

ERABI

EVIDENCE-BASED REVIEW
of moderate to severe
ACQUIRED BRAIN INJURY

8. Mental Health Issues Post Acquired Brain Injury

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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

Key Points

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

Citalopram may not be an effective treatment for major depression post TBI, but may be effective when taken in combination with carbamazepine.

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.

Cognitive behavioural therapy may be more effective when provided in combination with motivational interviewing than non-directive counselling.

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.

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.

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 be 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.

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

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 little negative effect on recovery following a TBI.

Pindolol may be effective in reducing aggression following an ABI.

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

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.

8. Mental Health Issues Post Acquired Brain Injury

8.1 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 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 individuals with 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 addressing 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. Studies have found that 30% to 60% of individuals who sustain an ABI have a dependence issues (Jorge, 2005). Many individuals relapse post injury, often within the first or second year. 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 depression, anxiety, suicidal ideation, challenging behaviours, and addictive behaviours post ABI. Issues regarding the use of restraints will also be discussed.

8.2 Depression

In Canada, it is estimated that approximately 11% of men and 16% of women will suffer from depression in their lifetime (Health-Canada, 2009). For those who sustain an ABI, depression is the most common mood disorder diagnosed (Jean-Bay, 2000; Jorge, 2005; 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, 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; Hudak et al., 2012).

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). The diagnosis is further complicated by the lack of consistency in the tools used to measure depression post injury (Jorge, 2005).

8.2.1 Lesion Location and Depression

Research has investigated the link between the area of brain damage and the occurrence of depression. Results indicate that those found to have left anterior (dorsolateral frontal or basal ganglia), parietal-occipital, or right hemisphere lesions were more likely to be diagnosed with depression (Fedoroff et al., 1992; Jorge et al., 2004).

8.2.2 Incidence and Prevalence of Depression

Studies examining depression following ABI have noted that depression or depressive symptoms can begin within the first three months of injury but may also become evident much later. Depression occurring within the first year has been noted in 18% to 39% of individuals with ABI (McKinlay et al., 1981). However, in studies studying depression in individuals who were one or more years post injury, rates ranged from 13% to 61% (Fleminger et al., 2003; Gordon et al., 1998; Osborn et al., 2014; Sigurdardottir et al., 2013). The risk for depression is high post ABI and remains this way for decades following injury (Hoffman et al., 2010). 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; these rates are high compared to the general population.

8.2.3 Pharmacological Interventions for Depression

Following ABI, depression is often 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. The use of tricyclic antidepressants is often restricted to the treatment of headaches in those who have sustained a mild TBI, because their side effects have proven to be problematic in individuals who have sustained more a moderate or severe brain injury (Bajo et al., 1999). 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/ Study Design/ N	Methods	Outcomes
<p>Rapoport et al. (2010) Canada RCT PEDro=9 N_{Initial}=21, N_{Final}=18</p>	<p>Population: TBI; Mean Age=47.67 yr; Gender: Male=11, Female=10; Mean Time Post Injury=106 days; Injury Severity: Mild=16, Moderate/Severe=5. Intervention: Patients in remission from major depression were assigned to either the treatment group (n=10) who received citalopram (~40 mg/day) or the control group (n=11) who received a placebo, both for 40wk. Outcome Measure: Hamilton Depression Rating Scale (HDRS), Cumulative Illness Rating Scale, Mini Mental State Examination, Rivermead Post Concussion Symptoms Questionnaire.</p>	<ol style="list-style-type: none"> 1. Comparing the treatment and control groups, relapse rates (p=0.835) and time to relapse (24.8 wk versus 22.3 wk, p=0.700) were not significantly different. 2. All participants experienced adverse events regardless of group (e.g., headache, muscle/joint pain, dizziness). 3. On the HDRS, patients with “more than mild agitation” relapsed sooner than those without that level of agitation (8.0wk versus 27.18 wk, p=0.013). 4. On the HDRS, those with “more than mild psychic anxiety” relapsed at a mean of 19.7 wk compared to those with “none to mild” who did not relapse (p=0.046).
<p>Ashman et al. (2009) USA RCT PEDro=10 N=41</p>	<p>Population: TBI; Mean Age=49.1 yr; Gender: Male=24, Female=17; Mean Time Post Injury=17.7 mo; 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 2 wk, up to 100 mg) and the control (n=19) received a placebo, both for 10 wk. 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).</p>	<ol style="list-style-type: none"> 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). 2. Changes in scores on the HAM-D, BAI, and QOL scales showed improvement (p<0.001) but no group effects were found.
<p>Lee et al. (2005) Korea RCT PEDro=8 N=30</p>	<p>Population: TBI; Gender: Male=24, Female=6. <i>Group A (n=10):</i> Mean Age=35.3yr; Mean Time Post Injury=34.8d. <i>Group B (n=10):</i> Mean Age=33.6yr; Mean Time Post Injury=31.9d. <i>Group C (n=10):</i> 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).</p>	<ol style="list-style-type: none"> 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 higher in Group B than Group A (13 versus 6, p=0.010).
<p>Wroblewski et al. (1996) USA RCT PEDro=4</p>	<p>Population: TBI; Mean Age=32.2 yr; Gender: Male=7, Female=3; Mean Time Post Injury=1.5 yr; Injury Severity=Severe. Intervention: Patients were diagnosed with major depression. The treatment group (n=6) received</p>	<ol style="list-style-type: none"> 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.

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
N=10	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).	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).
Rapoport et al. (2008) Canada Pre-Post N _{Initial} =65, N _{Final} =54	Population: TBI; Mean Age=39.7 yr; Gender: Male=38, Female=27; Injury Severity: Mild=33, Moderate to Severe=32. Intervention: Patients diagnosed with major depression received citalopram for 6wk (n=29) or 10 wk (n=36), starting at 20 mg/day and titrated up to 50 mg/day. Outcome Measure: Hamilton Rating Scale for Depression (HAM-D), Rivermead Post Concussion Symptoms Questionnaire (RPQ), Clinical Global Impression.	1. Mean HAM-D scores decreased from baseline to 6 wk (23.66 versus 16.30, p<0.0001) and from baseline to 10 wk (12.96, p<0.001). 2. Of the 54 subjects who started the study, 24.1% were in remission at 6wk. Of the 26 assessed, 26.9% were in remission at 10 wk. 3. Somatic score on the RPQ decreased significantly from 15.38 to 11.35 (p<0.001) at 6 wk but not at 10 wk (10.82, p=0.0632). 4. One or more adverse events were reported by 84.6% of participants; most often dry mouth.
Perino et al. (2001) Italy Pre-Post N=20	Population: TBI; Gender: Male=11, Female=9. <i>Group A (n=11):</i> Mean Age=26.9 yr; Mean GCS Score=5.5; Mean Time Post Injury=4.7 mo. <i>Group B (n=9):</i> Mean Age=31.3 yr; 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 into subgroups based on time post injury (Group A, <6 mo; Group B, 24-36 mo). Outcome Measure: Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI).	1. Total sample significantly improved from baseline to 12 wk 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.

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., 2014). 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. 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 three studies examined the effects citalopram on depression post TBI (Perino et al., 2001; Rapoport et al., 2008; Rapoport et al., 2010). Rapoport and colleagues (2008) administered 20 to 50 mg per day of citalopram for 6 to 10 weeks in individuals with major depression. For all participants, depression scores significantly decreased compared to baseline. In a subsequent study by Rapoport and colleagues (2010), individuals in remission from depression were randomly assigned to receive citalopram or placebo for 40 weeks. Post-treatment relapse rates and time to relapse were not significantly different between the groups; relapse occurred in 52.4% of all patients. In both studies by Rapoport and colleagues, adverse events associated with citalopram were common (Rapoport et al., 2008; Rapoport et al., 2010). While citalopram has shown potential to treat depression on its own, a study by (Perino et al., 2001) found that a combination of citalopram and carbamazepine significantly reduced depressive symptoms in patients diagnosed with depression after 12 weeks.

Conclusions

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

There is level 1b evidence that citalopram may not be effective in preventing relapse of major depression post TBI compared to no treatment.

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 an effective treatment for major depression compared to placebo post TBI.

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

Citalopram may not be an effective treatment for major depression post TBI, but may be effective when taken in combination with carbamazepine.

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

8.2.4 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), aerobic exercise, and other forms of counselling (Knottnerus et al., 2007). There is preliminary evidence for multiple non-

pharmacological interventions for mood, and the treatment of depression in particular. 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. However, given the limited amount of evidence, non-pharmacological interventions cannot be considered as alternatives to pharmacotherapy but may be effective adjunctive treatments.

8.2.4.1 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 ABI, multiple studies have examined the effectiveness of CBT in treating depressive symptoms (Table 8.2).

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

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
<p>Ponsford et al. (2016) Australia RCT PEDro=7 N_{Start}=75, N_{End}=51</p>	<p>Population: TBI. <i>CBT+MI Group (n=26)</i>: Mean Age=46.69 yr; Gender: Male=18, Female=8; Mean Time Post Injury=4.88yr; Mean GCS=10.43. <i>CBT+NDC Group (n=26)</i>: Mean Age=39.88 yr; Gender: Male=20, Female=6; Mean Time Post Injury=3.58 yr; Mean GCS=10.48. <i>WC Group (n=23)</i>: Mean Age=39.87 yr; Gender: Male=17, Female=6; Mean Time Post Injury=2.61 yr; Mean GCS=8.23.</p> <p>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 3 wk, followed by 9 wk of CBT, with three CBT booster sessions 21-30 wk from baseline. Assessments were conducted at baseline, 3 wk, 12 wk, 21 wk, and 30 wk.</p> <p>Outcome Measure: Depression, Anxiety & Stress Scale (DASS), Hospital & Anxiety Depression Scale (HADS), Sydney Psychosocial Reintegration Scale 2 (SPRS-2).</p>	<ol style="list-style-type: none"> All groups demonstrated significant improvements on the DASS-Depression, HADS-Anxiety, and SPRS-2 over time. 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. 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. On the SPRS-2, there was no significant difference in improvement between groups over time. 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). 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.
<p>Fann et al. (2015) USA PCT N_{Initial}=100, N_{Final}=72</p>	<p>Population: TBI; Mean Age=45.8 yr; Gender: Male=63, Female=37; Mean Time Post Injury=3.33 yr; Severity: Moderate=69, Severe=31.</p> <p>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 12 wk, where in-session work and</p>	<ol style="list-style-type: none"> 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 16 wk or 24 wk ($p>0.05$). On HAM-D, there were no significant differences for CBT-T versus UC, CBT-IP versus UC, or combined CBT versus UC at baseline, 8 wk, 16 wk, or 24 wk ($p>0.05$).

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
	<p>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, 8 wk, 16 wk, and 24 wk.</p> <p>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).</p>	<ol style="list-style-type: none"> 3. On SCL-20, CBT-T showed significantly greater improvement than UC at 8 wk ($p=0.002$) and 16 wk ($p=0.043$), but not 24 wk ($p=0.065$). 4. On SCL-20, there were no significant differences between CBT-IP and UC at baseline, 8 wk, 16 wk, or 24 wk ($p>0.05$). 5. On SCL-20, combined CBT showed significantly greater improvement than UC at 8 wk ($p=0.001$), but not at 16 wk ($p=0.074$) or 24 wk ($p=0.250$). 6. On PGI at 16 wk, 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 24 wk, 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 16 wk, 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.
<p>Ashworth et al. (2015) UK Pre-Post N=12</p>	<p>Population: TBI=7, Stroke=3, ABI=2; Mean Age=40.9 yr; Gender: Male=7, Female=5.</p> <p>Intervention: Participants received two phases of compassion-focused therapy (CFT) 1 day/wk for 18 wk. 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, 18 wk, and 3 mo follow-up.</p> <p>Outcome Measure: Hospital Depression and Anxiety Scale (HADS), Forms of Self-Criticism/Self-Attacking and Self-Reassuring Scale (FSCRS).</p>	<ol style="list-style-type: none"> 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 ($p<0.05$).
<p>Ashman et al. (2014) USA RCT PEDro=7 N_{Initial}=54, N_{Final}=43</p>	<p>Population: TBI. CBT Group ($n=28$): Mean Age=47.5 yr; Gender: Male=10, Female=18; Mean Time Post Injury=7.8 yr; Severity: Mild=10, Moderate/Severe=17. SPT ($n=26$): Mean Age=47.1 yr; Gender: Male=12, Female=14; Mean Time Post Injury=13.2 yr; Severity: Mild=9, Moderate/Severe=12.</p> <p>Intervention: Participants diagnosed with depression were randomized to receive</p>	<ol style="list-style-type: none"> 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 (CBT, $p=0.03$; SPT, $p=0.06$).

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
	<p>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 90 min sessions 2 day/wk for the first week, followed by 50 min sessions 1 day/wk for 3 mo. Assessments were conducted before and after each treatment session.</p> <p>Outcome Measure: Beck Depression Inventory-Second Edition (BDI-II), State-Trait Anxiety Inventory (STAI), Life-3.</p>	<ol style="list-style-type: none"> 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 ($p>0.05$).
<p>D'Antonio et al. (2013) USA RCT PEDro=6 N=44</p>	<p>Population: TBI; Mean Age=48.8 yr; Gender: Male=19, Female=25; Mean Time Post Injury=7.7 yr.</p> <p>Treatment: Participants diagnosed with depression were randomized to receive 16 sessions of cognitive behavioural therapy (CBT) or supportive psychotherapy (SPT) for over 3 mo. For both groups, the first session lasted 90 min and each subsequent session was 50 min. Assessments were conducted at baseline and 3mo.</p> <p>Outcome Measure: Beck Depression Inventory-II (BDI-II).</p>	<ol style="list-style-type: none"> 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.
<p>Bradbury et al. (2008) Arundine et al. (2012) Canada PCT N_{Initial}=20, N_{Final}=17</p>	<p>Population: TBI=10, ABI=10, Severity: Moderate-Severe. <i>CBT Group (n=10):</i> Mean age=39.8 yr; Gender: Male=5, Female=5; Mean Time Post Injury=7.00 yr. <i>EC Group (n=10):</i> Mean age=42.5 yr; Gender: Male=5, Female=5; Mean Time Post Injury=11.4 yr.</p> <p>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.</p> <p>Outcome Measure: Depression Anxiety Stress Scales 21 (DASS-21), Symptom Checklist 90 Revised (SCL-90-R).</p>	<ol style="list-style-type: none"> 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 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 ($p>0.05$). 4. At 6 mo 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.
<p>Anson & Ponsford (2006a) Anson & Ponsford (2006b) Australia RCT</p>	<p>Population: TBI; Gender: Male=26, Female=5. <i>CBT Group (n=15):</i> Mean Age=38.9 yr; Mean Time Post Injury=755.8 days. <i>WC Group (n=16):</i> Mean Age=37.8 yr; Mean Time Post Injury=340.8 days.</p> <p>Intervention: Participants were randomized to</p>	<ol style="list-style-type: none"> 1. Both groups significantly increased their adaptive coping skills on the CSA after CBT ($p<0.01$). 2. No significant improvements in scores on HADS-Depression, HADS-Anxiety, or RSES were found after CBT ($p>0.05$).

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
PEDro=5 N _{Initial} =33, N _{Final} = 31	receive cognitive behavioural therapy (CBT) or waitlist control (WC). CBT was delivered for 90 min, 2 days/wk for 5wk. Assessments were conducted at baseline, 5 wk, and 10 wk. Outcome Measure: Hospital Anxiety and Depression Scale (HADS), Coping Scale for Adults (CSA), Rosenberg Self Esteem Scale (RSES).	<ol style="list-style-type: none"> 3. Those who had a greater self-awareness post injury had better outcomes after CBT, noted in the decrease in HADS-Depression scores. 2. Those who had higher HADS-Depression and lower RSES scores did not perform as well after CBT.
Hodgson et al. (2005) Australia RCT PEDro=5 N=12	<p>Population: ABI; Gender: Male=7, Female=5. <i>Treatment Group</i> (n=6): Mean Age=44.2 yr; Mean Time Post Injury=96.7 mo. <i>Waitlist Group</i> (n=6): Mean Age=33.8 yr; Mean Time Post Injury=150.5 mo.</p> <p>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 1 hr sessions 1 day/wk for 9-14 wk. Assessments were conducted before and after treatment, and at 1 mo follow-up.</p> <p>Outcome Measure: Hospital Anxiety and Depression Scale (HADS), Social Phobia and Anxiety Inventory (SPAI), Coppersmith Self Esteem Inventory.</p>	<ol style="list-style-type: none"> 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.

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 (2006a) 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 lesser depressive symptoms demonstrated better outcomes with the program (Anson & Ponsford, 2006b). 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 control, whether in person, by phone, or combined (Fann et al., 2015). The telephone CBT significantly reduced psychological impairment relative to control, but in-person CBT and combined CBT were not superior. However, patients' subjective response to telephone CBT and combined CBT were more favourable than control, and all forms of CBT

had greater levels of satisfaction with depression care than control. In the third trial, CBT demonstrated significant reductions in depression compared to 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 either treatment. However, there were no significant differences in effectiveness between the two treatments. 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 (Ashman et al., 2014; D'Antonio et al., 2013). 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 ABI.

There is level 1b evidence that cognitive behavioural therapy may be a more effective treatment for depression post TBI when combined with motivational interviewing than with non-directive counselling.

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 conflicting (level 1b and level 2) evidence as to whether cognitive behavioural therapy is more effective when delivered in groups or by telephone post ABI.

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.

Cognitive behavioural therapy may be more effective when provided in combination with motivational interviewing than non-directive counselling.

8.2.4.2 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/ Study Design/ N	Methods	Outcomes
<p>Bedard et al. (2014) Canada RCT PEDro=6 N=76</p>	<p>Population: TBI; Gender: Male=42, Female=34; Mean Age=46.5 yr; Mean Time Post Injury=4.25 yr. Intervention: Participants were diagnosed with depression. The treatment group (n=38) received 1.5 hr weekly sessions of mindfulness-based cognitive therapy for 10 wk. The control group (n=38) received usual care. Assessments were conducted at baseline, 10 wk, and 3 mo 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).</p>	<ol style="list-style-type: none"> Following treatment, the treatment group showed significantly greater reduction in BDI-II scores than the control group ($p=0.029$), which was maintained at the 3 mo follow-up. No significant between-group differences on PHQ-9 and SCL-90-R were found ($p>0.05$). Neither PHLMS nor TMS reached significance in demonstrating increases in mindfulness for the treatment group ($p>0.05$).
<p>Bedard et al. (2012) Canada Pre-Post N=20</p>	<p>Population: TBI; Mean Age=47.1yr; Gender: Male=9, Female=11; Time Post Injury ≥ 1 yr. Treatment: Participants with a diagnosis of depression received 90 min sessions of mindfulness-based stress reduction 1 day/wk for 8 wk. Sessions included topics such as acceptance, staying in the present, and improving awareness of thoughts and feelings. Homework assignments were given after each session. Assessments were conducted at baseline and 8 wk. Outcome Measure: Beck Depression Inventory-II (BDI-II), Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire-9 (PHQ-9).</p>	<ol style="list-style-type: none"> After treatment, there were significant changes in scores on the BDI ($p=0.001$), PHQ-9 ($p=0.003$), and HADS-Depression ($p=0.023$). There was no significant improvement on HADS-Anxiety after treatment ($p=0.116$).
<p>Bedard et al. (2003) Canada Pre-Post N=13</p>	<p>Population: TBI; <i>MBSR Group (n=10):</i> Mean Age=43 yr; Gender: Male=3, Female=7. <i>Control Group (n=3):</i> Mean Age=39 yr; 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 12 wk. 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).</p>	<ol style="list-style-type: none"> After treatment, the MBSR group showed significant improvements on BDI-II ($p=0.006$), GSI ($p=0.004$), PSDI ($p=0.002$), and PSS ($p=0.026$). Compared to controls, the MBSR group showed no significant differences after treatment on BDI-II, GSI, PSDI, or PSS ($p>0.05$). 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

Three studies examining the efficacy of MBSR programs post TBI were conducted by Bedard and colleagues (Bedard et al., 2003; Bedard et al., 2012; Bedard et al., 2014). 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). In an RCT, 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.

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

8.2.4.3 Psychotherapy

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/ Study Design/ N	Methods	Outcomes
Andrewes et al. (2014) UK RCT PEDro=5 N=10	<p>Population: TBI; Mean Age=42.2 yr; Gender: Male=9, Female=1; Mean Time Post Injury=4.8 yr.</p> <p>Intervention: Participants were randomly assigned to control or to a 12 wk Positive Psychology program. The program involved “Three Good Things” sessions followed by “Signature Strengths” sessions. All participants also received weekly individual therapy sessions for substance misuse.</p> <p>Outcome Measure: Authentic Happiness Index (AHI), Head Injury Semantic Differential Scale (HISDS).</p>	<ol style="list-style-type: none"> After “three good things”, the intervention group scored significantly higher on the AHI than the control group (p=0.02); these differences were not significant at 12 wk. After “signature strengths”, there were no significant differences between groups on the HISDS (p>0.05).
Wiat et al. (2012) France Case Series N= 47	<p>Population: TBI; Mean Age=33.4 yr; Gender: Male=35, Female=12; Mean Time Post Injury=11.1 yr.</p> <p>Intervention: Retrospective review of patients with mood disorders referred to a single physician for at least 1 yr of neuro-systemic psychotherapy.</p> <p>Outcome Measure: Diagnostic and Statistical Manual of Mental Disorders (DSM), Glasgow Outcome Scale.</p>	<ol style="list-style-type: none"> Significant improvement of affective disorders was found: depression (p<0.001), anxiety (p<0.001), and hostility (p<0.01). No improvements were seen in apathy, bipolar symptomatology, loss of control, or addictive disorders. 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 (Wiat et al., 2012). The study found that patients had significant reductions in depression, as well as anxiety and hostility, after one year of treatment. As well, half of patients had a good outcome according to the Glasgow Outcome Scale. In a pilot RCT, patients with TBI were randomly assigned to a control group or two variations of positive psychology interventions: “Three Good Things” or “Signature Strengths” (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.

Conclusions

There is level 2 evidence that positive psychology therapy may improve happiness post TBI compared to substance abuse educational therapy.

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

Positive psychotherapy may increase happiness following TBI.

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

8.2.4.4 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/ Study Design/ N	Methods	Outcomes
Guetin et al. (2009) France Pre-Post N=13	Population: TBI; Mean Age=31 yr; Gender: Male=3, Female=10; Mean Time Post Injury=8 yr. Treatment: Participants received music therapy (1 hr/wk for 20 wk). 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, 1 wk, 5 wk, 10 wk, 15 wk, and 20 wk. Outcome Measure: Hospital Anxiety and Depression Scale (HADS).	<ol style="list-style-type: none"> Following each music therapy session, significant improvements in mood were noted on the HADS ($p<0.05$). Anxiety scores significantly decreased from baseline to 10 wk, 15 wk, and 20 wk ($p<0.05$). Depression scores significantly decreased from baseline to 10 wk and 15 wk ($p<0.05$).
Thaut et al. (2009) USA PCT	Population: TBI=24, Stroke=5, Other=4; Mean Age=31 yr; Gender: Male=3, Female=10. Intervention: Participants were assigned to a	<ol style="list-style-type: none"> On the MAACL, Depression and Anxiety improved significantly in the treatment

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
N=54	<p>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.</p> <p>Outcome Measure: Multiple Affect Adjective Checklist (MAACL), Brief Symptom Inventory 18 (BSI-18).</p>	<p>group ($p < 0.05$) but did not change in the control group ($p > 0.05$).</p> <ol style="list-style-type: none"> 2. On the MAACL, Positive Affect did not change in the treatment group ($p = 0.039$) but significantly worsened in the control group ($p = 0.04$). 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, $p = 0.010$).
<p>Nayak et al. (2000) USA PCT N=18</p>	<p>Population: TBI and Stroke; Mean Age=59.89 yr; Gender: Male=6, Female=12.</p> <p>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.</p> <p>Outcome Measure: Mood (Self-Report, Family-Rated, Staff-Rated), Social Interaction (Family-Rated), Participation (Staff-Rated).</p>	<ol style="list-style-type: none"> 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. However, it should be noted that 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.

8.2.4.5 Physical Activity

The positive impact of physical activity on mood has been well-established in the general population (Byrne & Byrne, 1993). 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/ Study Design/ N	Methods	Outcomes
Aerobic Exercise		
Damiano et al. (2016) USA Pre-Post N=12	<p>Population: TBI; Mean Age=31.3 yr; Gender: Male=7, Female=5.</p> <p>Intervention: Participants completed a home-based, aerobic exercise program for 5 days/wk over 8 wk. Training included exercise of moderate intensity for 30 min on the elliptical machine. Measures were assessed at baseline, 8 wk, and 16 wk.</p> <p>Outcome Measure: Hamilton Rating Scale for Depression (HAM-D), Beck Anxiety Inventory (BAI), Pittsburgh Sleep Quality Index (PSQI).</p>	<ol style="list-style-type: none"> 1. No significant changes in HAM-D or BAI scores from baseline to 8 wk or 16 wk 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. (2016) USA Pre-Post N _{Initial} =12, N _{Final} =10	<p>Population: TBI; Mean Age=32.9 yr; Gender: Male=4, Female=6; Mean Time Post Injury=6.6 yr; Severity: Mild=5, Moderate=4, Severe=1.</p> <p>Intervention: Participants completed one-on-one supervised aerobic exercise sessions (3 days/wk for 12 wk) where they reached 70-80% of maximum heart rate. Assessments were conducted before and after sessions at baseline, 4 wk, 8 wk, and 12 wk.</p> <p>Outcome Measure: Profile of Mood States - Short Form (POMS-SF).</p>	<ol style="list-style-type: none"> 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 ($p=0.04$). 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 ($p=0.09$).
Bellon et al. (2015) USA RCT PEDro=6 N _{Initial} =123, N _{Final} =69	<p>Population: TBI; Mean Age=43.7 yr; Gender: Male=41, Female=28; Mean Time Post Injury=100.5 mo; Severity: Mild=10, Moderate=10, Severe=35.</p> <p>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 12 wk, with a coaching call 3 days/wk to encourage increase in weekly step count. The</p>	<ol style="list-style-type: none"> 1. Depression on the CES-D decreased significantly from baseline to 12 wk and 24 wk for all participants ($p=0.007$), but there was no significant difference between groups at 12 wk or 24 wk. 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 ($p=0.006$).

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
	<p>home-based nutrition group learned about healthy eating habits through coaching calls 3 days/wk for 12 wk. After 12 wk, participants crossed over. Measures were assessed at baseline, 12 wk, and 24 wk.</p> <p>Outcome Measure: Centre for Epidemiological Studies-Depression (CES-D), Perceived Stress Scale (PSS).</p>	
<p>Hoffman et al. (2010) Wise et al. (2012) USA RCT PEDro=5 N_{Initial}=80, N_{Final}=40</p>	<p>Population: TBI. <i>Treatment Group (n=40):</i> Mean Age=39.7 yr; Gender: Male=15, Females=25. <i>Control Group (n=40):</i> Mean Age=37.1 yr; Gender: Male=20, Female=20.</p> <p>Intervention: The treatment group received a 10 wk exercise program with 15 min education session, 15 min of warm-up exercises, 30 min of aerobics, and 15 min of cool-down exercises. Each participant was asked to perform 30 min sessions for 4 days/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, 10 wk, and 6 mo.</p> <p>Outcome Measure: Beck Depression Inventory (BDI), Perceived Quality of Life Scale (PQOL), Short Form Health Survey (SF-12).</p>	<ol style="list-style-type: none"> At 10 wk, there were no significant differences between the exercise and control groups on the BDI (p=0.250). Participants exercising >90 min/wk were found to have lower depression scores than those exercising <90 min/wk (p=0.033). At 6 mo, there was a reduction in the number of participants able to exercise >90min per week (77% versus 52%). Those who exercised >90 min 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).
<p>Driver & Ede (2009) USA RCT PEDro=5 N=16</p>	<p>Population: TBI; <i>Treatment Group (n=8):</i> Mean Age=38.78 yr; Mean Time Post Injury=40.75 mo. <i>Control Group (n=8):</i> Mean Age=37.62 yr; Mean Time Post Injury=36.25 mo.</p> <p>Intervention: Participants were randomised to aquatic exercise (treatment) or a vocational rehabilitation class (control) for 3 days/wk over 8 wk. Measures were assessed at baseline and 8 wk.</p> <p>Outcome Measure: Profile of Mood States (POMS).</p>	<ol style="list-style-type: none"> At 8wk, significant differences in total POMS scores were noted between the groups in favour of treatment (p<0.05). Within-group scores for the treatment group showed significant differences on each of the POMS subscales (all p<0.05). No significant differences were noted on each of the sub-scales for the control group (p>0.05).
<p>Gordon et al. (1998) USA Case Control N=240</p>	<p>Population: TBI. <i>Non-Exercise Group (n=176):</i> Mean Age=37.1 yr; Mean Time Post Injury=9.1 yr. <i>Exercise Group (n=64):</i> Mean Age=37.8 yr; Mean Time Post Injury=11.2 yr. Intervention: Retrospective comparison of exercisers and non-exercisers.</p> <p>Outcome Measure: Beck Depression Inventory (BDI), The Institute for Rehabilitation Research (TIRR) Symptom Checklist.</p>	<ol style="list-style-type: none"> Individuals who exercised had less depressed mood (BDI) than those who did not exercise (p<0.01). Individuals who exercised reported significantly fewer symptoms on the TIRR checklist compared to those who did not exercise (p<0.0004).
Tai Chi		
<p>Blake & Batson (2009) UK RCT PEDro=6 N=20</p>	<p>Population: TBI; Gender: Male=15, Female=5; Injury Severity: Mild=7, Moderate=8, Severe=5. <i>Treatment Group (n=10):</i> Mean Age=44.5 yr; Mean Time Post Injury=16.4 yr. <i>Control Group (n=10):</i> Mean Age=46.2 yr; Mean Time Post Injury=13.62 yr.</p> <p>Intervention: The treatment group performed tai chi (qigong) for 1 hr/wk over 8 wk. The control</p>	<ol style="list-style-type: none"> At 8 wk, GHQ-12 showed a significant improvement in mood scores for those in the treatment group compared to the control group (p=0.026). Physical self-esteem was found to improve significantly from baseline to 8 wk for those in the treatment group (p=0.017).

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
	group attended non-exercise social and leisure activities for 1 hr/wk over 8 wk. Measures were assessed at baseline and 8wk. Outcome Measure: General Health Questionnaire-12 (GHQ-12), Physical Self-Description Questionnaire.	
Gemmell & Leathem (2006) New Zealand RCT PEDro=6 N=18	Population: TBI; Mean Age: Males=51.2 yr, Females=40.2 yr; Gender: Male=9, Female=9; Mean Time Post Injury=8.7 yr. Intervention: The treatment group (n=9) performed tai chi (chuan) for 6 wk. The control group (n=9) was waitlisted for tai chi. Measures were assessed at baseline, 6 wk, and 9 wk. Outcome Measure: Visual Analog Mood Scale (VAMS), Medical Outcome Scale Short Form 26 (MOS SF-36), Rosenberg Self-Esteem Scale (RSES).	<ol style="list-style-type: none"> At 6 wk, the treatment group reported significant improvements on VAMS (fear, confusion, sadness, anger, tiredness, tension, happiness, energy; not fatigue) compared to the control group. When compared to the control group, the differences on the MOS SF-36 and the RSES were not significant. At 9 wk, 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

Five prospective 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., 2016); the latter study reported significantly greater improvements in mood than conventional rehabilitation (Weinstein et al., 2016). However, 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).

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 control. However, the studies did not include participants with a diagnosis of depression and did not explicitly measure depression.

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.

8.2.4.6 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/ Study Design/ N	Methods	Outcomes
Ruff & Niemann (1990) USA RCT PEDro=7 N=24	<p>Population: TBI; Gender: Male=17, Female=7. <i>Group 1 (n=12):</i> Mean Age=28.3 yr; Mean Time Post Injury=44.3mo. <i>Group 2 (n=12):</i> Mean Age=31.1 yr; Mean Time Post Injury=52.2 mo.</p> <p>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.</p> <p>Outcome Measure: Katz Adjustment Scale (KAS).</p>	<p>1. Individuals in both groups experienced a decrease in depressed mood, as measured by the KAS.</p>

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.

Conclusions

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

Psychosocial or cognitive rehabilitation may reduce depressive symptoms following TBI.

8.3 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 includes 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.

8.3.1 Incidence and Prevalence of Anxiety

Following ABI, anxiety or anxiety disorders have been reported to occur in 4% to 28% of individuals (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., 2015; 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 PTSD, 15% with OCD, 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., 2015). 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).

8.3.2 Non-Pharmacological Interventions 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. However, CBT for anxiety post ABI may not be as effective due to the cognitive impairments in this population (Table 8.8).

Table 8.8 Cognitive Behavioural Therapy for the Treatment of Anxiety Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
<p>Ponsford et al. (2016) Australia RCT PEDro=7 N_{Start}=75, N_{End}=51</p>	<p>Population: TBI. <i>CBT+MI Group (n=26):</i> Mean Age=46.69 yr; Gender: Male=18, Female=8; Mean Time Post Injury=4.88 yr; Mean GCS=10.43. <i>CBT+NDC Group (n=26):</i> Mean Age=39.88 yr; Gender: Male=20, Female=6; Mean Time Post Injury=3.58 yr; Mean GCS=10.48. <i>WC Group (n=23):</i> Mean Age=39.87 yr; Gender: Male=17, Female=6; Mean Time Post Injury=2.61 yr; Mean GCS=8.23.</p> <p>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 3 wk, followed by 9 wk of CBT, with three CBT booster sessions 21-30 wk from baseline. Assessments were conducted at baseline, 3 wk, 12 wk, 21 wk, and 30 wk.</p> <p>Outcome Measure: Depression, Anxiety & Stress Scale (DASS), Hospital & Anxiety Depression Scale (HADS), Sydney Psychosocial Reintegration Scale 2 (SPRS-2).</p>	<ol style="list-style-type: none"> All groups demonstrated significant improvements on the DASS-Depression, HADS-Anxiety, and SPRS-2 over time. 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. 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. On the SPRS-2, there was no significant difference in improvement between groups over time. 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). When combining CBT+MI and CBT+NDC groups, there were significantly greater improvements on HADS-Anxiety ($p<0.05$), DASS-Depression ($p<0.005$),

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
<p>Hsieh et al. (2012b) Hsieh et al. (2012a) Australia RCT PEDro=6 N_{Initial}=27, N_{Final}=24</p>	<p>Population: TBI; Mean Age=38 yr; Gender: Male=21, Female=6; Mean Time Post Injury=37.9 mo.</p> <p>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 and 12 wk.</p> <p>Outcome Measure: Hospital Anxiety and Depression Scale (HADS), Depression Anxiety Stress Scale (DASS), Coping Style for Adults (CSA), Sydney Psychosocial Reintegration Scale (SPRS-2), Anxiety Change Expectancy Scale (ACES).</p>	<p>and SPRS-2 ($p<0.05$) in the combined group versus WC.</p> <ol style="list-style-type: none"> 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. CBT+MI did show a significantly greater increase in ACES than CBT+NDC after CBT ($p=0.04$) and at 9 wk follow-up ($p=0.015$), but not immediately after MI ($p=0.22$). 7. 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.
<p>Bradbury et al. (2008) Arundine et al. (2012) Canada PCT N_{Initial}=20, N_{Final}=17</p>	<p>Population: TBI=10, ABI=10, Severity: Moderate-Severe. <i>CBT Group (n=10):</i> Mean age=39.8 yr; Gender: Male=5, Female=5; Mean Time Post Injury=7.00 yr. <i>Control Group (n=10):</i> Mean age=42.5 yr; Gender: Male=5, Female=5; Mean Time Post Injury=11.4 yr.</p> <p>Intervention: Participants with psychological distress were randomized to receive cognitive behavioural therapy (CBT) or education control. 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, 1 mo follow-up, and 6 mo follow-up.</p> <p>Outcome Measure: Depression Anxiety Stress Scales 21 (DASS-21), Symptom Checklist 90 Revised (SCL-90-R).</p>	<ol style="list-style-type: none"> 1. At post treatment and 1 mo 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 significant improvements from post treatment to 1 mo 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 ($p>0.05$). 4. At 6 mo 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/ Study Design/ N	Methods	Outcomes
<p>Anson & Ponsford (2006a) Anson & Ponsford (2006b) Australia RCT PEDro=5 N_{Initial}=33, N_{Final}= 31</p>	<p>Population: TBI; Gender: Male=26, Female=5. <i>CBT Group (n=15):</i> Mean Age=38.9 yr; Mean Time Post Injury=755.8 days. <i>Control Group (n=16):</i> Mean Age=37.8 yr; Mean Time Post Injury=340.8 days.</p> <p>Intervention: Participants were randomized to receive cognitive behavioural therapy (CBT) or waitlist control. CBT was delivered for 90min, 2 days/wk for 5 wk. Assessments were conducted at baseline, 5 wk, and 10 wk.</p> <p>Outcome Measure: Hospital Anxiety and Depression Scale (HADS), Coping Scale for Adults (CSA), Rosenberg Self Esteem Scale (RSES).</p>	<ol style="list-style-type: none"> Both groups significantly increased their adaptive coping skills on the CSA after CBT ($p<0.01$). No significant improvements in scores on HADS-Depression, HADS-Anxiety, or RSES were found after CBT ($p>0.05$). Those who had a greater self-awareness post injury had better outcomes after CBT, noted in the decrease in HADS-Depression scores. Those who had higher HADS-Depression and lower RSES scores did not perform as well after CBT.
<p>Hodgson et al. (2005) Australia RCT PEDro=5 N=12</p>	<p>Population: ABI; Gender: Male=7, Female=5. <i>Treatment Group (n=6):</i> Mean Age=44.2 yr; Mean Time Post Injury=96.7mo. <i>Waitlist Group (n=6):</i> Mean Age=33.8 yr; Mean Time Post Injury=150.5 mo.</p> <p>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 1 mo follow-up.</p> <p>Outcome Measure: Hospital Anxiety and Depression Scale (HADS), Social Phobia and Anxiety Inventory (SPAI), Coppersmith Self Esteem Inventory.</p>	<ol style="list-style-type: none"> After treatment, the CBT group had significantly lower scores on HADS-Depression, HADS-Anxiety, and SPAI than the control group ($p<0.05$). At follow-up, the treatment group maintained improvement relative to the control group.

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, 2006a).

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.

8.3.3 Obsessive Compulsive Disorder

Following ABI, anxiety disorders such as OCD, panic attacks, and stress disorders are common. OCD is believed to be present in approximately 10% of the brain injury population (Berthier et al., 2001), but it is rarely reported in the literature (Drummond & Gravestock, 1988). Studies conducted by McKeon et al. (1984) and Kant et al. (1996) found that OCD symptoms appeared within the first few hours to the first week of injury; some patients developed symptoms within the first six months. Several authors have suggested the location of the brain lesion may predict OCD in patients (Bilgic et al., 2004; Donovan & Barry, 1994; Jenike & Brandon, 1988), although there is still no conclusive evidence to date. A review by Grados (2003) noted that OCD has been treated successfully with serotonin selective reuptake inhibitors. While success with other supportive therapies has been reported in the literature, no clinical trials have been identified.

8.3.4 Post-Traumatic Stress Disorder

Earlier literature of PTSD focused on patients with mild TBI, which was based on the belief that PTSD could not develop in the presence of amnesia for the 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., 2013b). Individuals with comorbid PTSD and TBI may experience cognitive impairment and sleep disruptions, along with anxiety and depressive symptoms (Barker-Collo et al., 2013a). 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.

8.4 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, and so it is not surprising that 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 at 20 years after TBI (Fisher et al., 2016).

8.4.1 Incidence and Prevalence of Suicidal Ideation

Within the TBI population, 23-28% of individuals report suicidal ideation after sustaining a TBI (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 (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).

8.4.2 Non-Pharmacological Interventions for Suicide Prevention

Specific interventions have been developed, primarily psychotherapy, in order to address suicidal ideation in individuals following ABI (Table 8.9).

Table 8.9 Non-Pharmacological Interventions for Suicide Prevention Post ABI

Author/Year/ Country/Study Design/ N	Methods	Outcomes
Brenner et al. (2017) Australia RCT PEDro=6 N _{Start} =44, N _{End} =35	Population: TBI. <i>Intervention Group (n=15):</i> Mean Age=47.7 yr; Gender: Male=13, Female=1, Transgender=1. <i>Waitlist Group (n=20):</i> Mean Age=54.6 yr; 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 2 hr and delivered weekly for 10 wk. Participants were crossed over to the alternate intervention after 10 wk. Assessments occurred at baseline, 10 wk, and 20 wk. Outcome Measure: Beck Hopelessness Scale (BHS), Beck Depression Inventory (BDI), Beck	<ol style="list-style-type: none"> 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. The waitlist group demonstrated significant reductions on the BHS (p=0.01) and depression (p=0.003) after completing the intervention. There were no significant between-group differences for the BDI or BSSI.

Author/Year/ Country/Study Design/ N	Methods	Outcomes
	Scale for Suicide Ideation (BSSI).	
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).	<ol style="list-style-type: none"> 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.
Simpson et al. (2011) Australia RCT PEDro=8 N=17	Population: TBI; Severity: Severe. <i>Treatment Group (n=8):</i> Mean Age=39.4yr; Mean Time Post Injury=6.3 yr. <i>Control Group (n=9):</i> Mean Age=44.1 yr; Mean Time Post Injury=7.6 yr. 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, 10 wk, 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).	<ol style="list-style-type: none"> 1. Significant group-by-time interaction on BHS (p=0.002) but no significant main effects for either group or time. 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.

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. In a small post-test, 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 waitlist controls, may be effective in reducing hopelessness post TBI, but does not reduce depressive symptoms or suicidal ideation.

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.

8.5 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.

8.5.1 Prevalence and Predictors of Agitation and Aggression

Agitation and aggression occur in approximately 33% to 54% of patients with TBI (Janzen et al., 2014; Sabaz 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 lesions (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).

8.5.2 Pharmacological Interventions for Agitation and Aggression

The diversity of behaviours typical of post-ABI agitation creates problems in terms of research regarding treatment efficacy. 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 efficacy of pharmacological interventions for agitation and aggression would be studied using a randomized, double-blinded, placebo design; although few of these trials have been conducted in ABI (Levy et al., 2005). Moreover, due to the lack of consistency in measuring agitation and aggression (Baguley et al., 2006), there is difficulty in comparing similar interventions across studies.

8.5.2.1 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 8.10).

Table 8.10 Effects of Sertraline and Amitriptyline on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Mysiw et al. (1988) USA Pre-Post N=20	Population: TBI; Mean Age=29.4 yr; Gender: Male=18, Female=2. Intervention: Participants received amitriptyline (25-150 mg/day). Assessments were conducted at 1 wk and follow-up. Outcome Measure: Orientation Group Monitoring Scale (OGMS).	<ol style="list-style-type: none"> Thirteen patients experienced significantly reduced levels of agitation after 1 wk ($p<0.001$), which was maintained in the ensuing weeks ($p<0.001$) but did not significantly decrease from 1 wk ($p>0.6$). Thirty percent of patients experienced no significant change in agitation levels, despite increasing the dose at 1 wk ($p>0.7$) and beyond ($p>0.3$).
Kant et al. (1998) USA Pre-Post N=13	Population: TBI; Mean Age=37.6 yr; Gender: Male=10, Female=3; Injury Severity: Mild=5, Moderate=6, Severe=6; Mean Time Post Injury=2 yr. Intervention: Participants with aggression received sertraline (50-200 mg/day) for 8 wk. Assessments were conducted at 4 wk and 8 wk. Outcome Measure: Overt Aggression Scale-Modified (OAS-M), Anger Irritability Assault Questionnaire (AIAQ), Beck Depression Inventory (BDI).	<ol style="list-style-type: none"> Significant improvement on OAS-M ($p<0.001$) and AIAQ ($p<0.01$) found at 4 wk and 8 wk. Significant improvement on BDI found at 4 wk ($p=0.04$) but not 8 wk ($p=0.14$).

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 70% of patients displayed significant reductions agitation within the first week of treatment (Mysiw et al., 1988). Both studies had similar limitations, due to small sample sizes and lack of control groups.

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.

8.5.2.2 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.

8.5.2.2.1 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). As well, amantadine can 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. Among the ABI population, the effects of amantadine on reducing agitation and aggression have yet to be established (Table 8.11).

Table 8.11 Effects of Amantadine on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
Hammond et al. (2015) USA RCT PEDro=10 N _{Initial} =168, N _{Final} =157	<p>Population: TBI. <i>Amantadine Group (n=82):</i> Mean Age=40.2 yr; Gender: Male=66, Female=16; Severity: Mild=20, Moderate=3, Severe=59. <i>Placebo Group (n=86):</i> Mean Age=38.2 yr; Gender: Male=64, Female=22; Severity: Mild=22, Moderate=1, Severe=63.</p> <p>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.</p> <p>Outcome Measure: Neuropsychiatric Inventory Irritability (NPI-I).</p>	<ol style="list-style-type: none"> 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.

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
<p>Hammond et al. (2014) USA RCT PEDro=9 N_{initial}=76, N_{Final}=72</p>	<p>Population: TBI. <i>Amantadine Group (n=38)</i>: Mean Age=34.7 yr; Gender: Male=25, Female=13; Mean Time Post Injury=5.3 yr; Mean GCS=9.5. <i>Placebo Group (n=38)</i>: Mean Age=42.1 yr; Gender: Male=22, Female=16; Mean Time Post Injury=4.7 yr; Mean GCS=7.5.</p> <p>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.</p> <p>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).</p>	<ol style="list-style-type: none"> 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.

8.5.2.2.2 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 methylphenidate 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 8.12).

Table 8.12 Effects of Methylphenidate on Agitation and Attention Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Mooney & Haas (1993) USA RCT PEDro=5 N=38	Population: TBI; Mean Age=29.45 yr; Gender: Male=38, Female=0; Mean Time Post Injury=27.08 mo. 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.	<ol style="list-style-type: none"> 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.

8.5.2.3 Anticonvulsants

Following a TBI, there is typically diffuse injury with primary involvement of the frontal-subcortical and temporal-limbic regions. As a result, seizure disorders following TBI are not uncommon and may result in episodic lack of control. In 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).

8.5.2.3.1 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 8.13).

Table 8.13 Effects of Carbamazepine on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
Azouvi et al. (1999) France Pre-Post N=10	Population: TBI; Mean Age=33.7 yr; Gender: Male=8, Female=2; Mean GCS Score=5.3; Mean Time Post Injury=58 wk. Intervention: Patients received carbamazepine	<ol style="list-style-type: none"> 1. Total NRS-R and ABS scores showed significant improvement ($p=0.02$); improvements plateaued after 2 wk.

Author/ Year/ Country /Study Design/ N	Methods	Outcomes
	(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).	<ol style="list-style-type: none"> 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 the 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.

8.5.2.3.2 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 8.14).

Table 8.14 Effects of Lamotrigine on Inappropriate Behaviour Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Results
Chahine & Chemali (2006) Lebanon Case Series N=4	Population: TBI; Mean Age=26 yr; Gender: Male=4, Female=0. Intervention: Patients received lamotrigine (range 125-300 mg/day) for inappropriate behaviours. Outcome Measure: Crying, Laughing, Impulsivity.	<ol style="list-style-type: none"> 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.

8.5.2.3.3 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 (Geraciotti Jr, 1994), and so it has been explored as an intervention for challenging behaviours post ABI (Table 8.15).

Table 8.15 Effects of Valproic Acid on Agitation and Aggression Post TBI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
Wroblewski et al. (1997) USA Case Series N=5	Population: TBI; Mean Age=38.2 yr; 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 depakene 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. However, no statistical analyses were conducted, and so it is 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.

Conclusions

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

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

8.5.2.3.4 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 as an intervention for reducing challenging behaviours in individuals post TBI (Table 8.16).

Table 8.16 Effects of Divalproex on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
Chatham Showalter & Kimmel (2000) USA Case Series N=29	<p>Population: TBI; Mean Age=48.2 yr; Mean Time Post Injury=28.6 days.</p> <p>Intervention: Patients received divalproex for agitation and aggression.</p> <p>Outcome Measure: Agitated Behaviour Scale (ABS).</p>	<ol style="list-style-type: none"> Eight patients had treatment with divalproex (mean 714 mg) that led to rapid resolution of symptoms and near total recovery. 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). 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 with brain injuries (Chatham Showalter & Kimmel, 2000). Symptoms decreased in the majority of patients, with a portion showing near total resolution of symptoms. However, due to a lack of statistical analysis, it is difficult to make firm conclusions based on these results.

Conclusions

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

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

8.5.2.4 Antipsychotics

Treatment with antipsychotic medication following brain injury remains controversial. A considerable proportion of the evidence is derived from preclinical research, of which some demonstrated attenuation of behavioural recovery (Elovic et al., 2003). Clinical research of typical and atypical antipsychotics is often limited to a single case series for each medication.

8.5.2.4.1 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 8.17).

Table 8.17 Effects of Quetiapine on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Kim & Bijlani (2006) USA Case Series N=7	<p>Population: TBI; Mean Age=48.9 yr; Gender: Male=4, Female=3; Mean Time Post Injury=23.1 mo.</p> <p>Intervention: Patients received quetiapine (25-300 mg/day; mean=110.7 mg/day) for 6 wk.</p> <p>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).</p>	<ol style="list-style-type: none"> 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.

8.5.2.4.2 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 8.18).

Table 8.18 Effects of Ziprasidone on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Noe et al. (2007) USA Case Series N=5	<p>Population: TBI; Mean Age=26.8 yr; Gender: Male=3, Female=2; Mean Time Post Injury=54.6 days; Mean GCS Score=6.</p> <p>Intervention: Ziprasidone (30-80 mg/day for 35-68 days) was given to participants.</p> <p>Outcome Measure: Agitation Behaviour Scale (ABS).</p>	<ol style="list-style-type: none"> 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 (PTA) has been defined as a period where the individual is disorientated and may suffer from behaviour alterations (Brooke et al., 1992b). 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 PTA 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.

Conclusions

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

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

8.5.2.4.3 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 after the 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 8.19).

Table 8.19 Effects of Lithium Carbonate on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Glenn et al. (1989) USA. Case Series N=10	<p>Population: TBI=8, CVA=2; Mean Age=31.6 yr; Gender: Male=5, Female=5.</p> <p>Intervention: Patients showing mood disorders and unstable, aggressive, combative, or self-destructive behaviour were administered lithium.</p> <p>Outcome Measure: Observed improvement.</p>	<ol style="list-style-type: none"> 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 7 wk. 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, as in a decrease in observed unstable, aggressive, combative, or self-destructive behaviour. However, 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 an antimanic agent (lithium carbonate) reduces aggressive/agitated behaviour following a brain injury.

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

8.5.2.4.4 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 8.20).

Table 8.20 Effects of Methotrimeprazine on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
Maryniak et al. (2001) Canada Case Series N=120	Population: TBI=95, ABI=25; Mean Age=37.8 yr; 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.	<ol style="list-style-type: none"> 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 (MTZ) for agitation was evaluated in a retrospective review of 56 patients during inpatient rehabilitation (Maryniak et al., 2001). The authors found that MTZ 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 MTZ 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.

8.5.2.4.5 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 8.21).

Table 8.21 Effects of Droperidol on Agitation and Aggression Post ABI

Author/Year/ Country/Study Design/ N	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: Observation.	<ol style="list-style-type: none"> Mean dose was 3.25 mg; a single dose reduced agitation in 96% of patients. Time to achieve calming following episodes of agitation was significantly shortened with droperidol compared to haloperidol, lorazepam, or diphenhydramine ($p=0.02$).

Discussion

One retrospective trial found that a single dose of droperidol effectively calmed patients displaying agitated behaviour, and did so more quickly than other drugs (haloperidol, lorazepam, and diphenhydramine) (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. However, it is worth noting that a standardized outcome measure was not utilized, and that a large proportion of the sample had psychiatric co-morbidities.

Conclusions

There is level 4 evidence that a single dose of droperidol may reduce agitation post TBI.

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

8.5.2.4.6 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. However, it has several known side effects, adverse events, and contraindications, and so there is concern that it may impede recovery post ABI (Table 8.22).

Table 8.22 Effects of Haloperidol on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcomes
Rao et al. (1985) USA Case Series N=26	Population: TBI; Age Range=16-48 yr; 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.	<ol style="list-style-type: none"> Those treated had a longer length of PTA ($p<0.03$). 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%). 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 little negative effect on recovery following a TBI.

8.5.2.5 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).

8.5.2.5.1 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 8.23).

Table 8.23 Effects of Pindolol on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Greendyke & Kanter (1986) USA RCT PEDro=7 N _{Initial} =11, N _{Final} =9	<p>Population: ABI; Mean Age=52 yr; Gender: Male=9, Female=0; Mean Time Post Injury=7.8 yr.</p> <p>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.</p> <p>Outcome Measure: Behavioural disturbances.</p>	<ol style="list-style-type: none"> 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 ranged between 40-60 mg per day, in terms of maximizing therapeutic efficacy and minimizing adverse events. 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 behavioural disturbances.

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.

8.5.2.5.2 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).

Table 8.24 Effects of Propranolol on Agitation and Aggression Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Brooke et al. (1992a) 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 420 mg) 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=52 yr; Gender: Male=9, Female=0; Mean Time Post Injury=7.8 yr. Intervention: Patients were randomized to receive either propranolol (520 mg/day) or placebo for 11 wk. Groups were then crossed over and received the alternate treatment for 11 wk. 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.

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

Discussion

Greendyke et al. (1986) investigated the effectiveness of propranolol for the improvement of behavioural issues associated with brain disease in a randomized, crossover trial. 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. (1992b) 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 TBI.

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

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

8.5.3 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).

8.5.3.1 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. There is limited evidence of interventions for sexually disinhibited behaviour among individuals with TBI (Table 8.21).

Table 8.25 Effects of Depo-Provera and Counselling on Sexually Disinhibited Behaviour Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Emory et al. (1995) USA Case Series N=8	Population: TBI; Mean Age=17.5 yr; 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: Hypersexual behaviour.	<ol style="list-style-type: none"> Family members reported all subjects stopped aberrant behaviour while taking medication. Three subjects returned to previous patterns after stopping medication, due to inconsistent family support. 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.

8.5.4 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).

8.5.4.1 General Behavioural Modification

Broad programs for the modification of various challenging behaviours have been evaluated in individuals with brain injury (Table 8.26).

Table 8.26 General Behavioural Modification Interventions for the Treatment of Behavioral Disorders Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Carnevale et al. (2006) USA RCT PEDro=5 N=37	Population: TBI=24, ABI=13; Mean Age=40.5 yr; Gender: Male=28, Female=7; Mean Time Post Injury=7.6 yr. Intervention: Participants were randomized to a control group (n=12) that received no treatment, an education group (n=13) that received	1. NSBM had more improvement in behaviour than the other two groups at 30 wk (p<0.002). 2. A significant difference was noted between the education group and the NSBM group (p<0.04).

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
	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).	
Schlund & Pace (1999) USA Pre-Post N=3	Population: TBI; Mean Age=36 yr; Gender: Male=3, Female=0; Mean Time Post Injury=5.7 yr. 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=26.8 yr; Gender: Male=18, Female=6; Mean GCS Score=7.8; Mean Time Post Injury=44.7 mo. 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, it should be noted that their study consisted of only three mildly cognitively impaired individuals 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.

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

8.5.4.2 Anger Management

Specific interventions have been developed to manage anger and aggression in individuals following brain injury (Table 8.27). 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 8.27 Anger Management Interventions for the Treatment of Anger Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
Hart et al. (2017) USA RCT PEDro=7 N _{Start} =90, N _{End} =84	<p>Population: TBI; Severity: Severe. <i>Treatment Group (n=60):</i> Mean Age=30.4 yr; Gender: Male=49, Female=11; Median Time Post Injury=69 mo. <i>Control Group (n=30):</i> Mean Age=36.2 yr; Gender: Male=24, Female=6; Median Time Post Injury=72 mo.</p> <p>Intervention: Participants were randomized to receive anger self-management training (treatment) or personal readjustment and education (control) in 90min weekly sessions for 8 wk. Assessments were conducted at baseline, 4 wk, 8 wk, and 16 wk.</p> <p>Outcome Measure: State-Trait Anger Expression Inventory 2 (STAXI-2); Brief Anger-Aggression Questionnaire (BAAQ).</p>	<ol style="list-style-type: none"> At 8 wk, 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 16 wk. There were no significant differences in response rates between groups on self-reported STAXI-2 Anger Expression-Out or BAAQ at 8 wk or 16 wk. There were no significant differences in response rates between groups on STAXI-2 or BAAQ as rated by a significant other at 8wk or 16 wk. There were no significant differences between groups in mean scores on STAXI-2 or BAAQ by self-report over time.
Aboulafia-Brakha et al. (2013) Switzerland Pre-Post N _{Initial} =10, N _{Final} =9	<p>Population: TBI; Median Age=47 yr; Gender: Male=8, Female=2; Median Time Post Injury=27.5 mo; Median GCS=5.</p> <p>Intervention: Participants completed a semi-structured group treatment program for the management of anger and aggressiveness (1 hr, 1 day/wk for 8 wk). 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 4-5 mo follow-up.</p> <p>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).</p>	<ol style="list-style-type: none"> Significant improvement in feelings of aggression on AQ-12 was found from baseline to follow-up ($p=0.02$). No significant improvement on AQ-12 was found from baseline to post treatment ($p=0.84$) or from post treatment to follow-up ($p=0.57$). 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	<p>Population: TBI; Mean Age=43.3 yr; Gender: Male=8, Female=2; Range of Time Post Injury=6-243 mo; Range of Injury Severity: Moderate to Severe.</p> <p>Intervention: Participants attended 8 sessions/</p>	<ol style="list-style-type: none"> 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 ($p=0.01$).

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
	wk of anger self-management training. Outcome Measure: State Trait Anger Expression Inventory 2 (STAXI-2), Brief Anger-Aggression Questionnaire (BAAQ).	2. There were no significant improvements on STAXI-2 or BAAQ as rated by a significant other.
Walker et al. (2010) Australia Pre-Post N=52	Population: TBI; Mean Age=32.3 yr; Gender: Male=40, Female=12; Mean Time Post Injury=4.1 yr; Injury Severity: Severe. Intervention: Participants received 2 hr sessions of group-based CBT focused on anger management, 1 x/wk for 12 wk. Assessments were conducted at baseline, 12 wk, and 3-16 mo follow-up. Outcome Measure: State-Trait Anger Expression Inventory (STAXI).	1. At post treatment, there were significant reductions in trait anger ($p=0.002$), anger expression-out ($p=0.003$), 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.
Medd & Tate (2000) Australia RCT PEDro=5 N=16	Population: TBI; Gender: Male=14, Female=2. <i>Treatment Group (n=8):</i> Mean Age=35.88 yr; Mean Time Post Injury=37.25 mo; <i>Waitlist Group (n=8):</i> Mean Age=34 yr; Mean Time Post Injury=74.25 mo. 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.
O'Leary (2000) USA Pre-Post N=5	Population: ABI; Age Range=21-42 yr; Gender: Male=5, Female=0; Time Post Injury Range=4 mo-5 yr. Intervention: Patients attended a 10 wk 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=18.3 yr; 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=23.2 yr; Gender: Male=5, Female=0. Intervention: Patients received behaviour therapy, with emphasis on reinforcement and antecedent conditions, for managing aggression.	1. Measurements showed a 97% decrease in aggressive behaviour from baseline levels at 1 wk and 100% at 3 wk.

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
	Outcome Measure: Frequency of aggression.	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 6 mo follow-up.

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

Discussion

Cognitive behavioural therapy (CBT) was investigated as an intervention for anger and aggression post TBI in three 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 a six sessions of an individualized CBT program significantly reduced trait anger and outward anger expression when compared to no treatment. Similarly, a later 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).

A psychoeducational treatment program called Anger Self-Management Training was evaluated in two 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.

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.

8.5.4.3 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 8.28 Social Skills Training for the Treatment of Maladaptive Behaviors Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Outcome
McDonald et al. (2008) Australia RCT PEDro=6 N=39	<p>Population: TBI; Gender: Male=28, Female=11. <i>Treatment Group (n=13):</i> Mean Age=35.5 yr; Mean Time Post Injury=4.0 yr. <i>Social Group (n=13):</i> Mean Age=34.3 yr; Mean Time Post Injury=4.3 yr. <i>Waitlist Group (n=13):</i> Mean Age=35.3 yr; Mean Time Post Injury=3.5 yr.</p> <p>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 12 wk program of group and individual sessions totaling 4 hr/wk. Control group received 4 hr/wk of social activities only for 12 wk.</p> <p>Outcome Measure: Partner Directed Behaviour Scale (PDBS), Personal Conversational Style Scale, Depression Anxiety and Stress Scale, Awareness of Social Inference Test.</p>	<ol style="list-style-type: none"> 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	<p>Population: TBI; Mean Age=23.5 yr; Gender: Male=3, Female=1; Mean Time Post Injury=5.75 yr.</p> <p>Intervention: Social skills training program comprised of education, instruction, manipulation, feedback, and reinforcement.</p> <p>Outcome Measure: Behavioural changes.</p>	<ol style="list-style-type: none"> 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 1 yr 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.

8.5.4.4 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 8.28).

Table 8.29 Music Therapy for Agitation and Aggression Post ABI

Author/Year/ Country/Study Design/ N	Methods	Outcome
Formisano et al. (2001) Italy Case Series N=34	<p>Population: TBI=18, Other=16; Mean Age=35.94 yr; Gender: Male=17, Female=17; GCS Score<8.</p> <p>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.</p> <p>Outcome Measure: Undesired behaviours, Glasgow Outcome Scale, Disability Rating Scale (DRS), Coma Recovery Scale (CRS).</p>	<ol style="list-style-type: none"> 1. During music therapy, patients showed a reduction in undesired behaviours. 2. Positive effects were reported in 27 of 34 patients 1 mo after starting treatment and at follow-up. 3. No improved interaction with the environment was recorded (DRS, CRS).

Discussion

Based on a retrospective case series, 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. However, 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.

8.6 Addictive Behaviours

8.6.1 Incidence and Prevalence of Substance Abuse

The rates of substance abuse in those who have sustained a TBI differ across the literature: 44 to 79% reported having an alcohol addiction at time of injury, while 12 to 38% reported having a drug addiction (Andelic et al., 2010; Bombardier et al., 2002; Kolakowsky-Hayner et al., 2002; Kwok et al., 2013; Taylor et al., 2003; West et al., 2009). The Diagnostic and Statistical Manual (DSM) outlines criteria that must be satisfied to determine if an individual has an issue with addiction, dependence, or abuse. However, the definitions of these terms vary between studies, and many of the studies have different inclusion criteria. For example, studies that only include subjects with a positive Blood Alcohol Concentration (BAC) at time of admission will report an inflated incidence, since non-users are automatically excluded.

Research has shown that substance abuse occurs more frequently in those who have sustained TBI than members of the general public (Taylor et al., 2003). It has been reported that as many as 40% of the TBI population meet the criteria for substance abuse or dependence as defined by the DSM (Hibbard et al., 1998). As well, the number of drinks per week pre injury reported in a sample of TBI patients was in the 84th percentile of average American alcohol consumption (Bombardier 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, TBI patients who abused alcohol pre-injury were ten times more likely to demonstrate problematic alcohol use post injury (Bombardier et al., 2003).

Individual characteristics have been found to determine the likelihood that a patient with TBI will have difficulties controlling their substance use. High consequences associated with drinking are thought to mediate the frequency of alcohol consumption and alcohol dependence (Turner 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).

8.6.2 Effect of Intoxication on Initial Assessments

Several issues have been raised about assessing the severity of injury, particularly with the use of the Glasgow Coma Scale (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. However, 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.

8.6.3 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.

8.6.4 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).

8.6.5 Substance Abuse Treatment Post ABI

Several programs have been proposed and developed in order to reduce substance abuse in the TBI population (Table 8.29). 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 8.30 Programs for the Treatment of Substance Abuse Post ABI

Author/ Year/ Country/ Study Design/ N	Methods	Results
<p>Sander et al. (2012) USA RCT PEDro=5 N=104</p>	<p>Population: TBI. <i>Intervention Group (n=54):</i> Mean Age=36.1 yr; Gender: Male=44, Female=10; Median GCS Score=14. <i>Control Group (n=50):</i> Mean Age=35.4 yr; 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 10 min 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 3 mo follow-up. Outcome Measure: CAGE Alcohol Questionnaire (CAGE-AQ), Alcohol Expectancy Questionnaire-III (AEQ), Readiness to Change Question (RTC).</p>	<ol style="list-style-type: none"> 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.
<p>Tweedly et al. (2012) Ponsford et al. (2012) USA RCT PEDro=5 N=60</p>	<p>Population: TBI; <i>ID Group (n=20):</i> Mean Age=36.5 yr; Gender: Male=15, Female=5; Mean Time Post Injury=8 mo. <i>INFO Group (n=20):</i> Mean Age=35.1 yr; Gender: Male=14, Female=6; Mean Time Post Injury=7.95 mo. <i>MI Group (n=20):</i> Mean Age=33.9 yr; Gender: Male=16, Female=4; Mean Time Post Injury=7.79 mo. Intervention: Participants were randomly assigned to one of three conditions: Informal Discussion (ID), a general 30 min 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 6-9 mo follow-up. Outcome Measure: Alcohol Use Disorders Identification Test (AUDIT), Timeline Follow-</p>	<ol style="list-style-type: none"> 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. 2. Being in the action stage on RTCQ was associated with lower risk of frequent drinking ($p<0.001$) and heavier drinking ($p<0.001$). 3. Higher HADS-Depression score was associated with higher risk of heavier drinking ($p<0.05$). 4. CVLT and MSET scores were not associated with frequency or intensity of drinking.

Author/ Year/ Country/ Study Design/ N	Methods	Results
	Back (TLFB), Readiness to Change Questionnaire (RTCQ), Hospital and Anxiety and Depression Scale (HADS), California Verbal Learning Test (CVLT), Modified Six Elements Test (MSET).	
Corrigan & Bogner (2007) USA RCT PEDro=5 N=74	Population: TBI; Mean Age=42.5 yr; 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). Participants then participated in a treatment program. Assessments were conducted at follow-up. Outcome Measure: Treatment attendance, Premature termination, Perceived therapeutic alliance.	<ol style="list-style-type: none"> 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. 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: 36.6 yr; 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 30 days, 3 mo, and 6 mo. Outcome Measure: ISP signup, ISP compliance, ISP attrition, Addiction Severity Index (ASI).	<ol style="list-style-type: none"> 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 3 mo (premature termination) did not differ between FI (4%), BR (6%), MI (9%), or AC (15%). 5. ISP attrition at 6 mo 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; <i>Treatment Group (n=40):</i> Mean Age=32.5 yr; Gender: Male=33, Female=7; Mean Time Post Injury=4.4 yr. <i>Comparison Group (n=54):</i> Mean Age=35.6 yr; Gender: Male=38, Female=16; Mean Time Post Injury=4.4 yr. 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	<ol style="list-style-type: none"> 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

Author/ Year/ Country/ Study Design/ N	Methods	Results
	baseline, after treatment, and at follow-up. Outcome Measure: Substance use, Motivational Structure Questionnaire (MSQ), Positive Affect Negative Affect Scale (PANAS).	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 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=26 yr; Gender: Male=56, Female=16; Mean Time Post Injury=44.3 mo. Intervention: Subjects received a substance abuse treatment plan and were monitored for 1 yr. 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 1 yr 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.

PE德罗=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). 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.

8.7 Restraints

8.7.1 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 common 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 recent 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. Whether or not individuals were restrained, a study by Schleenbaker and colleagues (1994) found that restraint orders were in the charts of more than 75% of individuals admitted for rehabilitation. Of those who were admitted for a TBI, approximately 90% had restraint orders appearing on their chart.

Despite guidelines and policies regarding restraint use, the literature suggests that there is need for improvement in the documentation and use of restraints in clinical practice. In a retrospective audit conducted at a Canadian hospital, Kow and Hogan (2000) found either chemical or physical restraints were used in 11.5% of patients. Despite hospital policy, orders approving the use of restraints were missing from some charts, and the nursing documentation pertaining to restraint use was often vague and questionable. The lack of documentation or an order for restraint use has been common in the literature (Macpherson et al., 1990; McNett et al., 2012; Minnick et al., 2007; Mion et al., 1996; Morrison et al., 1987; Schleenbaker et al., 1994). In fact, one study found that nurses and physicians believed getting an order and properly documenting were not always necessary (Mion et al., 1996).

8.7.2 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).

8.7.3 Effectiveness of Restraints

Many hospitals use physical restraints to ensure the safety of patients, staff, and family members. No clinical evidence supports their use with individuals who have sustained an ABI (Marks, 1992). 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).

8.7.4 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.

Restraint policies are often prefaced with the philosophy of the hospital regarding the use of restraints. They have been defined as an unusual and temporary measure, either physical or pharmacological, to limit the activity or control the behaviour of an individual. In a study conducted by Mion and colleagues (1996), they stated that “reducing the use of physical restraints is a challenge”. Over twenty years later, despite current hospital policies and the risk of patient injury, restraint use continues to be a challenge. It appears as though the clinicians’ perceptions regarding the benefits of restraints is without any empirical data to support the purported benefit (Mion et al., 1996). The use of restraints to meet the needs of staff striving to maintain order, routines, and rules is no longer considered acceptable.

8.8 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 as high as 28% in TBI populations (from intro), 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 level 1a 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.

8.9 Summary

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

There is level 1b evidence that citalopram may not be effective in preventing relapse of major depression post TBI compared to no treatment.

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 an effective treatment for major depression compared to placebo 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 ABI.

There is level 1b evidence that cognitive behavioural therapy may be a more effective treatment for depression post TBI when combined with motivational interviewing than with non-directive counselling.

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 conflicting (level 1b and level 2) evidence as to whether cognitive behavioural therapy is more effective when delivered in groups or by telephone post ABI.

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 2 evidence that positive psychology therapy may improve happiness post TBI compared to substance abuse educational therapy.

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 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 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 1a evidence that a group-based cognitive behavioural intervention, compared to waitlist controls, may be effective in reducing hopelessness post TBI, but does not reduce depressive symptoms or suicidal ideation.

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 valproic acid may reduce aggression post TBI.

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

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

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

There is level 4 evidence to suggest that an antimanic agent (lithium carbonate) reduces aggressive/agitated behaviour following a brain injury.

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

There is level 4 evidence that a single dose of droperidol may reduce agitation post TBI.

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 TBI.

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

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.

8.10 References

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