PREVENTION. CARE. RECOVERY.

Te Kaporeihana Āwhina Hunga Whara

Pragmatic Evidence Based Review

Depression in moderate to severe TBI

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Purpose

The purpose of the current report is to summarise the research on depression occurring in a person after a *moderate to severe*[1] traumatic brain injury (TBI). The following review will cover;

- The prevalence and risk factors for depression in TBI patients
- The impact of depression on rehabilitation outcomes
- Interventions/strategies for clients with concurrent TBI and depression
- Potential extra costs associated with depression and TBI rehabilitation
- Recommendations for changes where appropriate, based on best practice identified in the available literature

Key Findings

- **The international prevalence of depression in the TBI population is 31% and is approximately three times higher than in the general population**
- **There is an increased risk of suicide in TBI patients, up to 4 times more than the general population**
- **There is some preliminary evidence that risk for depression increases with severity of injury and decreases with age**
- **TBI patients need to be screened for depression, and clinicians should be aware that some screening tools may not be appropriate for TBI patients**
- **Screening for depression may be frequently needed throughout a patients rehabilitation**

[1]Based on the classifications of moderate to severe TBI used in; the ACC TBI Guideline (2006)NZGG (2006). Traumatic Brain Injury: Diagnosis, Acute Management and Rehabilitation. Evidence based best practice guideline (ACC). ACC. New Zealand, NZGG.

- **Selective serotonin reuptake inhibitors (SSRI) such as citalopram and setraline appear to be the most effective pharmacological treatment for depression**
- **Psychotherapeutic interventions such as cognitive behaviour therapy (CBT) approaches can be considered as an alternative to antidepressants**
- **Current research being undertaken by AUT & ACC will provide estimates of the prevalence of depression and TBI, and cost/liability information in New Zealand**

Recommendations

- **Ideally, TBI patients should be screened for depression at regular intervals during both acute rehabilitation and in the long term**
- **Suicide screening should occur in conjunction with regular screening for other mental health co morbidities**
- **It would be worth considering using a screening tool for depression that is used by other major rehabilitation centres as this enables a more accurate comparison**
- **The impact of concurrent TBI and depression on the family of the client needs to be investigated further**
- **The referral pathway for clients who screen positive for depression can include psychiatric services where both pharmacological and psychotherapeutic options are available**
- **There is a need for more methodologically sound research on the treatment for depression following a TBI**

1. Background

1.1 Depression Symptomology

Clinical depression is characterised by the presence of five or more of the following symptoms (American Psychiatric Association 2000);

- Depressed mood most of the day, every day
- Markedly diminished interest or pleasure in activities
- Significant weight loss or gain, or increase/decrease in appetite
- Insomnia or hyposomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Thoughts of death
- Diminished ability to concentrate or indecisiveness

For a diagnoses of depression, a person must have five (or more) of the above symptoms. They must have been present during the same 2-week period and represent a change from previous functioning. At least one of the symptoms has to be either (1) depressed mood or (2) loss of interest or pleasure. Additionally, the criteria include a caveat that the symptoms are not due to bereavement, substance abuse or a general medical condition.

It is important to differentiate between clinical depression and symptoms that may occur following a brain injury that *mimic* depression. Examples of these situations are

other emotional disorders associated with brain injury such as apathy or lability. Other symptoms that may occur as a result of the injury and/or hospitalisation include; loss of energy and appetite, poor concentration and change to sleeping habits.

1.2 Methodology

A comprehensive literature search focused on moderate to severe TBI search undertaken by an information specialist. The literature was critically appraised using SIGN grading for systematic reviews and Randomised Controlled Trials (RCTs), and the AGREE instrument for appraisal of guideline quality.

2. Review of the literature

2.1 Prevalence

Depression following a moderate to severe TBI is a common occurrence and the prevalence of depression in this part of the TBI population is three times higher than in the general population (Guillamondegui, Montgomery et al. 2011). Some research attempts to make the distinction between new cases of depression (those participants who do not have a pre-injury diagnoses of depression), and depression that may be a continuation of a pre-injury diagnoses. Individual studies reported prevalence rates between 12% and 77%. In a large sample of TBI patients across all severities, 41% had experienced a new major depressive episode at 12 months post injury. These patients had no pre-injury history of depression (Bombardier, Fann et al. 2010).

The weighted average across 112 studies looking at the prevalence of depression after TBI was 31% (Guillamondegui, Montgomery et al. 2011). Reasons why depression may occur after TBI include; an emotional response to the disability, a change in biochemical balance, or a history of depression.

The duration of depression following TBI has been documented at up to 30 years post injury. Kopenen et al., interviewed 60 patients who had suffered a TBI on average 30 years prior and found that 27% of them met the DSM-III-R criteria for major depression (Koponen, Taiminen et al. 2002).

There are no statistics currently available for the prevalence of depression in TBI patients in New Zealand. However, AUT are currently undertaking a large research project, Brain Injury Outcomes New Zealand in The Community (BIONIC)[1] which aims to determine the incidence of TBI and to explore a wide range of outcomes in the year following a TBI including; anxiety, depression, post traumatic stress, alcohol use, recurrent TBI and the occurrence of other physical and psychological health conditions (Alice Theadom, personal communication, 23 May 2011).

Additionally, ACC Research is in the process of contracting a project, The Impact of Co morbidities on Injury, Treatment and Rehabilitation, which will include TBI. The research aims to ascertain the current impact of co morbidities on claim numbers, duration, costs and liabilities to ACC, and forecast these through to 2025. The anticipated completion of this project is mid 2012.

2.2 Risk Factors

The following results were based on studies that covered mild, moderate and severe TBI and the review did not provide a breakdown of prevalence between the individual categories. There is some evidence that the prevalence may increase with an increase in severity however the results are mixed and inconclusive at this stage (Guillamondegui, Montgomery et al. 2011).

Risk factors for depression after TBI include; history of depression, history of drug and alcohol abuse, and age. However due to inconsistent findings on these risk factors, the authors do not make conclusions about what may place a TBI patient at an increased risk for depression (Guillamondegui, Montgomery et al. 2011).

There is some preliminary evidence to suggest that depression may develop as a consequence of the injury (Whelan-Goodinson, Ponsford et al. 2010). In a retrospective cross-sectional study of 100 TBI patients (full range of severity); the majority of anxiety and depressive disorders reported were novel episodes or new diagnoses post-injury. The authors conclude that this supports the long-term screening of TBI patients for depression, regardless of their pre-injury history.

Support for the above causal hypothesis is given by several studies looking at the neurological changes that may occur following TBI.

There is limited evidence to identify those most at risk of depression following TBI. A study covering the full range of severity, found that the risk of depression following TBI decreases with age. They also found some evidence that for women having a higher risk for developing new depression following TBI (Bombardier et al., 2010).

There is some evidence for injury-related problems that may act as moderators for the relationship between TBI and depression. For example, stress, social isolation and maladaptive coping styles may increase the risk of a patient developing depression (Kim, Lauterbach et al. 2007).

Of interest, the above review noted that litigation increased the risk of depression. This is interesting for the New Zealand perspective given that ACC eliminates the need for litigation and should therefore decrease stresses associated with this (Bay and Donders 2008).

2.3 Risk for Suicide

Research shows that TBI patients are at an increased risk for suicidal ideation, suicide attempts and successful suicide. In patients with severe TBI the risk of committing suicide is up to 4 times more likely than the general population (Simpson and Tate 2007). The increased risk remains stable over time, there is no specific time after injury where a patient has an elevated risk.

Research has identified several risk factors for suicide following TBI. Females have a higher Standardised Mortality Rate (SMR)[2] than males, and those with more severe injuries have a higher SMR than those with mild injuries. Whilst pre-injury history of suicide attempts increased the risk mortality following a TBI it was not a significant predictor when other variables such as age at injury and employment status are included in the model (Simpson and Tate 2007).

[2] Standardised Mortality Rate refers to the ratio of observed deaths to expected deaths. A ratio of 1.0 means that the number of observed deaths is equivalent to the number of expected deaths.

There is little evidence for any specific prevention models for suicidality following TBI, and existing guidelines should be utilised as a starting point. General practitioners and other primary health care services should be informed about the prevalence and risk for suicide post TBI so that extra efforts are made to screen the patient for depression and suicide ideation (Simpson and Tate 2007).

2.4 Screening

A useful flowchart for the management of depression in patients with brain injury is provided in appendix 1 and has also been reproduced for the 2006 ACC guidelines for TBI (Royal College of Physicians, British Society of Rehabilitation Medicine et al. 2005).

There are different tools to assess depression, from the structured clinical interview for the DSM-IV to self report measures such as the Beck Depression Inventory II (BDI-II). There is some evidence to suggest that not all depression measures/screening tools are appropriate for a brain injured patient, and preliminary research suggests that the BDI-II is *not* appropriate (Royal College of Physicians, British Society of Rehabilitation Medicine et al. 2005).

The Hospital Anxiety and Depression Scale (HADS) has been validated for use with the moderate to severe TBI population (Whelan-Goodinson, Ponsford et al. 2009). It is a short self report measure, with 14 items, taking approximately 5 minutes for patients to fill in. This measure is routinely used by the Monash-Epworth Rehabilitation Research Centre. Using such a validated and internationally comparable assessment tool would be useful in New Zealand.

Other Measures suggested for screening the TBI population for depression include (Royal College of Physicians, British Society of Rehabilitation Medicine et al. 2005; Accident Compensation Corporation 2006);

- Depression Intensity Scale Circles (DISCs)
- The Short-Form Geriatric Depression Scale (GDS-15)
- The Signs of Depression Screening Scale (SDSS)

Additionally, there is no clear evidence for the timing of administering the screening that would indicate a better time for detecting depression. Likewise there is insufficient evidence to recommend the frequency of screening for depression (Guillamondegui, Montgomery et al. 2011). One approach would be to screen patients more than once during the course of their rehabilitation (Whelan-Goodinson, Ponsford et al. 2010). The recent review by Guillamondegui et al suggest that frequent screening should take place until more quality evidence can guide specific recommendations around frequency.

2.5 Impact on outcomes for rehabilitation

Depression following TBI can severely limit the patient's rehabilitation. Studies indicate that compared to TBI patients without depression, they have poorer social functioning, and lower health-related quality of life. Depressed TBI patients have more severe post-concussive symptoms; headache, blurred vision, dizziness, and memory impairment (Rutherford 1977; Fann, Katon et al. 1995).

Families play a crucial role in the rehabilitation of a TBI patient, and it is often family member who are in direct caregiving roles (Ponsford and Schonberger 2010). Therefore, the support, education, and practical assistance families receive is often instrumental in the success of the patient's rehabilitation. Recent research has found that patients depression following TBI is directly related to family member depression at 5 years post injury (Ponsford and Schonberger 2010). If depression in TBI patients is addressed effectively this should have a flow on effect for family members and overall family functioning.

2.6 Impact on Costs associated with TBI

There is very little research on the effect of co morbid mental disorders on rehabilitation costs for TBI patients. Dobrez and colleagues (Dobrez, Heinemann et al. 2010) used secondary file analysis to determine costs for patients in an inpatient rehabilitation facility (IRF) who had mood disorders, anxiety disorders, or substance abuse. The review covered over 1300 IRF's in the United States with over 1 million patients. Patients with TBI and concurrent mood disorder or major depressive disorder (MDD) had significantly greater costs ($390USD and $1,397USD) than patients without these disorders. Costs were calculated by multiplying total charges by facility-specific cost-to-charge ratios.

2.7 Interventions/Strategies

Treatment for depression falls into 3 categories;

- Pharmacological interventions e.g. SSRI's
- Alternative therapies e.g. acupuncture
- Psychotherapeutic programmes e.g. CBT, mindfulness meditation, multidisciplinary team approaches

Overall, antidepressants relieve depressive symptoms better than placebo or no intervention, however the effect size is small and given the potential side effects other treatment options should be considered.

The evidence from a large systematic review (Fann, Hart et al. 2009) on interventions for depression following TBI are summarised below;

- The evidence regarding pharmacological options suggests that citalopram and setraline are the most effective and are the preferred choice
- There is limited evidence to support the use of ECT, low intensity magnetic field exposure, biofeedback, and acupuncture
- Studies using CBT report using only some aspects of CBT (e.g. individualised cognitive retraining) rather than pure CBT.
- CBT studies report positive outcomes, however the quality of the studies are low.
- The psychotherapeutic study with the best quality evidence supports the use of a multidisciplinary team targeted to multiple outcomes although there was only significant improvements in general psychological wellbeing, not specifically depression.

Evidence from a review (Royal College of Physicians, British Society of Rehabilitation Medicine et al. 2005) which included ABI patients made the following conclusions about interventions for depression;

- Conflicting evidence that sertraline is effective in the treatment of major depression
- Desipramine may be effective in reducing depression (level 2 evidence)
- Citalopram and carbamazepine may be effective in treating mood disorders

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Bay, E. and J. Donders (2008). "Risk factors for depressive symptoms after mild-to-moderate traumatic brain injury." Brain Injury: [BI] 22(3): 233-241.

Bombardier, C. H., J. R. Fann, et al. (2010). "Rates of major depressive disorder and clinical outcomes following traumatic brain injury." JAMA: The Journal Of The American Medical Association 303(19): 1938-1945.

Dobrez, D., A. W. Heinemann, et al. (2010). "Impact of mental disorders on cost and reimbursement for patients in inpatient rehabilitation facilities." Archives of Physical Medicine and Rehabilitation 91(2): 184-188.

Fann, J. R., T. Hart, et al. (2009). "Treatment for Depression after Traumatic Brain Injury: A Systematic Review." Journal of Neurotrauma 26: 2383–2402.

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Guillamondegui, O., S. Montgomery, et al. (2011). Traumatic brain injury and depression. Comparative Effectiveness Review No. 25. Rockville, MD, Agency for Healthcare Research and Quality.

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NZGG (2006). Traumatic Brain Injury: Diagnosis, Acute Management and Rehabilitation. Evidence based best practice guideline (ACC). ACC. New Zealand, NZGG.

Ponsford, J. and M. Schonberger (2010). "Family functioning and emotional state two and five years after traumatic brain injury." Journal of the International Neuropsychological Society 16(2): 306-17.

Royal College of Physicians, British Society of Rehabilitation Medicine, et al. (2005). Use of antidepressant medication in adults undergoing recovery and rehabilitation following acquired brain injury: national guidelines. Concise Guidance to Good Practice Number 4. London, Royal College of Physicians.

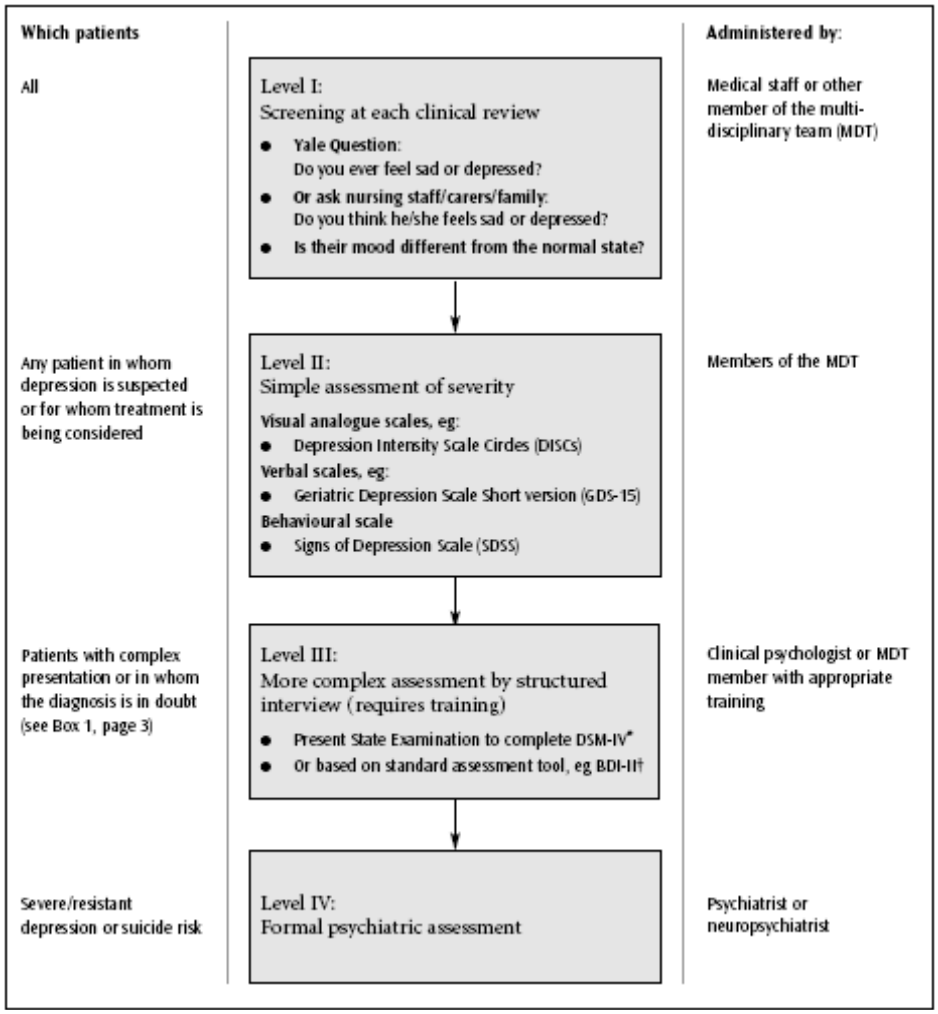
Rutherford, W. H. (1977). "Sequelae of concussion caused by minor head injuries." Lancet 1(8001): 1-4.

Simpson, G. and R. Tate (2007). "Suicidality in people surviving a traumatic brain injury: prevalence, risk factors and implications for clinical management." Brain Injury: [BI] 21(13-14): 1335-1351.

Whelan-Goodinson, R., J. Ponsford, et al. (2009). "Validity of the Hospital Anxiety and Depression Scale to assess depression and anxiety following traumatic brain injury as compared with the Structured Clinical Interview for DSM-IV." Journal Of Affective Disorders 114(1-3): 94-102.

Whelan-Goodinson, R., J. L. Ponsford, et al. (2010). "Predictors of psychiatric disorders following traumatic brain injury." The Journal of Head Trauma Rehabilitation 25(5): 320-329.

Appendix 1


Which patients
Administered by:
All
Level I:
Screening at each clinical review
Yale Question:
Do you ever feel sad or depressed?
Or ask nursing staff/carers/family:
Do you think he/she feels sad or depressed?
Is their mood different from the normal state?
Medical staff or other member of the multi-disciplinary team (MDT)
Any patient in whom depression is suspected or for whom treatment is being considered
Level II:
Simple assessment of severity
Visual analogue scales, eg:
Depression Intensity Scale Circles (DISCs)
Verbal scales, eg:
Geriatric Depression Scale Short version (GDS-15)
Behavioural scale
Signs of Depression Scale (SDSS)
Members of the MDT
Patients with complex presentation or in whom the diagnosis is in doubt (see Box 1, page 3)
Level III:
More complex assessment by structured interview (requires training)
Present State Examination to complete DSM-IV*
Or based on standard assessment tool, eg BDI-II†
Clinical psychologist or MDT member with appropriate training
Severe/resistant depression or suicide risk
Level IV:
Formal psychiatric assessment
Psychiatrist or neuropsychiatrist