8. Mental Health Issues Post ABI

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Key Points

The effectiveness of sertraline in treating depression post ABI is unclear.

Citalopram and carbamazepine may be effective n the treatment of mood disorders.

Desipramine may be effective in improving mood and reducing depression.

Results of various surveys indicate that those who have sustained an ABI have a higher incidence of depression post injury.

Music therapy may be more efficacious in improving anxiety and depression than standard rehabilitation alone.

Systematic Motivational Counselling may reduce negative affect.

Teaching coping skills to those who have sustained a TBI helps to reduce anxiety and depression.

Both cognitive remediation and day treatment are associated with a decrease in depressed mood.

Exercise is associated with feeling less depressed and an improved quality of life post TBI.

A mindfulness-based stress reduction programme may be efficacious in reducing depressed mood.

Thirty minutes of a weak complex (1 microT) burst-firing magnetic field across the temporoparietal regions once per week for 5 weeks may be efficacious in the treatment of depression.

Cognitive Behavioural Therapy does reduce anxiety and depression post ABI.

Biofeedback-assisted relaxation training may alleviate symptoms of anxiety.

Little research has been conducted looking at the effects of various treatments on OCD post ABI.

Amantadine may not be an effective treatment for behaviour following brain injury.

Carbamazepine has been shown to decrease aggressive behaviours post TBI.

Lamotrigine may be successful in reducing inappropriate behaviours post TBI.

Valproic acid may assist in the reduction of aggressive behaviours.

Anticonvulsants may be used to decrease the incidence of aggressive behaviour post ABI; however, more research is needed.

Sertraline HCL and amitriptyline may be used to decrease aggressive behaviour.

Pindolol decreases aggressive behaviour following brain injury.

Propranolol may reduce aggressive and agitated symptoms following brain injury.

The efficacy of buspirone for reducing hostile and agitated behaviour following brain injury is unclear. More research is required.

Although there is some evidence to suggest that quetiapine does help reduce aggressive behavior more research is needed.

Ziprasidone has been shown to assist in the controlling of aggressive behaviours; however, more research is needed.

Lithium may reduce behavioural problems but is associated with neurotoxicity.

Medroxyprogesterone intramuscularly can reduce sexual aggression.

Methotrimeprazine may be safe for controlling agitation following ABI.

Methylphenidate may be effective in increasing performance speed post TBI. It may also be effective in reducing anger following a brain injury.

Droperidol may be an effective agent for calming agitated patients.

Haloperidol appears to have little negative effect on recovery following TBI.

Antecedent management and/or feedback of consequences can reduce undesirable behaviour.

Anger management and social skills training reduce aggressive behaviour.

Music therapy may reduce psychomotor agitation, post-coma and improve mood following severe TBI.

Individually tailored behavioural treatment interventions, as well as training programs, have a positive effect on targeted behaviour(s).

Substance abuse and intoxication at time of injury is a frequent phenomenon in the TBI population.

Substance addiction pre injury is predictive of substance addiction post injury.

The impact blood alcohol levels have on GCS, ISS, mortality and long term outcomes have yet to be determined.

Although alcohol and elevated BALs has been linked to an increase risk of sustaining a TBI, there is however no evidence that elevated BALs are linked to an increase risk of mortality post injury. The possible neuroprotective role acute alcohol intoxication plays in a TBI warrants further investigation.

Earlier studies indicate elevated BALs are associated with poorer performance on a variety of cognitive communication tasks; however, these finding have not been supported in more recent studies. More research needs to be conducted investigating the impact of alcohol on cognitive outcomes post injury.

Education and motivational interviewing do not appear to have an strong impact on excessive alcohol consumption post TBI.

Providing financial incentives does encourage those with an ABI and a substance addiction to attend treatment more so than offering solutions to other barriers.

Despite their use, there is no evidence to support the use of restraints in those who have sustained an ABI/TBI.

Staff education programs to reduce the use of physical restraints, without increasing the risk of falls have been shown to be somewhat successful with staff in nursing home. Further research needs to be completed looking at the impact these education programs would have on those staff working in rehabilitation hospitals.

8. Mental Health Issues Post ABI

8.1 Introduction

Although mood is an internal subjective state, it is often inferred from our posture, behaviours, or our ability and the way we chose to express ourselves. Mood disorders such as agitation, major depression, and various anxiety disorders including post traumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD) may occur following an acquired brain injury and are associated with suffering, worsening of other ABI sequel, and poorer outcomes (Jorge and Starkstein 2005; Jorge 2005; Berthier et al., 2001). PTSD has been studied among those who sustain a mild ABI but not with those who sustain moderate or severe ABIs, thus is has not been included in this module

Depression in those who have sustained an ABI is often seen once the implications of the injury begin to become apparent. This may be a reaction to the injury or the result of the neurological changes that have taken place post injury. For some injured persons, depression 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). Silver et al. (2001) conducted 5034 interviews with individuals who had been diagnosed with a psychiatric disorder. Of these, 361 were found to have had a severe brain injury. Analysis of their data indicated the most prevalent issues were major alcohol and drug abuse or dependence (34%) and depression (11.1%). These findings are similar to those reported by several other researchers (Hibbard et al., 1998; Van Reekum et al., 1996; Deb et al., 1999). Individuals who experience depression post ABI may report feeling tired, may withdraw socially, have difficulties concentrating, and feel helpless and often hopeless.

Depression is often accompanied by anxiety and aggressive behaviours. Of note those who develop aggression early in their recovery are at a higher risk for developing depression which has been found to impact their length of stay in rehabilitation and their overall recovery (Jean-Bay 2000). Depression can exaggerate the effects of acquired brain injury and interfere with progress made during rehabilitation.

Challenging behaviour following a brain injury occurs with a relatively high frequency (25-50%). Challenging behaviours that may be seen include: non-compliance with treatment, anger, agitation, verbal and/or physical aggression and depression. The emergence of these behaviours likely arises from injury to the frontal lobes (and more specifically the orbitofrontal areas) resulting in disinhibited behaviour and lack of recognition of the consequences of one's behaviour. Behavioural management and pharmacological techniques are often used to address these challenges. Each has been used with varying levels of success.

Few investigators have examined predictors of aggressive symptoms following brain injury, although it has been suggested that disinhibition and depression may result in aggressive behaviour in some brain injured individuals (Backhaus et al., 2010; Kim 2002; Seel et al., 2010). In a sample of 228 patients with moderate to severe brain injury, Baguley et al. (2006) found depression and younger age to be a main predictor of aggression following brain injury at 6, 24,

and 60 months. These findings suggest that more severe levels of aggression may be more evident than previously reported, but due to the lack of consistency in how aggression is measured comparing studies and study results may be difficult (Baguley et al., 2006).

Addictive behaviours (alcohol and narcotics abuse and gambling) have been shown to be a serious problem for some individuals both pre and post ABI. Various studies have looked at the incidence of these behaviours pre and post injury and have found that 30 to 60% of individuals who sustain an ABI have a dependence issue (Jorge and Starkstein 2005). Many individuals relapse post injury, often within the first or second year. Alcohol abuse has also been linked to major depression both pre (Dikmen et al., 2004; Seel et al., 2010) and post injury (Jorge & Starkstein, 2005), although it remains unclear as to which problem evolved first, the alcohol abuse or the depression.

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 (e.g. reduced social role functioning, poorer quality of life, etc.). They frequently cause significant distress for individuals with brain injury, their family members, and may result in diminished access to services. This module will review the evidence for both pharmacological and non-pharmacological treatment of depression, anxiety, OCD, aggression and agitation, and addictive behaviours post ABI.

8.2 Depression

In Canada, it is estimated that approximately 11% of men and 16% of women will suffer from depression in their life time (Health Canada 2009) For those who sustain an ABI, depression is the most common mood disorder diagnosed (Seel et al., 2010; Underhill *et al.,* 2003; Jean-Bay 2000; Jorge and Starkstein2005). It is however, very difficult to diagnose due to the complexities of the brain injury itself (Underhill et al., 2003). Studies have suggested the development of depression may be related to the location of injury, a pre-existing condition, personality type, family support, social support post injury and/or neurochemical imbalances (Rosenthal et al., 1998; Ownsworth and Oei 1998; Jorge and Starkstein2005). Further complicating the diagnosis is the lack of consistency in the use of tools used to measure depression post injury (Jorge & Starkstein, 2005).

8.2.1 Lesion Location and Depression

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

8.2.2 Incidence and Prevalence post ABI

Studies looking at depression following an ABI have noted that depression or depressive symptoms can begin within the first 3 months of injury, or they may become evident much

later. Depression occurring within the first year has been noted in 18 to 39% of those injured (McKinlay et al., 1981). However, in studies looking at depression rates in individuals who were one or more years post injury prevalence rates ranged from 38 to 61% (Fleminger et al., 2003). The risk for depression is high post TBI or ABI and remains this way for decades post injury (Hoffman et al., 2010). Further, 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 one's ability to perform everyday tasks, the ability to cope with everyday stressors, and an increase in irritability and behavioural issues (e.g. anger, frustration, agitation) (Fleminger et al., 2003).

8.2.3 Pharmacological Treatments for Depressions

Post ABI, depression is often treated with various pharmacological treatments. Included among these are various antidepressants: serotonin re-uptake inhibitors (SSRI) such as paroxetine, sertraline, or citalopram; serotonin norepinephrine reuptake inhibitors (SNRI) such as duloxetine; and tricyclic antidepressants (TCA) such as amitriptyline. The use of TCA's is however, often restricted to the treatment of headaches in those who have sustained a mild TBI because their side effects (memory impairment, sedation, etc) 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.

Individual studies

Table 8.1 Pharmacological Interventions used to Treat Depression Post ABI

Treatment		
Author/Year/ Country/Study Design/PEDro Score	**Methods**	**Outcomes**
Rapoport et al., (2010) Canada RCT PEDro = 9	**N=21** Study participants, recruited from a previous study (2008), were randomly assigned to either the control group (n=11) or the treatment group (n=10). Those in the treatment group were given on average 40 mg/d of citalopram, while the control group was given a placebo for a period of approximately 15 weeks. To determine if the patients were compliant with the protocol pill counts were completed. The following scales were used to measure levels of depression pre and post administration of citalopram: Cumulative Illness	Once the study was completed, relapse rates were calculated for each group and no significant differences were found. Those receiving citalopram were found to relapse on average 24.8 weeks post study, while those in the placebo group were found to relapse 22.3 weeks post study. The rate of relapse was not linked to any one variable (gender, age, MMSE scores, HDRS scores). All participants experienced adverse events regardless of the group they were placed in.

	Rating Scale (CIRS), Hamilton Depression Rating Scale (HDRS)	
Ashman et al., (2009) USA RCT PEDro = 10	**N=52** Study participants were randomly assigned to either the treatment group or the placebo group. Those in the treatment group were given sertraline 25 mg to start, with adjustments to the dose being made after week 2. By the end of the study individuals were on doses ranging from 25 mg to 100 mg. Those in the control group were given a placebo for 10 weeks. Participants were assessed using the Hamilton Rating Scale for Depression (HAM-D) the Beck Anxiety Inventory (BDI), and the Life-3 scales (QOL).	Overall sertraline was found to have little impact on the depressive symptoms of those who had sustained a TBI. Changes in the scores on the HAM-D, the BAI and the QOL scales did show some improvement at the end of the 10 week study for both groups; however, no significant differences were found between the two groups.
Rapoport et al., (2008) Canada Prospective controlled trial	**N=54** Those in the 6 week study (n=29) were given 20 mg/day of citalopram, while those in the 10 week study (n=36) began on 20 mg/day and were titrated to a maximum of 50 mg/day. The Hamilton Rating Scale for Depression (HAM-D) and the Rivermead Post Concussion Symptoms Questionnaire were both used to measure change.	HAMD scores decreased from baseline (mean 23.66) to the end of the first 6 weeks (mean 16.30), $p<0.0001$. Scores decreased significantly ($p<0.001$) from for those in the 10 week program. It was also noted that of the 54 subjects were started the study, 24.1% were found to be in remission. At the 10 week period, of the 26 participants, 26.9% were found to be in remission. The somatic score on the Rivermead Post Concussion Symptoms Questionnaire (RPQ) decreased significantly from 15.38 to 11.35 ($p<0.001$) at 6 weeks. When reassessed at the 10 week assessment period no further changes were noted ($p>0.05$).
Lee et al., (2005) Korea RCT PEDro = 8	**N=30** Individuals with a mild or moderate TBI were selected for inclusion in the following study. All were randomly assigned to one of three groups: sertraline group who were started on 25 mg/day with an increase of 25 mg every 2 days until the dose reached 100mg/day; methylphenidate group who were given 5 mg/day with a 2.5 mg increase every day until the dose reached 20mg/day; and the placebo group. The Beck Depression Inventory (BDI) and the Hamilton Rating Scale for Depression (HAM-D) were used to measure depression.	In all 3 groups scores on the HAM-D and BDI improved from the baseline measure to the 4th week post treatment time period; however those in the methylphenidate and the sertraline groups improved significantly more than those in the placebo group.
Perino et al., (2001)	**N=20** Individuals were given citalopram (20mg/day) and	The BPRS score was shown to be 62.3 ± 17.6 before the study began and 51.7 ±

Italy Pre-Post	carbamazepine 600mg/day. Individuals were started on 10 mg/day of citalopram which was increased to 20 mg/day by weeks end. Carbamazepine was started at 100 mg/day and increased to 200mg/day by weeks end. Brief Psychiatric Rating Scale (BPRS) and the Clinical Global Impression (CGI) were used to measure mood, anxiety behavioural and psychotic symptoms.	12.8, ($p<0.05$). The CGI severity scale scores decreased from 4.4 ± 1.1 before the study began and 3.4 ± 0.8, ($p<0.005$).
Fann et al., (2000) USA Non-RCT	**N=15** Nonrandomized, 8-week, single-blind, placebo run-in trial of individuals diagnosed with major depression following mild TBI who received sertraline and placebo. The Hamilton Rating Scale for Depression (HAM-D) and the Clinical Global Impression (CGI) were used to measure depression	Statistically significant improvements in depression were found with the use of sertraline.
Wroblewski et al., (1996) USA RCT PEDro = 4	**N=10** Individuals were randomly assigned to either the placebo or treatment group. Those in the treatment group were given 150 mg/day of desipramine for 30 days then 150 to 300 mg/day at the 2 month period. Those in the control group were given placebo for the first 30 days before the desipramine was administered. DSM-III-R checklist and the Affect Mood Scale were used to measure improvement in mood.	6 individuals were randomized to the treatment group while 4 were in the control group. 3 from each group had nearly complete resolution of depression on desipramine. Seven of 10 subjects showed improvement over time on the affect/mood scale ($p=0.001$). There were different rates of improvement over time in those started on the despiramine rather than placebo.
Non-Treatment Studies		
Author/Year/ Country/Study Design	**Methods**	**Outcomes**
Malec et al., (2007) USA Survey	**N=135:** 93 participants (mild=42; mod/sev=51) had sustained a TBI and the remaining 42 had undergone orthopaedic surgery. All were asked to complete a questionnaire which included various scales: neurobehavioural functioning inventory (NFI), neurobehavioural functioning inventory-depression subscale (NFI-Dep), multidimensional scale of perceived social support (MSPSS), family assessment device (FAD)	Scores on the NFI-Dep showed no significant differences between groups. When looking at the data from the TBI groups only, depression appeared to be related to the individual's perception of their impairment. Those with increased levels of social support were found to have lower levels of depression, while those who were diagnosed with psychiatric disorders pre injury were more likely to be diagnosed with depression post injury.
Deb and Burns	**N=165** Patients, all of which had been	Those in the younger group were found

(2007) United Kingdom Cohort-Survey	diagnosed with a TBI, were divided into two groups (18-65 (n=120) and >65 years (n=45)). All were asked to complete a questionnaire or were interviewed by study staff.	to have a higher incidence of depression or depressive symptoms than those in the older age group.
Kreutzer et al., (2001) USA Survey	**N=722** Individuals who had sustained a TBI were assessed at a regional Level 1 trauma center. Level of ABI was not defined.	Results using DSM-IV classification indicate that 85% of the individuals reported feeling frustrated, with 41% feeling frustrated quite often or all of the time. Problems such as increased feelings of hopelessness, sadness, and worthlessness, increased tiredness, aggression and the inability to concentrate were found to be experienced by 19% to 60% of participants.
Hibbard et al., (2004) USA Survey-Interviews	**N=188** Participants with a TBI were interviewed by trained clinicians. Interviews were conducted twice, with 12 months between each interview. Mood and psychosocial functioning were evaluated using the following tools: Beck Depression Inventory (BDI), Living life after TBI (LLATBI), Unmet important needs (UIN) scale, Impact of TBI on Roles and Responsibilities Scale, Life-3, brain injury screen questionnaire, overall rating of health, and overall rating of pain. Level of ABI was not defined.	Results indicate that 17% of those defined as having mood disorder, were diagnosed with major depression post injury and 35% of those without a previous mood disorder were diagnosed with major depression at both assessment periods. Individuals in the chronic- depression group showed no improvement on the various psychosocial scales at each time period. BDI scores in the late onset depression group had increased during the 12 month time period.

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

Discussion

Several studies were found looking at the effects of sertaline, citalopram, carbamazepine, desipramine and methylphenidate on the treatment of depression or depressive symptoms post ABI.

Three studies looked at the effects of sertraline on depression post ABI. Ashman et al. (2009) in a blind RCT found no significant differences between baseline measures on the Beck Anxiety Inventory (BAI), Hamilton Rating Scale for Depression (HAMD) and Quality of Life (QOL) scales between the control and treatment group. Over time significant improvement in both groups on the HAMD scale ($p<0.001$), BAI scale ($p<0.001$) and QOL scale ($p<0.01$) was found; however, no significant changes were seen between groups. As a result changes in the treatment group may not have been related to sertraline.

Lee et al. (2005) in a study which included both individuals who had sustained a mild or moderate TBI, randomly assigned participants into one of three groups: the placebo group, the sertaline group and the methylphenidate group. Those in the sertaline group were started on

25 mg/day with an increase of 25 mg every 2 days until the dose reached 100mg/day and the methylphenidate group were given 5 mg/day with a 2.5 mg increase every day until the dose reached 20mg/day. The Beck Depression Inventory and the Hamilton Rating Scale for Depression were used to measure depression in each group. Although all participants were seen to improve, study results indicate those assigned to the sertaline and the methylphenidate groups did significantly better on the scales than the placebo group at study's end (Lee et al., 2005).

Fann et al. (2000) assessed the effects of sertraline on fifteen patients diagnosed with major depression post-mTBI. The patients experienced significant improvements in depression while using sertraline. Although both Fann and Lee studied sertraline's effectiveness on depression post ABI, the study groups themselves were different (mild TBI compared to a diverse group of mild to severe TBI). The difference in the study groups may help to explain the study results when looking at the effectiveness of sertraline on depression. Of note, neither studies (Lee or Fann) included individuals who had sustained a severe TBI in their studies (Fann et al., 2000; Lee et al., 2005).

Rapoport and colleagues (2008, 2010) examined the benefits of citalopram on depression post ABI. The first study included fifty-four (54) participants who were divided into two groups. One group (n=29) was given 20 mg/day of citalopram for 6 weeks while the second group (n=36) began with 20 mg/day which was titrated to a maximum of 50 mg/day. The second group was studied for 10 weeks. Scores on the Hamilton Rating Scale for Depression (HAMD) was decreased from baseline (mean 23.66) to the end of the first 6 weeks (mean 16.30), $p<0.0001$. Scores decreased significantly ($p<0.001$) from for those in the 10 week program. The somatic score on the Rivermead Post Concussion Symptoms Questionnaire (RPQ) decreased significantly from 15.38 to 11.35 ($p<0.001$) at 6 weeks, but no further changes were noted at the 10 week assessment period. In the follow-up study, Rapoport et al. (2010), randomly assigned 21 individuals to either the citalopram group (n=11) or the placebo group (n=10). Post treatment relapse rates were calculated for each group and there were no significant differences noted between the groups with individuals relapsing 22 to 24 weeks post treatment. Again, as in the Fann et al. (2000) and the Lee et al. (2005) studies there were more individuals with a mTBI than with a moderate or severe TBI.

In the study conducted by Perino et al. (2001), the 20 individuals who participated were divided in two groups based on the length of time since injury. Each was given 20 mg of citalopram per day and 600 mg of carbamazepine per day. When looking at the scores from the Brief Psychiatric Rating Scale and the Clinical Global Impression, scores were significantly improved 12 weeks following the administration of citalpram and carbamazepine.

Wroblewski et al. (1996) randomized 10 subjects to receive either desipramine or placebo. Of the six individuals who were started on desipramine, only 3 were found to have depression symptoms resolved following treatment; however, all 4 participants in the placebo group had their symptoms of depression resolved.

In studies conducted by Malec et al. (2007), Deb and Burns (2007), Kreutzer et al., (2002) and Hibbard et al. (2004), all authors report various levels of depression and other psychiatric or psychological difficulties among those who had sustained an ABI regardless of the severity of injury. Deb and Burns (2007) noted that individuals who were younger (18-65 years of age) experienced higher incidences of depression than the older cohort they looked at. It was also noted that those who suffered from depression prior to their injury were more likely to have depressive symptoms post ABI (Hibbard et al., 2004; Malec et al., 2007). Kreutzer et al. (2001) also noted in their results that many grouping their study group experienced feeling of depression.

Conclusions:

There is conflicting evidence that sertraline is effective in the treatment of major depression post-TBI.

There is Level 2 evidence that citalopram aids in the reduction of depression post ABI.

There is Level 4 evidence that citalopram and carbamazepine may be efficacious in the treatment of depression, anxiety and mood disorders.

There is Level 2 evidence to suggest that the administration of desipramine assists in improving mood and reducing depression.

The effectiveness of sertraline in treating depression post TBI is unclear.

Citalopram and carbamazepine may be effective in the treatment of mood disorders.

Desipramine may be effective in reducing depression.

Results of various surveys indicate that those who have sustained an ABI have a higher incidence of depression post injury.

8.2.4 Non-Pharmacological Treatments for Depression

Several non-pharmacological treatments have been used to treat depression post ABI including: exercise, involving individuals in team sports, providing them with supports through an interdisciplinary team, or counselling (Knottnerus et al., 2007)

Individual Studies

Table 8.2 Non-Pharmacological Treatments used to Treat Depression Post ABI

Mindfulness-Based Stress Reduction (MBSR) Program		
Author/Year/ Country/Study Design/PEDro Score	**Methods**	**Outcomes**
Bedard et al., (2012) Canada Pre-Post	**N=20** Participants experienced one 90 minute session per week for 8 weeks. Sessions included topics such as staying in the present, acceptance, and improving awareness of thoughts and feelings. Sessions were modified to address attention, concentration and memory difficulties. Homework assignments were given after each session.	Following the intervention, a reduction in depression and anxiety was noted in all participants. The anxiety subscale of the HADS scale did not change pre to post intervention. There was also a non-significant reduction in the level of pain experienced by participants post intervention.
Bedard et al., (2003) Canada Pre-Post	**N=10** Prospective controlled trial of depressed individuals who participated in 12 weekly group sessions of a mindfulness-based stress reduction programme. Three dropouts were used as controls.	Of those who completed the stress reduction program, no significant differences (p=0.059) were found on the overall Beck Depression Inventory II and the Positive Symptom Distress Inventory of the SCL-90R. A trend was however noted. When looking at the subsections of the BDI II, a significant improvement was noted on the cognitive-affective domain only (p=0.029).
Exercise Programs		
Wise et al., (2012) USA Follow-up to the 2010 RCT	**N=40** Those in the treatment group originally participated in a 10 week exercise program that included a one hour session in the gym and participants were encouraged to participate in four 30 sessions at home. The Beck Depression Inventory was used to assess levels of depression. In this follow-up study 37 participants were interviewed by phone.	At the 6th month follow-up there was a reduction in the number of participants who were able to exercise >90 minutes per week. Those who exercised more than 90 minutes per week and lower BDI scores and felt they had a higher quality of life and better mental health.
Hoffman et al., (2010) USA RCT PEDro=5	**N=80** Those randomly assigned to the exercise group (n=40) participated in an exercise program run at the local gym with a educational and athletic trainer, Session included a 15 minute education session, 15 minutes of warm up exercises, 30 minutes of aerobics and 15 minutes of cool down exercises. The Aerobic exercise program was chosen by the individual. All maintained an exercise log and presented this at the start of each session. Each participant was asked to perform 30 minutes of exercise 4x/week while in the program. The program	Throughout the exercise program, more than half the sessions were attended. Results of the Beck Depression Inventory indicate there were no differences between the groups post intervention. No differences in sleep quality, general health status, heart rate or ability to walk were noted between the groups. Those in the treatment group did report less pain post intervention. For those who reported exercising more than 90 minutes each week, they

	lasted 10 weeks. Controls (n=40) were allowed to participate in the program once the treatment group had completed it. No specific discussion about abstaining from exercise was given to the control group.	were found to have lower depression scores and participated in more community activities and better quality of life then those who exercises less than 90 minutes.
Blake and Batson (2009) UK RCT PEDro=6	**N=20** Participants were randomly assigned to the treatment group (exercise group who received Qigong instruction) or the control group who attended non-exercise social and leisure activities for one here each week over an eight week period. The Qigong program was conducted by a qualified teacher. The control group was supervised by day centre staff.	Results of the General health Questionnaire -12 showed a significant decrease in mood scores for those in the Qigong group compared to the control group. Physical self-esteem was also found to improve for those in the Qigong group.
Driver and Ede (2009) USA RCT PEDro=5	**N=16** Patients involved with an outpatient recreation program were randomly selected to participate in the study. Eight patients were assigned to each group (intervention and control). Patients ranged in age from 33 to 45 and were 13 to 56 months post injury. The Profile of Mood States was used to assess patients' mood pre and post intervention.	When looking at the results of POMS, significant differences were noted between the groups post intervention ($p<0.05$). When looking at the within group scores pre to post significant differences were noted for the treatment group on each of the sub-scales of the POMS (depression, anger, vigour, fatigue, confusion and friendliness ($p<0.05$)). No significant differences were noted on each of the sub-scales for the control group.
Gennell and Leathem (2006) New Zealand RCT PEDro=6	**N=18** Individuals who had sustained a mild to severe TBI were randomly assigned to either the treatment or waitlist control group. Those in the treatment group attended a tai chi course that included breathing and steeping exercises. Rest was encouraged when needed. It was anticipated that improvements in general physical, social interactions and mental well-being would be noted 3 weeks post intervention.	No significant differences were noted between the groups prior to the exercise program beginning. Post intervention the treatment group reported feeling less afraid, confused, sad, angry, tired, and tense. They also reported greater feelings of happiness and more energy. When compared to the control group the differences on the Medical Outcomes Scale Short Form 36 and the Rosenberg self-esteem scale were not significant. At follow-up (3 weeks post intervention) the treatment group reported feeling less impaired because of emotional problems.
Gordon et al., (1998) USA Case Series	**N=240** Retrospective comparative study of individuals with TBI, of which 64 exercised and 176 did not exercise. The Beck Depression Inventory was used to assess depressed mood.	Participants with TBI who exercised had less depressed mood than participants with TBI who did not exercise.
Teaching of Coping Skills		
Anson and Ponsford (2006b)	**N=33** All individuals participated in the Coping Skills Group (CSG). This program was originally designed to assist individuals	Those who had a greater self-awareness following their injuries had demonstrated better outcomes post-

Australia RCT PEDro=5	in finding ways to handle the changes resulting from the brain injury. Individuals were randomized into either Group A, receiving 10 weeks of CSG intervention or Group B, receiving 5 weeks of the same intervention. The sessions ran for 90 minutes twice a week. 7 assessment scales were used among them the State-Trait Anger Expression Inventory (STAXI-2) and the Self-awareness of Deficits Interview (SADI), the Hospital Anxiety and Depression Scale (HADS).	CSG intervention. This was noted in the decrease in depression scores. Those who had poorer self-awareness had higher scores on the depression scales did not perform as well post CSG intervention.
Anson and Ponsford (2006a) Australia RCT PEDro=5	**N=31** Participants working as their own controls, were assigned to one of 2 group protocols and a wait-list control design was used. For group A, baseline phase was 5 weeks, followed by 5 weeks of intervention, and a 5-week follow-up phase. For group B, baseline was 10 weeks, followed by 5 weeks of intervention and a 10-week follow-up phase. The coping skills group (CSG) consisted of 10 group sessions and ran for 90 minutes 2x wk for 5 wks.	No significant changes in anxiety or self-esteem scores were noted following the CSG ($p>0.05$). Although levels of depression and psychosocial dysfunction were significantly different between the two groups ($p<0.05$) participation in the CSG did not have an effect on their scores. Both groups significantly increased their adaptive coping skills following the CSG ($p<0.01$).
Ruff & Niemann (1990) USA RCT	**N=24** An experimental control group design was used in the current study. Individuals were randomized to either their control or experimental groups. Those in the experimental group participated in a cognitive retraining programme as outpatients. The program was divided into 4 modules and ran for 12 weeks. The control group participated in the same group therapy and wrap up sessions but did not participate in the cognitive retraining portion of the study. The Katz Adjustment Scale was used to measure depression.	Individuals in both groups experienced a decrease in depressed mood, as measured by the Katz Adjustment Scale.
Music Therapy		
Guetin et al., (2009) France Pre-Post	**N=13** Subjects were exposed to two music therapies: the receptive music therapy or the active music therapy. While participating in the receptive music therapy program, participants were asked to remain in a quiet room and listen to music sequences through a set of head phones for 20 to 30 minutes. In the active music therapy session, participants played a musical instrument, sing, write a song etc. Improvement in anxiety & depression was noted by using Hospital Anxiety and Depression (HAD) scale.	Following each music therapy session, improvements in mood were noted on the HAD scale. Anxiety scores also decreased following the sessions and could be seen when looking at the scores of Session 1 and Sessions 10, 15 and 20 ($p=0.05$). Depression scores also improved however significant improvement was only noted when looking at the scores of Session 1 and Session 10.

Thaut et al., (2009) USA Case-Control	**N=54** Individuals with an ABI were selected for participation in the following study. Those in the treatment group (n=31) participated in 4 different sessions (attention, memory, executive function and emotional adjustment). Sessions were conducted on different days. Day 1 participants focused on emotional adjustment; Day 2 was executive function; Day 3 was attention; and Day 4 was memory. The third and fourth sessions took place 2 weeks after the second. Each session began with a cognitive measure pertaining to the skill being addressed. Participants were tested pre and post session. The controls (n=23) were each assessment with one of the various assessment measures and were then asked to rest in a quiet room.	Both the treatment and control group showed significant improvement on the BSI-18 scale looking at emotional adjustment; depression and anxiety scores also improved significantly (p=0.02 and p=0.04 respectively). Neither groups showed improved in attention functioning, memory testing or mental flexibility pre to post intervention.
Nayak et al., (2000) USA Non-RCT	**N=18** Individuals were assigned to receive either standard rehabilitation alone or standard rehabilitation plus music therapy (3 treatments per week for up to 10 treatments). Participants rated their moods using the Faces Scale.	Receiving standard rehabilitation plus music therapy was associated with more improved ratings of mood (patients', families', and therapists' ratings) than receiving standard rehabilitation alone.
Motivational Counselling		
Cox et al., (2003) USA Pre-post	**N=94 Forty (40)** participants received 12 individual systematic motivational counselling sessions for their substance abuse and 54 participants in a comparison group did not receive any counselling for their substance abuse. Their mood was assessed.	Participants who received systematic motivational counselling sessions experienced a significant reduction in negative affect.

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

Discussion

Several studies were found that specifically evaluated the non-pharmacological treatment of depression in those diagnosed with an ABI. Among these studies the efficacy of exercise and its role in reducing the levels of depression felt by those with an ABI was investigated (Hoffman et al., 2010; Wise et al., 2012; Driver and Ede, 2009; Blake & Bason, 2009; Gremmell & Leathem, 2006; Gordon et al., 1998). In an RCT conducted by Hoffman and colleagues (2010), 80 participants were randomly assigned to either the exercise component of the study of the wait-list control group. Those in the exercise group (n=40) participated in weekly exercise classes supervised by an exercise therapist and a educational therapist. All were encouraged to exercise at home for 30 minutes 4 times per week. Those in the control group were offered the exercise program at the end of the 10 week period, but were neither encouraged nor discouraged from exercising at home, if they wanted to. At the end of the 10 week exercise program, results indicate there were no significant differences on the BDI depression scores

between the two groups. Individuals who exercised more in a week were found to have lower BDI scores then those who exercised less. The follow up to this, Wise et al. (2012) looked only at those in the treatment group. Telephone interviews were completed for 36 of the original 40 participants 6 months after the exercise program ended. Results indicate that fewer were exercising >90 minutes per week, but those who did exercise more than 90 minutes each week were found to have lower BDI scores, and reported higher perception of quality of life and mental health.

In an earlier RCT investigating the impact of physical activity on mood post TBI, study authors found those who participated in the exercise program showed improvement on the Profile of Mood State ($p<0.05$) on the following variables: tension, depression, anger, vigour, fatigue confusion and friendliness compared to those in the control group (Driver and Ede 2009). Study authors suggested that mood post TBI can be positively affected or influenced by physical activity. Again in a much earlier case series by Gordon et al. (1998), the effect of exercise on depression was assessed. Comparisons between subjects with TBI who exercised and subjects with TBI who did not exercise led the authors to conclude that subjects in the former group had less depressed mood.

Two studies investigated the benefits of the Chinese exercise methods Tai Chi Qigong (Blake & Baston, 2009) and Tai Chi Chaun (Gemmell & Leathem, 2006) on those who had sustained a TBI. In both these groups individuals had sustained mild, moderate or severe TBIs. Results from both these studies found improvement mood. However, despite this findings and due to the small sample sizes in each study, there was not enough evidence to definitely state these exercise techniques are effective in reducing depression or anxiety post ABI. Further study is needed.

In two RCTs conducted by Anson and Ponsford (2006b; 2006a), individuals who participated in the Coping Skills Group (CSG), increased their coping skills. One study Anson and Ponsford (2006a), 31 subjects acting as their own controls, were divided into two separate protocols. Each group was exposed to the same intervention for the same length of time (5 weeks), however Group A's baseline and follow-up was only 5 weeks compared to Group B whose baseline and follow-up were 10 weeks. Anson and Ponsford (2006a) found that both groups increased their adaptive coping skills following the CSG ($p<0.01$); however, no significant changes in their anxiety or self-esteem, depression or psychosocial scores were noted following the CSG ($p>0.05$). Overall when asked, those participating did feel they had better understanding of emotional issues and an increased ability to implement coping strategies as a result of their participation in the CSG. In their second study, those who had a greater self-awareness following their injuries demonstrated better outcomes post-CSG intervention. This was noted in the decrease in depression scores. Those with a poorer sense of self had higher scores on the depression scales and did not perform as well post-CSG intervention (Anson and Ponsford 2006a).

Ruff and Niemann (1990) compared 12 subjects who participated in an eight week cognitive remediation programme (treatment group) with 12 subjects who participated in an 8 week day

treatment programme (control group). Groups were comparable at the start of the study. All subjects had moderate or severe head injuries and all had sustained their injuries 1 to 7 years prior to the study. As measured by the Katz Adjustment Scale, both groups experienced a decrease in depressed mood.

Two studies looking at the efficacy of mindfulness-based stress reduction programs on depression post ABI were conducted by Bedard and colleagues (2012, 2003). The first study by Bedard et al. (2003), used dropouts as controls, looked at the effects of a mindfulness-based stress reduction programme on depression in 10 patients at least one year post-brain injury. The programme consisted of 12 weekly group sessions designed to encourage a new way of thinking about life and disability. Following the intervention phase improvements were seen when looking at scores on the Quality of Life scale, the Beck Depression Inventory and the Positive Symptom Distress Inventory for those in the treatment group only. More recently Bedard and colleagues (2012) once again looked at the efficacy of mindfulness-based cognitive therapy in reducing depression. In this more recent study 20 individuals who had sustained an ABI were recruited. The intervention consisted 90 minute sessions discussing awareness of thoughts and feelings, staying in the present and acceptance. All ere taught mediation techniques, breathing and yoga exercises. Homework assignments were also handed out. Results found improvement in the levels of depression participants were feeling. They also showed a non-significant reduction in the level of pain being reported.

Three studies investigated the benefits of music therapy on anxiety and depression post ABI. Guetin et al. (2009) had subjects participate in two music therapy programs. In one program, participants in the receptive music therapy program were placed in a quiet room and asked to listen to various music sequences through head phone for 20 to 30 minutes. Those in the active music therapy sessions were asked to play a musical instrument, sing, or write a song. The Hospital Anxiety and Depression (HAD) scale was used to assess changes in mood post interventions. Overall, participant scores improved significantly ($p<0.05$) from the initial assessment (S1) to the final assessment (S20) as a result of both interventions (i.e., no group differences were reported).

In a study conducted by, Thaut et al. (2009), 54 participants were divided into one of two groups. Those in the treatment group were asked to participate in 4 sessions focusing on attention, memory, executive function and emotional adjustment followed by a 30 minute neurologic music therapy program. Those in the control group completed the various assessment measures then sat in a quiet room for 30 minutes. Both groups were reassessed following the 30 minute intervention or quiet time. Improvement was noted following intervention on the depression and anxiety subscales of the Multiple Affect Adjective Check List for those in the treatment group only and on the BSI-18 scale in both groups.

Nayak et al. (2000) evaluated the benefits of music therapy by utilizing a between group repeated measures design. In this study, 18 patients were assigned to receive either standard rehabilitation alone or standard rehabilitation plus music therapy. Patients' self-rating of mood,

family's rating of patients' mood, and therapists' rating of patients' mood were all assessed. More improved ratings of mood were found for patients who received music therapy in addition to standard rehabilitation than for patients who received standard rehabilitation alone.

In the only other study that focused on mood, Cox et al. (2003), carried out a study with a multiple baseline design. Systematic Motivational Counselling (SMC), described as counselling designed to help persons with TBI cope with their injury in ways other than substance abuse, was the intervention of interest. The authors found that participants who received SMC experienced a significant reduction in negative affect.

Although there is preliminary evidence for a number of non-pharmacological interventions for mood, in particular the treatment of depression, given the limited evidence, non-pharmacological interventions cannot be considered as alternatives to pharmacological interventions. However, non-pharmacological treatments and in particular cognitive-behavioural therapies may help augment the action of antidepressants and should therefore be part of the treatment of depression post ABI. Although the evidence supporting the use of exercise to treat affective disorders, in general, has been shown to be cost effective and unlike the use of pharmacological treatments there are no side effects (Byrne & Byrne, 1993), more research regarding its effectiveness post ABI needs to be conducted.

Conclusions:

There is Level 1a evidence that individuals with a TBI who participate in exercise programs report feeling less depressed and report experiencing greater quality of life post injury.

There is Level 2 evidence that both cognitive remediation and day treatment are associated with a decrease in depressed mood.

There is Level 4 evidence from 2 studies indicating mindfulness-based stress reduction programmes may be efficacious in reducing depressed mood.

There is Level 4 evidence that thirty minutes of a weak complex (1 microT) burst-firing magnetic field across the temporoparietal regions once per week for five weeks may be efficacious in the treatment of depression.

There is Level 3 evidence that music therapy does improve depression and anxiety post ABI.

There is Level 4 evidence that Systematic Motivational Counselling may reduce negative affect.

There is Level 2 evidence that teaching coping skills to individuals post TBI helps to reduce their levels of anxiety and depression.

Music therapy may be more efficacious in improving anxiety and depression than standard rehabilitation alone.

Systematic Motivational Counselling may reduce negative affect.

Teaching coping skills to those who have sustained a TBI helps to reduce anxiety and depression.

Both cognitive remediation and day treatment are associated with a decrease in depressed mood.

Exercise is associated with feeling less depressed and an improved quality of life post TBI.

A mindfulness-based stress reduction programme may be efficacious in reducing depressed mood.

Thirty minutes of a weak complex (1 microT) burst-firing magnetic field across the temporoparietal regions once per week for 5 weeks may be efficacious in the treatment of depression.

8.3 Anxiety Related Disorders

Anxiety is a subjective sensation of apprehension of danger and dread that may be accompanied by signs of restlessness, tension, tachycardia and shortness of breath that are part of the fight or flight response. Anxiety can be quite disabling whether it is generalized or includes a specific phobia to a certain stimulus. Anxiety disorders (e.g. Generalized Anxiety Disorder, Post Traumatic Stress Disorder, etc.) are common following ABI. Anxiety can be related to confusion and cognitive impairment or may be specifically related to the psychological trauma of the injury itself. Anxiety may also be a common symptom post-ABI (e.g. associated with depression, related to stress, etc). In the non-brain injured population, a cognitive-behavioural program directed at managing and reducing the disabling symptoms that cause avoidance of the stimulus may effectively treat anxiety. However treatment of anxiety post ABI may not be as effective because of cognitive impairments in this population.

8.3.1 Incidence *and Prevalence post ABI*

Post ABI, anxiety or anxiety disorders have been reported to occur in 4 to 28% of those who have been injured (Deb et al., 1999; Van Reekum et al., 1996; Fann et al., 1995; O'Donnell et al., 2008). In a study conducted by Hibbard et al., (1998) looking at various anxiety disorders post ABI, 19% of the study population was diagnosed with PTSD, 15% with OCD, and 14% with panic disorder.

8.3.2 *Non-Pharmacological Intervention for Anxiety*

Although anxiety disorders appear to be well recognized post ABI there is little in the literature regarding use of non-pharmacological treatments; only 1 study using non-pharmacological treatment of anxiety post-ABI was found.

Individual Studies

Table 8.3 Studies of Non-Pharmacological Interventions for the Treatment of Anxiety Post ABI

Author/Year/ Country/Study design/PEDro Score	Methods	Outcomes
Hsieh et al., (2012) Australia RCT PEDro=6	**N=27** All were randomized to the MI+CBT (experimental group, 1 n=9) or the NDC+CBT (experimental group, 2 n=10) group or the treatment as usual group (control group). Participants assigned to the experimental group 1 began by receiving 3 weekly session of motivational interviewing (MI) then started cognitive behavioural therapy (CBT). Those in experimental group 2received 3 sessions of non-directive counselling followed by CBT. The treatment as usual (control, n=8) group received customary care. CBT was offered to the control group at the end of the wait list period.	Following treatment those in the experimental groups each showed significant reductions on the HADS anxiety. Results on the DASS-anxiety subscale showed improvement however this was not significant. Those in experimental group 1 showed a greater response to CBT then those in experimental group 2, in regards to a reduction in anxiety, stress and non-productive coping.
Hodgson et al., (2005) Australia RCT Pedro=5	**N=12** Participants were divided into 6 matched pairs. Following this one member of the pair was randomly assigned to either the cognitive behavioural treatment (CBT) group or the wait list control group. The CBT treatment program consisted of relaxation training, cognitive strategies, graded exposure and assertiveness skills training. Those in the treatment group were seen weekly for hourly sessions, for a total of 9 to 14 weeks. Decisions regarding the number of sessions were based on the individual's progress in therapy. The Hospital Anxiety and Depression Scale (HADS), Coppersmith Self Esteem Inventory, and the Social Phobia and Anxiety Inventory (SPAI) were used to assess change.	Results of the SPAI indicated anxiety levels were similar between the two groups prior to the start of treatment. Post treatment the SPAI scores had decreased for the treatment group, but not for the wait list control group. At the one month follow up a significant difference ($p<0.006$) was found when comparing the two groups. Results from the HADS showed that prior to treatment, in total there were 7 individuals who displayed probable – definite levels on the depression subscale, and 11 who displayed probable – definite levels on the anxiety scale. Post intervention those in the wait list control group scored higher on the depression and anxiety subscales of the HADS, compared to the treatment group whose scores decreased significantly on both subscales.
Arundine et al.,	**N=17** Individuals were assigned to one	Results of the SCL-90-R-GSI and the

(2012) Canada Cohort	of 2 CBT treatment groups based on geographical proximity. The first CBT session was conducted face to face for all. The remaining 10 were conducted either face-to-face in a group format (G-CBT), or individually by phone (T-CBT). All participants were evaluated pre and post intervention using the following tools: Repeatable Battery of Adult Neuropsychological Status (RRANS), Symptom Checklist-90-revised (SCL-90-R), Depression Anxiety Scales 21 (DASS-21), Community Integration scale (CIS)	DASS-21 indicate emotional distress was significantly decreased following the intervention ($p<0.01$) for all participants. Results from the CIS also improved significantly ($p<0.01$). A comparison of the two groups showed no significant difference between them following the intervention. All participants also showed greater improvement at the 6th month follow-up compared to the initial follow-up time period (30 days post treatment).
Holland et al., (1999) USA Case Study	**N=2** Case studies of males who received biofeedback-assisted relaxation training for their anxiety-related symptoms.	Both of the male patients experienced an improvement in their anxiety-related symptoms after receiving biofeedback-assisted relaxation training.

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

Discussion

Several studies have investigated the benefits of cognitive behaviour therapy (CBT) to reduce anxiety levels in those who sustained a TBI (Hsieh et al., 2012; Arundine et al., 2012; Hodgson et al., 2012). Hsieh and colleagues (2012) randomized a group of individuals who had sustained a TBI into one of three groups: the Motivational Interviewing (MI) and CTB (group 1), the non-directive counselling (NDC) group and CBT (group 2), or the treatment as usual (TAU) group (group 3). Those in groups 1 and 2 showed a significant reduction in anxiety following treatment than group 3. Those in group 1 showed a greater response to the CBT compared to group 2 (Hsieh et al., 2012).

Arundine et al. (2012) examined the effects of CBT on 17 chronic ABI patients. All were assigned to one of two groups: the group CBT (G-CBT) or the telephone administered CBT (T-CBT). Once all had completed the initial session, the reaming 10 took place weekly in the as per the protocol for each group. Teletheapy took place over a 45 to 60 minute period, while the group sessions lasted 60-90 minutes. Following treatment, at the 6th month follow-up, all showed significant improvements on all test scores. Study authors suggest teletherapy may be just as beneficial to patients post TBI as group therapy.

Hodgson et al. (2005) found that anxiety scores on the Hospital Anxiety and Depression Scale (HADS) and the Social Phobia and Anxiety Inventory (SPAI) did decrease following treatment. Study participants were randomly assigned to either the treatment group or a wait list control group. The CBT treatment program, which lasted 9 to 12 weeks, included relaxation training, development of cognitive strategies and assertiveness training. Anxiety levels as measured by the SPAI were similar for the two groups at the start of the treatment but post treatment anxiety and depression levels of treatment group had decreased compared to the wait list group. Scores on the HADS also decreased significantly post treatment for those in the

treatment group compared. These results indicate that CBT training can reduce anxiety and depression in those who have sustained a TBI.

Holland et al. (1999) examined the efficacy of biofeedback-assisted relaxation training in alleviating anxiety-related symptoms. Biofeedback-assisted relaxation training consisted of a variety of techniques utilized to control one's physiological responses through direct feedback of information regarding one's physiological state. Both of the male patients included in the study appeared to benefit from the intervention.

Conclusions:

There is Level 1b evidence that Cognitive Behavioural Therapy does reduce anxiety post ABI.

There is Level 5 evidence, from a case study, that biofeedback-assisted relaxation training may be efficacious in alleviating anxiety-related symptoms.

Cognitive Behavioural Therapy does reduce anxiety and depression post ABI.

Biofeedback-assisted relaxation training may alleviate symptoms of anxiety.

8.3.3 Obsessive Compulsive Disorder (OCD)

Following a traumatic brain injury, anxiety disorders such as OCD, panic attacks and stress disorders are common both within the adult and paediatric populations. OCD is believed to be present in less than 10% of the brain injury population (Berthier et al., 2001), although it is rarely reported in the literature (Drummond and Gravestock 1988). Studies conducted by McKeon et al. (1984) and Kant et al. (1996) have found OCD symptoms appearing shortly after injury, within the first few hours to the first week. Some patients were found to develop symptoms within the first 6 months of sustaining their injury. Several authors have suggested the location of the brain lesion may predict OCD in patients (Donovan and Barry 1994; Jenike and Brandon 1988; Bilgic et al., 2004). To date, although several theories have been put forth (lesion location, age of the individual) there is still no conclusive evidence to support one theory over the other. Grados (2003) noted that OCD has been treated successfully with SSRIs such as fluoxetine, paroxetine, fluvoxamine or sertraline. Other supportive therapies have also been reported to be successful although there were no clinical trials found in the literature.

Interventions

Table 8.4 Treatments Used for Obsessive Compulsive Disorders (OCD) Post ABI

Author/Year/ Country/Study design	Methods	Outcomes
Arco, (2008) Australia Case Study	**N=1** A 24 year old male was treated with interventions designed to assist him in controlling his compulsive counting and voiding. The intervention consisted of in home consultations and self-regulatory procedure such as recording each hour what he had been doing and reviewing his reminder card.	Following intervention the subject's episodes of compulsive counting and voiding decreased. The subject had also been placed on ditropan 15mg daily but this was discontinued as his compulsive behaviours decreased. Following cessation of the interventions the subject was able to maintain his schedule of voiding 8 times per day, and the compulsive counting had stopped.
Bilgic et al., (2004) Turkey Case Study	**N=1** A 23 year old male who had sustained a severe TBI in a motor vehicle collision participated in the study was admitted to hospital 9 months post injury due to behavioural changes.	At time of hospital admission this young man was obsessed with hand washing and the need for symmetry. Fluoxetine (60mg/d) and behavioural therapy helped decrease this behaviour.
Max et al., (1995) USA Case Study	**N=1** Study participant was a female, 12 years of age. The child had been in a coma for 16 days and her on scene GCS was 3. PTA lasted another 15 days. Post injury the child became obsessed with hand washing, ordering of things and counting.	To assist in decreasing these obsessive behaviours the following medication were given: fluoxetine 20mg/day, carbamazepine 200 mg (b.i.d.) up to 400 mg (b.i.d.) and phenytoin 500mg (b.i.d.). The previous administration of phenobarbital was discontinued.
Childers et al., (1998) USA Case Study	**N=4** Individuals who had sustained a severe TBI were included in the following study developed OCD post injury. Treatments for OCD were individualized.	Individuals would become upset, anxious, or disruptive if routines were disrupted for any reason. In a effort to resolve OCD symptoms patients underwent individual therapies: Patient 1 was given 10 mg of prozac daily; Patient 2 was placed on 25 mg of clomipramine at bedtime; Patient 3 was given 20 mg of paroxetine at bedtime; and patient 4 was given 25 mg clomipramine hydrochloride at bedtime. Clinical improvement was noted for each patient.

Discussion

In each of these case studies, individuals were treated with a variety of medications to reduce or extinguish the frequency of OCD post ABI. In each case the individualized drug treatment therapy chosen was shown to be effective.

Conclusion

Although OCD has been identified post ABI there does not appear to be one method of treatment that works for all, but rather treatments remain individualized.

Little research has been conducted looking at the effects of various treatments on OCD post ABI.

8.4 Challenging Behaviours

Behaviour can be defined as any interaction between an organism and their environment. This encompasses almost everything that humans do; however, most people tend to think of behavioural problems in a more restricted sense of antisocial, uncooperative or negative interactions associated with interpersonal problems. Challenging behaviour following a brain injury occurs with a relatively high frequency (25-50%). Challenging behaviour can include, but is not limited to, the following: non-compliance with treatment, anger, agitation, verbal and/or physical aggression and depression. The emergence of these behaviours likely arises from injury to the frontal lobes and more specifically the orbitofrontal areas resulting in disinhibited behaviour and lack of recognition of the consequences of one's behaviour. Typically behavioural management techniques and pharmacological interventions are used to minimize and/or alleviate these challenges with varying degrees of success.

Few investigators have examined predictors of aggressive symptoms following brain injury, although it has been suggested that disinhibition and depression may result in aggressive behaviour in some brain injured individuals (Bakchine et al., 1989; Kim and Humaran 2002). In a sample of 228 patients with moderate to severe brain injury, Baguley et al. (2006) found depression and younger age to be a main predictor of aggression following brain injury at 6, 24, and 60 months. These findings suggest that more severe levels of aggression may be evident than previously reported but due to the small numbers reported in other studies, the level of injury and the tools used to measure aggression, comparing studies and study results may be difficult (Baguley et al., 2006).

8.4.1 Agitation and Aggression

Agitation is generally defined as wondering, edginess, distractibility, non-compliance, and/or impulsiveness, while **aggression** is defined as physical or verbal violence that may put the individual and others at risk for injury (Eisenberg et al., 2009). Results from a study conducted by Tateno and colleagues, indicate the aggressive behaviors post TBI are associated with the presence of depression, frontal lobe lesions, and a history of substance or alcohol abuse (Tateno et al., 2003). TBI injuries that can lead to aggressive or agitated behavior may result from a diffuse injury, lesions in the frontal lobe (Warriner and Velikonja 2006) and/or injuries to the left hemisphere (Tateno et al., 2003). Individuals found to have poorer social functioning often engage in a variety of aggressive or agitated behaviors including: hitting, kicking, refusing

to participate in activities, memory deficits and slowness, decreased attention span, impulsivity, wondering off the unit, throwing objects, verbal aggression and engaging in self-abusive behaviors (McNett et al., 2012; Rao et al., 2009).

Following an ABI, studies have suggested that aggressive behavior is linked to the levels of serotonin in the brain. An ABI often results in serotonergic dysfunction thus increasing the risk of aggressive behaviors (Jorge and Starkstein 2005).

8.4.2 Pharmacological Treatments for Agitation and Aggression

Agitation occurs in approximately 33-55% of traumatic brain injury patients. The term agitation encompasses a wide variety of behaviours including restlessness, wandering, shouting, etc. This diversity of behaviours is typical of the agitation seen post ABI, but creates problems in terms of research regarding treatment efficacy (e.g. targeting interventions to particular types of agitation). Agitation is often a recovery-limiting factor as it creates both a disruptive and unsafe environment for rehabilitation (Rosati 2002). Pharmacological interventions are often used to treat this problem and include a variety of medications such as: anti-epileptics, anti-depressants, beta-blockers, anti-psychotics along with several others. This section will look at each of these drug families in detail.

8.4.3 Amantadine

Amantadine is a non-competitive N-methyl-D-aspartate receptor antagonist and is currently used as an antiviral agent used for the prevention of influenza A, for the treatment of neurological diseases such as Parkinson's Disease and in the treatment of neuroleptic side-effects such as dystonia, akinthesia and neuroleptic malignant syndrome (Schneider et al., 1999). It is also thought to work pre- and post-synaptically by increasing the amount of dopamine (Napolitano et al., 2005). During the early stages of recovery from a brain injury, when intracranial pressure is increased, amantadine should be used with caution (Levy et al., 2005).

Individual Studies

Table 8.5 Effects of Amantadine on Cognitive Functioning and Behaviour Post ABI

Author/Year Country/Study Design/PEDro Score	Methods	Outcome
Schneider et al., (1999) USA RCT PEDro= 5	**N=10** TBI rehabilitation subjects randomly assigned to treatment and placebo groups to test the effectiveness of amantadine on cognitive and behavioural rehabilitation.	Although there was a general trend towards improvement, results did not reach significance when treatment and placebo groups were compared using ANOVA and regression analysis (p=0.732).
Nickels et al., (1994) USA	**N=12** Retrospective chart review of subjects with brain injury treated with amantadine.	10 of the 12 subjects experienced some improvement in cognitive and/or physical function while using

Author/Year Country/Study Design/PEDro Score	Methods	Outcome
Case Series		amantadine. Five of the 12 subjects experienced side effects that included pedal oedema, hypomania, generalized seizure, and visual hallucinations.

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

Discussion

Schneider et al. (1999) completed a double-blinded, randomized placebo controlled trial evaluating the effects of amantadine on cognition and behavior. Twenty patients were included in the study and each took amantadine for 2 weeks. Statistical comparison of results evaluating the five subsets of attention, executive/flexibility, memory, behavior and orientation did not demonstrate any significant effect for the use of amantadine.

Conclusion

There is Level 2 evidence that amantadine did not help to improve behaviour following brain injury.

Amantadine may not be an effective treatment for behaviour following brain injury.

8.4.4 Anti-Convulsants

Typically following a TBI there is diffuse injury with primary involvement in fronto-subcortical and temporolimbic regions. As a result seizure disorder following TBI is not uncommon which may result in episodic lack of control. In the use of any medication, a balance must be struck between managing the behaviour and maintaining cognitive functioning. As a result, some anticonvulsants have been found to be a good alternative to antipsychotic and/or benzodiazepines in managing aggression, as they tend to have fewer cognitive side effects (e.g., sedation, confusion, memory impairment).

8.4.4.1 Carbamazepine

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

Individual Study

Table 8.6 Effect of Carbamazepine on Reducing Aggressive Behaviour Post ABI

Author/Year Country/ Study Design	Methods	Results
Azouvi et al., (1999) France Pre-Post	**N=10** Consecutive, severe (GCS ≤ 8), closed-head TBI patients scoring severe in two or moderate in three items of the Neurobehaviour Rating Scale (NRS) (French) were treated with Carbamazepine (mean dose: 9.47 +/- 2.9 mg/kg/day) for 8 weeks. NSR-R measures, Agitated Behaviour Scale (ABS) and Mini-Mental Status Examination (MMSE – to control for spontaneous recovery) were taken twice at baseline and every 2 weeks, 4 weeks and 2 weeks thereafter respectively.	Dosage and blood work remained within clinical limits for epilepsy. Sum NRS-R and ABS scores showed significant improvement ($p=0.02$); improvements plateaued after 2 weeks. At follow-up, significant for only irritability ($p<0.01$), disinhibition ($p<0.05$) portions of NRS-R. Global NRS-R significantly decreased from baseline ($p=0.01$). No significant changes on MMSE were observed ($p>0.01$).
Lewin and Sumners (1992) UK Case Study	**N=1** A 21 year old male was administered 300 mg of carbamazepine twice daily to help treat episodic dyscontrol. Administration of medication began 14 months post injury.	Aggressive outbursts began to subside once the individual began taking carbamazepine; however in the initial follow up session post administration of carbamazepine, the patient appeared calmer but depressed. Following inpatient care, at one year follow-up, no further acts of aggression were noted but the individual did remain on 200 mg of carbamazepine nightly.

Discussion

Azouvi et al. (1999) in an open, 8-week drug trial used carbamazepine (Tegretol) in 10 severely brain injured clients with significant behavioural challenges that were interfering with care and/or family integration. Baseline data was collected on a number of measures rating the individuals' neurobehavioural function and level of agitation, as well as global social functioning and general cognitive ability (all ratings taken from self-report and staff or family members' ratings). Every two weeks, 2 measures of agitation and disinhibition were measured, along with blood samples. Global measures were administered at baseline, 4 weeks and 8 weeks. Dosage ranged from 400 mg to 800 mg (mean dosage to body weight was 9.47 + 2.9 mg/kg/day at the end of the trial). Results indicated improvement on the behavioural scales at the first assessment (2 weeks), which were maintained only for the scales of irritability and disinhibition by the end of the trial, although overall neurobehavioural and social functioning had improved. Although not all patients showed any change (n=2), 8 patients did. Of these, 3 patients showed a 25 to 43% improvement and 5 showed a 50% improvement (Azouvi et al. 1999).

In a case study, Lewin and Sumners (1992) found the administration of carbamazepine lead to a decrease in aggressive outbursts. Although the subject experienced episodes of depression when he first began taking the drug, an increase in the dose of the medication seemed to help

reduce the bouts of depression. Eventually the medication was reduced to 200 mg nightly with the subject doing well on this.

Conclusion

There is Level 4 evidence that carbamazepine decreases the incidence of aggressive behaviours following a TBI.

Carbamazepine has been shown to decrease aggressive behaviours post TBI.

8.4.4.2 Lamotrigine

The benefits of lamotrigine as an antiepileptic and mood stabilizer have been well established; however, its effectiveness as a mood stabilizer with ABI patients has yet to be established (Gao and Calabrese 2005; Tidwell and Swims 2003).

Individual Study

Table 8.7 Effects of Lamotrigine on Reducing Aggressive Behaviour Post ABI

Author/Year Country/Study Design	Methods	Results
Chahine & Chemali (2006) Lebanon Case Study	**N=4** Males aged 18 to 48 were asked to participate in the study.	All 4 individuals were placed on lamotrigine to help reduce or extinguish inappropriate behaviours such as: laughing, impulsivity or verbal aggression. All behaviours decreased once the individual was placed on lamotrigine.
Pachet et al., (2003) Canada Case Study	**N=1** A 40 yr old male participated in the current study. He was given 25 mg daily of lamotrigine. Agitated behaviour was assessed using the Agitated Behaviour Scale (ABS) the Functional Independence Measure (FIM) and the Functional Assessment Measure (FAM)	Results of the FIM and FAM indicated that scores improved (up to 42 points) following the introduction of lamotrigine. When looking at the scores on the ABS a reduction in aggressive behaviour could be seen. The study participant was discharged home sooner than expected.

Discussion

Results from the two case studies, indicate that lamotrigine helps to reduce unwanted behaviours such as verbal aggression. In both studies, participants were initially placed on other medications to help control these behaviours; however, in each case these medications were eventually eliminated once lamotrigine was introduced. Unwanted behaviours decreased and in some cases were extinguished (Pachet et al. 2003; Chahine and Chemali 2006).

Conclusion

There is limited Level 5 evidence, from two case studies, to suggest that lamotrigine helps to reduce inappropriate behaviours post TBI. More research is needed, with a greater number of subjects, to validate these findings.

Lamotrigine may be successful in reducing inappropriate behaviours post TBI.

8.4.4.3 Valproic Acid/Depakene

Valproic acid, an antiepileptic, has been used successful to treat seizure disorders in both adults and children and more recently it has been used to treat bipolar, post-traumatic stress disorder and mania (McElroy et al., 1987). It has also been found to reduce episodic explosiveness with an individual with TBI (Geracioti, Jr. 1994).

Individual Study

Table 8.8 Effects of Valproic Acid on Reducing Aggressive Behaviour Post TBI

Author/Year Country/Study Design	Methods	Results
Wroblewski et al., (1997) USA Case studies	**N=5** Four TBI and one non-TBI subject were assessed, observed and treated individually with valproic acid to measure changes in behaviour.	Each patient was reviewed individually, with no cross-case comparisons. All showed a substantial reduction in target behaviours.

Discussion

Wroblewski and colleagues (1997) examined the effects of valproic acid (Depakene) on reducing aggressive behaviour in a case series (N=5). Although the study reports that all patients showed a substantial reduction in challenging behaviour (i.e., outbursts, agitation, anger), no statistical analyses were carried out (instead researchers relied on visual inspection of data graphs and graphs were only presented for 3 of the 5 patients). Patients were also part of a specialized neurobehavioural unit, which may have contributed to the positive results.

Conclusion

There is Level 5 evidence that valproic acid decreases the incidence of aggressive behaviours.

Valproic acid may assist in the reduction of aggressive behaviours; however more research is needed.

8.4.4.4 Divalproex/Epival

Divalproex, another anticonvulsant, is believed to help reduce aggressive behaviours in individuals post TBI.

Individual Study

Table 8.9 Effects of Divalproex on Reducing Aggressive Behaviour Post ABI

Author/Year Country/Study Design	Methods	Results
Chatham Showalter and Kimmel (2000) USA Case Series	**N=29** Chart reviews of individuals that had been patients at an inpatient brain injury rehabilitation unit (ages ranged from 13- 89 years) were treated with divalproex in an attempt to reduce symptoms of agitation following injury. Symptoms of agitation included easily aggravated, escalating temper, insistent, biting, profane, punching, restless, removing braces etc.	Eight patients had been rated on the Agitated Behavior Scale prior to treatment with divalproex. For these individuals, a rapid resolution of symptoms to near total recovery was demonstrated. For a second subgroup (n=18), progress notes prior to and during treatment demonstrated decreased and significantly improved symptoms within 7 days of receiving a mean daily dose of divalproex.

Discussion

Divalproex was used to treat symptoms of agitation in 29 brain-injured patients (Chatham Showalter & Kimmel, 2000). Symptoms decreased significantly in the majority of patients, indicating that divalproex may be an effective treatment to reduce agitation following brain injury.

Conclusion

There is Level 4 evidence that divalproex decreases the incidence of aggressive behaviour post TBI

Anticonvulsants may be used to decrease the incidence of aggressive behaviour; however, more research is needed.

8.4.5 Anti-Depressants

Two studies examined the effect of an antidepressant on reducing agitation and/or aggression in brain injured patients (Kant et al., 1998; Mysiw et al., 1988). Kant et al. (1998) examined the effect of sertraline, a serotonin specific reuptake inhibitor (SSRI) on reducing aggression and irritability in brain injured patients, whereas Mysiw et al. (1988) examined the effect of amitriptyline (a tricyclic antidepressant with both serotonergic and noradrenergic reuptake

inhibition) on decreasing agitation while the individual was still experiencing post-traumatic amnesia.

Individual Studies

Table 8.10 Effects of Sertraline and Amitriptyline on Reducing Aggression and Irritability Post ABI

Author/Year Country/Study Design	Methods	Outcome
Mysiw et al., (1988) USA Non-RCT	**N=43** TBI subjects experiencing non-directed agitation following PTA were treated with a traditional structured program. The 20 patients whose agitation interfered with rehabilitation, or persisted more than 7 days were administered amitriptyline daily.	There were no significant demographic differences between groups. Thirteen of 20 patients treated with amitriptyline experienced significantly reduced levels of agitation after the first week ($p<0.001$); levels that were maintained in the ensuing weeks ($p<0.001$), but did not significantly drop when compared to the first week ($p>0.6$). 7 of 20 patients experienced no significant change in agitation levels at week 1 ($p>0.7$) and beyond ($p>0.3$).
Kant et al., (1998) USA Pre-Post	**N=10** CHI subjects (mean age: 37.6, chronicity: 2 years) with complaints of irritability and/or aggression completed an 8-week trial of Sertraline. Follow-up every two weeks measured OAS-M, BDI, and AIAQ	Overt Aggression Scale-Modified (OAS-M) aggression ($p<0.001$) and irritability ($p<0.01$) measures showed significant improvement from baseline. Results from the BDI indicate there was a significant improvement 4 weeks post baseline ($p=0.04$), but at the 8 week assessment period no significant improvement ($p=0.14$) was found

Discussion

Following a multiple baseline procedure, Kant et al. (1998) examined the effect of sertraline HCL (Zoloft) on reducing aggression and irritability in 13 brain injured patients (5 mild, 6 moderate and 2 moderate-severe) two years post-injury. Patients were started on "50 mg/day dose that was adjusted during follow-up visits to a maximum tolerable dose or up to 200 mg per day" (results were reported for baseline, 4 and 8-week follow-up). Three patients dropped out of the study (reasons and subject characteristics were not reported). Positive effects were reported to occur (i.e., decrease in reported aggression and irritability) at each follow-up visit compared to baseline.

Mysiw et al. (1988) administered amitriptyline to 20 brain injured patients after one week they had not responded favourably to standard behavioural intervention (i.e. where agitation persisted to the point of interfering with rehabilitation). Results indicated that within 7 days of amitriptyline therapy (mean dosage was 75 mg), 90% of the patients had a dramatic decrease in agitation with no concomitant increase in cognitive difficulties (as measured by the Orientation Group Monitoring System).

Conclusion

There is Level 4 evidence that sertraline HCL and amitriptyline decrease the incidence of aggressive behaviours.

Sertraline HCL and amitriptyline may be used to decrease aggressive behaviour.

8.4.6 Beta-Blockers

It has been suggested that Beta-blockers may improve agitation, anxiety and aggressive symptoms following brain injury, as well as to reduce restlessness. Oftentimes, dosage is high, leaving patients vulnerable to such adverse effects as sedation, depression and lethargy, although it does not seem to negatively affect motor recovery post-injury (Levy et al., 2005).

8.4.6.1 Pindolol

Pindolol is a beta- blocker unlike many others in that it exerts a partial agonist effect, providing a slight stimulation of the blocked receptor and maintaining a better resting sympathetic tone.

Individual Studies

Table 8.11 Effects of Pindolol on Behaviour Post ABI

Author/Year Country/Study Design/PEDro Score	Methods	Outcome
Greendyke and Kantor (1986) USA RCT PEDro = 7	**N=11** ABI subjects were randomly assigned to receive pindolol or an equal number of identical-appearing placebo capsules for the first half of study. Following titration period, treatment group received a daily dose of 60 mg/day for 10 days. Following this, the dose was increased (up to 100 mg) to determine whether benefits could be gained with higher doses. Following a tapering-down period, placebo was given in place of the drug, and patients that had received placebo first were given a daily dose of pindolol to the same effect as the first group.	Significant reduction of assaultive episodes, need for supplemental medication and hostility were demonstrated during pindolol treatment ($p< 0.05$). Significant improvements in patients' willingness to communicate, and cooperation during treatment ($p< 0.025$) and significant reduction of stereotyped behaviors ($p< 0.01$).

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

Discussion

Greendyke and Kantor (1986) investigated the effectiveness of the beta-blocker, pindolol, for the improvement of behaviour associated with brain disease or injury in a randomized, crossover trial. Of 11 patients, brain disease was caused by brain injury, anoxia, or encephalitis in seven of them. A significant reduction in behaviours that lead to assaults was demonstrated during treatment with pindolol.

Conclusion

There is Level 1b evidence that pindolol decreases aggression following brain injury.

Pindolol decreases aggressive behaviour following brain injury.

8.4.6.2 Propranolol

Propranolol is a non-selective beta-blocker that has been used for the reduction of aggressive behaviours associated with compromised brain function. It is not known how this drug works to affect behaviour, however it appears to lack the serious cognitive and affective side effects of other medications or physical restraints used to treat agitation post-injury (Levy et al. 2005).

Individual Studies

Table 8.12 Effects of Propranolol on Behaviour Post ABI

Author/Year Country/Study Design/PEDro Score	Methods	Outcome
Greendyke et al., (1986) USA RCT PEDro = 7	**N=10** Patients were randomly assigned to receive either long-lasting propranolol (520 mg/day) or an equal number of identical-appearing placebo capsules for the first half of study. Following titration period, treatment group received a daily dose of 520 mg/day for 11 weeks. Following a tapering-down period, placebo was given in place of the drug, and patients that had received placebo first were given a daily dose of propranolol to the same effect as the first group.	Significantly fewer assaults and attempted assaults occurred during the 11-week propranolol treatment as compared to the 11 weeks of placebo, $F(1, 7) = 6.50$, $p < 0.05$. No significant changes in social interests, irritability or psychomotor retardation were noted. No abnormalities were noted on laboratory measures.
Brooke et al., (1992a) USA RCT PEDro=7	**N=21** The experimental group (n=11) was given propranolol while the control group (n=10) was given placebo for 3 weeks at which time the medication or placebo was tapered off. Medication given was begun at 60 mg/day and increased every third day by 60 mg to a max of 420 mg/day.	Both groups were similar at start of study. As a result the control group had a greater number of episodes related to agitation than the treatment group ($z=0.889$, $p<0.05$). The patterns of increase or decrease in both groups were not significantly similar ($r=0.491$). When looking at the number of agitation episodes by week, there were no significantly greater differences between the two groups ($z= -1.5213$). Patterns of behavior increasing and decreasing were similar between the

		two groups (r=0.892, p<0.05). It was also found that more participants in the control group were placed in restraints during the study (z= -2.2022, p<0.05) although there were no significant differences in the pattern of restraint used of the two groups (r=-0.080). There were no differences between the two groups in the numbers receiving sedating drugs or drugs for agitation.

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

Discussion

Greendyke et al. (1986b) investigated the effectiveness of the beta-blocker, propranolol, for the improvement of behaviour 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 the 11 weeks of placebo, $F(1,7) = 6.50$, $p < 0.05$. Of the nine patients, five showed marked improvement, two demonstrated moderate improvement, and two showed little or no improvement of assaultive behavior.

Following the acute stage of recovery, 11 closed-head-injured (CHI) patients were treated with a maximum dose of 420 mg/day of propranolol while 10 were given a placebo (Brooke et al. 1992). The intensity of agitated symptoms decreased but not the frequency, suggesting that the drug helps to reduce the emotional intensity of agitated responses.

Conclusion

There is Level 1a evidence, from 2 RCTs, that propranolol reduces agitated symptoms following brain injury.

Propranolol may reduce aggressive and agitated symptoms following brain injury.

8.4.7 Buspirone

Buspirone is an azaspiredecanedione unrelated to the benzodiazepams that have been traditionally used to treat anxiety. An advantage to this treatment is that side effects are relatively minimal. Buspirone helps to effectively treat anxiety without causing sedation, fatigue or a lack of in coordination (Levine 1988). Exact mechanisms enabling the reduction of anxiety and agitation are unclear.

Individual Studies

Table 8.13 Effects of Buspirone on Agitation Post ABI

Author/Year Country/Study Design	Methods	Outcome
Levine (1988) USA Case study	**N=1** A 17-year-old male, recovering from a brain injury sustained following a motor vehicle accident was treated with buspirone for agitation.	Following treatment of buspirone, the patient became more cooperative and demonstrated no agitated or hostile behaviour.

Discussion

One case study has investigated the effects of buspirone as a treatment for the improvement of hostile and agitated behaviours following brain injury. Further investigation of the efficacy of this drug is required.

Conclusion

There is Level 5 evidence, from one case study, to suggest that buspirone may be effective for reducing symptoms of agitation following brain injury. More research is needed.

The efficacy of buspirone for reducing hostile and agitated behaviour following brain injury is unclear. More research is required.

8.4.8 Antipsychotics

8.4.8.1 Quetiapine (Seroquel)

Quetiapine has been used to reduce aggressive behaviour among those diagnosed with schizophrenia and alzheimer disease (Volavka et al., 2004; Webb and Glueckauf 1994). Quetiapine may be a better, compared to haloperidol and chlorpromazine choice since it is just as effective in treating aggressive behaviours without the side effects (Kim and Bijlani 2006).

Individual Study

Table 8.14Effects of Quetiapine on Aggressive Behaviour post ABI

Author/Year Country/Study Design	Methods	Outcome
Kim and Bijlani, (2006) USA Case series	**N=7** Subjects were given quetiapine (dose ranged from 25 to 300mg). Both male and female subjects participated in the study	Average does of quetiapine was 110.7 mg. As a result of the medication, subjects OAS scores were significantly reduced (p=0.002). The CGI score improved from a mean of 414 to 2.29

		(p=0.002). Significant improvements were also noted on the aggression subscale (p=0.036). RBANS overall scores indicated a mean improvement of 8.02% (p=0.027)

Discussion

In one case series conducted by Kim and Bijlani (2006) they found that quetiapine assisted in helping to reduce aggressive behaviour in 7 subjects. They also noted that they were significant improvements in the Overt Aggression Scale-Modified (OAS-M), the Clinical Global Impression (CGI) scores, and the overall scores of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

Conclusion

There is Level 4 evidence (from one small study) to suggest that quetiapine helps reduce aggressive behaviour.

Although there is evidence to suggest that quetiapine does help reduce aggressive behaviour more research is needed.

8.4.8.2 Ziprasidone

Ziprasidone has been approved for acute agitation in those who have been diagnosed with schizophrenia. It has also been found to work in the treatment of acute mania, often associated with bipolar disorder. For those who sustain a TBI, the period of post traumatic amnesia (PTA), has been defined as a period where the individual is disorientated, and may lack the ability to learn new things and suffer from behaviour alterations (Brooke et al., 1992b). Researchers believe that these behaviour alternations may result from the individual's lack of self – awareness which may be related to memory alterations that appear after the injury (Noe et al., 2007).

Individual Study

Table 8.15 Effects of Ziprasidone on Agitation Post ABI

Author/Year Country/Study Design	Methods	Outcome
Noe et al., (2007) USA Case Series	**N=5** Those included in the study, were still in PTA at the start of the study, but were out of it at the end. All subjects were given ziprasidone upon entering the study. Medication given to subjects ranged from 20 mg/day to 80mg/day, lasting from 35 to 68 days. Agitation was assessed with the Agitation Behavior Scale (ABS).	Results of the ABS showed a decrease in the score within the first 14 days from 27.3 to 18. Scores on the disinhibition portion of the scale decreased from 28.6 to 17.1, while scores on the aggressiveness subsection of the scale decreased from 26.1 to 20.4.

Discussion

In the current study conducted by Noe et al. (2007), individuals who were still in the PTA stage at admission to rehabilitation, were given 20 to 80 mg/day ziprasidone. The medication was given for 35 to 68 days. Aggressions scores decreased during the first 2 weeks while on the medication. The total ABS score decreased from 27.2 to 18, while the disinhibition score on the scale decreased by 9 points (from 28.6 to 17.1), and the scores on aggressiveness decreased 7.7 points (from 24.5 to 16.8). It was also noted that all who participated tolerated the ziprasidone with no clinical side effects observed.

Conclusion

There is Level 4 evidence from one study to suggest that ziprasidone assists in the controlling of aggressive behaviours post TBI.

Ziprasidone in one small study has been shown to assist in the controlling of aggressive behaviours; however more research is needed.

8.4.8.3 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, such as mania, occurring after the TBI, may contribute to the development of aggression (Kim2002; Wroblewski et al., 1997). In the search for a pharmacological agent that reduces aggression following TBI with limited side effects in comparison to antipsychotics and benzodiazipines, lithium has been tried. Lithium carbonate also functions as a mood stabilizer.

Individual Studies

Table 8.16 Effects of Lithium Carbonate on Aggressive Behaviour Post ABI

Author/Year Country/Study Design	Methods	Outcome
Bellus et al., (1996) USA Case study	**N=2** Male subjects (aged 40 and 24) having a brain-injury were treated with lithium. One patient displayed highly aggressive behaviours (self-injurious), while the 2nd subject's behaviour was described as "bizarre and inappropriate" such as unwanted touching of females, biting and hoarding material beneath his mattress.	Following lithium treatment, the reduction of aggressive behaviours by 60% was demonstrated for one patient. For the other patient, problematic behaviour decreased dramatically (84%) during the second three-month analysis period and was free of the problematic behaviours during the remaining 6-months of evaluation.
Glenn et al., (1989) USA. Case Study	**N=10** brain-injured subjects showing mood disorders, aggressive, combative, self-destructive behaviour or affective instability were administered lithium. Intervention measured by observed improvement.	Five showed a significant improvement in rehab programs with no decrease in motor or cognitive performance. One showed moderate response, one improved dramatically but regressed after 7 weeks; four regressed after medications stopped.

Discussion

Lithium carbonate was used in a series of case reports with 11 brain injured (8 TBI and 3 stroke) (Glenn et al., 1989). Glenn et al. (1989) reported favourable outcomes for all but one patient who received lithium (i.e., a decrease in "severe unremitting, aggressive, combative, or self-destructive behaviour or severe affective instability"). No objective measures of behaviour were reported (only descriptive, no frequency, duration/intensity or rating scales). Lithium must also be monitored carefully because of concerns regarding neurotoxicity. Similarly, Bellus et al. (1996) reported lithium treatment reduced aggressive and inappropriate behaviours in two, male patients.

Conclusion

There is Level 5 evidence to suggest that an antimanic agent (lithium carbonate) reduces aggressive/agitated behaviour following a TBI.

Lithium may reduce behavioural problems but is associated with neurotoxicity.

8.4.9 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 (decreased libido) but results in a greater negative effect for the individual and results in a great burden of care and limited independence (i.e. is less tolerated in the community). Hypersexual behaviour can range from

"*indiscriminate sexual overtures, promiscuity, and exhibitionism, to assault and/or rape*."
Treatment for non-brain injured sexual offenders has included pharmacological intervention and/or counselling/education. Typically, medication is used to reduce the sexual drive, but it is unclear if it has effect on cognitive processing (i.e. preservative thoughts regarding sex).

Individual Studies

Table 8.17 Effects of Depo-Provera on Sexually Aggressive Behaviour

Author/Year/ Country/Study design	Methods	Outcome
Emory et al., (1995) USA Case Series	**N=8** Blunt trauma, TBI subjects, who were 16 to 27 yrs of age when they began exhibiting inappropriate, contact, hyper-sexual behaviour received weekly injections of Depo-Provera in conjunction with directive, individual-specific counseling for 6 months – with follow-up every 3-6 months for 2 years.	Family members report all subjects stopped aberrant behaviour while taking medication. Blood work revealed a drop in testosterone from 834 to 85 mg/dL. Three subjects returned to previous patterns after stopping medication – due to inconsistent family support. 3 subjects dramatically improved and did not stop medication.

Discussion

In a retrospective study, medroxyprogesterone acetate (Depo-Provera; an anti-androgen drug) was evaluated in terms of its efficacy for controlling sexual aggression in 8 TBI males experiencing onset of sexual aggression 3 years post-injury (Emory et al., 1995). Weekly intramuscular injections of Depo-Provera (400 mg) in conjunction with monthly psychoeducational counseling occurred for 6 months and then follow-up examinations occurred every 3 months for 2 years (mean duration of treatment was 42 months). Results indicate a cessation of hypersexual behaviour and reduced testosterone levels. Three subjects re-offended when the drug was stopped, 3 remained on it and 2 stopped taking the drug and have maintained cessation of hypersexual behaviour.

Conclusion

There is Level 4 evidence that an antiandrogen and counselling reduces sexually aggressive behaviour.

Medroxyprogesterone intramuscularly can reduce sexual aggression.

8.4.10 Methotrimeprazine

Methotrimeprazine (Nozinan) is a psychotropic medication. It has antipsychotic (mediated by dopamine blocking), tranquilizing, and analgesic properties. It appears to have an effect on opiate (pain) receptors as well (Maryniak et al., 2001).

Individual Studies

Table 8.18 Effects of Methotrimeprazine on Agitation Post ABI

Author/Year/ Country/Study Design	Methods	Outcomes
Maryniak et al., (2001) Canada Case Series	**N=56** Retrospective chart review of subjects with ABI who were treated with 2-50 mg of methotrimeprazine (MTZ) 2-4 times per day.	MTZ, for the most part, was both safe and effective for controlling agitation.

Discussion

The oral administration of methotrimeprazine (MTZ) for agitation in doses of 2-50 mg for a maximum of 4 times per day was evaluated in a retrospective chart review of 56 patients out of a series of 110 patients admitted for rehabilitation (Maryniak et al., 2001). This was the first report on MTZ's use in treating agitation after ABI and the authors found that in most cases MTZ was both safe and effective for controlling agitation.

Conclusion

There is Level 4 evidence that methotrimeprazine is safe and effective for controlling agitation after ABI.

Methylphenidate may be safe for controlling agitation following ABI.

8.4.11 Methylphenidate

One randomized controlled trial examined the effect of methylphenidate on the control of anger following a brain injury, while another examined its effectiveness in dealing with attention and attention difficulties (Mooney and Haas 1993; Whyte et al., 2004).

Individual Studies

Table 8.19 Effects of Methylphenidate on Anger and Attention Post ABI

Author/Year/ Country/Study design/PEDro Score	Methods	Outcome
Whyte et al., (2004) USA RCT PEDro =8	**N=34** Double-blind crossover study of methylphenidate (0.3 mg/kg/dose) versus placebo measured by sustained/divided arousal, attention, distraction tasks with varying target rates on subjects, between 16 and 60 with a non-penetrating TBI resulting in loss of consciousness (LOC) (GCS<12), PTA > 1 hour or a focal abnormality (neuro-imaging); outcome measures included subject response as well as reports from treating clinicians and caregivers.	54 dependent variables reduced to 13 composite factors revealing significance in three treatment effects: information processing speed (p<0.001), work task attentiveness (p=0.01), and caregiver attention ratings (p=0.01). Of 13 independent variables, one showed significant treatment effects: reaction time before errors in sustained attention to response task (p=0.03). Treatment-related improvements were not observed in susceptibility to distraction, and divided or sustained attention.
Mooney & Haas (1993) USA RCT PEDro= 5	**N=38** Individuals having experienced a severe head injury (all males) were randomly divided into two groups, one that received 30mg of methylphenidate per day over a six-week period and the placebo control group. Anger was measured using the State-Trait Anger Scale (STAS), the Belligerence cluster score from the Katz Adjustment Scale (KAS) and the Anger-Hostility factor score of the Profile of Mood States (POMS).	Despite randomization, individuals in the treatment group scored higher on pretreatment measures of the STAS Trait Anger than the placebo group (p< 0.05). Following statistical control over the possible bias, there was a significant main effect for the drug treatment (p< 0.001).

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

Discussion

In a RCT examining the effects of methylphenidate, a psychostimulant on attention, Whyte et al. (Whyte et al., 2004) indicated that speed of processing, attentiveness during individual work tasks and caregiver ratings of attention were all significantly improved with methylphenidate treatment. No treatment related improvement was seen in divided or sustained attention or in susceptibility to distraction. Mooney and Haas (1993) demonstrated that methylphenidate helped to significantly reduce anger following brain-injury as demonstrated using several anger outcome measures. Despite the differences between the groups on one anger measure, a significant group main effect of the drug treatment was demonstrated.

Conclusion

There is Level 1b evidence (from one RCT) demonstrating the effectiveness of methylphenidate on performance speed.

There is Level 2 evidence (from one RCT) to suggest that treatment with methylphenidate following brain injury can significantly reduce anger.

Methylphenidate may be effective in increasing performance speed post TBI. It may also be effective in reducing anger following a brain injury.

8.4.12 Neuroleptic butyrophenones

8.4.12.1 Droperidol (Inapsine)

Droperidol is a butyrophenone antipsychotic agent that closely resembles haloperidol in structure. It has been used for the treatment of psychosis in Europe (Stanislav and Childs 2000).

Individual Studies

Table 8.20 Effects of Droperidol for Improving Behaviour Post ABI

Author/Year/ Country/Study design	Methods	Outcome
Stanislav & Childs (2000) USA Pre-Post	**N=27** brain-injured subjects were treated with intramuscular droperidol as needed to relieve agitated symptoms. Patients were followed for 2-months and data collected included: dose, number of doses, time to achieve calming, emergent side effects and patient demographics. Data demonstrating the relief of symptoms for three other drugs (lorazepam, diphenhydramine and haloperidol) was collected retrospectively. Patients acted as their own controls.	The time to achieve calming following episodes of agitation was significantly shorted with intramuscular droperidol (mean = 27.0 minutes) compared to intramuscular haloperidol, lorazepam, or diphenhydramine (p = 0.02).

Discussion

One retrospective controlled trial, Stanislav and Childs (2000) found that a single-dose of droperidol calmed an agitated, brain-injured significantly more quickly than other drugs. It is worth noting that a large proportion of the sample had psychiatric co-morbidities: organic personality syndromes (48%) and mental retardation (41%).

Conclusion

There is Level 4 evidence that administration of single-dose droperidol calms brain-injured, agitated patients more quickly than other agents.

Droperidol may be an effective agent for calming agitated patients.

8.4.12.2 Haloperidol

Haloperidol is a psychotropic drug found to reduce agitation. It also blocks or disrupts dopamine receptors. Thus, while it improves agitation, there is a theoretical concern it may impede recovery by reducing arousal.

Individual Studies

Table 8.21 Effects of Haloperidol on Agitation Post ABI

Author/Year/ Country/Study design	Methods	Outcomes
Rao et al., (1985) USA Case Series	**N=26** Retrospective study of patients with severe traumatic closed head injury, of which 11 were treated with haloperidol and 15 were not.	No differences in success of rehabilitation outcome were found between the two groups.

Discussion

In a retrospective chart review, agitation was managed in eleven patients with haloperidol and in fifteen patients without haloperidol (Rao et al., 1985). No differences were found between the two groups with regards to success of rehabilitation outcome.

Conclusion:

There is Level 4 evidence that haloperidol does not have a negative effect on the success of rehabilitation.

Haloperidol appears to have little negative effect on recovery following TBI.

Summary Regarding the Use of Pharmaceuticals to Reduce Aggressive Behaviour

When investigating aggressive symptomology following brain injury, specific definitions regarding the behaviours would be helpful. Several, Azouvi et al. (1999), Kant et al. (1998) and Mysiw et al. (1988) used behaviour rating scales and unblinded raters. The

other studies reported behaviour, but did not provide objective measures for example: specific frequency, intensity, duration etc.

The use of pharmacological agents can help to prevent injury to the patient and others and 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" (pg 263-4) (Stanislav & Childs, 2000).* Ideally, neuropharmacologic interventions for agitation in brain-injured patients would be studied using a randomized, double-blinded, placebo design, however, few of these trials have been conducted (Levy et al., 2005). It has been suggested that more research be conducted examining the safety of atypical, antipsychotic drugs, beginning with further animal studies (Lombard & Zafonte, 2005).

Conclusion

There is only limited evidence that pharmacological interventions can reduce verbal, physical and/or sexual aggressive behaviours. More research using randomized placebo controlled design is needed.

8.4.13 Behavioural Management Post ABI

Common sequelae to brain injury are behavioural disturbances impacting on the patients' compliance with rehabilitation following injury. In some cases, individuals with brain injury develop behavioural difficulties that result in early discharge and/or limited participation in rehabilitation activities. (Alderman 1991). When challenging behaviours take the form of aggressive acts, this may prevent functional gains in neurorehabilitation (Alderman et al., 1999). In a cross-sectional study of 69 subjects admitted to a Brain Injury Unit, Lequerica et al. (2007) found an inverse relationship between agitation and the individual's engagement in physical and occupational therapy.

It is difficult to compare across studies when evaluating interventions using behavioural management techniques, as behavioural techniques are tailored to the individual needs/requirements of the person in question. Studies may examine diverse techniques to manage challenging behaviours following an acquired brain injury, including antecedent controls, positive reinforcement, and token economies, whereas other studies have examined the efficacy of specific training programs (i.e. anger management, social skills training, etc) in reducing agitation/aggression.

8.4.14 Specific Behavioural Techniques

Behavioural techniques have been in used for many years with a variety of disorders. Techniques are often used to teach new skills, socially appropriate behaviour and

improve independent functioning. It does not control people or make them do anything against their will. Behavioural analysis examines the relationship events and behaviour with the goal of increasing social interactions and independence available to people (Ashley et al., 1995). In the past, the alternative to behavioural strategies has been sedation, physical restraint, and/or institutionalisation. Not only are behavioural techniques applicable in a variety of settings and with a variety of behaviours, but it also addresses the main goals of rehabilitation – the development of functional life skills (Jacobs 1993).

Individual Studies

Table 8.22 Effects of Antecedent Behavioural Interventions on Reducing Aggressive Behaviour Post ABI

Author/Year/ Country/Study design	Methods	Outcome
Hart et al., (2012) USA Pre-Post	**N=10** Individuals participated in an 8 session intervention built around self-monitoring training to build awareness of their anger problem and to improve their ability to attend to anger signals and training of specific problem solving skills to develop better responses to anger or conflict (anger self-management training (ASMT). Trails making test A/B; Rey auditory verbal learning test (RAVLT), Brief Symptom Inventory (BSI), Global Severity Index (GSI) were used to assess participants pre and post intervention	The group overall, were of low to average intelligence and were found to have significant executive dysfunction. Following the intervention, self-reports of anger declined significantly (p.03).
Wesolowski et al., (1999) USA Pre-Post	**N=3** Subjects with TBI from MVA participated in a before/after case series that implemented 10 minute "mini" breaks per hour during work. Outcomes measured by frequency of unauthorized breaks before and after the intervention and at 6 weeks follow-up.	Number of unauthorized breaks for each participant decreased with the introduction of "mini" breaks. This decrease in the number of unauthorized breaks persisted to the 6-week follow up period.
Schlund & Pace (1999) USA Pre-Post	**N=3** TBI subjects (aged 27-48) received systematic feedback on their frequency of maladaptive behaviour.	Variability and frequency of maladaptive behaviour generally decreased from baseline (2 to 5.1 per week) to completion (0.18 to 1.8 per week).
Burke et al., (1988) USA. Pre-Post	**N=5** ABI subjects (closed-head trauma) previously placed in psychiatric hospitals for aggressive behaviour received positive reinforcement through increased density, reinforce sampling, antecedent control, no negative consequences. Progress was measured by recording numbers of physically aggressive behaviours.	Measurements at 1 week post treatment showed a 97% decrease in aggressive behaviour from baseline levels; 100% by the third week. There was a significant reduction in behaviour at all time points compared to baseline (p<.001).

Author/Year/ Country/Study design	Methods	Outcome
Eames et al., (1985) UK Pre-Post	**N=24** Severely injured ABI subjects (mean LOC 7.8 +/- 6 weeks) whose disturbed behaviours prevented rehabilitation in ordinary settings were placed in a specialized TBI unit that used a wide range of physical, cognitive behavioural, occupational and social techniques based on positive reinforcement and a token economy.	As the nature and severity of the patients' injuries were virtually never associated with a return to work, the authors constructed a simple hierarchy of possible placements and measured outcomes in terms of steps up or down this scale between admission, discharge and follow-up. More than 2/3 of patients had improved placements after treatment; only one person had a substantial improvement. Fewer than 1/3 made no change, and no one was worse placed.
Feeney & Ylvisaker (1995) USA Case study	**N=3** Late-adolescent males with TBI from MVA displaying aggressive behaviour participated in an A-B-C-A designed antecedent behavioural and cognitive intervention comprised of photographic and written cues. Frequency of individual-specific behaviours, sections of the Aberrant Behavior Checklist and percentage of assigned work completed were used to measure progress under treatment.	All three cases showed a sharp improvement in completed work while under therapy, a decrease in aggressive behaviours and ABC ratings indicated decreased intensity. Subjects 1 and 2 showed a mild increase in aggressive behaviours with written cues, which decreased when substituted with photographic cues.
Persel et al., (1997) USA Single subject intervention	**N=1** ABAB design was used. During the A condition the subject was kept busy with productive activities. During the B condition noncontingent reinforcement was used to decrease unwanted or inappropriate behaviors. The noncontingent reinforcement consisted of staff delivering attention to the subject every 30 min for the first 4 hours (wake up time to 11 am) of the day, then every hour until the subject went to bed. Self-injurious behaviors and physically aggressive behaviors were monitored	The noncontingent reinforcement was effective in reducing the rate of physical aggression and self-injurious behaviors. Both were reduced with the introduction of NCR but returned to baseline levels once NCR was discontinued.
Alderman et al., (1999) UK Case study	**N=3** subjects participated in a behaviour modification intervention designed to decrease inappropriate shouting using satiation through negative practice. Following this intervention, reduced frequency of shouting was demonstrated and a second intervention was put in place to encourage further improvements. Individual rehabilitation activities were provided for the patient whereby he was allowed to continue shouting until he stopped voluntarily. Staff would then	There was a downward trend in the mean frequency of shouting per minute over time ($p < 0.01$) following the initial intervention and decreased significantly from baseline following the second intervention ($p < 0.01$).

Author/Year/ Country/Study design	Methods	Outcome
	encourage him to continue shouting for 2- to 3-min period.	
Fluharty & Glassman (2001) USA Case study	**N=1** The intervention plan for one individual focused on the modification of the environment to address the problems of aggression and difficulty with ADLs. Sources of agitation were minimized for the participant.	The facilitation of ADLs, coupled with the modification of the environment, helped to decrease the incidence of aggressive acts for one individual following brain injury.
Burke et al., (1991) USA Case study	**N=6** Subjects with TBI were provided with verbal and visual feedback and various checklists for improving social behaviors, problem solving, and initiation	No statistical comparisons completed. Upon removal of checklists and feedback, trained behaviors were maintained.

Discussion

In a recent study 10 individuals who had sustained a TBI participated in an 8 session psychoeducational treatment program (anger self-management training (ASMT) for irritability and anger (Hart et al., 2012). Eight of the 10 participants had a significant other participate with them. The 8 session program was designed to assist the individual identify anger signals, and to learn specific problem solving skills to death with frustration and conflict. Following treatment, anger declined significantly ($p<0.03$).

Feeney and Ylvisaker (1995) used an ABCA (changing treatment) design to test the effectiveness of an antecedent behavioural intervention for three severely brain injured clients in reducing aggressive behaviour over a six week period. Their study showed that by structuring the environment initially with high support, and then reducing it, and involving the clients in a collaborative manner, aggressive behaviour was significantly reduced.

Three studies explored the impact of systematic data based feedback on maladaptive behaviour. Schlund and Pace (1999) demonstrated that by using frequency data as feedback (as opposed to only verbal-based feedback), the occurrence of “maladaptive” behaviour could be reduced. However, their group consisted of three mildly cognitively impaired individuals attending a medical rehab program five days a week. Maladaptive behaviours consisted of pseudoseizures, non-compliance with rules, verbal aggression and sexually inappropriate behaviour. Wesolowski et al. (1999) utilized a “non-contingent escape” paradigm i.e. planned mini-breaks in work periods to increase compliance in three TBI clients in order to effect positive change with vocational placement. Burke et al. (1988) used a program that was structured so that positive

behaviours, that were incompatible with aggression, would be more likely to occur, thereby decreasing aggressive behaviour in five patients. Percentage of change scores from baseline revealed success.

Eames et al. (1985) examined the quality of life (as measured by living environment and behavioural ratings) of 24 severely injured ABI patients following intensive behavioural treatment utilizing a token economy (admission to a structured unit, mean length of stay was12 months). Behaviours were rated as severe (i.e., could not be dealt with in the community and generally resulted in admission to institutions with restriction in independence) and time since injury was on average four years (i.e., spontaneous recovery had taken place). The study examined the effects of treatment from discharge to follow up (mean follow-up 19 months). Results indicated that generally the quality of life had improved and was maintained, as measured by improved relationships with care-givers and an improvement in living arrangements. However, when examining results reported, actual behaviours of aggression, sexual inappropriate behaviours, drive/motivation & odd behaviours increased in occurrence from discharge to follow-up. Results were not presented from pre-admission to discharge to follow-up so it is not clear how behaviours had changed following treatment.

The results from two case studies suggested that the use of antecedent control may improve outcome following brain injury (Alderman et al., 1999; Fluharty & Glassman, 2001). One patient participated in a behaviour modification program designed to decrease the frequency of inappropriate shouting using satiation through negative practice (Alderman et al., 1999). The initial training procedure included four techniques: (1) patient was exposed to tape of his own shouting during initial training sessions; (2) patient was encouraged to practice sitting using a posture designed to maximize stability and to control and decrease the effects of abnormal tone; (3) patient was prompted to shout for periods of 2 to 3 min, followed by a one minute rest period; and (4) promotion of shouting during later stages of training. Significant reductions in the frequency of shouting were found, which enabled physical and functional gains to be made through rehabilitation activities that were previously avoided. Significant reductions in aggressive acts were also noted for one individual in Fluharty and Glassman (2001) following facilitation of ADLs and modification of the environment.

In the single subject intervention by Persel et al. (1997) unwanted self-injurious behaviors were reduced by using noncontingent reinforcement (NCR). Although there were no statistically significant differences noted before and after the introduction of the NCR, aggressive behaviors did decrease. Burke et al. (1991) in their case study, noted that those who were given checklists for improving social behaviors, problem solving and initiation were able to maintain improvements in social communications and behaviors after those cues were removed.

Conclusion

There is Level 4 evidence to suggest that anger self- management training is effective in reducing irritability and anger after TBI.

There is Level 4 evidence that behavioural approach using antecedent management and/or feedback of consequences reduces undesirable behaviour (e.g., aggression/agitation).

Anger self-management training is effective in teaching those with a TBI identify anger signals and develop more appropriate ways of dealing with anger and frustration.

Antecendent management and or feedback of consequences can reduce undesirable behaviour.

8.4.15 Multi-intervention Training Programs

Training programs that combine a number of behavioural interventions have been utilized with some success. For example, anger management, social skills, and coping skills training programs have been used in the past to alleviate aggressive/agitated behaviour in individuals with an ABI.

Individual Studies

Table 8.23 Effects of Training Programs on Alleviating Aggressive Behaviour Post ABI

Author/Year/ Country/Study design /PEDro Score	Methods	Outcome
McDonald et al., (2008) Australia RCT PEDro = 6	**N=39** Participants were randomly assigned to one of three groups - control (non-therapeutic social group n=13), waitlist (deferred treatment group n=13) or the social skills group (treatment group n=13). Once randomized, those in the skills training were required to attend a 12 week program that include both group and individual sessions totaling 4 hrs per week. Those in the control group were subjected to 4 hours/wk of social activities only. The program lasted 12 weeks. The remaining group (waitlist) would receive treatment at the end of the study.	Results indicate no interaction effects for the social group relative to the waitlist group. Those in the skills training group made significant improvement on the Partner Directed Behaviour Scale (PDBS) scale ($p<0.004$) compared to the placebo group and the waitlist group. Changes were not noted for any group when looking at social functioning and social participation post treatment. Treatment effects were found to be modest at best and limited to direct measures of social behaviour.

Author/Year/ Country/Study design /PEDro Score	Methods	Outcome
Carnevale et al., (2006) USA RCT PEDro=5	**N=37** Subjects were divided into one of three groups: control group received not treatment, the education group received education only, and the Natural Setting Behavior Management (NSBM) group received both education and participated in an individual be- mod program. Looking for changes in targeted behaviors, used a subscale of the Questionnaires on Resources and Stress, Maslach Burnout Inventory and the Neurobehavioral Functioning Inventory	Following treatment, it was noted that changes in behavior were not apparent at the first 2 follow-up points but differences at the third point were statistically different (F=3.32, p=0.05). A significant difference was also noted between the education group and the NSBM group (p<0.04). There was also a significant change in the emotion exhaustion score before and after treatment (last follow-up session) (p<0.03). There was also a significant difference between the control group and the education group (p<0.005) but not between the NSBM and these two groups. Treatment did not affect the NFI aggression scale.
Anson & Ponsford (2006a) Australia RCT PEDro=5	**N=31** Participants working as their own controls, were assigned to one of 2 group protocols and a wait-list control design was used. For group A, baseline phase was 5 weeks, followed by 5 weeks of intervention, and a 5-week follow-up phase. For group B, baseline was 10 weeks, followed by 5 weeks of intervention and a 10-week follow-up phase. The coping skills group (CSG) consisted of 10 group sessions and ran for 90 minutes 2x wk for 5 wks.	Although not stable in the short term, both groups significantly increased their adaptive coping skills following the CSG (p<0.01). No significant changes in their anxiety or self-esteem scores were noted following the CSG (p>0.05). Although levels of depression and psychosocial dysfunction were significantly different between the two groups (p<0.05) participation in the CSG did not have an effect on their scores.
Medd & Tate (2000) Australia RCT PEDro = 5	**N=16** TBI subjects between 16 and 60 with post-trauma onset of anger management problems participated in a two by two factorial program utilizing a matched-randomized, repeated measures design. Program consisted of 5-8 weekly individualized sessions of components based on the Commonwealth Rehabilitation Service Anger Management Program (derived from Novaco's 1975 stress inoculation training principles). Anger (STAXI), anxiety/depression (HADS), self esteem (SEI), and self-awareness (PCRS) were measured pre/post-intervention and at 2 months follow-up	Significant Results: Higher **pre-intervention** levels of Anger Expression-Out (AX-O) than WAIT (p=.004); Group and Time interaction for AX-O (p=.006) and Trait Anger-TANG (p=.054); Reduction of anxiety **post-intervention**(HADS: p=.006); TANG (p = .002) and AX-C (p = .008); **pre-intervention to follow-up** AX-O showed improvement (p = .015)
O'Leary (2000) USA	**N=5** Adult TBI males with a history of verbal and physical aggression that prevents them from being successful	Training reduced the number of incidents of both verbal and physical aggression for all participants.

Author/Year/ Country/Study design /PEDro Score	Methods	Outcome
Post-test	received a 10 week training program including written materials, role-plays, audiotapes, group discussions and lectures. Instances of verbal and physical aggression were measured for 10 weeks following the training period.	
Brotherton et al., (1988) USA Case Series	**N=4** Subjects with closed head injuries were selected for a social skills training program comprised of self-manipulation, posture, speech dysfunctions, personal attention, reinforcing feedback, and positive statements through a single case methodology in the form of a multiple baseline across behaviours (4 replications).	The intervention was effective in three of the four patients treated (however, not all behaviors were equally amenable to treatment -- eg. more effective for self-manipulation and posture) Behaviors showing clear training effects also showed good maintenance one year after training.
Uomoto & Brockway (1992) USA Case study	**N=2** Subjects (both male, ages 22 and 43) and their families participated in the Behavioral Management Treatment Program to help control anger following brain injury. The program involved eight to 12 weekly sessions (between one and one half hours) of treatment by clinical psychologists. The frequency of outbursts of anger by patient was measured.	Both patients experienced a notable decrease in the average number of outbursts per week during treatment.

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

Discussion

In a RCT conducted by McDonald et al. (2008) subjects were randomized to either: 1) the social skills training group (n=13), or 2) a social activity group (n=13) or 3) a waitlist control group (n=13). Those in the social skills training group attended group and individual sessions, focusing on improving social behaviour, changing social perceptions, and improving mood and self-esteem for a total of 12 weeks. Those in the social activity group participated in social activities 4 hours each week for 12 weeks. The final group (waitlist group) were told they would receive treatment at the end of the study. Those in the social skills group did have a positive effect compared to the two control groups (the social activity group and waitlist group) on PDBS; however, this improvement was noted on the Partner Directed Behaviour Scale only. When looking at levels of anxiety, depression and stress no significant improvement was noted following treatment.

In the randomized controlled trial conducted by Carnevale et al. (2006), 40 subjects were divided into one of three groups and following treatment changes in targeted behaviours was examined. Following treatment, significant changes in behaviour were apparent at the third follow-up period ($p=0.05$). There also appeared to be a difference between two of the three groups (the education group and the NSBM, $p<0.04$). No

significant changes were noted when looking at the aggression scores between any of the groups after treatment, but difference were noted between the control and the experimental groups in the emotion exhaustion scale ($p<0.005$).

In another randomized control trial, this time by Anson and Ponsford (2006a) had 31 subjects; acting as their own controls, divide into two separate protocols. Each groups was exposed to the same intervention for the same length of time (5 weeks), however Group A's baseline and follow-up was only 5 weeks compared to Group B whose baseline and follow-up were 10 weeks. Anson and Ponsford (2006a) found that both groups significantly increased their adaptive coping skills following the CSG ($p<0.01$), although this was not stable during the immediate follow-up, it did increase again with time. No significant changes in their anxiety or self-esteem scores were noted following the CSG ($p>0.05$). It was also found that participation in the CSG did not have an effect on the depression or psychosocial dysfunction scores either group received, but overall levels of depression and psychosocial dysfunction were significantly different between the two groups ($p<0.05$). Overall when asked those participating did feel they had better understanding of emotional issues and an increased ability to implement coping strategies as a result of their participation in the CSG.

O'Leary (2000) in a case series demonstrated that verbal and physical aggression could be decreased following 10 weeks of training (which included one hour of coping skills training and one-hour of anger management) and that effects could be maintained through follow-up (another 10 weeks).

In a matched, randomized procedure, Medd and Tate (2000) evaluated the effectiveness of an anger management therapy program in 16 ABI patients (13 TBI, three stroke). The treatment group received on average six individualized hourly sessions following cognitive-behavioural and stress-inoculation strategies tailored for individuals with brain injury. The "control" group monitored their anger daily. Results indicated a decrease in anger (as measured by an inventory) immediately and two months following treatment, primarily on the sub scale of outward expression of anger. Trends in a positive direction were observed for the other measures of anger, but were not significant.

Brotherton et al. (1988), in a multiple baseline across behaviour design implemented social skills training (28 weeks) with four preselected individuals following severe TBI. Data analysis relied on visual inspection of graphs. A general improvement in targeted behaviour was observed, although some aspects of social skills training improved more readily than other aspects (e.g., more concrete, objective aspects such as posture, decreased fidgeting as compared to complex verbal aspects such as positive statements, reinforcing feedback). The authors concluded that treatment effects were maintained at follow-up one year later, although visual inspection of the graphs does not support this.

Conclusions

There is Level 1b evidence that social skills training has limited impact on changing inappropriate behaviours and mood disturbances of those who have sustained a severe TBI.

There is Level 4 evidence that social skills training reduces aggressive behaviour.

There is Level 2 evidence that Natural Setting Behavior Management may help to change behavior.

There is Level 2 evidence that participating in a Coping Skills Group assists in improving adaptive coping in the long term.

There is Level 2 evidence based on one RCT that anger management reduces aggressive behavior.

Anger management and social skills training reduce aggressive behaviour.

8.4.16 Music Therapy

Music therapy is an approach that *"consists of using music therapeutically to address physical, psychological, cognitive and/or social functioning for patients of all ages"* (American Music Therapy Association 2004). It was first used with WWI veterans in hospital and was formally recognized as a therapeutic tool in 1950. Music therapy has been used with a variety of patients (neurological, psychiatric, medical, pervasive and developmental disorders) and has been found to result in physiological changes (e.g., respiration, blood pressure, heart rate, decrease cortisol levels and increase endorphine) and increased wellbeing. This type of therapy has been tried with stroke patients and although the results only approached statistical significance, feelings of depression and anxiety were improved (Purdie et al., 1997). More recently music therapy has been used with TBI patients to decrease agitation.

Individual Studies

Table 8.24 Effects of Music Therapy on Post-Coma Agitation Post ABI

Author/Year/ Country/Study Design	Methods	Outcome
Baker et al., (2005) Australia Case Series	**N=4** Subjects between the ages of 24-29, with a GCS of 3-5, were recruited to participate in the following study. Subjects participated in 15 individual music therapy	Results from the mood scale found differences between subjects on their responses to all 8 of the scales. Feelings of happiness were found to

	sessions, lasting approximately 40-50 minutes, over a 5-8 week period. Subjects were asked to sing 3 songs they had selected. Lyrics were provided to each of the subjects. State of mood was assessed using the visual analogue mood scale.	differ between subjects, with some indicating improved feelings ($p<0.01$). Immediate effects of the treatment were different between subjects for mood ($p<0.01$). When looking at the fundamental frequency data, significant differences were found between subjects' responses over time for: afraid ($p<0.05$), angry ($p<0.01$), and sad ($p<0.05$).
Baker (2001) Norway Non-RCT	**N=22** 3 conditions were presented to the subjects: live music, taped music, and no music (control session). Each received all three conditions, one condition per day over 6 days. Each condition was presented twice, with each condition presented on days1-3 and 4-6. No condition was presented two days in a row. Subjects were exposed to the live and taped music session for approximately 12 minutes. Changes were measured using the Westmead PTA Scale, Agitation Behavior Scale.	Orientation scores seemed to improve, following exposure to the live and taped music. Significant differences were noted when comparing the scores between the live music and the control conditions ($p<0.001$) and between the taped music and the control conditions ($p<0.001$). The difference between the live and taped music was not significant ($p=0.8$). There was some evidence to suggest that memory for music returned faster than memory for pictures but findings were not significant ($p=0.7$) Agitation decreased significantly after exposure to the live and taped music ($p<0.001$).
Formisano et al., (2001) Italy Case Series	**N=34** TBI subjects (LOC > 15 days, GCS <= 8, GOS <= 3) showing a lack of verbal initiative received music therapy based on the approach of Nordoff and Robbins (1977) without any change in pharmacological treatment. Music Therapy's effect on psychomotor initiative, agitation and interaction with the environment were assessed with the following outcome measures: GOS, Disability Rating Scale, Coma Recovery Scale, Post-Coma Scale (taken at admission, before starting Music Therapy, and at 15 days, 1 month, 2 months, at treatment completion, and 1 month follow-up).	Psychomotor initiative improved but did not reach statistical significance. (PCS). Events of psychomotor agitation decreased significantly (GOS). No improved interaction with the environment was recorded (DRS, CRS). No p values provided. Positive effects reported in 27 of 34 patients (21 of 34 according to blind examiner) one month after starting treatment and at follow up.

Discussion

One study, Formisano et al. (2001) reported that music therapy had a beneficial effect in reducing post-coma agitation and inertia in 62% of their subjects in a slow-to-recover group one month after starting music therapy.

In the study conducted by Baker (2001) 22 subjects were exposed to music therapy (either live music, taped or no music) over a six day period. Presentation of the

intervention was randomized and no one intervention was presented two days in a row. Changes in the subjects agitation was measured using the Westmead PTA scale and the Agitation Behavior Scale. When comparing the scores of the Westmead PTA scale between the live and taped music sessions and the control conditions significant differences were noted ($p<0.001$). Agitation decreased significantly after exposure to the live and taped music ($p<0.001$). There was some evidence to suggest that memory for music returned faster than memory for pictures but findings were not significant ($p=0.7$).

A more recent study by Baker et al. (2005) in which 4 subjects participated in 15 individual music therapy, found difference between subjects on their responses to all 8 of the mood scales. Feelings of happiness were found to differ between subjects, with some indicating improved feelings ($p<0.01$). Immediate effects of the treatment were different between subjects for mood ($p<0.01$). When looking at the fundamental frequency data, significant differences were found between subjects' responses over time for: afraid ($p<0.05$), angry ($p<0.01$), and sad ($p<0.05$).

Conclusions

There is Level 2 evidence from one non-RCT to suggest that music therapy reduces agitation post PTA.

There is Level 4 evidence that music therapy reduces psychomotor agitation post-coma following severe TBI in a slow-to-recover group.

There is Level 4 evidence to suggest that music therapy improves the mood of ABI adults.

Music therapy may reduce psychomotor agitation post coma and improve mood following severe TBI.

8.5 Addictive Behaviours Post ABI

8.5.1 ABI and Substance Abuse

Several studies have examined the rates of substance abuse in those who have sustained a traumatic brain injury (TBI) and have found that 44 to 79% of individuals have an alcohol addiction at time of injury, while another 12 to 33% reported having a drug addiction (Kolakowsky-Hayner et al., 2002; West et al., 2009; Taylor et al., 2003) Kelly et al. (1997) in a study examining the effects of alcohol and other substances on various neuropsychological measures found those who reported using alcohol or other substances prior to their injury, scored significantly lower than those who did not have a

history of substance use. It has been noted that of those who sustain their injury in a motor vehicle collision, one of the leading causes of TBIs, almost half were found to be impaired (Wehman et al., 2000; West et al., 2009; DeLambo et al., 2008). Acute intoxication has been found, in some studies, to impact the duration of coma, length of time in post-traumatic amnesia (PTA), overall length of stay, post recovery cognitive outcomes and self-care abilities (Vickery et al., 2008; Bombardier and Thurber 1998).

Studies have found that substance abuse issues occur more frequently with those who have sustained TBI then members of the general public (Taylor et al., 2003) and many will return to drinking within two years of injury (Bombardier & Thurber, 1998). Hibbard et al. (Hibbard et al., 1998) reported that as many as 40% of the TBI population meet the criteria for substance abuse or dependence as it is measured on the DSM-IV. Post-injury even small amounts of alcohol can result in more significant cognitive impairments as the individual works through the recovery process (Tweedly et al., 2012). The link between depression or other mood disorders and substance abuse has also been shown to be quite strong both pre and post ABI (Jorge and Starkstein2005).

Individual Studies

Table 8.25 Prevalence of Substance Use and Abuse Pre- and Post-ABI

Author/Year/ Country/Study Design	Methods	Results
Andelic et al., (2010) Norway Prospective Study	**N=111** subjects with moderate to severe TBI and a known status of intoxication at the time of injury. Within 24 hours of injury, 2 CT scans were performed. The brain injuries were classified as either less severe (Marshall score < 3) or more severe (Marshall score > 3). CAGE questionnaire was used to screen for pre-injury substance abuse.	26% of the subjects reported pre-injury substance abuse. Less severe TBI patients more frequently reported substance use at time of injury (p=0.01) while more severe TBI patients more frequently reported pre-injury substance abuse (30% vs 23%). An adjusted regression analysis revealed that subjects with a CAGE score ≥ 2 (indicative of pre-injury substance abuse) were likely to have a more severe TBI than a less severe TBI (p=0.04).
Ponsford et al., (2007) Australia Case-Control	**N=121** Individuals who had sustained a TBI and had emerged from PTA, completed a questionnaire administered by a non-treating clinician. The questionnaire included the following scales: The AUDIT, the DAST, the HADS. Those who had sustained a TBI were administered the questionnaire 1, 2 and 3 yrs post injury. Those in the control group were members selected from the general population. Controls completed the survey at one time period only.	Initial assessments indicated there were no differences between the two groups related to their alcohol consumption. At one year post injury significantly more (30%) had abstained from alcohol completely compared to those who abstained before their injury (8.4%, p<0.001). 17.4% of the ABI survivors reported drinking at hazardous levels and another 11.5% indicated there was an alcohol dependence. At the two year assessment, more were abstaining (21% vs 30%) but amongst those who were drinking, the frequency of drinking had increased. The number drinking at hazardous levels or dependent on alcohol had also increased. The

		use of other drugs also decreased at one year post injury, but increased at the 2 year mark. It was also noted that many who were alcohol dependent were also drug dependent. Drinking and substance abuse was noted as a problem for approximately 30% of the 76 individuals who completed the surveys.
Bombardier et al., (2003) USA Cohort	**N=174** Individuals with a TBI were asked to compete various surveys. Alcohol consumption pre and post TBI were assessed.	Of the 174 individuals involved in the study, only 65 were found to have an alcohol related problem pre injury. Of these at one year post injury, 25 continued to have an alcohol related problem. Those identified as having alcohol abuse problems pre injury are 10.9 times more likely to have a problem post injury in comparison to those who did not report alcohol abuse pre-injury.
Turner et al., (2003) USA Cohort/Survey	**N=218** consecutive TBI (119), SCI (70) and combined TBI/SCI (29) patients admitted to a rehabilitation facility on average 29.9 days after injury. The subjects were administered questionnaires in an interview format. Outcome measures were the SMAST, the PDS, the RTC questionnaire, number of drinks per week, illicit drug use, preferences for alcohol-related behavioural change strategies and extent to which substance use was cause of injury. Medical diagnostic information was obtained from subject's charts such as admission serum toxicology and whether the physician identified a history of alcohol abuse.	The subjects were divided into 4 subtypes of alcohol use: high drinking-high consequence (I), high drinking-low consequence (II), low drinking-high consequence (III), low drinking-low consequence (IV). Differences among alcohol subtypes were found in total drinks per week, SMAST and physical dependency ($p<0.001$ for all). Subtypes differed in their drug use ($p<0.01$) with type IV reporting less drug use than the other groups. The contribution of alcohol to cause of injury differed among subtypes ($p<0.001$) with type I reporting more alcohol-related injuries. Type IV were least likely to have documentation of alcohol-related problems while type I were most likely to have documentation than type II ($p<0.001$). At time of admission, type I and type II were more likely to have a positive BAL than type IV ($p<0.001$).
Bombardier et al., USA Cohort/Survey	**N=142 c**onsecutive TBI patients were admitted to a rehabilitation facility on average 27.1 days after TBI. All of the subjects were given several questionnaires to complete which included: the Ph scale from the Brief Drinkers Profile, the SMAST, and the RTC questionnaire. The subjects were also queried on several subjects including: number of drinks per month pre-injury, number of drinks consumed at each drinking occasion, number of times within the past month the subject consumed ≥ 5 drinks on a single occasion, number of times subjects drank ≥2 drinks and drove in the past month, which illicit drugs were used in the 3 months pre-injury, preferences for alcohol-related change	59% of the sample was classified as at-risk for alcohol related problems. At-risk drinkers were more likely to be men ($p=0.001$), single, separated or divorced ($p<0.001$) and people with a high school education or less ($p=0.011$). At time of admission, 42.3% of subjects with obtained BALs were positive and 32.3% were intoxicated. The average number of drinks per week (11.2) was in the 84^{th} percentile overall. 49.3% of the sample had a significant history of alcohol problems. 37.7% of the sample tested positive for illicit drug use at admission while only 31.4% of the sample admitted to using illicit drugs. Overall,40.1% of the total sample reported or tested positive for the use of illicit drugs. 21% of the whole sample used alcohol safely,

	strategies, the degree to which they were responsible for their injury and the degree to which alcohol and drug use was the cause of injury. Acute serum BALs and toxicology screens were extracted from the medical records.	abstained from drug use and didn't have a history of alcohol abuse. Readiness to change was positively correlated with high SMAST scores ($r=0.39$, $p<0.01$), high physical dependency ($r=0.31$, $p<0.01$) and number of drinks per week ($r=0.30$, $p<0.01$).

Note: ABI = Acquired Brain Injury; AUDIT = Alcohol Use Disorders Identification Test; BAL = Blood Alcohol Level; CAGE = Cut down, Annoyed, Guilty, Eye-opener; CT = Computed Tomography; DAST = Drug Abuse Screening Test; HADS = Hospital Anxiety and Depression Scale; PDS = Physical Dependence Scale; RTC = Readiness to Change; SCI = Spinal Cord Injury; SMAST = Short Michigan Alcoholism Screening Test; TBI = Traumatic Brain Injury; PTA = Post-Traumatic Amnesia

Discussion

There is currently a large variation in the amount of substance abuse in the TBI population reported in the literature; the studies listed above reveal the same finding. The prevalence of pre-injury alcohol abuse was reported between 11.5% and 49% (Andelic et al., 2010; Bombardier et al., 2003; Bombardier et al., 2002; Ponsford et al., 2007) while illicit drug use was reported to be 38% (Bombardier et al., 2002). The problem with comparing the reported pre-injury substance abuse rates is that the inclusion criteria for many of the studies differ. Studies which only include subjects with a positive BAC at time of admission will report an inflated incidence since non-users are automatically excluded. Bombardier and colleagues (2002) reported that the number of drinks per week pre-injury reported by their sample was in the 84th percentile of average American alcohol consumption. This suggests that substance abuse is a much greater problem in the TBI population than in the general population. Furthermore, a history of substance abuse may be a risk factor for future TBI. Interestingly, substance abuse is more often affiliated with moderate to severe injuries while intoxication at time of injury is more often affiliated with mild injuries (Andelic et al., 2010). The incidence of intoxication at time of injury also varies across studies and has been reported here by Bombardier and colleagues (2002) as 32% of TBI admissions with 42% positive for alcohol in the blood.

The post-injury substance abuse rates range from 30% to 59% being at-risk for alcohol related problems (Ponsford et al., 2007; Bombardier et al., 2002). Two studies suggested that alcohol consumption declined within the first year of injury, but those who returned to drinking two years post-injury were likely to consume more than before the injury, drink excessively, and be dependent on alcohol (Bombardier et al., 2002; Ponsford et al., 2007). Ponsford and colleagues (2007) reported the same trend for the use of illicit drugs. TBI victims who abused alcohol pre-injury were 10 times more likely to demonstrate problematic alcohol use post-injury (Bombardier et al., 2003).

Individual characteristics were also found to determine the likelihood that a TBI patient 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).

In several studies looking at the rates of drinking and the use of other substances post injury, rates declined slightly within the first year of injury (Ponsford et al., 2007; Kelly et al., 1997; Bombardier et al., 2003; Jorge et al., 2005). Ponsford et al. (2007) reported that although substance abuse or misuse declined post injury within the first year, the rates had risen during the second year. It was also noted that individuals who had significant substance abuse problems before injury, were likely to return to this behaviour post injury. It has also been noted that many who continue to "use" have an increased risk of re-injury (Corrigan 2005). Problem drinkers are more likely to be male and single/separated/ divorced with high school education or less (Bombardier et al., 2002).

Substance abuse and intoxication at time of injury is a frequent phenomenon in the TBI population.

Substance addiction pre injury is predictive of substance addiction post injury.

8.5.2 Substance Abuse and Assessing the Severity of Injury

When assessing the severity of injury several issues have been raised. The first is the use of the Glasgow Coma Scale (GCS). It has been suggested that the GCS is unreliable when using it to establish functioning level at time of injury for those who have been drinking and/or using other substances (Jagger et al., 1984). However, Stuke et al. (2007) in a recent study found the GCS was not affected by the blood alcohol concentration (BAC) of individuals admitted to a local trauma centre. Similar findings have also been reported (Kelly et al., 1997; Sperry et al., 2006); however other studies have found just the opposite (O'Phelan et al., 2008). To date there is conflicting evidence when looking at the effects of alcohol on the level of injury, survival rates and GCS.

8.5.2.1 Effect of Substance Use on Initial Assessments and Severity of Injury

Alcohol use has been identified as a contributing factor to cause of brain injury but more destructively as a factor which promotes poorer long-term recovery from injury and more difficult assessment of injury (Vickery et al., 2008). Some recent clinical studies have suggested quite the opposite. They have found evidence which implies that alcohol has a neuroprotective effect on neuronal recovery post-TBI (Andelic et al., 2010; Berry et al., 2010; Shahin et al., 2010). The evidence surrounding the effects of alcohol at time of injury and outcome measures is quite conflicted.

Individual Studies

Table 8.26 Effect of Substance Use at Time of Injury on Severity of Injury Post-ABI

Author/Year/ Country/Study Design/PEDro Score	Methods	Results
Andelic et al. (2010) Norway Prospective Study	**N=111** subjects with moderate to severe TBI and a known status of intoxication at the time of injury. Within 24 hours of injury, 2 CT scans were performed. The brain injuries were classified as either less severe (Marshall score < 3) or more severe (Marshall score > 3). CAGE (Cut down, Annoyed, Guilty, Eye-opener) questionnaire was used to screen for pre-injury substance abuse.	26% of the subjects reported pre-injury substance abuse. Less severe TBI patients more frequently reported substance use at time of injury (p=0.01) while more severe TBI patients more frequently reported pre-injury substance abuse (30% vs 23%). An adjusted regression analysis revealed that subjects with a CAGE score ≥ 2 (indicative of pre-injury substance abuse) were likely to have a more severe TBI than a less severe TBI (p=0.04).
Berry et al. (2010) USA Retrospective Study	**N= 7304** subjects who had ETOH levels measured on admission were selected from the Los Angeles County Trauma System database. The patients who tested positive for ETOH were compared to the patients who tested negative for ETOH on several parameters.	44% of patients tested positive for ETOH on admission. In comparison to ETOH-negative patients, ETOH-positive patients were younger (p<0.0001), more frequently male (p<0.0001), had less severe injuries (p<0.0001) and lower GCS (p<0.0001).
Shahin et al., (2010) USA Prospective Study	**N=188** Consecutive TBI patients admitted to the Neurosurgical Intensive Care Unit between May 2006 and Feb 2008 had their information prospectively collected in a TBI database. Demographic information, pre-hospital records, emergency department records and the initial CT scan were accessed. Injury severity was assessed using the AIS. The subjects were divided into two groups: intoxicated (BAC ≥0.08%) and nonintoxicated (BAC <0.08%).	The pre-hospital GCS was significantly lower in the intoxicated group (p<0.001). The median change in GCS from pre-hospital to emergency department worsened in the non-intoxicated group (p=0.039) and remained stable in the intoxicated group (p=0.09). The change in GCS between the emergency department and day 1 in the intoxicated group was significantly greater than the non-intoxicated group (p<0.001). The piecewise regressed analyses revealed that in the intoxicating range, BAC is positively related to changes in GCS indicating higher BAC is associated with better improvement (p<0.0001). Emergency department GCS was also significantly related to changes in GCS indicating more severe emergency department GCSs are associated with better improvement (p<0.0001). AIS was also significantly associated with GCS changes indicating high AISs are related to greater improvement (p<0.0001).
Vickery et al., (2008) USA Cohort	**N= 1,748** All were enrolled in the Traumatic Brain Injury Model Systemsresearch and demonstration program at the time of the study, were 16 years or older, arrived at a trauma	Acute LOS was not associated with blood alcohol levels, binge drinking or frequency of drinking (p>0.05), it was however, correlated to GCS (p<0.01). No interaction effects were noted when looking at DRS at admission or

	centre within 72 hours of injury and received both acute and inpatient care.	FIM scores between alcohol history and blood alcohol levels. Age, education level, LOS, GCS and blood alcohol levels were related to DRS ($p<0.05$ for all). For individuals who were over the legal limit and less than double the limit, their DRS scores were .70 units higher than person with no alcohol in their blood ($p=0.05$). Alcohol related variables were not associated with FIM cognitive scores or FIM motor scores.
Stuke et al., (2007) Cohort	**N=108,929** GCSs of those who tested positive to alcohol testing were compared to those who tested negative following an ABI. Data from the National Trauma Data Bank of the ACS (1994-2003) was used.	Although there were more males in the alcohol group, there were no significant differences on the GCS between the genders. Overall alcohol use did not result in a clinically significant reduction in GCS.
Sperry et al., (2006) USA Retrospective Chart Audit	**N=1,075** Patients charts from 1995 to 2004 were reviewed. Patients were placed in one of two groups: the non-intoxicated (n=571), and the intoxicated (n=504) group.	More intoxicated subjects were injured through a physical assault (18%) or being struck by a car (10%) than being injured in a MVA (40%) compared to the non-intoxicated subjects. Overall it was noted that there was no relationship between alcohol intoxication and GCS; no linear relationship was found between blood alcohol concentration and GCS, nor was there a mean difference between the GCS in both groups (intoxicated and non-intoxicated).

Note: ABI = Acquired Brain Injury; ACS = American College of Surgeons; AIS = Abbreviated Injury Score; BAC = Blood Alcohol Concentration; CAGE = Cut down, Annoyed, Guilty, Eye-opener; CT = Computed Tomography; DRS = Disability Rating Scale; ETOH = Ethanol; GCS = Glasgow Coma Score; LOS = Length of Stay; MVA = Motor Vehicle Accident; TBI = Traumatic Brain Injury

Discussion

Several studies have investigated the effects of alcohol and/or other chemical substances on GCS, and length of stay in ICU (Vickery et al., 2008; Sperry et al., 2006). It has been noted by Andelic and colleagues, that patients diagnosed with a less severe TBI more frequently report substance use at the time of injury ($p=0.01$) while those diagnosed with a more severe injury frequently report pre-injury substance abuse (30 vs 23%) (Andelic et al., 2010). Sperry et al. (2006) no relationship between alcohol intoxication and GCS, nor did they find a linear relationship between blood alcohol concentration (BAC) and GCS. One study found a higher BAC was found to be associated with a better improvement in GCS over time (Shahin et al., 2010). Although it has been suggested that the presence of alcohol or other substances leads to a greater risk for poorer outcomes, no conclusive evidence was found. Further research needs to be conducted to determine conclusively the effects alcohol and other substances have on severity of TBI.

The impact blood alcohol levels have on GCS, ISS, mortality, and long term outcomes has yet to be determined.

8.5.2.2 Effects of Substance Use on Mortality

The protective role of elevated levels of serum ethanol levels (ETOH) and TBI continues to be debated. Recent research indicates alcohol acts as a neuroprotective agent and plays a role in survival post injury (Berry et al., 2010). Further, earlier studies have found that mortality was not more common in those who had been intoxicated at time of injury (Kelly, 1995). Despite the numbers of studies looking at levels of intoxication, length of hospitalization, TBI severity and mortality a solid link has not yet be made (Berry et al., 2010; Kelly et al., 1997).

Individual Studies

Table 8.27 Effect of Substance Use on Mortality Post-ABI

Author/Year/ Country/Study Design/PEDro Score	Methods	Results
Berry et al., (2010) USA Retrospective Study	**N= 7304** subjects who had ETOH levels measured on admission were selected from the Los Angeles County Trauma System database. The patients who tested positive for ETOH were compared to the patients who tested negative for ETOH on several parameters.	44% of patients tested positive for ETOH on admission. In comparison to ETOH-negative patients, ETOH-positive patients were younger (p<0.0001), more frequently male (p<0.0001), had less severe injuries (p<0.0001) and lower GCS (p<0.0001). A lower mortality rate was observed in ETOH-positive patients (p=0.005). A logistic regression revealed the presence of ETOH in patient's blood was associated with reduced mortality (p=0.035).
Salim et al., (2009) USA Retrospective Study	**N=482** Trauma patients admitted from Jan 2000 to Dec 2005 who had sustained a severe TBI and a measure of serum ETOH level at admission were selected for the study. The subjects were divided into two groups: ETOH-positive and ETOH-negative. Outcome variables were survival, ventilator days, ICU and hospital length of stay, and complications.	Of the 482 subjects selected for inclusion, 37% of them were ETOH-positive. The subjects in the ETOH-positive group had a higher percentage of males (p=0.001), lower percentage of penetrating injuries (p=0.002) and lower ISS (p=0.05). Hospital mortality was lower in the ETOH-positive group compared to the ETOH-negative group (p=0.004). ETOH-positive subjects had higher rates of sepsis (p=0.01). The mean serum ETOH level was greater for survivors than non-survivors (p=0.001).
Salim et al., (2009) USA	**N=38,019** Trauma patients from the National Trauma Data Bank injured between 2000 and 2005 who had	37.9% of the subjects tested serum alcohol levels were positive. The ETOH-positive subjects were younger (p<0.001), had lower

Retrospective Study	sustained a moderate to severe TBI were included in the sample. Only subjects who had their serum ETOH levels measured at admission were divided into two groups: ETOH-positive and ETOH-negative. The outcome variables included complications, hospital and ICU length of stay, days spent on ventilator, discharge disposition, functional independence score and mortality.	ISSs ($p<0.001$) and lower GCSs ($p<0.001$). They were also more likely to have positive toxicology for illicit drug use ($p<0.001$). After adjusting for the differences between the tested and non-tested groups, ETOH-positive subjects had reduced mortality ($p=0.005$) and more complications ($p<0.001$).
Shandro et al., (2009) USA Cohort	**N=1,529** Those with an AIS score of 3 or more were included in the following study. BACs were measured on all participants. Patients were contacted at 3 and 12 months post injury. All were diagnosed with a moderate to severe brain injury.	Results indicate that alcohol status had no effect on the survival rates of patients either in the acute stage, 3 months post injury or 1 year post injury.
O'Phelan et al., (2008) Chart Audit	**N=483** Chart audits were completed on those who were admitted to hospital between 2001-2006.	Of the 483 charts reviewed, 331 patients were found to be intoxicated at the time of injury. Several of these also tested positive for other chemical substances. Those who tested positive for methamphetamine and alcohol were found to have decreased mortality. Individuals who tested positive for methamphetamine often tested positive for marijuana.
Tien et al., (2006) Canada Cohort	**N=3675** of the patients seen over a 16 year period, 3675 were found to meet inclusion criteria.	Males were more likely to have a higher BAC than females and younger individuals were more likely to have higher BAC than older individuals. It was also noted that those with a severe head injury and a higher BAC level tended to have a higher mortality rate; however those with lower BAC levels or moderate levels had a significantly lower risk of dying then those with no BAC ($p=0.008$).
Alexander et al., (2004) USA Chart Audit	**80** Patient charts were audited 3, 6 and 12 months post injury. The subjects were divided into three groups based on their BALs at admission: 0 mg/dL, 1-100 mg/dL and >100 mg/dL.	A relationship was found between the serum alcohol levels and GCS. There was also a relationship between CBF and serum alcohol levels ($p=0.02$) but there was no significant association between serum alcohol levels and GOS at 3, 6 or 12 months. Serum alcohol levels >100mg/dL were associated with a decrease in global CBF. The three groups had similar mortality rates.

Note: AIS = Abbreviated Injury Scale; BAC = Blood Alcohol Concentration; BAL = Blood Alcohol Level; CBF = Cerebral Blood Flow; ETOH = Ethanol; GCS = Glasgow Coma Score; GOS = Glasgow Outcome Score; ICU = Intensive Care Unit; ISS = Injury Severity Score; TBI= Traumatic Brain Injury

Discussion

Over the past couple of decades several studies have investigated the effect of BAL on mortality post TBI. Tien et al. (2006) found that moderate or low BAC levels lowered the risk of dying in those who had sustained a severe TBI. Study findings, from each of the studies looked at, suggest elevated BAL is not associated with an increase risk of mortality post injury (Salim et al., 2009a, 2009b; Shandro et al., 2009; O'Phelan et al., 2008; Tien et al., 2006; Berry et al., 2010). Further, O'Phelan et al. (2008) in a recent study looking at the effect of BAL, cannabis and amphetamines found not only was alcohol associated with a decrease in mortality, methamphetamine was also associated with a decrease in mortality. Further research needs to be conducted to determine conclusively the effects alcohol and other substances have on severity of TBI.

Although alcohol and elevated BALs has been linked to an increase risk of sustaining a TBI, there is however no evidence that elevated BALs are linked to an increase risk of mortality post injury. The possible neuroprotective role acute alcohol intoxication plays in a TBI warrants further investigation.

8.5.3 Post-injury Recovery and Substance Addiction

If individuals continue to use or abuse alcohol or drugs post injury, the impact on their recovery is a negative one. In a recent survey of 43 treatment centres across Canada, West et al. (2009) found that those with a disability (TBI, spinal cord injury, multiple sclerosis, psychiatric disabilities, etc.) had very low participation rates in rehabilitation programs. Continued use of alcohol or other substances may increase levels of aggressiveness, risk of seizures, decrease their satisfaction with life and increase family stress.

Substance abuse often impacts the neurotransmitter process making it difficult to assess the impact the brain injury has had on the individual. Many individuals have been found to spend more time in rehabilitation programs as alcohol addiction, in particular, has been found to accentuate sensory motor, cognitive and communication problems post injury (Wehman et al., 2000). Continued substance abuse further complicates the recovery process (DeLambo et al., 2008), as many admitted to rehabilitation programs find their treatments delayed as they go through the withdrawal process (Wehman et al., 2000). Continued involvement with alcohol and other substances increases the risk of developing medication complications.

Assessing their responses in rehabilitation programs has been proven difficult. Many, as a result of past involvement with substances, do not meet the inclusion criteria for experimental trials. For many, involvement in rehabilitation deters or prevents individuals from using various substances as patients are monitored rather closely (Bjork and Grant 2009). Once patients are discharged from brain inpatient rehabilitation, no

monitoring exists and patients may return to their previous behaviours or begin using drugs and alcohol as a coping strategy. Alcohol and other substance addictions may lead to a failure to survive independently in the community (Burke et al., 1988).

Individual Studies

Table 8.28 Influence of Substance Use or Abuse on Neuropsychological Outcomes Post-ABI

Author/Year/ Country/Study Design/PEDro Score	Methods	Results
Schutte & Hanks, (2010) USA Case Series	**N=482** subjects were selected from the Southeastern Michigan Traumatic Brain Injury System who had a GCS of < 13 or between 13-15 with evidence of intracranial bleeding on the CT. Only subjects without penetrating injuries were included. Outcome measures were BAL, GCS, TMT, RAVLT, WCST and a total FIM score. Tests were administered after each subject emerged from post-traumatic coma.	A significant negative correlation between GCS and BAL was found (r=-0.23, p<0.01). Three regression analyses to predict functional outcomes were significant: FIM at admission, FIM at discharge and FIM at 1 year (p<0.01 for all). BAL only predicted functional outcome at admission to rehabilitation (p<0.05) while age at time of injury predicted functional outcomes at admission, discharge and 1 year. Three regression analyses to predict cognitive outcomes at 1 year were significant: TMT-A, TMT-B and WCST (p<0.01 for all). BAL did not predict cognitive outcomes while age at time of injury predicted TMT-A, TMT-B and WCST performance at 1 year (p<0.05 for all).
Wilde et al., (2004) USA Retrospective Study	**N=77** consecutive patients admitted to a rehabilitation unit who met inclusion criteria were included in the study. The subjects were divided into two groups: TBI+BAL (>10 mg/dL of serum alcohol at admission) and TBI-only (no evidence of positive BAL at admission). Information about cause of injury, toxicology findings, substance dependence/abuse diagnoses and pre-injury alcohol use were extracted from charts. The highest GCS within 24 hrs of injury was used. The WAIS-R and WMS-R were used to assess intellectual capacity and memory functioning. Outpatient MRIs were used to assess TICV, total brain volume, CSF volume and total ventricular volume.	There was a significant difference between the ventricle-to-brain ratio in the two groups (p=0.009). TBI+BAL subjects had more atrophy when examining brain volume (p=0.002), CSF (p=0.002) and total ventricular volume (p=0.045). Differences between subjects with no alcohol serum, mild, moderate and heavy alcohol serum were significant for quantitative MRI measures such as ventricle to brain ration (p=0.05), whole brain volume (p=0.001) and CSF volume (p=0.001) such that increased alcohol abuse was associated with increased atrophy.
Tate et al., (1999)	**N=67** The medical charts of **s**ubjects from three different TBI admission	Subjects with high admission BAL were more likely to have a history of alcohol

USA Retrospective Study	sites who had an alcohol abuse history were reviewed. 88% of the sample suffered a moderate to severe brain injury. BAL at admission, history of alcohol abuse and severity of injury were used as independent measures. Dependent measures included the WAIS-R, TMT, WMS-R and WCST.	abuse ($p<0.0001$). Subjects with mild TBI had lower average BAL than those with moderate-severe TBI ($p<0.05$). Poorer performance on WMS-R was negatively correlated with higher admission BAL ($p<0.05$). Fewer failures on WCST was correlated with increased BAL ($p=0.022$). For partial correlations, BAL was negatively correlated with two aspects of the WMS-R ($p<0.05$) and the block design section of the WAIS-R ($p=0.023$). Admission BAL predicted poor verbal recall ($p=0.0156$), poor information retention ($p=0.0359$) and poor visuospatial constructional ability ($p=0.0196$). Education and TBI severity also predicted visuospatial constructional ability (WAIS-R, $p<0.05$). TBI severity predicted number of conceptual categories and set failures on the WCST ($p<0.05$). Age and education predicted time to complete TMT-A and TMT-B ($p<0.05$), while TBI severity predicted TMT-A performance only ($p<0.05$).
Bombardier & Thurber (1998) USA Retrospective Study	**N=58** patients within 60 days of TBI were administered a series of neuropsychological tests as part of their in-patient rehabilitation program. 91% of the subjects incurred a moderate to severe TBI. The NCSE assessed cognitive functioning, the TMT forms A and B assessed psychomotor speed, concentration and cognitive flexibility, the RAVLT assessed memory span, verbal learning and recall. Levels of blood alcohol serum above 100 mg/dL from routine laboratory testing indicated legal intoxication.	NCSE orientation ($p<0.01$), NCSE naming ($p<0.005$), NCSE verbal memory ($p<0.005$) and NCSE similarity ($p<0.05$) scores were inversely correlated with BAL at time of injury. Time to complete TMT-A was positively correlated with BAL ($p<0.05$). When looking at those with a positive BAL at time of injury, NCSE attention span ($p<0.05$) and NSCE judgment ($p<0.05$) and RAVLT total score ($p<0.01$) were added to the list of variables negatively correlated with BAL. Subjects tested <30 days post-injury to those tested >30 days post injury were compared. After 30 days only two variables were negatively correlated with BAL, NCSE memory ($p<0.05$) and NCSE similarities ($p<0.05$). Before 30 days, NCSE orientation, NCSE naming, RAVLT total and TMT-A time were correlated with BAL.
Kelly et al., (1997) USA/Israel Cohort	**N=119** Patients admitted to hospital following a TBI were divided into one of three groups: normal toxicology screen (NS=50), positive alcohol screen (ETOH=52), and those with a positive drug screen (DRUG=17). All individuals underwent a	Results indicated that those in the NS group showed better neuropsychological performance on the WAIS-R and the WMS-R than those in the ETOH and DRUG groups. Scores on the TMT and the WCST showed no significant difference between the ETOH and DRUG groups.

	neuropsychological assessment and the results were compared across the three groups. The WAIS-R, WMS-R, TMT and the Wisconsin Card Sorting Test (WCST) were all administered	

Note: AA/D = Alcohol Abuse or Dependence; BAL = Blood Alcohol Level; CSF = Cerebrospinal Fluid; CT = Computed Tomography; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; FIM = Functional Independence Score; GCS = Glasgow Coma Score; MRI = Magnetic Resonance Imaging; NCSE = Neurobehavioral Cognitive Status Examination; RAVLT = Rey Auditory Verbal Learning Test; TBI = Traumatic Brain Injury; TICV = Total Intracranial Volume; TMT = Trail Making Test; WAIS-R = Wechsler Adult Intelligence Scale-Revised; WCST = Wisconsin Card Sorting Test; WMS-R = Wechsler Memory Scale-Revised

Discussion

Studies investigating the impact of substance use or abuse on neuropsychological outcomes post-ABI have resulted in conflicting results. Of the 482 individuals examined post admission to the emergency room, Schutte and Hanks (2010) found the relationship between TBI severity, GCS and BAL was significant ($p<0.01$), as was age at time of injury, BAL, GCS in predicting FIM scores at time of admission to rehabilitation. When assessed at the one year follow up cognitive functioning and overall FIM scores did not appear to be impacted by BAL at time of injury.

In an earlier study Tate et al. (1999) found BALs were predictive of poorer performance on a variety of neuropsychological measures during post acute recovery. Poorer recall was found on the WMS-R logical memory 2, the WMS-R logical memory residual test, and the WAIS-R block design. Overall study authors suggest an increase in BALs predicts greater cognitive impairment. Similar results were noted in a study conducted by Bombardier and Thurber (1998). Here BALs predicted poor performance on orientation tasks, concentration and mental speed, naming abilities, verbal memory and abstract reasoning. Wilde and colleagues (2004) also noted that an increase in alcohol abuse was associated with increased brain atrophy post injury.

Earlier studies indicate elevated BALs are associated with poorer performance on a variety of cognitive communication tasks; however, these finding have not been supported in more recent studies. More research needs to be conducted investigating the impact of alcohol on cognitive outcomes post injury.

8.5.4 Substance Abuse Treatment Post ABI

Until recently very few studies looking at treatments to address addictive behaviours post ABI were available. Several theories have been put forth as to the types of programs that might reduce substance abuse in the TBI population, but little research was found supporting these theories. A recent study by Corrigan and Bogner (2007) was conducted looking at using financial incentives to encourage those with a TBI and substance abuse problem to remain in treatment. In a systematic review, Corrigan and

colleagues (2010) concluded that research focused on interventions for substance abuse specifically excluded participants with severe TBI.

Individual Studies

Table 8.29Compliance with Substance Addiction Treatment Programs Post ABI

Treatments		
Author/Year/ Country/Study design/ PEDro Score	**Methods**	**Results**
Sander et al., (2012) USA RCT PEDro=5	**N=104** Participants who had emerged from PTA, and were diagnosed with a mild, moderate or severe TBI participated in the current study. Individuals were randomly assigned to either the treatment group or the control group. Intervention took approximately 20 minutes to complete. Those in the treatment group participated in a 10 minute educational DVD that described the potential negative effects of alcohol abuse after TBI. Participants were asked to carefully consider the pros and cons of substance abuse. Following this, they completed a visual analogue scale related to how important they felt abstinence from alcohol and drug use was. A motivational interview using open ended questions with each participant followed. The control group received information and referral services typically given to those with an substance addiction issue. All were assessed 3 months later.	Individuals who attributed their TBI to alcohol use, indicated alcohol use could result in physical and cognitive impairment. Overall the treatment did not have any effect on readiness to change or problem alcohol use.
Tweedly et al., (2012) RCT USA PEDro=5	**N=60** Participants were randomly assigned to (1) informal discussion group,or (2) the brief information group, or (3) the information plus brief motivational interviewing. Informal Discussion: general 30 minute discussion about changes that had occurred since their injury. Brief Information sessions had participants engaging in the informal discussion along with receiving an information	Prior to the introduction of the interventions, there were no differences between the two groups and the amount of alcohol consumed with 16.7% reported drinking at harmful or hazardous levels. AT the 6-9 month follow up all reported a large consumption rate for alcohol. Those in the ID group reported consuming more alcohol over time; however the total time line follow back (TLFB) scores were not significantly difference between the three groups. Over all there were no significant differences between

	package that consisted of a short DVD a booklet outlining cognitive, physiological and behavioural changes that can occur following a TBI. Those in the information plus brief motivational interviewing received both interventions. Assessment took approximately 2 hours to complete. Follow-up assessment was conducted 6 months post intervention	the groups and the amount of alcohol consumed or number of days drinking.
Corrigan and Bogner (2007) USA RCT PEDro=5	**N=74** Subjects with TBI in the following study were randomly assigned to one of 3 groups: provision of financial incentives to not miss appointments (n=24); reduction of logistical barriers to attending appointments (n=26); and attention control (n=24). Intervention was delivered via a phone call. Intervention included a $20 fee for participation. Treatment program was designed for substance abusers who had sustained a TBI. To assess the effectiveness of the intervention the following scales were completed: Employability rating scale (ERS), Satisfaction with Life Scale (SWLS), Readiness to Change Questionnaire (RTC), Trail making test (TMT)	Receiving financial incentives resulted in few missed appointments, compared to those who had specific barriers (poor memory, transportation issues) removed ($p<0.001$). There was no statistically significant differences in the number of missed appointments between the barrier group and the control group ($p<0.318$). Interventions offered did not affect the client or counsellor therapeutic relationship. Receiving financial incentives or having barriers reduced did not have any significant effect on premature termination from treatment.
Corrigan et al., (2005) USA	**N=195** Subjects with TBI were randomly assigned to one of 4 groups: barrier reduction, motivational interview, financial incentive and attention control group. The interventions were delivered over the phone. The outcome measures were the proportion of subjects who signed and ISP, the average time to signing the ISP, average number of missed appointments and the proportion of subjects who terminated treatment prematurely. These variables were taken at 3 months after injury and 6 months after injury. The following instruments were used: TMT, RTC questionnaire, NCSE, ASI. ERS and SWLS.	The proportion of participants who signed the ISP differed among the conditions ($p<.001$). Financial incentive and barrier reduction were better than the other groups at signing their ISPs. The conditions also differed in days to sign the ISP ($p=0.01$) such that financial incentive and motivational interview differed from each other ($p<0.001$). At 6 months following injury, 29.2% of participants had terminated substance use direr treatment prematurely, this differed significantly by condition ($p<0.05$). The financial incentive and barrier reduction conditions had fewer premature terminations than the attention control condition ($p<0.05$).
Treatment Outcome		
Author/Year/ Country/Study Design	**Methods**	**Outcomes**

Bogner et al., (1997) USA Retrospective Study	**N=72** Subjects were consecutively selected to receive a substance abuse treatment plan. Some of the subjects had a community team while others did not. A comprehensive assessment was conducted before treatment planning and 1 year after the initiation of the treatment plan. The assessment included a structured interview with the client and a family member, QFVI, GHHQ, ASI and the ERS.	75% of participants had a positive substance abuse outcome – 18% maintained abstinence, 32% attained abstinence and 25% reduced alcohol use. A significant difference in abstinence was found between initial assessment and 1 year follow-up was found ($p<0.05$). 60% of participants had a positive productivity outcome – 21% maintained competitive employment, 27% attained competitive employment, 4% maintained productivity and 9% attained productivity. Participants with a community team had more positive substance abuse outcomes ($p<0.05$).

Note: PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002).
ASI = Addiction Severity Index; ERS = Employability Rating Scale; GHHQ = General Health and History Questionnaire; ISP = Individualized Service Plan; NCSE = Neurobehavioral Cognitive Status Exam; QFVI = Quantity-Frequency-Variability Index; RTC = Readiness to Change; SWLS = Satisfaction With Life Scale; TBI = Traumatic Brain Injury; TMT = Trail Making Test

Discussion

Recently several studies have been conducted looking at the effect of motivational interviewing (MI) coupled with information sessions had on return to drinking post TBI (Tweedly et al., 2012; Sander et al., 2012; Ponsford et al., 2012). In two of these studies individuals were randomly assigned to an informal discussion group, an information group or an information plus brief motivational group. Participants were also stratified by gender (Tweedly et al., 2012; Ponsford et al., 2012). Sanders and colleagues (2012) randomly assigned participants to either a control or treatment group. Those in the control group viewed a 10 minute DVD describing the negative effects of alcohol and drug use post TBI. Those in the treatment group viewed the video and then engaged in a motivational interview. Results from each of these studies indicate that the intervention provided did have a significant effect on drinking post injury or on willingness to change drinking habits. Sanders et al. (2012) found those with a more severe injury expected alcohol used would negatively impact cognitive and physical impairments. Ponsford et al. (2012) noted that higher education and higher levels of depression were also associated with greater alcohol consumption.

In a study conducted in Corrigan and Bogner (2007) subjects with a diagnosed substance abuse problem were randomly assigned to one of 3 groups. Interventions were given during a telephone interview conducted with a trained staff. One group of participants was randomly assigned to the barrier reduction group. These individuals identified that they had problems with remembering the appointments, not being able to afford parking, not having child care, and not being able to afford lunch while they attended the intervention program. These issues were addressed by the interviewer offering to provide compensation to the subject. Another group was offered $20.00 to attend the intervention program. Results indicate that offering a financial incentive was more effective in promoting compliance attending treatment sessions than reducing barriers.

The third group was initially contacted by phone and asked to verify specific pieces of information on the subject. A letter reminding the subject of their next scheduled appointment was sent to the subject following the interview. Results indicate that those in the financial incentive group attended more treatment sessions than subjects in the barrier reduction group. Financial incentives appeared to enhance the relationship between the subjects and the councillors involved with the treatment program.

Conclusion

There is Level 2 evidence suggesting that neither education nor motivational interviewing has a significant impact on excessive alcohol consumption post TBI.

There is Level 2 evidence supporting the use of financial incentives to encourage participants to continue with their substance addiction therapy following an ABI; however addressing the barriers preventing individuals from attending was not found to be successful.

Education and motivational interviewing do not appear to have a strong impact on excessive alcohol consumption post TBI.

Providing financial incentives does encourage those with a TBI and a substance addiction to attend treatment more so than offering solutions to other barriers.

8.6 Restraints

8.6.1 Prevalence and Incidence of Restraint Use

Due to the continued concern to insure safety of both patients and staff in hospitals and long term facilities, the use of restraints continues to be part of common clinical practice; however this use remains controversial. Following an acquired or traumatic brain injury (ABI/TBI) the incidence and prevalence of agitation or aggressive behaviors ranges from 10% to 96%. Studies have found as many as 17%-32% of survivors may be restrained while undergoing care in either an acute or rehabilitative hospital (Gregory, Jr. and Bonfiglio 1995; McNett et al., 2012; Stubbs and Alderman 2008). However; due to the broad definition of agitation the reported numbers of agitated patients may be misleading, raising questions about the numbers of those who may actually need to be restrained (Eisenberg *et al.,* 2009). Results from a recent study indicate impulsiveness, pulling at devices or removing endotracheal tubes, central venous lines and other life support measures and decreased attention span are often cited as reasons for the use of a restraint (McNett et al., 2012). As well many care professionals indicate the use of restraints prevents the individual from falling and further injuring themselves (Schleenbaker et al., 1994; Mion et al., 1996; Kow and Hogan 2000). Another common

reason cited for the use of restraints is to protect individuals (hospital staff, other patients or family members) from patients felt to be dangerous or aggressive (Mion et al., 1996; Kow and Hogan, 2000).

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 behaviors that occur during agitated states include many pharmaceutical agents with primary or secondary psychotropic effects, including: beta blockers, anti-depressants, psychostimulants, anti-Parkinson's agents and anti-convulsants (Gregory, Jr. and Bonfiglio1995; McNett et al.,2012). Medication treatments used in non-emergent situations to reduce the need for physical restraints include propranolol, atypical neuroleptics and valproic acid (Busch and Shore 2000).

Physical restraints have been defined as any manual method that immobilizes or reduces the ability of individuals to move their arms, legs, body, or head freely (Busch and Shore 2000; Stevens 2012) and may be used as an alternative to prescribing medications (Beaulieu et al., 2008). Often restraints are attached or placed adjacent to the patient's body and they cannot be easily removed by the patient; they are designed to restrict movement; and are not meant to be a part of the standard practice of care (Amato et al., 2006). Physical restraints include the use of bed rails, feeding trays, mittens (tying of hands), chest straps (seat belts), ankle and wrist restraints, and jacket restraints (Gregory, Jr. and Bonfiglio 1995; Busch and Shore 2000; Marks 1992; Morrison et al. 1987).

Policies related to the application of restraints often state: the restraint should be individualized and offer as much dignity to the individual as the situation allows: they must be humanely and professionally administered; safety protocols must be in place; patients must be observed while in the restraint; careful documentation of the reasons for and means of restraint and the means for observation while in the restraint must be made; the method or choice of restraint must be the least restrictive as possible (Ontario College of Nurses, 2009; St. Joseph's Health Care Restraint Policy 2012; American Nurses Association, 2012)

The decision to use restraints, whether mechanical or chemical is generally made by physicians or nurses on the unit and it must be accompanied by a "permission slip" signed by the family or caregivers indicating they are in agreement. Previously, in a study conducted in a Canadian hospital, Kow and Hogan (2002) found either chemical or physical restraints were used in 18 of 156 patient charts reviewed. They also noted that despite hospital policy the "orders" approving the use of restraints were missing from some charts, while a blanket or restrain as needed (PRN) orders was placed on other charts. Within the nurses' notes there were indications of when restraints should be used but this was often "vague or questionable" (Kow and Hogan, 2002). The use of a chemical restraint was accompanied by prescriptions for time and dosage; however,

neither type of restraint was accompanied by guidelines for the length of time it should be used.

Earlier Mion and colleagues (1996) noted that physicians and nurses rarely discuss the use of a physical restraint and the necessary documentation or "order" to use one is often not on the chart. They noted both physicians and nurses found this to be an "unnecessary and benign thing" to do. These findings were also noted in a study conducted by MacPherson et al. (1990). Here both nurses and physicians were surveyed regarding the use of restraints on medical patients. In 71 cases nurses made the decision to restrain and physicians made the decision in 23 cases. Twenty-eight percent of physicians indicated they left orders to restrain on the patient chart. Study authors found the documentation related to a patient being restrained was missing from the nurse's or physician's daily progress notes (Macpherson et al., 1990).

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. Least likely were geriatricians. Further, male doctors were more likely to order restraints than female doctors and they were more likely to order them for male patients. Again, when asked why they would order a restraint 50% of those surveyed indicated they would do so to prevent falls, or to reduce the risk of therapy being disrupted (Sandhu et al., 2010). Despite this stated need to restrain to prevent falls there is no evidence to suggest this procedure is effective; however there is some evidence to suggest it puts patients at a greater risk of injury (Busch and Shore2000; Mion et al., 1996; Mion et al., 2010; Evans and Fitzgerald 2002).

8.6.2 Reasons Cited for their Use

A great deal of study has been conducted looking at the use of physical restraints in nursing homes or in acute care hospitals (Ludwick et al., 2008; Evans and Fitzgerald 2002). The nursing literature indicates the use of restraints is influenced by the values, education, beliefs of the nurses themselves, behaviors and the demographic characteristics of the patients (Ludwick et al., 2008). Patients in physical restraints have been found to have higher rates of clinical agitation as did patients who require constant supervision (Minnick et al., 2007; Morrison et al., 1987; McNett et al., 2012; Visscher et al., 2011). Recently McNett et al. (2012) noted reorientation, redirection, constant supervision, the administration of benzodiazepines, restraints, and/or modifying the patient's environment were used most often to manage agitation post TBI. Of concern and despite hospital policies, the findings from many of these studies indicate the necessary documentation and permissions for using restraints was not readily available (Morrison et al., 1987; McNett et al., 2012; Minnick et al., 2007).

In an earlier chart audit, completed by Morrison and colleagues (1987), 13.2% of the patient population was managed with restraints. Many restrained were individuals who had a diagnosis of organic brain syndrome and were over the age of 65. Further in the acute care setting an elevated use of restraints was noted on the general medicine or

neurosurgery units. Jacket restraints and lap belts were primarily used. Of concern was the absence of the documentation regarding the decision making process and approval was notably absent from the charts. In a chart audit conducted by Schleenbaker and colleagues (1996), restraint orders appearing on patient charts were simply written "restrain as needed". These orders were written for more than 75% of individuals admitted for rehabilitation. Of those who were admitted for a traumatic brain injury approximately 90% had restraint orders appearing on their chart. Study authors did not indicate if the behaviors being displayed by patients justified this "generic" order.

More recently Evans and Fitzgerald (2002) found the main reasons for using restraints were controlling agitation or acts of aggression, behavior control related to altered mental status and confusion, prevent wandering of the unit, patient safety related to impaired mobility, supporting patient's posture or sitting balance. These reasons were noted in both the acute care literature and the nursing home literature. More recently Minnick and colleagues (2007) found the most commonly cited reasons for using restraints were to prevent disruption of therapy, confusion, to manage behavior and to prevent the individual from falling. In this study physical restraints used included the use of wrist restraints which was used in approximately 80% of incidents. Other restraints used were the vest, mittens, leg restraints or waist belts. In many cases two or more restraints were used.

Visscher and colleagues (2011) found 42% of the study population, which included ABI patients (n=24), had engaged in one or more aggressive acts prior to the patients being restrained. During a 17 week period three or more aggressive acts were dealt with daily. Aggression was measured using the Staff Observation Aggression Scale-Revised. Although the majority (67%) of aggressive incidents was judged to be mild in severity, 33% were documented as severe. Often these incidences were triggered by asking the individual to engage in an activity or take medications, or the individual required help with his or her ADLs (Visscher et al., 2011).These aggressive outbursts, which were primarily directed toward staff, were dealt with by talking to the patient, staff walking away, medication, physical restraints, and time outs (Visscher et al., 2011). Acts of aggression - either physical or verbal - were more prevalent with male patients. A higher level of aggression was also related to an increase length of stay. Lower Functional Independence Measure (FIM) scores and Mini Mental State Examination (MMSE) scores were also found in those with a higher frequency of aggression (Visscher et al., 2011).

Suen and colleagues (2006) conducted a survey of nurses in 2 rehabilitation settings in Hong Kong. The majority of nurses who responded did know a consent form was needed prior to using a restraint, they explained to the patient why the restraint was being applied and they knew the restraint had to be released every 2 hours. Respondents also indicated they felt restraints could prevent falls and over 70% felt the use of restraints enabled nurses to spend less time on nursing care. Results indicate the majority of respondents were not aware of any of the suggested alternatives (manipulating the

environment, supervision, companionship, reviewing prescribed medications) to the use of a restraint.

8.6.3 Physical Restraints and their Effectiveness

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 a TBI or ABI (Marks 1992) The use of restraints is considered acceptable if the restraint is used to ensure the patient's safety; if less restrictive interventions have been ineffective in preventing harm to the patient or others; if the restraint is implemented safely, 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 and Shore 2000). Currently there is not enough data available to determine the efficacy of using physical restraints to reduce agitated or aggressive behavior post ABI (Duxbury and Wright 2011).

Despite their use, there is no evidence to support the use of restraints in those who have sustained an ABI/TBI.

According to legislation currently in the province of Ontario, when patients are restrained or confined, hospital staff have a duty to monitor and reassess the patient in accordance with the regulations. They are also required to keep accurate records about why the individual is being restrained and how they will be monitored (Patient Restraints Minimization Act, 2001-MOH-LTC). In accordance with the province's legislation, the College of Nurses for Ontario suggests that the following information is to be recorded when using restraints: significant patient behaviors, alternative considered and used, date and time of application, reason given to patient, type used, reason for choice and patient's response. According to Morrison and colleagues (1987) the individual who is restrained must be monitored every two hours and the situation must be reevaluated every eight.

Alternatives to using restraints has been legislated in several countries. In England and New Zealand altering staff patterns and manipulating the environment is used to manage patients, restraints is not considered a management option (Mion et al., 1996). In New Zealand, restraint use must be reported and the reason for it must be documented on an incident form. The process that is expected to be followed by hospital staff includes: an assessment of the patient, consent from patient or family/caregiver, report and document and notify the patient's physician, and monitor and observe the patient (Mercy Hospital Dunedin, Nursing Services Policy Manual). In the USA the OMNIBUS Budget Reconciliation ACT (1987) states individuals in nursing homes have the right to be restraint free. This policy change resulted in a reduction in

the number of restraints used; however, it remains unclear as to the impact this act has had on the use of restraints in a hospital setting.

8.6.4 Reducing the Use of Physical Restraints (PR)

In many facilities the number one reason cited for the use of physical restraints is the prevention of falls. Several studies have looked at a variety of education programs aimed at staff to reduce the use of physical restraints; however no studies were found that investigated the effectiveness of these programs on an ABI/TBI unit.

Individual Studies

Table 8.30 Education Programs to Reduce the Use of PR.

Author, Year, Country	Objective, Intervention Implemented and Facility	Results
Gulpers et al., (2011) Netherlands	Staff in 13 nursing homes participated in a study looking at a program designed to eliminate the use of restraining belts (EXBELT). Staff members were assigned to the EXBELT group or a control group. The study was conducted over an 8 month period.	Over time a reduction in belts used while in wheelchairs was noted, however the use of belts in bed was not. Staff in the EXBELT program were found to use fewer restraints than staff in the control group. The use of medications (psychoactive drugs) was not impacted by the EXBELT program. Further no significant differences between the groups were found regarding falls, and fall-related injuries as a result of the EXBELT program.
Huizing et al., (2009) Netherlands	In this RCT staff in nursing homes participated in either five 2hour education session delivered over a 2 month period or those in the control group received no education sessions. The program was designed to assist staff in developing a *"restraint free care philosophy".*	Study results indicate the educational program was **not** effective in reducing the use of physical restraints in nursing homes. The most commonly used restraint were bedrails, followed by belts in chairs or beds and sleep suits.
Rask et al., (2007) USA	To reduce the number of falls experienced by patients in nursing homes. The Emory/Ethica Falls Management Program was introduced in 19 nursing homes	The fall management program was found to reduce the number of falls, further the number of restraints used decreased significantly ($p<0.001$) over the study time period.

Discussion

Often the primary reason for the use of restraints in hospitals or nursing homes is to reduce the risk in those who have sustained serious injury or who have been diagnosed with dementia. We examined 3 recent studies investigating the effectiveness of education programs designed to reduce the use of physical restraints on individuals in nursing home. Huizing and colleagues (2009) randomly assigned nursing staff to either a treatment group (educational program) or the control group (no educational program) in an effort to reduce the number of physical restraints used and their frequency. In a study conducted by Rask et al. (2007) a falls management program was introduced to group of nursing homes. This program resulted in the management of fall risk improving significantly and the use of restraints decreasing. In the nursing homes where the program was not introduced the use of restraints did decrease but the risk of falls increased. Study authors concluded the falls management program may be helpful in reducing the risk of falls while reducing the use of restraints. Gulpers et al. (2011) found the introduction of an expelling belts program (EXBELTS), resulted in the reduction of the use of belts.

Staff education programs to reduce the use of physical restraints, without increasing the risk of falls have been shown to be somewhat successful with staff in nursing home. Further research needs to be completed looking at the impact these education programs would have on those staff working in rehabilitation hospitals.

Conclusion

Restraint policies are often prefaced with the hospital's philosophy 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 behavior of an individual. In the earlier study conducted by Mion and colleagues (1996) they state "reducing the use of physical restraints is a challenge" and twenty-five years later despite current hospital policies and the risk of patient injury it continues to be a challenge. It appears as though the clinicians' perceptions of the benefits of physical restraints is without any empirical data to support the purported benefit (Mion et al., 1996 pg 422). Where clinical practice is not in compliance with policy, clinical outcomes are suboptimal. Care in health care facilities should be "*based on the principles of partnership and recovery in practice*" (Brodie, 2009 *p3*). The use of restraints to meet the needs of staff striving to maintain order, routines and rules is no longer considered acceptable.

8.7 Conclusions

1. ***There is conflicting evidence that sertraline is effective in the treatment of major depression post-TBI.***

2. ***There is Level 2 evidence that citalopram aids in the reduction of depression post ABI.***

3. ***There is Level 4 evidence that citalopram and carbamazepine may be efficacious in the treatment of depression, anxiety and mood disorders.***

4. ***There is Level 2 evidence to suggest that the administration of desipramine assists in improving mood and reducing depression.***

5. ***There is Level 2 evidence that individuals with a TBI who participate in exercise programs report feeling less depressed and report experiencing greater quality of life post injury.***

6. ***There is Level 4 evidence that a mindfulness-based stress reduction programme may be efficacious in reducing depressed mood.***

7. ***There is Level 4 evidence that thirty minutes of weak complex (1 microT) burst firing magnetic field across the temporoparietal rigors once per week for five weeks may be efficacious in the treatment of depression.***

8. ***There is Level 3 evidence that music therapy does improve depression and anxiety post ABI***

9. ***There is Level 4 evidence that Systematic Motivational Counselling may reduce negative affect.***

10. ***There is Level 2 evidence that teaching coping skills to individuals post TBI helps to reduce their levels of anxiety and depression.***

11. ***There is Level 2 evidence from one RCT that Cognitive Behavioural Therapy does reduce anxiety post ABI.***

12. ***There is Level 5 evidence from a case study that biofeedback-assisted relaxation training may be efficacious in alleviating anxiety-related symptoms.***

13. ***Although OCD has been identified post ABI there does not appear to be one method of treatment that works for all, but rather treatments remain individualized.***

14. ***There is Level 2 evidence that amantadine did not help to improve behaviour following brain injury.***

15. ***There is Level 4 evidence that carbamazepine decreases the incidence of aggressive behaviours following a TBI.***

16. ***There is Level 5 evidence to suggest that lamotrigine helps to reduce inappropriate behaviours post TBI. More research is needed to validate these findings.***

17. ***There is Level 5 evidence that valproic acid decreases the incidence of aggressive behaviours.***

18. ***There is Level 4 evidence that divalproex decreases the incidence of aggressive behaviour post TBI.***

19. ***There is Level 4 evidence that sertraline HCL and amitriptyline decrease the incidence of aggressive behaviours.***

20. ***There is Level 1b evidence that pindolol decreases aggression following brain injury.***

21. ***There is Level 1a evidence, from 2 RCTs, that propranolol reduces agitated symptoms following brain injury.***

22. ***There is Level 5 evidence to suggest that buspirone may be effective for reducing symptoms of agitation following brain injury. More research is required.***

23. ***There is Level 4 evidence (from one small study) to suggest that quetiapine helps reduce aggressive behaviour.***

24. ***There is Level 4 evidence from one study to suggest that ziprasidone assists in the controlling of aggressive behaviours post TBI.***

25. ***There is Level 5 evidence that an antimanic agent (lithium carbonate) reduces aggressive/agitated behaviour following a TBI.***

26. ***There is Level 4 evidence that an antiandrogen and counselling reduces sexually aggressive behaviour.***

27. ***There is Level 4 evidence that methotrimeprazine is safe and effective for***

controlling agitation after ABI.

28. *There is Level 1b evidence (from one RCT) demonstrating the effectiveness of methylphenidate on performance speed.*

29. *There is Level 4 evidence that the administration of single-dose droperidol calms brain injured agitated patients more quickly than other agents.*

30. *There is Level 4 evidence that haloperidol does not have a negative effect on the success of rehabilitation.*

31. *There is only limited evidence that pharmacological intervention can reduce verbal, physical and or sexual aggression behaviours. More research using a randomized placebo controlled design is needed.*

32. *There is Level 4 evidence that behavioural approach using antecedent management and/or feedback of consequences reduces undesirable behaviour (e.g., aggression/agitation).*

33. *There is Level 1b evidence that social skills training has limited impact on changing inappropriate behaviours and mood disturbances of those who have sustained a severe TBI*

34. *There is Level 4 evidence that social skills training reduces aggressive behaviour.*

35. *There is Level 2 evidence that Natural Setting Behaviour Management may help to change behaviour.*

36. *There is Level 2 evidence that participating in a Coping Skills Group assists in improving adaptive coping in the long term.*

37. *There is Level 2 evidence based on a single RCT that anger management reduces aggressive behaviour.*

38. *There is Level 2 evidence from one non-RCT to suggest that music therapy reduced agitation post PTA.*

39. *There is Level 4 evidence that music therapy reduces psychomotor agitation post-coma following severe TBI in a slow-to-recover group.*

40. *There is Level 4 evidence to suggest that music therapy improves the mood of ABI adults.*

41. ***There is Level 2 evidence suggesting that neither education nor motivational interviewing has an significant impact on excessive alcohol consumption post TBI.***

42. ***There is Level 2 evidence supporting the use of financial incentives to encourage participants to continue with their substance addiction therapy following an ABI; however addressing the barriers preventing individuals from attending was not found to be successful.***

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