considered acceptable if the restraint is used to ensure patient safety, the restraint is implemented safely, less restrictive interventions have been ineffective in preventing harm, and appropriate techniques are used as determined by hospital or organizational policy (Recupero et al., 2011). The risk of harm to the patient must be taken into consideration when using physical restraints, thus all restraints must be discontinued at the earliest possible time and patients must be monitored to ensure their safety (Busch & Shore, 2000). Currently, there is insufficient data available to determine the efficacy of using physical restraints to reduce agitated or aggressive behaviour post ABI (Duxbury & Wright, 2011).

8.6.4 Reducing the Use of Restraints

In many facilities, the number one reason cited for the use of physical restraints is the prevention of falls. Three studies investigating the effectiveness of education programs designed to reduce the use of physical restraints on individuals in nursing homes were identified (Gulpers et al., 2011; Huizing et al., 2009; Rask et al., 2007). Rask et al. (2007) included the creation of a falls coordinator as well as staff buy-in to increase accountability, while Gulpers et al. (2011) make reference to policy changes. Although Huizing et al. (2009) did not find education alone was effective in reducing the use of restraints, the two studies that included

multiple components in their interventions and took a more active approach had more favourable outcomes (Gulpers et al., 2011; Rask et al., 2007). It should be noted, however, that none of these studies investigated the effectiveness of these programs on an ABI/TBI unit. Brooke et al. (1992) examined the treatment of agitated patients, which is another reason for the use of restraints, in a TBI population. The results of the RCT indicated that treatment with propranolol reduced the use of physical restraints in agitated patients with TBI (Brooke et al., 1992).

8.7 Conclusions

Mental health and mental disorders post ABI can represent a challenging area of rehabilitation. As many of the behaviors and disorders discussed above are internalizing, it is important to always screen for depression, anxiety, or other maladaptive behaviors after an ABI. Once a negative pattern or behavior has been identified then a treatment plan can be developed in collaboration with the rest of the care team. With rates of suicidal ideation being high among the TBI population, it is critical to be aware and sensitive to the psychological needs of those with an ABI.

Many of the maladaptive behaviors discussed above have both pharmacological and non-pharmacological interventions available to choose from, and each individual patient should be consulted on their preference when appropriate. Many pharmacological agents, as well as non-pharmacological interventions have evidence supporting their efficacy and use and should be explored as options with the care team. It is also important to keep in the mind the stigma that exists around mental health and to approach the topic with compassion and understanding.

8.8 Summary

There is level 1b evidence that methylphenidate may be an effective treatment for major depression post TBI compared to placebo.

There is level 2 evidence that desipramine may be an effective treatment for major depression post TBI compared to placebo.

There is level 4 evidence that a combination of citalopram and carbamazepine may be an effective treatment for major depression post TBI.

There is conflicting (level 1b) evidence as to whether sertraline is a more effective treatment than placebo for major depression post TBI.

There is level 1a evidence that cognitive behavioural therapy may be an effective treatment for depression compared to waitlist controls post TBI.

There is level 1a evidence that cognitive behavioural therapy may be no more effective than supportive psychotherapy as a treatment for depression post TBI.

There is level 1b evidence that cognitive behavioural therapy combined with motivational interviewing or non-directive counselling may be equally effective treatments for depression post TBI.

There is level 2 evidence that cognitive behavioural therapy, compared to controls, may improve adaptive coping but may not reduce depressive symptoms post TBI.

There is level 4 evidence that compassion-focused therapy reduces depressive symptoms post ABI.

There is level 1b evidence that cognitive behavioural therapy is effective when delivered over the phone or in person.

There is level 1b evidence that mindfulness-based stress reduction may be an effective treatment for depression post TBI compared to usual care.

There is level 4 evidence that long-term, neuro-systemic psychotherapy is an effective treatment for depression post TBI.

There is level 2 evidence that neurorehabilitation programs focused on cognitive training, relaxation and physical activity may improve depression and anxiety.

There is level 2 evidence that music therapy reduces symptoms of depression post ABI compared to standard rehabilitation.

There is level 1a evidence that Tai Chi may improve mood compared to wait-list controls following TBI.

There is level 1a evidence that aerobic exercise, compared to waitlist controls, does not reduce symptoms of depression following TBI.

There is level 1b evidence that aerobic exercise, compared to waitlist controls, improves mood following TBI.
There is level 4 evidence that rehabilitation programs, whether focused on cognitive or psychosocial remediation, may reduce depressive symptoms post TBI.

There is level 4 evidence that community-based rehabilitation programs alone do not change the psychological status of patients with ABI.

There is level 1b evidence that repetitive transcranial magnetic stimulation improves cognition and depression in patients with TBI.

There is level 1a evidence that cognitive behavioural therapy combined with motivational interviewing may be an effective treatment for anxiety post ABI, compared to waitlist controls.

There is level 2 evidence that group cognitive behavioural therapy and telephone cognitive behavioural therapy are similarly effective in reducing anxiety following ABI.

There is conflicting (level 1b) evidence as to whether motivational interviewing is more effective than non-directive counselling as an adjunct to cognitive behavioural therapy for anxiety post ABI.

There is level 2 evidence that neurofeedback training may improve stress in patients with ABI.

There is level 1a evidence that a group-based cognitive behavioural intervention, compared to a waitlist control, may be effective in reducing hopelessness post TBI.

There is level 4 evidence that problem-solving therapy may decrease suicidal ideation post TBI.

There is level 4 evidence that sertraline may reduce aggression and irritability post TBI.

There is level 4 evidence that amitriptyline reduces agitation post TBI.

There is level 1b evidence that amantadine compared to placebo may reduce aggression post TBI in individuals with moderate to severe aggression.

There is conflicting (level 1b) evidence as to whether amantadine reduces irritability compared to placebo post TBI.

There is level 2 evidence that methylphenidate compared to placebo reduces anger post TBI.

There is level 4 evidence that carbamazepine may reduce agitation and aggression post TBI.

There is level 4 evidence that lamotrigine may reduce inappropriate behaviours post TBI.

There is level 4 evidence that quetiapine may reduce aggression post TBI.

There is level 4 evidence that ziprasidone may reduce agitation post TBI.

There is level 4 evidence that methotrimeprazine may be effective for controlling agitation post ABI.

There is level 4 evidence that haloperidol may not be effective in treating behavioral disorders post TBI.

There is level 1b evidence that pindolol may reduce aggression compared to placebo post ABI.

There is level 1b evidence that propranolol compared to placebo reduces the intensity of agitated symptoms post ABI.

There is conflicting evidence (level 1b) that propranolol compared to placebo reduces the frequency of aggressive behaviour post ABI.

There is level 4 evidence to suggest that lithium carbonate may reduce aggressive/agitated behaviour following a brain injury.

There is level 4 evidence that Depo-Provera, in combination with counselling, may reduce sexually aggressive behaviour post TBI.

There is level 2 evidence that behavioural modification incorporating reinforcement compared to education alone may improve negative behaviours post brain injury.

There is level 1b evidence that self-management training reduces anger and aggression compared to education post TBI.

There is level 2 evidence that cognitive behavioural therapy, compared to waitlist control, reduces anger and aggression post TBI.

There is level 4 evidence that antecedent interventions reduce anger and aggression post TBI.

There is level 1b evidence that a social skills training programs, compared to controls, may improve social behaviour post ABI.

There is level 4 evidence that music therapy may reduce post-coma agitation in slow-to-recover patients after severe TBI.

There is level 2 evidence that motivational interviewing and education do not reduce frequency or intensity of substance consumption post TBI.

There is level 2 evidence that motivational interviewing does not increase signup, promote attendance, or reduce premature dropouts in a substance abuse treatment program post TBI when compared to barrier reduction, financial incentive, or attention control.

There is level 2 evidence that providing financial incentives increases signup, promotes attendance, and reduces premature dropouts in a substance abuse treatment program post TBI compared to attentional controls.

There is level 2 evidence that reducing logistical barriers increases signup for a substance abuse treatment program post TBI, but the evidence is conflicting as to whether it promotes attendance and reduces premature dropouts compared to controls.

There is level 4 evidence that a long-term substance abuse program reduces consumptions and increases abstinence post TBI.

8.9 References

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