6. Mood and Emotional Disorders Post Acquired Brain Injury

On behalf of the ERABI Research Group

6.1 Introduction

Association and Onset of Mood Disorder Symptoms with Acquired Brain Injury

Q. Describe the associations between mood disorders and Acquired Brain Injury.

Answer

- Although mood is an internal subjective state, it is often inferred from our posture, behaviours, and the way we choose to express ourselves.
- Mood disorders such as agitation, major depression, as well as various anxiety disorders including post-traumatic stress disorder and obsessive compulsive disorder may occur following ABI; these conditions are associated with suffering, worsening of other ABI sequelae, and poorer outcomes (Bedard et al. 2003; Berthier et al. 2001; Jorge 2005; Jorge & Starkstein 2005).
- Mood disorders likely arise from the direct involvement of limbic nerve cells in the brain injury process.
- Affective symptoms appear to be important determinants of functional and quality of life outcomes (e.g. reduced social role functioning, poorer quality of life, etc.). These symptoms frequently cause significant distress for individuals with brain injury as well as for their family members and rehabilitation therapists.

6.2 Depression Post ABI

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 (Jean-Bay 2000; Jorge & Starkstein 2005; Seel et al. 2010; Underhill et al. 2003). 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 (Jorge & Starkstein 2005; Ownsworth & Oei 1998; Rosenthal et al. 1998). Psychological stressors, being employed pre injury but not post, and older age are also predictors of depression among the ABI population (Sigurdardottir et al. 2013). Complicating the diagnosis is the lack of consistency in the use of tools used to measure depression post injury (Jorge & Starkstein 2005).

Q. What are the symptoms most often reported by individuals who experience depression post ABI?

Answer

- Individuals who experience depression post ABI may report feeling tired, withdraw socially, have difficulties concentrating, and often feel helpless or hopeless

Q. When do the symptoms of depression begin to become apparent post ABI?

Answer

- Depression in those who have sustained an ABI is often seen once the implications of the injury begin to become apparent.
- For some, 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).

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 13 to 61% (Fleminger et al. 2003; Gordon et al. 1998; Sigurdardottir et al. 2013). The risk for depression is high post 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) may be symptoms of depression or brain injury (Fleminger et al. 2003).

Pharmacological Treatments for Depression

Post-ABI depression is often treated with various pharmacological agents. Included among these are various antidepressants: selective serotonin reuptake inhibitors (SSRIs) such as paroxetine, sertraline, or citalopram; serotonin norepinephrine reuptake inhibitors such as duloxetine; and tricyclic antidepressants such as amitriptyline. The use of tricyclic antidepressants is, however, often restricted to the treatment of headaches in those who have sustained a mild traumatic brain injury (TBI) because their side effects (memory impairment, sedation, etc.) have proven to be problematic in individuals who have sustained a more moderate or severe brain injury (Bajo et al. 1999). Anticonvulsants such as carbamazepine have also been used to treat depression post ABI. Several studies were found which examined the effects of sertaline, citalopram, carbamazepine, desipramine and methylphenidate in the treatment of depression or depressive symptoms post ABI.

Depression Recommendations from ABIKUS Guidelines (Bayley et al. 2007).
Those determined to be depressed should receive appropriate treatment, which can consist of:

- Non-pharmacological treatments, which may include exercise and/or psychotherapy/ counseling
- Pharmacological treatments (SSRIs are the first line of treatment) (ABIKUS B) (G70-p.27)
- Patients and their caregivers should be made aware of the risk of depression following TBI. (ABIKUS C) (G71-p.27)
- Persons with moderate to severe ABI are at future risk of depression and should be monitored on an ongoing basis for development of depression (ABIKUS C) (G72-p.27)

Sertraline

Q. What does the evidence tell us about the effectiveness of sertraline in treating depression post TBI?

Answer

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

Two randomized controlled trials (RCTs) looked at the effects of sertraline on depression post ABI (Ashman et al. 2009; Lee et al. 2005). Ashman et al. (2009) compared sertraline and a placebo and found improvements over time for both groups on all three outcomes, the Hamilton Rating Scale for Depression, the Beck Depression Inventory, and the Life-3 quality of Life scales. No statistically significant differences were shown between the two groups; therefore the changes may not have been related to sertraline. The second RCT added a third arm to their trial. The authors randomized individuals with mild or moderate TBI to a sertraline, methylphenidate or placebo group (Lee et al. 2005). Similarly, to the first study, all participants improved on the depression measures. However, the study results indicated that those assigned to the sertraline and the methylphenidate groups reported significantly less depressive symptoms on these measures than the placebo group at study's end (Lee et al. 2005). Further, fewer adverse events were reported for individuals receiving, methylphenidate than those administered sertraline.

Study Snapshot

A Randomized Controlled Trial of Sertraline for the Treatment of Depression in Persons with Traumatic Brain Injury (Ashman et al. 2009).

- Study participants (N=52) were randomly assigned to either the treatment group (sertraline 25 mg daily to start) or the control group (placebo).
- By the end of the study individuals were on sertraline at doses ranging from 25 mg to 100 mg daily.
- Participants were assessed bi-weekly over a 10-week treatment period using the Hamilton Rating Scale for Depression the Beck Anxiety Inventory, and the Life-3 scales.
- 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 Hamilton Rating Scale for Depression, the Beck Anxiety Inventory and the Quality of Life scales indicated improvement; however, this improvement was noted for both groups suggesting the changes were not related to the administration of sertraline.

Citalopram

Q. What does the evidence tell us about the effectiveness of citalopram in treating depression post ABI?

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

Rapoport and colleagues (2008) administered 20 mg/day of citalopram for 6 weeks to one group while the second group began with 20 mg/day which was titrated to a maximum of 50 mg/day. The second group was studied for 10 weeks. For participants in both groups, their depression scores significantly decreased compared to baseline. In another study participants were randomly assigned to receive citalopram or placebo (Rapoport et al. 2010). Post-treatment relapse rates were calculated for each group and there were no significant differences noted between the groups with individuals relapsing (meeting criteria for major depressive disorder) 22 to 24 weeks post treatment; relapse occurred in 52.4% of patients. In both studies, adverse events were common (Rapoport et al. 2008; Rapoport et al. 2010).

Carbamazepine and Citalopram

Q. What evidence is there for using carbamazepine and citalopram to treat depression post ABI?

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

While citalopram on its own has shown potential to aid with depression, a study by (Perino et al. 2001) found that when citalopram and carbamazepine were given to patients post TBI diagnosed with depression, after 12 weeks, scores on the Brief Psychiatric Rating Scale and the Clinical Global Impression were significantly improved.

Desipramine

Q. What does the evidence tell us about the effectiveness of desipramine in treating depression post ABI?

Answer

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

Wroblewski et al. (1996) conducted a small sample RCT of 10 subjects who received either desipramine or placebo for 30 days, then crossed-over into the alternate group. The study found that desipramine was effective in treating long-standing depression. Three of those in the treatment group and three in the control group had near complete resolution of depression; however, because the control was crossed over to the treatment group, further studies are necessary before firm conclusions are drawn on this medication.

Study Snapshot

Antidepressant pharmacotherapy and the treatment of depression in patient with severe traumatic brain injury: A controlled prospective study (Wroblewski et al. 1996).

- Participants (N=10) were randomly assigned to receive either desipramine (N=6; 150mg/day for 30 days, then 150-300mg/day after) or a placebo (N=4). The groups then crossed-over.
- Diagnostic and Statistical Manual of Mental Disorders-III-revised checklist and the Affect Mood Scale were used to measure improvement in mood.
- Study results indicated all six patients who received desipramine (three patients from each group) had nearly complete resolution of their depressive symptoms.
- Seven subjects showed improvement over time on the Affect Mood Scale (p=0.001). Those in the treatment group showed improvement sooner than those in the placebo group.

Non-Pharmacological Treatments for Depression

Several non-pharmacological treatments have been used to treat depression post ABI including: exercise, team sport involvement, interdisciplinary team support, and counselling (Knottnerus et al. 2007).

Cognitive Remediation

Q. What is the evidence supporting the use of cognitive therapies for depression post ABI?

Answer

- There is Level 1b evidence that both Cognitive Behavioural Therapy and supportive psychotherapy may decrease symptoms associated with depression.

Ruff and Niemann (1990) compared subjects who participated in an eight week cognitive remediation programme with subjects attending a treatment day program. As measured by the Katz Adjustment Scale, both groups experienced a decrease in depressed mood. A more recent RCT compared patients who received 16 weeks of Cognitive Behavioural Therapy (CBT) to patients who received 16 weeks of supportive psychotherapy. Overall depression scores decreased compared to baseline yet no between-group differences were found (D'Antonio et al. 2013).

Exercise

Q. What does the evidence tell us about the impact exercise has on depression post ABI?

Answer

- 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.

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 was investigated (Blake & Batson 2009; Driver & Ede 2009; Gemmell & Leathem 2006; Gordon et al. 1998; Hoffman et al. 2010; Wise et al. 2012). Overall, although improvements in mood were seen with exercise (Driver & Ede 2009; Gordon et al. 1998), it was not always significantly better than the controls (Gemmell & Leathem 2006). A major difference noted was for individuals who exercised more than 90 minutes per week and those who exercised less. Those in the first group (>90 minutes) showed significantly lower depression scores, better mental health and a higher perceived quality of life (Hoffman et al. 2010; Wise et al. 2012). Two studies investigated the benefits of the Chinese exercise methods Tai Chi Qigong (Blake & Batson 2009) and Tai Chi Chaun (Gemmell & Leathem 2006) on those who had sustained a TBI. Results from both these studies found an improvement in mood. However, due to the small sample sizes in each study limited conclusions can be drawn on their effectiveness in reducing depression.

Mindfulness-Based Stress Reduction

Q. What evidence is there supporting the use of mindfulness-based stress reduction programs to treat depression post ABI?

Answer

- There is Level 1b evidence that mindfulness-based stress reduction programs may be efficacious in reducing depressed mood.

Three studies looking at the efficacy of mindfulness-based stress reduction programs on depression post ABI were conducted by Bedard and colleagues (Bedard et al. 2003; Bedard et al. 2012; Bedard et al. 2014). After a small pilot study (Bedard et al. 2003) and a pre-post study (Bedard et al. 2012) with positive results in favour of mindfulness-based stress reduction interventions reducing depression, Bedard et al. (2014) investigated this therapy through an RCT. The programme consisted of 10 weeks of therapy designed to encourage a new way of thinking about life and disability. Results found that those in the intervention group showed a significantly greater reduction in Beck Depression Inventory scores compared to the control group with this reduction maintained at 3 month follow-up. In a recent pilot RCT, patients with TBI were randomly assigned to two variations of positive psychology interventions ("Three Good Things" or "Signature Strengths"; Andrewes et al. 2014). No significant differences were found from pre to post test on the Authentic Happiness Scale or the Head Injury Semantic Differential Scale, although participants in the "Three Good Things" intervention, scored significantly higher on the happiness measure than patients in the "Signature Strengths" intervention.

Music Therapy

Q. What evidence is there for music therapy in improving mood post ABI?

Answer

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

Studies investigating music as an intervention have demonstrated positive results related to patient mood. In an early repeated measures design, patients who received standard rehabilitation plus music had greater improvements in reported mood in comparison to patients who received standard rehabilitation only (Nayak et al. 2000). More recently, both listening to music and active music therapy (e.g. playing a musical instrument, singing or writing a song) improved mood (symptoms of anxiety and depression) from initial assessments to final assessments (Guétin et al. 2009). Another study had participants in a treatment group participate in four sessions focussing on attention, memory, executive function and emotional adjustment followed by a 30 minute neurologic music therapy program while a control group completed various assessments and sat quietly for 30 minutes after the assessments (Thaut et al. 2009). Although there were no improvements on cognitive measures, participants in the

intervention group improved on depression and anxiety subscales and both groups improved on the Brief Symptom Inventory (Thaut et al. 2009).

Systematic Motivation Counselling

Q. What does the evidence tell us about the effects of systematic motivation counselling on depression post ABI?

Answer

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

Cox et al. (2003) carried out a study examining Systematic Motivational Counselling, described as counselling designed to help persons with TBI cope with their injury in ways other than substance abuse. The study compared those that received Systematic Motivational Counselling to a control group that received no counselling. The authors found that participants who received Systematic Motivational Counselling experienced a significant reduction in negative affect and substance abused decreased.

6.3 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. It 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.

Incidence and Prevalence of Anxiety Disorders Post ABI

Q. What is the prevalence of anxiety or anxiety disorders post ABI?

Answer

- Post ABI, anxiety or anxiety disorders have been reported to occur in 4–28% of those who have been injured (Deb et al. 1999; Fann et al. 1995; O'Donnel et al. 2008; van Reekum et al. 1996)

Non-Pharmacological Interventions for Anxiety and Anxiety Disorders

Cognitive-Behavioural Therapy for Anxiety

Q. What is the evidence behind the use of cognitive behavioural therapy in the treatment of anxiety disorders post ABI?

Answer

- There is Level 1b evidence that cognitive behavioural therapy does reduce anxiety post ABI.

Several studies have investigated the benefits of CBT to reduce anxiety levels in those who sustained a TBI (Arundine et al. 2012; Hodgson et al. 2005; Hsieh et al. 2012). Hodgson et al. (2005) found that found that anxiety scores on the Hospital Anxiety and Depression Scale and the Social Phobia and Anxiety Inventory decreased significantly more following 9 to 12 weeks of CBT treatment than for the wait list control group, indicating that CBT training can reduce anxiety and depression in a TBI sample. Hsieh and colleagues (2012) examined CBT in combination with other therapies; specifically, motivational interviewing and CBT (group 1), the non-directive counselling group and CBT (group 2), or the treatment as usual group (group 3). Those in groups 1 and 2 showed a significant reduction in anxiety following treatment as compared to group 3. Those in group 1 showed a greater response to the CBT compared to group 2 (Hsieh et al. 2012). In terms of the way in which CBT is delivered, Arundine et al. (2012) found that both face-to-face group CBT and one-to-one telephone CBT were effective in improving community integration and mood, with no significant differences between groups. Study authors suggest teletherapy may be just as beneficial to patients post TBI as group therapy (Arundine et al. 2012).

Obsessive Compulsive Disorder

Q. What does the evidence tell us about the treatments used in Obsessive Compulsive Disorder post ABI?

Answer

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

Following a TBI, anxiety disorders such as Obsessive Compulsive Disorder (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); it is rarely reported in the literature (Drummond & 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 (Bilgic et al. 2004;

Donovan & Barry 1994; Jenike & Brandon 1988). To date, although several theories have been put forth (lesion location, age of the individual) there is still no conclusive evidence. 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.

6.4 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 results in disinhibited behaviour and a lack of recognition for the consequences of one's behaviour (Kim 2002). Typically behavioural management techniques and pharmacological interventions are used to minimize and/or alleviate these challenges with varying degrees of success.

Agitation and Aggression Post ABI

Agitation is generally defined as wandering, 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). Aggressive behaviours post TBI are associated with the presence of depression, frontal lobe lesions, and a history of substance or alcohol abuse (Singh et al. 2014; Tateno et al. 2003). TBI injuries that can lead to aggressive or agitated behaviour may result from a diffuse injury, lesions in the frontal lobe (Warriner & Velikonja 2006) and/or injuries to the left hemisphere (Tateno et al. 2003). Agitation is more common among younger individuals and those with lower FIM scores on admission (Wolffbrandt et al. 2013). Individuals found to have poorer social functioning often engage in a variety of aggressive or agitated behaviours 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 behaviours (McNett et al. 2012; Rao et al. 2009). Following an ABI, studies have suggested that aggressive behaviour is linked to the levels of serotonin in the brain. An ABI often results in serotonergic dysfunction thus increasing the risk of aggressive behaviours (Jorge & Starkstein 2005).

Q. What is the link between depression, anxiety and aggressive behaviours post ABI?

Answer

- Depression is often accompanied by anxiety and aggressive behaviours
- 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)

Assessment of Agitated and Aggressive Behaviour

Q. What test is available to assess for agitated and aggressive behaviour? What are its strengths and weaknesses?

Answer

- The Agitated Behaviour Scale (ABS) was designed to assess agitation in patients. It is a 14-item scale with each item being scored on a scale of one to four (total scores range from 14-56).
- **Strengths:** short, can be completed quickly (<30 minutes), and readily available.
- **Weaknesses:** Risk of over diagnosis (Corrigan & Mysiw 1988).

Click here to view the Agitated Behavior Scale: http://www.tbims.org/combi/abs/absrat.html

Q. What are some of the practical advantages of using an objective scale for assessing agitation post ABI?

Answer

- Assesses the pattern of agitation
- Assesses the level of agitation which then can dictate treatment
- Assesses the response of agitation to interventions
- Agitated Behaviour Scale >21 = agitation, <23 unlikely to be violent, >28 = treatment with pharmacological agents

To measure agitation post injury the Agitated Behaviour Scale (ABS) was developed (Bogner & Corrigan 1995). The ABS was designed to assess agitation in patients by those working with them**.** According to Levy et al. (2005), despite the availability of the scale, agitation remains unmeasured by most who work with the TBI population. The scale, which originally consisted of 39 items, was reduced to 14 items with each item scored 1–4 describing the behaviour as absent or present to a slight/moderate/extreme degree). The scale which was originally tested by nurses, occupational therapists, physiotherapists and other hospital staff, was designed to be used by allied health professionals (Corrigan 1989).

Non-pharmacological Treatment of Agitation and Aggression

Agitation occurs in approximately 33-55% of patients with TBI (Singh et al. 2014; Tateno et al. 2003). 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, and anti-psychotics, as well as others.

Specific Behavioural Techniques

Q. What evidence is there for antecedent management or feedback of consequences to reduce undesirable behaviour?

Answer

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

Different behavioural interventions have been trialed in hopes of reducing aggressive behaviour. An antecedent behavioural intervention was studied by structuring the environment with high support and then reducing it. This intervention was able to significantly reduce aggressive behaviour (Feeney & Ylvisaker 1995).

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. Percentage of change scores from baseline revealed success.

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.

Q. What does the evidence tell us about the effectiveness of social skills training on inappropriate behaviour post ABI?

Answer

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

A RCT conducted by McDonald et al. (2008) compared social skills training, social activity, and a control group. Those in the social skills group showing a positive improvement in behaviour compared to the other interventions but the treatment effect was modest at best. Therefore, improving social behaviour, changing social perceptions, and improving mood and self-esteem seem to be somewhat influential in improving behaviour (McDonald et al. 2008). In reviewing the studies education alone was not effective in improving behaviour; however, education in combination with other interventions resulted in positive behavioural change. Carnevale et al. (2006) found that at 30 weeks following treatment, significant changes in behaviour were apparent for participants receiving an individualized program and education compared to education alone. Other interventions have been shown to benefit individuals post injury with alleviating aggression, such as an anger management therapy program (Medd & Tate 2000), a combination of anger management and coping skills training (O'Leary 2000) and social skills training (Brotherton et al. 1988); although the evidence is weak.

Study Snapshot

Social Skills Treatment for People with severe chronic acquired brain injuries: A multicenter trial (McDonald et al. 2008).

- Participants (N=39) were randomly assigned to one of three groups: 1) control (non-therapeutic social group, N=13), 2) waitlist (deferred treatment group, N=13) or 3) the social skills group (treatment group, N=13).
- The skills training group was required to attend a 12 week program (4hr/wk) that included both group and individual sessions. The control group was subjected to 4 hr/week of social activities only and the waitlist group received 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 compared to the control and waitlist groups ($p<0.004$).
- Changes were not noted for any group when looking at social functioning and social participation.
- Treatment effects were found to be modest at best and limited to direct measures of social behaviour.

Natural Setting Behaviour Management Programs

Q. What evidence is there for Natural Setting Behaviour Management programs post ABI?

Answer

- There is Level 2 evidence that community based program combining education and an individualized behaviour plan (e.g. Natural Setting Behaviour Management intervention) helps to change behaviour.

Anger Management

Q. What evidence is there supporting the use anger management programs to reduce aggressive behaviour post ABI?

Answer

- There is Level 2 evidence that anger management reduces aggressive behaviour.

Music Therapy

Q. What is the evidence for music therapy for agitation?

Answer

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

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, decreased cortisol levels and increased endorphins) and increased wellbeing. For brain injury, only one study was conducted. 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 1 month after starting music therapy. More research is needed.

Pharmacological Treatment of Agitation and Aggression

Q. What are some principles for using pharmacological measures in the treatment of aggressive and/or agitated behaviours?

Answer

- Pharmacological agents should only be used as a last resort (ABS >28).
- The sensitivity of people with TBI to psychotropic medications should be carefully considered and these agents should be used with caution.
- Physicians should "start low and go slow" when titrating up to an optimal dose; however, it is important to achieve a therapeutic dose before abandoning use.
- Develop clear cut goals and metrics to assist in determining when to stop treatment (i.e. consider weaning off medication when ABS <21).
- Be alert to the development of side effects.
- Minimize the use of benzodiazepines and neuroleptic antipsychotic medications such as haldol as animal studies suggest these medications may slow brain recovery.

ABIKUS Recommendations for the Principles of Use of Medications in Persons with Brain Injury (Bayley et al. 2007).

- There should be careful consideration of the sensitivity of people with traumatic brain injury to psychotropic medication before trial use. Psychotropic medication should be used with caution. Where medications are clinically indicated 'start low and go slow', keep under direct clinical monitoring to ensure that the drug is tolerated and producing the expected improvement and use with caution where indicated. (ABIKUS C, adapted from NZG; 14.4.10.3, 182) (G10-p.18).
- Perform a detailed physical exam prior to commencing any trial of medications. People with traumatic brain injury and their caregiver should be asked about any prescribed medications, over the counter remedies, herbs or supplements they are taking to check for potential interactions and adverse effects. (ABIKUS C) (G11-p.18).
- Appropriate investigations should be completed prior to medication trials to rule out and minimize metabolic abnormalities including evaluation of: plasma blood sugar, electrolytes, hormones, hemoglobin, oxygenation and infection. (ABIKUS B) (G12-p.18).
- Clinicians should also consider the possibility of brain injury related sleep disorders as a cause of cognitive and other behavioural changes. (ABIKUS B, adapted from Mahmood et al. 2004) (G13-p.18).
- Any trial of medication for a person with traumatic brain injury should be preceded by a clear explanation to the patient and their caregivers, and a caution that the effects of medications are less predictable in people with traumatic brain injury. (ABIKUS C) (G14-p.18).

Q. When non-pharmacological measures are unsuccessful, which medications are recommended to decrease aggressive and agitated behaviours?

Answer

Initially

- Atypical antipsychotics prn – risperidone up to 3g daily; alternatives include seroquel or olanzapine

Later (if ABS ≥28 then provide scheduled dose medications)

- Beta-blockers
- Anticonvulsants
- SSRIs
- Tricyclic antidepressants
- Methylphenidate
- Avoid the use of typical antipsychotic drugs such as Haldol

Anticonvulsants

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

Carbamazepine (Tegretol)

Q. What type of medication is Carbamazepine?

Answer

- Carbamazepine inhibits voltage-dependent neuronal sodium channels (Schachter 1997)
- As Indicated in the Canadian Pharmacists Association (2008), carbamazepine has moderate anticholinergic activity that is responsible for some of its side effects
- This medication has been shown to successfully treat various seizure disorders, as well as obsessive compulsive disorder and may be effective in treating aggressive behaviour post TBI

Q. What evidence is there supporting the administration of carbamazepine to treat aggressive behaviours post ABI?

Answer

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

Azouvi et al. (1999) in an 8-week open drug trial administered carbamazepine (Tegretol) to 10 individuals with severe brain injury who had significant behavioural challenges that were interfering with care and/or family integration. 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. It should be noted that drowsiness was a frequent adverse event which limited the dosage being increased in 40% of the participants.

Lamotrigine (Lamictal)

Q. What evidence is there supporting the administration of lamotrigine to treat aggressive behaviours post ABI?

Answer

- There is limited Level 4 evidence 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.

Results from a single study indicate that lamotrigine helped reduce unwanted behaviours such as pathologic laughter but did not address impulsivity (Chahine & Chemali 2006). All four participants were on other medications to control for additional behaviours, however in each case these medications were eventually eliminated once lamotrigine was introduced. No formal outcome assessments were conducted making it challenging to draw conclusions from this study. Further research is needed.

Valproic Acid (Depakene)

Q. What type of medication is valproic acid and what are its advantages?

Answer

- Valproic acid is primarily an anticonvulsant drug
- Divalproex sodium is a variant of valproic acid
- Has one of the most favourable neuropsychological side-effect profiles
- Is effective for the management of both seizures and aggressive behaviour (Geracioti 1994; Wroblewski et al. 1997)
- Is effective in a number of psychiatric disorders including bipolar disorder (McElroy et al. 1987)

Q. What evidence is there supporting the administration of valproic acid to treat aggressive behaviours post ABI?

Answer

- There is Level 4 evidence that valproic acid decreases the incidence of aggressive behaviours.

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. Researchers relied on visual inspection of data and graphs were only presented for

three of the five patients, which may bias results. Further, patients were also part of a specialized neurobehavioural unit, which may have contributed to the positive results.

Divalproex (Epival)

Q. What evidence is there supporting the administration of divalproex to treat aggressive behaviours post ABI?

Answer

- There is Level 4 evidence that divalproex decreases the incidence of agitation post TBI.

Divalproex, another anticonvulsant, is believed to help reduce aggressive behaviours in individuals post TBI. Divalproex was used to treat symptoms of agitation in 29 patients with brain injury (Chatham et al. 2000). Symptoms decreased significantly in the majority of patients, indicating that divalproex may be an effective treatment to reduce agitation following brain injury.

Antidepressants

Sertraline (Zoloft)

Q. What type of medication is sertraline and how does it work to control aggression post ABI?

Answer

- Sertraline is a selective serotonin reuptake inhibitor, which potentiates the effects of serotonin
- Decreased serotonin levels have been associated with both aggression and depression after brain injury and sertraline has been proposed as an effective treatment for both problems

Q. What evidence is there supporting the administration of sertraline to treat aggressive behaviour?

Answer

- There is Level 4 evidence that sertraline can decrease the incidence of aggression and irritability.

Kant et al. (1998) examined the effect of sertraline HCl (Zoloft) on reducing aggression and irritability in patients with closed head injuries of varying severities, two years post injury. The patients responded positively at both the four and eight week follow-ups, showing significant reduction in aggressive and irritable behaviour (Kant et al. 1998). The patients treated also had improvements in depression at week four.

Amitriptyline (Elavil)

Q. What is the evidence supporting the administration of amitriptyline to treat aggressive behaviour?

Answer

- There is Level 4 evidence that amitriptyline may be useful in reducing the incidence of agitated behaviour.

Mysiw et al. (1988) administered amitriptyline to 20 patients with TBI after a failed 1-week trial of a standard behavioural intervention (i.e. where agitation persisted to the point of interfering with rehabilitation). Results indicated that 70% of patients displayed significant reductions agitation within the first week.

Beta Blockers

Q. What beta blockers are used to treat aggression and why?

Answer

- Propranolol and Pindolol are used because they both cross the blood-brain barrier (Greendyke & Kanter 1986; Brooke 1992)

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. Greendyke and Kanter (1986) investigated the effectiveness of the beta-blocker, pindolol, for the improvement of behavioural disturbances. A significant reduction in behaviours that lead to assaults was demonstrated during treatment with pindolol, with the authors stating the optimal dose ranged between 40-60 mg per day. No therapeutic advantage was gained with doses beyond that but rather it lead to adverse events (Greendyke & Kanter 1986). Although the frequency of supplemented psychotropic medications was reduced in the pindolol group, these medications were still given and may have attributed to the reduction in assaultive episodes.

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).

Study Snapshot

Therapeutic effects of pindolol on behavioural disturbances associated with organic brain disease: A double-blind study (Greendyke & Kanter 1986).

- Subjects with ABI (N=11) were randomly assigned to receive pindolol or placebo for the first half of study and then crossed-over.
- Following the titration period, the treatment group received a daily dose of 60 mg/day for 10 days, followed by another increase (up to 100 mg) to determine whether benefits could be gained with higher doses.
- Results indicate that while on pindolol there was a significant reduction in the number of assaultive episodes and the need for supplemental medication ($p<0.05$).
- There was a significant improvement in the subjects' willingness to communicate and cooperate during the treatment period ($p<0.025$), as well as a significant reduction in stereotyped behaviours ($p<0.01$).

Greendyke and Kanter (1986) investigated the effectiveness of the beta-blocker, pindolol, for the improvement of behavioural disturbances. A significant reduction in behaviours that lead to assaults was demonstrated during treatment with pindolol, with the authors stating the optimal dose ranged between 40-60 mg per day. No therapeutic advantage was gained with doses beyond that but rather it lead to adverse events (Greendyke & Kanter 1986). Although the frequency of supplemented psychotropic medications was reduced in the pindolol group, these medications were still given and may have attributed to the reduction in assaultive episodes.

Study Snapshot

Propranolol treatment of assaultive patients with organic brain disease (Greendyke et al. 1986).

- Patients (N=10) were randomly assigned to receive either long-lasting propranolol (520 mg/day) or placebo and then crossed-over.
- Propranolol administration began at 80 mg/day with an increase of 80 mg every 3 to 4 days to a maximum dose of 520 mg.
- Assaultive behaviour was significantly reduced during the 11-week propranolol treatment as compared to the 11 weeks of placebo ($p<0.05$).
- No significant changes in social interests, levels of irritability or psychomotor deficits were noted.

Greendyke et al. (1986) 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 placebo group. Of the nine patients, five showed marked improvement, two demonstrated moderate improvement, and two showed little or no improvement of assaultive behaviour. It should be noted that the participants also had severe dementia; therefore, this study was not used to draw conclusions for an ABI population as a whole. A later study by Brooke et al. (1992) found that propranolol was effective in reducing the intensity of the agitation but was not significantly more effective in reducing the number of episodes compared to a placebo.

Study Snapshot

The treatment of agitation during initial hospitalization after traumatic brain injury (Brooke et al. 1992).

- Those in the experimental group (N=11) was given propranolol while the control group (N=10) was given placebo.
- Propranolol was begun at 60 mg/day and increased every third day by 60 mg to a max of 420 mg/day.
- Although the number of aggressive episodes was similar between the two groups, the level of intensity was significantly different, with the treatment groups showing lower levels of agitation ($p<0.05$).
- It was also found that more participants in the control group required physical restraints during the study period ($p<0.05$); although, there were no significant differences in the pattern of restraint use between the two groups ($r=-0.080$).
- There were no differences between the two groups in the number of patients receiving sedating drugs or drugs for agitation.

Antipsychotics

Quetiapine (Seroquel)

Q. What is the evidence for using quetiapine to treat aggressive or agitated behaviours post ABI?

Answer

- There is Level 4 evidence to suggest that quetiapine helps reduce aggressive behaviour.

In one case series quetiapine assisted in helping to reduce aggressive behaviour in seven individuals (Kim & Bijlani 2006). They also noted significant improvements in the Overt Aggression Scale-Modified, the Clinical Global Impression scores, and the overall scores of the Repeatable Battery for the Assessment of Neuropsychological Status. Quetiapine may be considered as an alternative to haloperidol or chlorpromazine if additional research finds it is just as effective in treating aggressive behaviours without the side effects (Kim & Bijlani 2006).

Ziprasidone (Geodon, Zeldox)

Q. What evidence is there for using Ziprasidone to treat aggression post ABI?

Answer

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

Noe et al. (2007) studied individuals who were still in post-traumatic amnesia stage at admission to rehabilitation. Within these participants, a decrease in agitation scores was reported during the first 2 weeks of ziprasidone administration. It was also noted that all who participated tolerated the medication with no clinical side effects observed. A larger RCT would be beneficial before any firm conclusions are made.

Droperidol (Inapsine)

Q. What evidence is there to support the administration of droperidol to calm aggressive or agitated patients with brain injury?

Answer

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

When an individual is agitated, not only is the effectiveness of the medication administered important but also the time it takes to have a calming effect. One retrospective controlled trial found that a single-dose of droperidol calmed patients displaying agitated behaviour faster than other drugs (haloperidol, lorazepam, and diphenhydramine; Stanislav & Childs 2000). The study also found that droperidol calmed individuals without heavily sedating the patients like some of the comparative medications did. It is worth noting however that a large proportion of the sample had psychiatric co-morbidities, this should be kept in mind when generalizing the findings.

Haloperidol

Q. What does the evidence tell us about haloperidol's effect on recovery post ABI?

Answer

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

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

Other Drugs

Lithium Carbonate

Q. What is the evidence for using lithium carbonate to treat aggression post ABI?

Answer

- There is Level 4 evidence to suggest that an anti-manic agent (lithium carbonate) reduces aggressive/agitated behaviour following a brain injury.

Lithium carbonate was used in a series of case reports with ten individuals with either TBI or stroke (Glenn et al. 1989). Glenn et al. (1989) reported favourable outcomes for the majority of patients (i.e. a decrease in observed aggressive, combative, or self-destructive behaviour or severe affective instability). However, this study highlight that there is a high risk of potential neurotoxicity among individuals with brain injuries, specifically in combination with neuroleptic drugs.

Medroxyprogesterone for Sexually Disinhibited Behaviour

Q. What is the evidence for using medroxyprogesterone to treat sexually aggressive behaviour post ABI?

Answer

- There is Level 4 evidence that Depo-Provera and counselling reduces sexually aggressive behaviour.

As shown by the findings from Simpson et al. (2013), inappropriate sexual behaviour is a concern for individuals post injury; specifically, verbal inappropriateness among younger and more severely injured individuals. In a retrospective study, Depo-Provera, an anti-androgen drug, was evaluated in terms of its efficacy for controlling sexual aggression in eight males with TBI 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 resulted in a cessation of hypersexual behaviour and reduced testosterone levels. Three subjects re-offended when the drug was stopped, three remained on it and two stopped taking the drug and had maintained cessation of hypersexual behaviour.

Methotrimeprazine (Nozinan)

Q. What is the evidence supporting the administration of methotrimeprazine to reduce aggressive or agitated behaviours post ABI?

Answer

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

The oral administration of methotrimeprazine (MTZ) for agitation was evaluated in a retrospective chart review of 56 patients during inpatient 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. No standardized outcome measures were used within this study, and there was no control group; therefore, a more rigour study examining the safety and efficacy of MTZ within an ABI population is necessary before a level of evidence statement can be provided.

Methylphenidate

Q. What evidence is there supporting the administration of methylphenidate to reduce agitation and aggression post ABI?

Answer

- There is Level 2 evidence to suggest that treatment with methylphenidate following brain injury can significantly reduce anger.

In a RCT, 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.

Study Snapshot

Effect of methylphenidate on brain injury-related anger (Mooney & Haas 1993).

- Young, adult male subjects with TBI (N=38) were included.
- Subjects were split into two groups to receive gradually increasing doses of methylphenidate (up to a maximum of 30 mg, starting dosage was unspecified) or a placebo for 6 weeks.
- The treatment group reported significant reductions in anger ($p=0.002$).
- Whilst between-group comparisons at post-treatment yielded no significant difference, the treatment group exhibited significantly greater levels of baseline State and Trait Anger Scale Anger subtest scores. After controlling for this, a significant effect was still found for drug treatment ($p<0.001$).

- Treatment group patients also demonstrated significant reductions in psychopathology ($p<0.01$).
- No significant side effects were noted from patients taking methylphenidate.
- There were no significant differences between-groups on memory or attention; thus, there were no cognitive effects of the drug.

Summary Regarding the Use of Pharmaceuticals to Reduce Aggressive Behaviour

The use of pharmacological agents can help to prevent injury to the patient and others. 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). A fairly consistent limitation across the studies in this section is the lack of a control group. Ideally, the efficacy of pharmacological interventions for agitation would be studied using a randomized, double-blinded, placebo design; however, few of these trials have been conducted (Levy et al. 2005). When investigating aggressive symptomology following brain injury there is difficulty in comparing across studies, and different treatment types, due to the lack of consistency in how aggression is measured. For example, some studies used standard outcome measures while others relied on reported/ observational behaviour ratings.

6.5 Addictive Behaviours Post ABI

ABI and Substance Abuse

Several studies have examined the rates of substance abuse in those who have sustained a TBI and 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; Taylor et al. 2003; West et al. 2009). The Diagnostic and Statistical Manual (DSM-IV-TR) outlines criteria that must be satisfied to determine if an individual has an addiction or dependence issue; however, the definitions of 'abuse' and 'addiction' vary between studies. 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 (Kelly et al. 1997). 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 intoxicated (DeLambo et al. 2008; Wehman et al. 2000; West et al. 2009). Acute intoxication has been found, in some studies, to impact the duration of coma, length of time in post-traumatic amnesia, overall length of stay, post recovery cognitive outcomes and self-care abilities (Bombardier & Thurber 1998; Vickery et al. 2008).

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. (1998) reported that as many as 40% of the TBI population meet the criteria for substance abuse or dependence as defined by 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 & Starkstein 2005).

Substance Abuse and Assessing the Severity of Injury

Q. What does the evidence tell us about the link between blood alcohol content and Glasgow Coma Scale (GCS), loss of consciousness or overall outcomes post ABI?

Answer

- There is no clear evidence linking blood alcohol content with GCS, loss of consciousness or overall outcomes post ABI

Several studies have investigated the effects of alcohol and/or other chemical substances on Glasgow Coma Scale (GCS), and length of stay in an intensive care unit (Sperry et al. 2006; Vickery et al. 2008). It has been noted by Andelic and colleagues (2010), that patients diagnosed with a less severe TBI more frequently report substance use at the time of injury while those diagnosed with a more severe injury frequently report pre-injury substance abuse. Sperry et al. (2006) found no relationship between alcohol intoxication and GCS, nor did they find a linear relationship between blood alcohol concentration and GCS. However, a study found a higher blood alcohol concentration was 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, evidence is still inconclusive.

Post injury Recovery and Substance Addiction

Q. What impact does the continued use of alcohol or drugs have on an individual's recovery from TBI?

Answer

- Continuing to use or abuse alcohol/drugs post injury can impact an individual's recovery
- Continued use of alcohol or other substances may increase levels of aggressiveness, risk of seizures, decrease satisfaction with life, and increase family stress, as well as decrease participation in rehabilitation.
- Results from several studies suggest that many individuals who have an addiction prior to their injury are likely to return to these behaviours within 2 years of the injury.

If individuals continue to use or abuse alcohol or drugs post injury, their recovery is negatively impacted. 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 that the brain injury has on the individual. Many individuals have been found to spend more time in rehabilitation programs, as alcohol addiction has been found to accentuate sensory motor, cognitive and communication problems post

injury (Wehman et al. 2000). Continued involvement with alcohol and other substances increases the risk of developing medical complications.

Involvement in rehabilitation deters or prevents individuals from using various substances as patients are monitored rather closely (Bjork & Grant 2009). However, once patients are discharged from inpatient rehabilitation, no monitoring exists and patients may return to their previous behaviours 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).

Substance Abuse Treatment for those with an ABI

Q. How effective is the use of financial incentives in encouraging individuals post ABI to continue with substance addiction therapy?

Answer

- 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.

In a study conducted in Corrigan and Bogner (2007), subjects with a diagnosed substance abuse problem were randomly assigned to one of three groups. All interventions were administered during a telephone interview. The three intervention groups were 1) provision of financial incentives to not miss appointments 2) reduction of logistical barriers to attending appointments and 3) attention control. Results demonstrated that offering a financial incentive (group one) was more effective in promoting compliance in attending treatment sessions than either other intervention which aimed to reduce barriers.

Reference List

Andelic, N., Jerstad, T., Sigurdardottir, S., Schanke, A. K., Sandvik, L., & Roe, C. (2010). Effects of acute substance use and pre-injury substance abuse on traumatic brain injury severity in adults admitted to a trauma centre. *J Trauma Manag Outcomes, 4*, 6.

Andrewes, H. E., Walker, V., & O'Neill, B. (2014). Exploring the use of positive psychology interventions in brain injury survivors with challenging behaviour. *Brain Inj, 28*(7), 965-971.

Arundine, A., Bradbury, C. L., Dupuis, K., Dawson, D. R., Ruttan, L. A., & Green, R. E. A. (2012). Cognitive behavior therapy after acquired brain injury: Maintenance of therapeutic benefits at 6 months posttreatment. *J Head Trauma Rehab, 27*(2), 104-112.

Ashman, T. A., Cantor, J. B., Gordon, W. A., Spielman, L., Flanagan, S., Ginsberg, A., Greenwald, B. (2009). A Randomized Controlled Trial of Sertraline for the Treatment of Depression in Persons With Traumatic Brain Injury. *Arch Phys Med Rehabil, 90*(5), 733-740.

Azouvi, P., Jokic, C., Attal, N., Denys, P., Markabi, S., & Bussel, B. (1999). Carbamazepine in agitation and aggressive behaviour following severe closed-head injury: Results of an open trial. *Brain Inj, 13*(10), 797-804.

Bajo, A., Hazan, J., Fleminger, S., & Taylor, R. (1999). Rehabilitation on a Cognitive Behavioural Unit Is Associated with Changes in FAM, not FIM. *Neuropsychol Rehabil, 9*(3-4), 413-419.

Bayley, M., Teasell, R., Marshall, S., Cullen, N., Colantonio, A., Kua A. (2007). ABIKUS Evidence Based Recommendations for Rehabilitation of Moderate to Severe Acquired Brain Injury. *Toronto, Ontario, Canada: Ontario Neurotrauma Foundation*.

Bedard, M., Felteau, M., Mazmanian, D., Fedyk, K., Klein, R., Richardson, J., . . . Minthorn-Biggs, M.-B. (2003). Pilot evaluation of a mindfulness-based intervention to improve quality of life among individuals who sustained traumatic brain injuries. *Disabil Rehabil, 25*(13), 722-731.

Bedard, M., Felteau, M., Marshall, S., Campbell, S., Gibbons, C., Klein, R., & Weaver, B. (2012). Mindfulness-based cognitive therapy: benefits in reducing depression following a traumatic brain injury. *Adv Mind Body Med, 26*(1), 14-20.

Bedard, M., Felteau, M., Marshall, S., Cullen, N., Gibbons, C., Dubois, S., . . . Moustgaard, A. (2014). Mindfulness-based cognitive therapy reduces symptoms of depression in people with a traumatic brain injury: Results from a randomized controlled trial. *J Head Trauma Rehabil, 29*(4), E13-E22.

Berthier, M. L., Kulisevsky, J., Gironell, A., & López, O. L. (2001). Obsessive-compulsive disorder and traumatic brain injury: Behavioral, cognitive, and neuroimaging findings. *Neuropsych Neuropsychol Behav Neurol, 14*(1), 23-31.

Bilgic, B., Baral-Kulaksizoglu, I., Hanagasi, H., Saylan, M., Aykutlu, E., Gurvit, H., & Emre, M. (2004). Obsessive-compulsive disorder secondary to bilateral frontal damage due to a closed head injury. *Cogn Behav Neurol, 17*(2), 118-120.

Bjork, J. M., & Grant, S. J. (2009). Does traumatic brain injury increase risk for substance abuse? *J Neurotraum, 26*(7), 1077-1082.

Blake, H., & Batson, M. (2009). Exercise intervention in brain injury: A pilot randomized study of Tai Chi Qigong. *Clin Rehabil, 23*(7), 589-598.

Bogner, J., & Corrigan, J. D. (1995). Epidemiology of agitation following brain injury. *Neurorehabil , 5*(4), 293-297.

Bombardier, C. H., & Thurber, C. A. (1998). Blood alcohol level and early cognitive status after traumatic brain injury. *Brain Inj, 12*(9), 725-734.

Brooke, M. M., Patterson, D. R., Questad, K. A., Cardenas, D., & Farrel-Roberts, L. (1992). The treatment of agitation during initial hospitalization after traumatic brain injury. *Arch of Phys Med Rehabil, 73*(10), 917-21.

Brotherton, F. A., Thomas, L. L., Wisotzek, I. E., & Milan, M. A. (1988). Social skills training in the rehabilitation of patients with traumatic closed head injury. *Arch Phys Med Rehabil, 69*(10), 827-32.

Burke, W. H., Wesolowski, M. D., & Lane, I. (1988). A positive approach to the treatment of aggressive brain injured clients. *Int J Rehabil Res, 11*(3), 235-41.

Canadian Pharmacists Association. (2008). *Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health Professionals*. Ottawa, ON, Canada.

Carnevale, G. J., Anselmi, V., Johnston, M. V., Busichio, K., & Walsh, V. (2006). A Natural Setting Behavior Management Program for Persons With Acquired Brain Injury: A Randomized Controlled Trial. *Arch Phys Med Rehabil, 87*(10), 1289-97.

Chahine, L. M., & Chemali, Z. (2006). Du rire aux larmes: Pathological laughing and crying in patients with traumatic brain injury and treatment with lamotrigine. *Epilepsy and Behavior, 8*(3), 610-615.

Chatham Showalter, P. E., & Kimmel, D. N. (2000). Agitated symptom response to divalproex following acute brain injury. *J Neuropsychiat Clin Neurosci, 12*(3), 395-397.

Corrigan, J. D. (1989). Development of a scale for assessment of agitation following traumatic brain injury. *J Clin Exp Neuropsychol, 11*(2), 261-277.

Corrigan, J. D., & Bogner, J. (2007). Interventions to promote retention in substance abuse treatment. *Brain Inj, 21*(4), 343-356.

Corrigan, J. D., & Mysiw, W. J. (1988). Agitation following traumatic head injury: equivocal evidence for a discrete stage of cognitive recovery. *Arch Phys Med Rehabil, 69*(7), 487-492.

Cox, W. M., Heinemann, A. W., Vincent Miranti, S., Schmidt, M., Klinger, E., & Blount, J. (2003). Outcomes of Systematic Motivational Counseling for substance use following traumatic brain injury. *J Add Dis, 22*(1), 93-110.

D'Antonio, E., Tsaousides, T., Spielman, L., & Gordon, W. (2013). Depression and traumatic brain injury: Symptom profiles of patients treated with cognitive-behavioral therapy or supportive psychotherapy. *Neuropsych, 3*(6), 601-609.

Deb, S., Lyons, I., Koutzoukis, C., Ali, I., & McCarthy, G. (1999). Rate of psychiatric illness 1 year after traumatic brain injury. *Am J Psych, 156*(3), 374-378.

DeLambo, D. A., Chandras, K. V., Homa, D., & Chandras, S. V. (2008). Psychiatric disabilities and substance abuse: Applications for rehabilitation professionals. *Compelling counseling intervention: Celebrating VISTAS'fifth anniversary*, 149-159.

Donovan, N. J., & Barry, J. J. (1994). Compulsive symptoms associated with frontal lobe injury. *Am J Psych, 151*(4), 618.

Driver, S., & Ede, A. (2009). Impact of physical activity on mood after TBI. *Brain Inj, 23*(3), 203-212.

Drummond, L. M., & Gravestock, S. (1988). Delayed emergence of obsessive-compulsive neurosis following head-injury. Case report and review of its theoretical implications. *Brit J Psych, 153*(DEC.), 839-842.

Eisenberg, M. E., Im, B., Swift, P., & Flanagan, S. R. (2009). Management of Traumatic Brain Injury-Related Agitation. *Crit Rev Phys Rehabil Med, 21*(3-4), 215-229.

Emory, L. E., Cole, C. M., & Meyer, W. J. (1995). Use of Depo-Provera to control sexual aggression in persons with traumatic brain injury. *J Head Trauma Rehabil, 10*(3), 47-58.

Fann, J. R., Katon, W. J., Uomoto, J. M., & Esselman, P. C. (1995). Psychiatric disorders and functional disability in outpatients with traumatic brain injuries. *Am J Psych, 152*(10), 1493-1499.

Feeney, T. J., & Ylvisaker, M. (1995). Choice and routine: Antecedent behavioral interventions for adolescents with severe traumatic brain injury. *J Head Trauma Rehabil, 10*(3), 67-86.

Fleminger, S., Oliver, D. L., Williams, W. H., & Evans, J. (2003). The neuropsychiatry of depression after brain injury. *Neuropsychol Rehabil, 13*(1-2), 65-87.

Formisano, R., Vinicola, V., Penta, F., Matteis, M., Brunelli, S., & Weckel, J. W. (2001). Active music therapy in the rehabilitation of severe brain injured patients during coma recovery. *Ann dell'Istituto Superiore di Sanita, 37*(4), 627-630.

Gemmell, C., & Leathem, J. M. (2006). A study investigating the effects of Tai Chi Chuan: Individuals with traumatic brain injury compared to controls. *Brain Inj, 20*(2), 151-156.

Geracioti Jr, T. D. (1994). Valproic acid treatment of episodic explosiveness related to brain injury. *J Clin Psych, 55*(9), 416-417.

Glenn, M. B., Wroblewski, B., Parziale, J., Levine, L., Whyte, J., & Rosenthal, M. (1989). Lithium carbonate for aggressive behavior or affective instability in ten brain-injured patients. *Am J Phys Med Rehabil, 68*(5), 221-226.

Gordon, W. A., Sliwinski, M., Echo, J., McLoughlin, M., Sheerer, M., & Meili, T. E. (1998). The benefits of exercise in individuals with traumatic brain injury: A retrospective study. *J Head Trauma Rehabil, 13*(4), 58-67.

Grados, M. A. (2003). Obsessive-compulsive disorder after traumatic brain injury. *Int Rev Psych, 15*(4), 350-358.

Greendyke, R. M., & Kanter, D. R. (1986). Therapeutic effects of pindolol on behavioral disturbances associated with organic brain disease: A double-blind study. *J Clin Psych, 47*(8), 423-426.

Greendyke, R. M., Kanter, D. R., Schuster, D. B., Verstreate, S., & Wootton, J. (1986). Propranolol treatment of assaultive patients with organic brain disease. A double-blind crossover, placebo-controlled study. *J Nerv Ment Dis, 174*(5), 290-294.

Guétin, S., Soua, B., Voiriot, G., Picot, M. C., & Hérisson, C. (2009). The effect of music therapy on mood and anxiety-depression: An observational study in institutionalised patients with traumatic brain injury. *Ann Phys Rehabil Med, 52*(1), 30-40.

Health-Canada. (2009). *Depression*. Retrieved from http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/depression-eng.php.

Hibbard, M. R., Uysal, S., Kepler, K., Bogdany, J., & Silver, J. (1998). Axis I psychopathology in individuals with traumatic brain injury. *J Head Trauma Rehabil, 13*(4), 24-39.

Hodgson, J., McDonald, S., Tate, R., & Gertler, P. (2005). A Randomised Controlled Trial of a Cognitive-Behavioural Therapy Program for Managing Social Anxiety After Acquired Brain Injury. *Brain Imp, 6*(03), 169-180.

Hoffman, J. M., Bell, K. R., Powell, J. M., Behr, J., Dunn, E. C., Dikmen, S., & Bombardier, C. H. (2010). A randomized controlled trial of exercise to improve mood after traumatic brain injury. *Phys Med Rehabil, 2*(10), 911-919.

Hsieh, M. Y., Ponsford, J., Wong, D., & McKay, A. (2012). Exploring variables associated with change in cognitive behaviour therapy (CBT) for anxiety following traumatic brain injury. *Disabil Rehabil, 34*(5), 408-415.

Jean-Bay, E. (2000). The biobehavioral correlates of post-traumatic brain injury depression. *J Am Assoc Neurosci Nurs, 32*(3), 169-176.

Jenike, M. A., & Brandon, A. D. (1988). Obsessive-compulsive disorder and head trauma: A rare association. *J Anx Dis, 2*(4), 353-359.

Jorge, R. E. (2005). Neuropsychiatric consequences of traumatic brain injury: A review of recent findings. *Curr Opin Psych, 18*(3), 289-299.

Jorge, R. E., & Starkstein, S. E. (2005). Pathophysiologic aspects of major depression following traumatic brain injury. *J Head Trauma Rehabil, 20*(6), 475-487.

Kant, R., Smith-Seemiller, L., & Duffy, J. D. (1996). Obsessive - Compulsive disorder after closed head injury: Review of literature and report of four cases. *Brain Inj, 10*(1), 55-63.

Kant, R., Smith-Seemiller, L., & Zeiler, D. (1998). Treatment of aggression and irritability after head injury. *Brain Inj, 12*(8), 661-666.

Kelly, M. P., Johnson, C. T., Knoller, N., Drubach, D. A., & Winslow, M. M. (1997). Substance abuse, traumatic brain injury and neuropsychological outcome. *Brain Inj, 11*(6), 391-402.

Kim, E. (2002). Agitation, aggression, and disinhibition syndromes after traumatic brain injury. *Neurorehabil, 17*(4), 297-310.

Kim, E., & Bijlani, M. (2006). A pilot study of quetiapine treatment of aggression due to traumatic brain injury. *J Neuropsych Clin Neurosci, 18*(4), 547-549.

Knottnerus, A. M., Turner-Stokes, T., van de Weg, F. B., Heijnen, L., Lankhorst, G. J., & Turner-Stokes, L. (2007). Diagnosis and treatment of depression following acquired brain injury: A comparison of practice in the UK and the Netherlands. *Clin Rehabil, 21*(9), 805-811.

Kolakowsky-Hayner, S. A., Gourley I, E. V., Kreutzer, J. S., Marwitz, J. H., Meade, M. A., & Cifu, D. X. (2002). Post-injury substance abuse among persons with brain injury and persons with spinal cord injury. *Brain Inj, 16*(7), 583-592.

Lee, H., Kim, S. W., Shin, I. S., Yang, S. J., & Yoon, J. S. (2005). Comparing effects of methylphenidate, sertraline and placebo on neuropsychiatric sequelae in patients with traumatic brain injury. *Human Psychopharmacol, 20*(2), 97-104.

Levy, M., Berson, A., Cook, T., Bollegala, N., Seto, E., Tursanski, S., . . . Bhalerao, S. (2005). Treatment of agitation following traumatic brain injury: A review of the literature. *Neurorehabil, 20*(4), 279-306.

Maryniak, O., Manchanda, R., & Velani, A. (2001). Methotrimeprazine in the treatment of agitation in acquired brain injury patients. *Brain Inj, 15*(2), 167-174.

McDonald, S., Tate, R., Togher, L., Bornhofen, C., Long, E., Gertler, P., & Bowen, R. (2008). Social Skills Treatment for People With Severe, Chronic Acquired Brain Injuries: A Multicenter Trial. *Arch Phys Med Rehabil, 89*(9), 1648-1659.

McElroy, S. L., Keck, P. E., Jr., & Pope, H. G., Jr. (1987). Sodium valproate: its use in primary psychiatric disorders. *J Clin Psychopharmacol, 7*(1), 16-24.

McKeon, J., McGuffin, P., & Robinson, P. (1984). Obsessive-compulsive neurosis following head injury. A report of four cases. *Brit J Psych, 144*(2), 190-192.

McKinlay, W. W., Brooks, D. N., Bond, M. R., Martinage, D. P., & Marshall, M. M. (1981). The short-term outcome of severe blunt head injury as reported by relatives of the injured persons. *J Neurol Neurosurg Psych, 44*(6), 527-533.

McNett, M., Sarver, W., & Wilczewski, P. (2012). The prevalence, treatment and outcomes of agitation among patients with brain injury admitted to acute care units. *Brain Inj, 26*(9), 1155-1162.

Medd, J., & Tate, R. L. (2000). Evaluation of an anger management therapy programme following acquired brain injury: A preliminary study. *Neuropsycholog Rehabil, 10*(2), 185-201.

Mooney, G. F., & Haas, L. J. (1993). Effect of methylphenidate on brain injury-related anger. *Arch Phys Med Rehabil, 74*(2), 153-160.

Mysiw, W. J., Jackson, R. D., & Corrigan, J. D. (1988). Amitriptyline for post-traumatic agitation. *Am J Phys Med Rehabil, 67*(1), 29-33.

Nayak, S., Wheeler, B. L., Shiflett, S. C., & Agostinelli, S. (2000). Effect of music therapy on mood and social interaction among individuals with acute traumatic brain injury and stroke. *Rehabil Psychol, 45*(3), 274-283.

Noé, E., Ferri, J., Trénor, C., & Chirivella, J. (2007). Efficacy of ziprasidone in controlling agitation during post-traumatic amnesia. *Behaviour Neurolog, 18*(1), 7-11.

O'Donnell, M. L., Bryant, R. A., Creamer, M., & Carty, J. (2008). Mental health following traumatic injury: Toward a health system model of early psychological intervention. *Clin Psychol Rev, 28*(3), 387-406.

O'Leary, C. A. (2000). Reducing aggression in adults with brain injuries. *Behav Int, 15*(3), 205-216.

Ownsworth, T. L., & Oei, T. P. S. (1998). Depression after traumatic brain injury: Conceptualization and treatment considerations. *Brain Inj, 12*(9), 735-751.

Perino, C., Rago, R., Cicolin, A., Torta, R., & Monaco, F. (2001). Mood and behavioural disorders following traumatic brain injury: Clinical evaluation and pharmacological management. *Brain Inj, 15*(2), 139-148.

Rao, N., Jellinek, H. M., & Woolston, D. C. (1985). Agitation in closed head injury: Haloperidol effects on rehabilitation outcome. *Arch Phys Med Rehabil, 66*(1), 30-34.

Rao, V., Rosenberg, P., Bertrand, M., Salehinia, S., Spiro, J., Vaishnavi, S., . . . Miles, Q. S. (2009). Aggression after traumatic brain injury: Prevalence and correlates. *J Neuropsych Clin Neurosci*, 21(4), 420-429.

Rapoport, M. J., Chan, F., Lanctot, K., Herrmann, N., McCullagh, S., & Feinstein, A. (2008). An open-label study of citalopram for major depression following traumatic brain injury. *J Psychopharmacol, 22*(8), 860-864.

Rapoport, M. J., Mitchell, R. A., McCullagh, S., Herrmann, N., Chan, F., Kiss, A., Lanctôt, K. L. (2010). A randomized controlled trial of antidepressant continuation for major depression following traumatic brain injury. *J Clin Psych, 71*(9), 1125-1130.

Rosati, D. L. (2002). Early polyneuropharmacologic intervention in brain injury agitation. *Am J Phys Med Rehabil, 81*(2), 90-93.

Rosenthal, M., Christensen, B. K., & Ross, T. P. (1998). Depression following traumatic brain injury. *Arch Phys Med Rehabil, 79*(1), 90-103.

Ruff, R. M., & Niemann, H. (1990). Cognitive rehabilitation versus day treatment in head-injured adults: Is there an impact on emotional and psychosocial adjustment? *Brain Inj, 4*(4), 339-347.

Schachter, S. (1997). Treatment of seizures. In S. D. Schachter SC (Ed.), *The Comprehensive Evaluation and Treatment of Epilepsy: A Practical Guide* (1st ed., pp. 61-74). San Diego, CA: Academic Press.

Schlund, M. W., & Pace, G. (1999). Relations between traumatic brain injury and the environment: Feedback reduces maladaptive behaviour exhibited by three persons with traumatic brain injury. *Brain Inj, 13*(11), 889-897.

Seel, R. T., MacCiocchi, S., & Kreutzer, J. S. (2010). Clinical considerations for the diagnosis of major depression after moderate to severe tBI. *J Head Trauma Rehabil, 25*(2), 99-112.

Shahin, H., Gopinath, S. P., & Robertson, C. S. (2010). Influence of alcohol on early glasgow coma scale in head-injured patients. *J Trauma, 69*(5), 1176-1181.

Sigurdardottir, S., Andelic, N., Røe, C., & Schanke, A. K. (2013). Depressive symptoms and psychological distress during the first five years after traumatic brain injury: Relationship with psychosocial stressors, fatigue and pain. *J Rehabil Med, 45*(8), 808-814.

Simpson, G. K., Sabaz, M., & Daher, M. (2013). Prevalence, clinical features, and correlates of inappropriate sexual behavior after traumatic brain injury: A multicenter study. *J Head Trauma Rehabil, 28*(3), 202-210.

Singh, R., Venkateshwara, G., Nair, K. P. S., Khan, M., & Saad, R. (2014). Agitation after traumatic brain injury and predictors of outcome. *Brain Inj, 28*(3), 336-340.

Sperry, J. L., Gentilello, L. M., Minei, J. P., Diaz-Arrastia, R. R., Friese, R. S., & Shafi, S. (2006). Waiting for the patient to "sober up": Effect of alcohol intoxication on glasgow coma scale score of brain injured patients. *J Trauma Inj, 61*(6), 1305-1311.

Stanislav, S. W., & Childs, A. (2000). Evaluating the usage of droperidol in acutely agitated persons with brain injury. *Brain Inj, 14*(3), 261-265.

Tateno, A., Jorge, R. E., & Robinson, R. G. (2003). Clinical correlates of aggressive behavior after traumatic brain injury. *Neuropsych Clin Neurosci, 15*(2), 155-160.

Taylor, L. A., Kreutzer, J. S., Demm, S. R., & Meade, M. A. (2003). Traumatic brain injury and substance abuse: A review and analysis of the literature. *Neuropsychol Rehabil, 13*(1-2), 165-188.

Thaut, M. H., Gardiner, J. C., Holmberg, D., Horwitz, J., Kent, L., Andrews, G., . . . McIntosh, G. R. (2009). Neurologic music therapy improves executive function and emotional adjustment in traumatic brain injury rehabilitation. *Ann N Y Acad Sci*, 1169(1), 406-416.

Tweedly, L., Ponsford, J., & Lee, N. (2012). Investigation of the effectiveness of brief interventions to reduce alcohol consumption following traumatic brain injury. *J Head Trauma Rehabil, 27*(5), 331-341.

Underhill, A. T., Lobello, S. G., Stroud, T. P., Terry, K. S., Devivo, M. J., & Fine, P. R. (2003). Depression and life satisfaction in patients with traumatic brain injury: A longitudinal study. *Brain Inj, 17*(11), 973-982.

van Reekum, R., Bolago, I., Finlayson, M. A., Garner, S., & Links, P. S. (1996). Psychiatric disorders after traumatic brain injury. *Brain Inj, 10*(5), 319-327.

Vickery, C. D., Sherer, M., Nick, T. G., Nakase-Richardson, R., Corrigan, J. D., Hammond, F., . . . Sander, A. (2008). Relationships Among Premorbid Alcohol Use, Acute Intoxication, and Early Functional Status After Traumatic Brain Injury. *Arch Phys Med Rehabil, 89*(1), 48-55.

Warriner, E. M., & Velikonja, D. (2006). Psychiatric disturbances after traumatic brain injury: Neurobehavioral and personality changes. *Curr Psychiatry Rep, 8*(1), 73-80.

Wehman, P., Targett, P., Yasuda, S., & Brown, T. (2000). Return to work for individuals with TBI and a history of substance abuse. *Neurorehabil, 15*(1), 71-77.

Wesolowski, M. D., Zencius, A. H., & Rodriguez, I. M. (1999). Mini-breaks: The use of escape on a fixed-time schedule to reduce unauthorized breaks from vocational training sites for individuals with brain injury. *Behav Int, 14*(3), 163-170.

West, S. L., Graham, C. W., & Cifu, D. X. (2009). Rates of Alcohol/Other Drug Treatment Denials to Persons With Physical Disabilities: Accessibility Concerns. *Alcoholism Treatment Quarterly, 27*(3), 305-316.

Wise, E. K., Hoffman, J. M., Powell, J. M., Bombardier, C. H., & Bell, K. R. (2012). Benefits of exercise maintenance after traumatic brain injury. Arch Phys Med Rehabil, 93(8), 1319-1323.

Wolffbrandt, M. M., Poulsen, I., Engberg, A. W., & Hornnes, N. (2013). Occurrence and severity of agitated behavior after severe traumatic brain injury. *Rehabil Nurs, 38*(3), 133-141.

Wroblewski, B. A., Joseph, A. B., & Cornblatt, R. R. (1996). Antidepressant pharmacotherapy and the treatment of depression in patients with severe traumatic brain injury: A controlled, prospective study. *J Clin Psych, 57*(12), 582-587.

Wroblewski, B. A., Joseph, A. B., Kupfer, J., & Kalliel, K. (1997). Effectiveness of valproic acid on destructive and aggressive behaviours in patients with acquired brain injury. *Brain Inj, 11*(1), 37-47.