OPEN ACCESS Freely available online

ISSN: 2378-5756
Journal of Psychiatry

Research Article

Treatments for Obsessive-Compulsive Disorder in Patients with Traumatic Brain Injury: A Systematic Review

Ty Drake, Nabil Malik*

Department of Liaison Psychiatry, Liverpool Hospital, Liverpool, New South Wales, Australia

ABSTRACT

Background: The prevalence of Obsessive-Compulsive Disorder (OCD) following Traumatic Brain Injury (TBI) ranges from 2-15%. OCD in patients with TBI can be distressing, difficult to manage, and hinder the rehabilitation process. Compared to non-TBI patients who have OCD, those with TBI and OCD present unique diagnostic and treatment challenges. The aim of this literature review was to identify treatments for OCD following TBI, and to evaluate the quality of evidence to explore recommendations for clinical practice and future research.

Methods: The following databases were searched for treatments of OCD in patients with TBI using Medical Subject Headings (MeSH) and key index terms: MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, Scopus, Web of Science, and Google Scholar. The search criteria included studies on humans from 16-years-old to 65-years-old from database inception to November 2020. Grey literature was also searched.

Results: After deduplication, the literature search identified 232 results. The title, abstract, and key index terms were then screened against inclusion and exclusion criteria; leaving 30 results for further review. These 30 results were screened at full-text level against the criteria, ending with 13 results for the final analysis. In total, there were 10 case reports and three case series; a total of 19 patients with TBI treated for OCD. All results were NHMRC Level IV evidence and descriptive; therefore, a narrative analysis was performed. Pharmacological treatments included several antidepressant classes and stimulants.

Conclusion: Pharmacological, psychological, combination treatments and ECT have been utilised to treat OCD in patients with TBI. Treatments not immediately described in guidelines for treating OCD in the general population appeared to have achieved some success in treating OCD in a TBI population. However, there is currently not enough high quality evidence to support an evidence-based clinical guideline or recommendation. There is a paucity of high-level research, and further research would assist future clinical practice.

Keywords: Brain injury traumatic; Brain injury; Obsessive compulsive disorder; Anxiety treatments; Disability; Mental illness; Neuropsychiatry

BACKGROUND

Traumatic Brain Injury (TBI) occurs when external force(s) results in damage to the brain [1]. The incidence of TBI in Australia is not definitively established; however, best incidence estimates range from 100-400/100,000 [2,3]. The pathophysiology of TBI is multifactorial, but essentially results in disrupted neurocircuitry causing dysfunction [4]. It can range from brief physiological disruption to widespread axonal tearing. Secondary processes such as hypoxemia, intracranial hypertension, fat embolism, subarachnoid haemorrhage and oxidative free radical production can further compound the initial insult [5]. Motor Vehicle Accidents (MVAs), falls, physical assaults, and injuries associated with sporting activities are the most common aetiological factors [6].

Obsessive-Compulsive Disorder (OCD) is a chronic disorder characterised by obsessions and/or compulsions. Obsessions are intrusive and unwanted thoughts, urges or impulses that increase anxiety whilst compulsions are repeated behaviours or acts which decrease anxiety [7]. OCD is recognised as one of the most common and disabling psychiatric conditions [7,8]. The pathophysiology and aetiology of OCD is complex and multifactorial; involving multiple neuroanatomical, neurophysiological, and neurochemical pathways [8].

Correspondence to: Nabil Malik, Department of Liaison Psychiatry, Liverpool Hospital, Liverpool, New South Wales, Australia, E-mail: nabil.malik@health.nsw.gov.au

Received: 13-Apr-2022, Manuscript No. JOP-22-16084; **Editor assigned:** 19-Apr-2022, PreQC No. JOP-22-16084 (PQ); **Reviewed:** 03-May-2022, QC No JOP-22-16084; **Revised:** 10-May-2022, Manuscript No. JOP-22-16084 (R); **Published:** 17-May-2022 DOI : 10.35248/2378-5756.22.25.505

Citation: Drake T, Malik N (2022) Treatments for Obsessive-Compulsive Disorder in Patients with Traumatic Brain Injury: A Systematic Review. J Psychia. 25:505.

There is a growing body of evidence recognising OCD in patients with TBI [9-12]. The emergence of OCD following TBI can vary from days to years' post-incident [13,14]. The prevalence of OCD following TBI ranges from 2-15% [15]. In comparison, 1.1-1.8% of the general population can be expected to present with OCD [16].

The neurological and neuropsychiatric complications secondary to TBI can significantly affect the rehabilitation process [17-19]. Achieving long-term functional independence is difficult, and as such there is an impaired Quality of Life (QOL) [6]. Many patients require extensive multidisciplinary rehabilitation, creating a significant public health and economic burden to the community [6].

Inpatient medical rehabilitation teams may ask the Consultation-Liaison Psychiatry service for guidance regarding the diagnosis and treatment of OCD in TBI patients. The diagnosis of OCD in patients with TBI is uniquely challenging. TBI can result in a combination of primary physical, cognitive, behavioural and affective impairments which can complicate diagnosing and treating secondary comorbidities such as OCD [20]. Neuropsychological studies on non-TBI OCD patients have revealed that OCD itself can cause impairments in executive control, attention shifting, visuospatial tasks, and memory [21]. The combination of TBI and OCD can result in significant disability and distress, creating significant obstacles in rehabilitation and recovery [14]. Communication issues and perseverations can make the identification and diagnosis of obsessions and compulsions complex, leading to a longer duration of untreated illness [22].

It is not immediately clear whether guidelines exist for managing OCD in TBI; however, there are well established guidelines for managing OCD in the general population [23-25]. The guidelines routinely recommend a combination of pharmacotherapy and psychotherapeutic measures. Selective Serotonin Reuptake Inhibitors (SSRIs) or clomipramine are typical first-line pharmacotherapy, and psychotherapeutic measures often include Cognitive Behavioural Therapy (CBT).

However, there are specific factors that need to be considered when initiating treatments for OCD in patients with TBI. Individuals with TBI have increased neuronal sensitivity to pharmacological agents, decreased neuropsychological capacity for psychological therapy, and a greater incidence of concurrent medical comorbidities [3,26]. Specific recommendations or guidelines for managing OCD in patients TBI would be clinically useful.

The current Coronavirus (COVID-19) pandemic and subsequent media coverage make a review of OCD in patients with TBI acutely meaningful. Increased suggestibility, secondary to TBI-related executive dysfunction [27-29], may lead to fearful obsessions of viral contamination and infection [30-32].

The purpose of this literature review was to identify what treatments are being utilised to treat OCD following TBI, and evaluate the current evidence. Recommendations for clinical practice and further research are explored.

MATERIAL AND METHODS

Ethics

An application was lodged with the Research Ethics and Governance Information System (REGIS) for the project to be reviewed by the Local Health District (LHD) ethics committee. No ethics approval was required by the LHD ethics committee.

Search strategy

Medical Subject Heading (MeSH) and index terms were identified through database tools and incorporated into the search strategy. Some of the search terms used included "obsessive-compulsive disorder," "OCD," "neurosis," "neuroses," "obsessive," "compulsive," "traumatic brain injury," "TBI," "brain damage," "management," "treatment," "therapy," "psychology", "pharmacotherapy" and "medication." A complete list of the search terms can be found in Appendix 1. The following databases were searched for published articles: MEDLINE, Embase, CINAHL, PsycINFO, Cochrane, Scopus, Web of Science, and Google Scholar. All study design types and languages were included, involving humans between the ages of 16-years-old to 65-years-old from database inception to November 2020. A result in German was translated to English. A flowchart depicting the study selection is shown in Appendix 2. This database search was wide and broad, in an effort to capture as many results as possible. This search identified 277 results.

Grey literature was also searched; the health service, professional organisations, and expert colleges. The LHD intranet was searched for guidelines, protocols or policies. TBI organisations (Brain Injury Australia, Synapse) were contacted. The websites for the Royal Australian and New Zealand College of Psychiatrists (RANZCP) and The Royal Australasian College of Physicians (RACP) were searched and contacted for any other resources. An additional two results were identified and included; bringing the total to 279 results.

The reference lists of the identified results were hand-searched. No additional results were found. Manual deduplication through referencing software removed 47 results. In total, there were 232 results remaining for further review.

Criteria and methods for inclusion

After the initial search, inclusion and exclusion criteria were developed.

Inclusion criteria:

- Treatment of OCD as a primary or secondary outcome;
- Patients with TBI (regardless of severity);
- Treatment of any modality: pharmacological, psychotherapeutic, rehabilitation-based, exercise, Electroconvulsive Therapy (ECT), Transcranial Magnetic Stimulation (TMS).

Exclusion criteria:

- Patients with OCD without TBI;
- Patients with TBI without OCD;
- Results that describe a patient with OCD and TBI, however do not discuss treatment;
- Management of OCD symptoms in patients with cerebrovascular related brain impairment or neurodegenerative brain impairment.

Using these criteria, titles and abstracts of the 232 results were screened by two reviewers (principal author and the co-author). The reviewers also screened the indexing terms and key words. Discrepancies were resolved by reviewer consensus. The full-text was reviewed if the reviewers were unable to determine if the result

fulfilled inclusion criteria. If a result did not meet the criteria, it was excluded. This process removed 202 results, leaving 30 results.

The remaining 30 results were assessed at the full-text level by each of the reviewers. There were many case reports and case series that were inapplicable to the topic of interest (e.g. case report regarding OCD in TBI that did not discuss treatment). After independently reviewing these results, the reviewers reconciled and there were no discrepancies regarding which results fulfilled selection criteria. This process removed 17 results that did not meet the criteria; leaving 13 results for analysis.

Data extraction

Two reviewers independently extracted data from each of the 13 results at different times, to improve inter-rater reliability. Some of the data extracted included the design of the study, patient information, TBI severity, interventions, and outcome measures. The data was compiled in a Microsoft Access database, where changes could be tracked. The software detected data input, removal and editing. The data extracted from one article was adjusted (after consensus between the reviewers), meaning there was à 92.31% reviewer agreeability with the extracted data. The level of evidence for the records included for the final review was also considered, based on the National Health and Medical Research Council (NHMRC) guidelines [33]. A summary of the data extracted in the database can be found in Appendix 3.

RESULTS

The literature on the treatment of OCD in patients with TBI was limited to descriptive case reports and case series varying widely in intervention and duration. The search found 10 case reports and three case series, totalling 19 patients.

Out of these 19 patients who had TBI and received treatment for OCD, 12 received pharmacological treatment. Four patients received combination treatment. Two patients received psychological treatment. Other treatment (ECT) was used on one patient.

There was no high quality evidence, such as Randomised Controlled Trials (RCTs). There were no guidelines, policies, or protocols. The severity of TBI was graded 'severe' in the majority of the patients (n=17), and the cases were predominantly male (n=17) (Appendix 4). All literature was graded as Level IV evidence based on NHMRC guidelines. The treatments that were utilised are summarised in Table 1 and Appendix 3.

Table 1: An overview of the interventions being used to treat OCD in patients with TBI.

Intervention	Patients
Pharmacological treatment	12
Combination treatment	4
Psychological treatment	2
Other treatment	1
Total patients	19

Pharmacological treatment

The pharmacological interventions (Table 2) used in isolation included SSRIs (fluoxetine, paroxetine), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs; venlafaxine), Tricyclic Antidepressants (TCA; clomipramine) and Monoamine Oxidase Inhibitors (MAOIs; phenelzine). Stimulant medication (amphetamine and dextromethorphan/quinidine) had been used in some patients.

Table 2: Pharmacological treatments being used to treat OCD in patients with TBI.

Pharmacological treatment	Case report	Case series	Patients
SSRIs	2	2	5
TCA	0	2	3
Stimulants	2	0	2
SNRIs	1	0	1
MAOIs	1	0	1
			Total patients=12

Selective Serotonin Reuptake Inhibitors (SSRIs): Five patients were treated with SSRIs, making SSRIs the most used single intervention for treatment of OCD in TBI. Fluoxetine was used in four cases and paroxetine in one case.

Stengler-Wenzke and Müller described an 18-year-old male with severe TBI following a MVA [34]. Severe checking compulsions and obsessions developed 10-months post incident, and his Yale–Brown Obsessive Compulsive Scale (Y-BOCS) score was 30/40 (severe). He had no previous psychiatric history. He was treated with fluoxetine 60 mg for 90 days and demonstrated a good clinical response with no adverse effects. His Y-BOCS score decreased from 30/40 to 10/40, with the authors reporting a subsequent improvement in his QOL.

Childers and colleagues described a 36-year-old male with no previous psychiatric history with severe TBI following à bar fight [35]. He started to obsessively ruminate about returning to work and was convinced that someone was waiting to collect him from the hospital; impairing his ability to participate in physical rehabilitation. Within a few days of commencing fluoxetine 10 mg, his OCD symptoms resolved and he was able to participate in rehabilitation. No adverse effects reported.

Bilgic described a 23-year-old male with severe TBI following a MVA [36]. After several months in hospital, he was discharged home with his mother who started to notice he was washing his hands excessively and taking more frequent showers. He had no previous psychiatric history. He scored 26/40 on Y-BOCS and commenced fluoxetine 60 mg with symptoms improving after several weeks. Bilgic did not provide the Y-BOCS score post-treatment. The case report focused on the significance of frontal lobe injury leading to OCD symptoms; treatment was not the primary outcome.

Kant and colleagues reported on a 26-year-old male with severe TBI following an industrial accident [37]. Six months post-TBI, he started to develop obsessions regarding safety and compulsively checked doors. He was diagnosed with depression as well as OCD. He was commenced on fluoxetine which was titrated up to 100 mg. His mood symptoms improved but his OCD symptoms remained. He was given a trial of clomipramine; however, it was not tolerated due to anticholinergic side-effects and he was switched back to fluoxetine.

Childers and colleagues described a case where paroxetine was used for the treatment of OCD in TBI as the primary outcome [35]. The report detailed a 38-year-old male with severe TBI as a result of falling from a moving vehicle. He started obsessing about a former girlfriend and compulsively handled photographs and letters. His symptoms particularly distracted from elements of his rehabilitation. Paroxetine 20 mg was commenced and worked well in reducing his OCD symptoms within several days. The treatment allowed him to complete inpatient rehabilitation. Standardised assessment tools were not described.

Tricyclic Antidepressants (TCAs): Three patients were treated with TCAs, with clomipramine being reported in two cases. One case reported the use of a 'tricyclic antidepressant.'

Childers and colleagues described two cases where clomipramine was used [35]. The first was a 37-year-old male with severe TBI due to being struck by a train. He had no previous psychiatric history. During recovery, he began obsessing about object arrangement on his desk and becoming anxious. He was commenced on clomipramine 25 mg at night and demonstrated clinical improvement within days. The authors did not report using assessment scales. The second case described by Childers and colleagues was of a 41-year-old male with severe TBI following an assault [35]. There was no previous psychiatric history; however, he had two prior TBIs. During rehabilitation, he demonstrated persistent and repetitive acts of meticulously cleaning objects in the rehabilitation area and attempting to aid janitorial staff in sweeping and cleaning. He became obsessed with punctuality and orderliness which interfered with rehabilitation. He was commenced on clomipramine 25 mg at night, and clinical improvement was reported to have occurred within days.

McKeon and colleagues described a 23-year-old male with severe TBI after being struck by a car [38]. He started developing rituals that involved repeated checking of clothes, brushing his teeth for over an hour, and taking extensive precautions to avoid contamination. The author's reported that he was commenced on a 'tricyclic antidepressant'; however, his OCD symptoms continued unaltered.

Stimulants: Fellus and colleagues described a 51-year-old male with severe TBI from the age of 10 following a MVA [39].OCD symptoms commenced shortly after injury. He obsessed about money and later compulsively started withdrawing cash from an ATM machine, only to redeposit it back moments later. The authors question whether his diagnosis was OCD, Pseudobulbar Palsy (PBA), or a combination of both. The authors reported the patient had trialled 12 different medication over the decades with no success. The authors did not state what medications had been previously trialled. Approximately 39-years post-TBI, the patient was commenced on dextromethorphan/quinidine (20 mg/10 mg) over a two-week period. His compulsive behaviours diminished considerably at four weeks, and remitted after six weeks. No further details regarding treatment were described.

Khanna and colleagues reported on an 18-year-old male with severe TBI following a bus accident [40]. He had no previous psychiatric history. Following the injury, he started repeating daily activities like opening and closing books and touching pens. He described distressing thoughts about not completing tasks correctly. He was initially treated with adequate doses of amitriptyline, imipramine, and trifluoperazine over a 12-month period. He was eventually prescribed amphetamine 30 mg/day and showed considerable improvement. The authors did not report using assessment scales or any other details regarding the treatments.

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs): One case in the literature reported using SNRIs. Khouzam and Donnelly reported a 51-year-old male with a severe TBI [41]. The authors did not report the mechanism of the head injury. There was no previous psychiatric history. Compulsions involved rhythmic activities of pacing and walking the majority of the day and excessive cleaning of floors. The authors used Y-BOCS to ascertain the severity of OCD prior to treatment, receiving a score of 35/40 (extreme). The patient was initially treated with clomipramine 50 mg, however he suffered dizziness and it was discontinued. He refused to trial a SSRIs, but eventually agreed to take venlafaxine after considerable encouragement. Treatment began with 75 mg of venlafaxine which was increased on the fourth day to a total dose of 75 mg twice daily. There were no side effects and his compulsive behaviours decreased within 15 days. His Y-BOCS score decreased to 25/40 at the 15 day mark, then 9/40 at the 4 week mark, and then 3/40 at 10 weeks. During a four-month follow-up appointment, his Y-BOCS score was still at 3/40 which indicated good symptom control.

Monoamine Oxidase Inhibitors (MAOIs): One case reported using MAOIs to treat OCD in TBI. Jenike and Brandon reported on a 24-year-old male with severe TBI following a MVA when he was 17-years-old [42]. He was in a coma for one month at the time of the accident, and was found to have frontal and basilar fractures with temporal haematoma. Six months post-TBI, he developed severe intrusive obsessive thoughts that he may have a severe illness. Later, other obsessive thoughts developed revolving around viruses and environmental pollutants. He unsuccessfully attempted controlling the thoughts by excessive exercise and would frequently spend hours washing his hair. Prior to the injury he had no psychiatric or neurological disease and was high functioning. He had been treated with adequate doses of phenytoin, clonazepam, chlorpromazine, trimipramine, amitriptyline, amoxapine, trazodone, methylphenidate, imipramine, doxepin, and haloperidol. Approximately eight years post-TBI, the patient was commenced on the MAOI phenelzine and within 10 months his OCD symptoms improved to the point he was capable to work and participate in social activities. Assessment tools and doses were not reported.

Combination treatment

Combination therapy (Table 3) was the second most common treatment category found in the literature.

Table 3: Combination treatments being used to treat OCD in patients with TBI.

Combination Treatment	Case Reports	Case Series	Patients
Clomipramine + ERP	1	1	2
Paroxetine + ERP	1	0	1
Clomipramine + sertraline	0	1	1
			Total patients=4

Drummond and Gravestock described a 26-year-old male with no previous psychiatric history who received a blow to the back of his

head at work resulting in severe TBI [43]. He started performing counting rituals whilst washing, shaving or combing his hair. Exposure to dirt or dust caused him to repeatedly blow his nose and cough for two hours post exposure. He scored 46/111 on the Compulsion Checklist. He was commenced on clomipramine but ceased the medication shortly after for unreported reasons. One year later, he was admitted to hospital and was commenced back on clomipramine and given ERP for three weeks. The authors reported his OCD symptoms did not improve with ERP and therefore it was ceased. His symptoms continued unchanged with clomipramine.

McKeon and colleagues described a 16-year-old female with a mild TBI after her mother hit her head with a brush [38]. She went to school the next day, feeling anxious and uneasy. She began searching for items she thought were lost. She spent lengthy periods of time searching for a handkerchief or coins which resulted in her missing classes. The compulsive searching later extended to her bedroom and other rooms in the house. Eight years later, she was admitted to hospital with depression and OCD. She was commenced on clomipramine and received intensive ERP. Despite the dual treatment approach, her OCD symptoms continued unabated. The authors did not comment on the dose of clomipramine. The treatment of OCD in TBI was not an outcome of these studies. No further details on the use of ERP were reported.

Hofer and colleagues reported on a 27-year-old male with severe TBI due to a rock-climbing accident [44]. Neuropsychological assessment showed impairments in almost every area of cognitive functioning (memory, executive functioning, and attention). He also had impairments in behaviour, emotions and personality. He demonstrated limited awareness of his deficits. He was initially prescribed risperidone (0.25 mg twice daily) for agitation whilst participating in a three month rehabilitation program. Six months post TBI, he developed obsessive thoughts that were followed by compulsive acts or ideas such as counting or repeating certain movements. Treatment of OCD in TBI was a primary outcome of this study. Hoefer and colleagues utilised Y-BOCS to monitor his symptoms pre- and post-treatment. Paroxetine was prescribed and slowly up-titrated to a total dose of 80 mg during a three-month period with no side-effects. The authors reported paroxetine was prescribed for mental stabilisation prior to psychological treatment. Following medication stabilisation, ERP was commenced. The psychological treatment occurred over a 12-month period and consisted of restructuring dysfunctional thoughts and utilising imaginal exposure and ritual prevention. The entire treatment lasted 15-months. The Y-BOCS score improved by 31% from pre-treatment to six months post-intervention. Scores on the Brief Symptom Inventory (BSI) also improved, with a reduction in self-reported clinically relevant psychological symptoms. This case was the most detailed in the literature found. Criteria for diagnosis, pre- and post-treatment measures, and treatment as the primary outcome were all included.

Kant and colleagues described a 43-year-old man with severe TBI following an industrial accident [37]. Within one week of injury, he started developing aggressive sexual obsessions about his wife which caused distress to the point he was unable to work. He had three psychiatric admissions within the next four months due to depression and anxiety symptoms. He received haloperidol, desipramine, trifluoperazine and ECT without any improvement. OCD was diagnosed five months post injury, and he was prescribed a combination of sertraline and clomipramine which controlled his symptoms to the point he was capable to return to work. Kant and colleagues did not report the doses of medications used.

Psychological treatment

Two patients received psychological treatment only (Table 4). The psychological treatments used included neurobehavioural treatment and CBT.

Table 4: Psychological treatments being used to treat OCD in patients with TBI.

Psychological Treatment	Case Reports	Case Series	Patients
Neurobehavioural	1	0	1
CBT	1	0	1
			Total patients=2

Neurobehavioural: Arco described a 24-year-old male with severe TBI following a MVA who presented one year post injury for treatment of his OCD symptoms which included counting and voiding [45]. He was of average intelligence but had difficulties in memory and problem solving post-TBI. He received neurobehavioural treatment over 11 weeks; consisting of regular in-home consultations, self-regulation procedures, stress-coping strategies, errorless remediation, and social reinforcement. At the end of the intervention, he no longer reported compulsive counting and had stabilised his voiding at an acceptable level of eight times per day (from 11). At six months follow-up, therapeutic gains were not only maintained but additional improvements observed – a further decrease in voiding to seven times per day and a reduction in the urge to void. The authors concluded the neurobehavioural treatment was effective in decreasing and controlling obsessive-compulsive counting and bladder voiding.

Cognitive Behavioural Therapy (CBT): Williams and colleagues reported on a male with severe TBI who presented two years post-TBI with compulsive behaviours which consisted of tidying the house and checking doors [46]. He was of average intelligence and had an attention and memory impairment post-TBI. He received cognitive-behavioural treatment as part of a multicompetent eight-month rehabilitation program. Results showed a decrease in his OCD symptoms to non-clinical levels. However, it was unclear how the cognitive-behavioural treatment interacted with other program components. Furthermore, the treatment appeared intensive and costly.

Other treatment

One patient received Electroconvulsive Therapy (ECT) (Table 5).

Table 5: Psychological treatments being used to treat OCD in patients with TBI.

Other Treatment	Case Reports	Case Series	Patients
ECT	0	1	1
			Total patients=1

Electroconvulsive Therapy (ECT): Kant and colleagues described a case report of a 45-year-old female with a mild-moderate TBI following a MVA with no previous history of psychiatric disorders [37]. She developed OCD symptoms within two months of injury,

repeatedly checking doors and appliances. She would compulsively tap her fingers and count in a ritualised sequence. She received several trials of medications including clomipramine, sertraline, lithium, carbamazepine, sodium valproate, and haloperidol. The authors reported that all medications were given at full therapeutic doses for sufficient duration. She eventually received seven right unilateral ECT treatments which were tolerated. The authors did not report pre-ECT Y-BOCS, however they stated scores significantly improved post-ECT and the OCD had responded to ECT.

DISCUSSION

Research regarding the psychiatric sequelae of TBI has developed since 1848, when a case study on Phineas Gage was published that detailed personality change following head injury. The understanding of TBI-associated neuropsychiatric disorders has improved in the last several decades, and the occurrence of OCD after TBI has been well documented [34,35,44-47].

Despite increasing recognition of OCD post-TBI, there is no high level evidence or evidence based guideline supporting any particular treatment of OCD in this population. Results were heterogeneous in TBI mechanism, illness duration, study outcome, and confounding comorbidity. All results were graded as Level IV evidence, according to NHMRC guidelines, indicating low quality evidence. From a Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework; case reports and case series are rated as very low evidence when developing health recommendations or guidelines [48]. The body of evidence is weak; therefore, it is difficult to make sound clinical recommendations.

Treatment generally followed guidelines for treating OCD in the general population (e.g. SSRI, clomipramine). One would assume Consultation-Liaison Psychiatrists are suggesting treatment based on current well recognised guidelines for idiopathic OCD [23-25]. However, adjustments in these approaches must be made to account for the physical and cognitive sequelae of TBI and the increased sensitivity to the adverse effects of medications. Medications with prominent anticholinergic, antihistaminergic or antidopaminergic effects should be used with caution in patients with TBI [5,26].

Clomipramine was the most commonly used pharmacological agent (either in isolation or combination); however, reported efficacy was inconsistent. Kant and colleagues described a case of a patient being treated with clomipramine but switched to fluoxetine due to the anticholinergic side-effects [37]. Khouzam and Donnelly also reported a patient who could not tolerate the side-effects of clomipramine [41].

SSRIs were the most commonly used pharmacological class in the literature studied; however, the reported efficacy was also variable. The literature search found reports on ECT and stimulants being useful in treatment resistant cases [37,39,40]. Isolated reports on the successful use of an SNRI and MAO are interesting and may warrant further investigation [41,42].

ERP was the most commonly used psychological intervention, mostly in combination with pharmacological treatment. Established guidelines highly recommend a combination approach when treating OCD in the general population [23-25]. However, a combination approach in treating OCD symptoms in this TBI population had mixed results (Appendix 5). Surprisingly, psychological treatment alone and non-SSRI pharmacological treatments demonstrated more consistent results.

The most comprehensive study was by Hoefer and colleagues, detailing a combination treatment (ERP and CBT with paroxetine) which demonstrated a 31% improvement in Y-BOCS during the study period [44]. This study was notable due to following standardised international guidelines for case reporting (CARE) [49].

Some of the cases demonstrated how OCD in patients with TBI can interfere with physical rehabilitation. While this review predominantly focused on specific treatments for OCD in TBI, one must remember that patients with TBI receive multidisciplinary management and that any treatment utilised should be compatible with the various other aspects of the treatment plan.

CONCLUSION

Pharmacological, psychological, combination treatments and ECT have been utilised to treat OCD in the TBI population. There is no high quality evidence to support definite recommendations; however, it is intriguing to note that treatments not immediately described in guidelines for treating OCD in the general population appear to have had some success in treating OCD in a TBI population. This literature review highlights that there is a paucity of high quality research, and that further research in this area would support recommendations for future clinical practice.

LIMITATIONS

The level of evidence was limited to descriptive case reports and case series. There were limited studies with heterogeneous data, and no RCTs. This review was initially intended to be systematic; however, given the paucity of research and the quality of evidence available, a narrative approach was taken.

Most cases did not report on the use of a standardised assessment tool to quantify the effect of treatment, and instead relied on subjective clinical response. The use of different outcome measures made direct comparisons between cases difficult.

One study did not specify the exact medication used (e.g. 'tricyclic antidepressant'), and some did not report on the doses and frequency of medication or therapy used [38]. The majority of studies did not comment on side-effects.

The diagnosis of OCD in TBI would be complicated, due to physical and cognitive impairments and diagnostic masking. Perseverations may present similar to compulsions [22,50]. It was unclear, in many cases, how the author(s) arrived at the diagnosis of OCD.

Efficacy, for the purpose of this literature review, was determined when the case reported some benefit from treatment. It is possible some articles may have been missed because of inconsistent indexing in electronic databases. Biases (e.g. observer bias, publication bias) may have influenced the author's results and conclusions.

FUTURE DIRECTIONS AND RECOMMENDATIONS

Additional studies of higher quality are required before a practical guideline can be developed. Future research should use a standardised assessment tool pre- and post-treatment (e.g. Y-BOCS) and specify the exact treatment and dose/frequency of treatment, as well as timeframe. Furthermore, a standardised diagnostic procedure should be applied.

Future researchers may consider head-to-head studies comparing treatments within a treatment category. However, given the current

paucity of research and the potential difficulties in identifying and recruiting patients, any further research of a higher level of evidence would be helpful on this topic and future researchers may consider cohort and/or case-control studies.

There was an over-representation of males who had a 'severe' TBI and received treatment for OCD (Appendix 4). Future epidemiological studies may help extrapolate whether there is any association between gender, TBI severity and the incidence and prevalence of OCD.

DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

FUNDING

The author(s) received no financial support for the research, authorship and/or publication of this article.

REFERENCES

1. Grande CV, Melo LL, Jucá Moscardi MF, Marttos A. Traumatic Brain Injury. The Trauma Golden Hour 2020:49-53.
2. Nguyen R, Fiest KM, McChesney J, Kwon CS, Jette N, Frolkis AD, et al. The international incidence of traumatic brain injury: A systematic review and meta-analysis. Can J Neurol Sci. 2016;43(6):774-785.
3. Tate RL, McDonald S, Lulham JM. Incidence of hospital□treated traumatic brain injury in an Australian community. Aust N Z J Public Health. 1998;22(4):419-423.
4. Marklund N, Tenovuo O. Pathophysiology of Severe Traumatic Brain Injury. Management of Severe Traumatic Brain Injury. 2020:35-50.
5. Rao V, Lyketsos C. Neuropsychiatric sequelae of traumatic brain injury. Psychosomatics. 2000;41(2):95-103.
6. Ahmed S, Venigalla H, Mekala HM, Dar S, Hassan M, Ayub S. Traumatic brain injury and neuropsychiatric complications. Indian J Psychol Med. 2017;39(2):114-121.
7. Derksen M, Feenstra M, Willuhn I, Denys D. The serotonergic system in obsessive-compulsive disorder. Behav Neurosci. 2020;31:865-891.
8. Dougherty DD, Wilhelm S, Jenike MA. Obsessive-compulsive and related disorders. Textbook of Psychiatry. 2014.
9. Tsao JW, editor. Traumatic brain injury: A clinician's guide to diagnosis, management, and rehabilitation. Springer Nature. 2019.
10. Hiott DW, Labbate L. Anxiety disorders associated with traumatic brain injuries. NeuroRehabilitation. 2002;17(4):345-355.
11. Osborn AJ, Mathias JL, Fairweather-Schmidt AK, Anstey KJ. Anxiety and comorbid depression following traumatic brain injury in a community-based sample of young, middle-aged and older adults. J Affect Disord. 2017;213:214-221.
12. Popovitz J. Multidimensional approach to investigating neural mechanisms of anxiety outcomes following traumatic brain injury in mice. Johns Hopkins. 2020.
13. Carota A, Staub F, Bogousslavsky J. Emotions, behaviours and mood changes in stroke. Curr Opin Neurol. 2002;15(1):57-69.
14. Coetzer BR. Obsessive-compulsive disorder following brain injury: a review. Int J Psychiatry Med. 2004;34(4):363-377.
15. Deb S, Lyons I, Koutzoukis C. Neurobehavioural symptoms one year after a head injury. Br J Psychiatry. 1999;174(4):360-365.
16. American Psychiatric Association. Obsessive-Compulsive and Related Disorders, 5th edn, Washington, DC. 2013.
17. Baguley I, Slewa-Younan S, Lazarus R, Green A. Long-term mortality trends in patients with traumatic brain injury. Brain Inj. 2000;14(6):505-512.
18. Ratcliff G, Colantonio A, Escobar M, Chase S, Vernich L. Long-term survival following traumatic brain injury. Disabil Rehabil. 2005;27(6):305-314.
19. Whelan-Goodinson R, Ponsford J, Johnston L, Grant F. Psychiatric disorders following traumatic brain injury: Their nature and frequency. J Head Trauma Rehabil. 2009;24(5):324-332.
20. Coetzer BR. Acquired Brain Injury: A Clinical Neuropsychology Perspective. Adv Psychol Res. 2006;43:23.
21. Cameron DH, Rowa K, McKinnon MC, Rector NA, McCabe RE. Neuropsychological performance across symptom dimensions of obsessive-compulsive disorder: A comment on the state and critical review of the literature. Expert Rev Neurother. 2020;20(5):425-438.
22. Grados MA. Obsessive-compulsive disorder after traumatic brain injury. Int Rev Psychiatry. 2003;15(4):350-358.
23. Australian R. Australian and New Zealand clinical practice guidelines for the treatment of panic disorder and agoraphobia. Aust N Z J Psychiatry. 2003;37(6):641-656.
24. Brakoulias V. Managing obsessive compulsive disorder. Aust Prescr. 2015;38(4):121.
25. Johnson C, Blair-West S. Obsessive-compulsive disorder: the role of the GP. Aust Fam. 2013;42(9):606-609.
26. Hicks AJ, Clay FJ, Hopwood M, James AC, Perry LA, Jayaram M, et al. Efficacy and harms of pharmacological interventions for anxiety after traumatic brain injury: Systematic review. J Neurotrauma. 2021;38(5):519-528.
27. Gualtieri CT, Johnson LG. Traumatic brain injury: Special issues in psychiatric assessment. NeuroRehabilitation. 1999;13(2):103-115.
28. Johnson MK, Raye CL. Cognitive and brain mechanisms of false memories and beliefs. APA Psycnet. 2000.
29. Baron Levi J. Executive Functions (EF), Traumatic Brain Injury (TBI), Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), Conduct Disorder (CD) and Learning Difficulty (LD). The Hairy Bikie and Other Metacognitive Strategies 2020:17-23.
30. Aardema F. COVID-19, obsessive-compulsive disorder and invisible life forms that threaten the self. J Obsessive Compuls Relat Disord. 2020;26:100558.
31. Chakraborty A, Karmakar S. Impact of COVID-19 on obsessive compulsive disorder (OCD). Iran J Psychiatry. 2020;15(3):256.
32. Shafran R, Coughtrey A, Whittal M. Recognising and addressing the impact of COVID-19 on obsessive-compulsive disorder. Lancet Psychiatry. 2020;7(7):570-572.
33. National Health and Medical Research Council. APPENDIX F: Levels of evidence and recommendation grading. National Institute of Clinical Studies. 2009.
34. Stengler-Wenzke K, Müller U. Fluoxetine for OCD after brain injury. Am J Psychiatry. 2002;159(5):872.
35. Childers MK, Holland D, Ryan MG, Rupright J. Case study: Obsessional disorders during recovery from severe head injury: report of four cases. Brain Inj. 1998;12(7):613-616.
36. Bilgic B, Baral-Kulakszoglu I, Hanagasi H, Saylan M, Aykutlu E, Gurvit H, et al. Obsessive–compulsive disorder secondary to bilateral frontal damage due to a closed head injury. Cogn Behav Neurol. 2004;17(2):118-120.

37. Kant R, Smith-Seemiller L, Duffy JD. Obsessive-compulsive disorder after closed head injury: review of literature and report of four cases. Brain Inj. 1996;10(1):55-64.

38. McKeon J, McGuffin P, Robinson PH. Obsessive-compulsive neurosis following head injury: a report of four cases. Br J Psychiatry. 1984;144(2):190-192.

39. Fellus J, Halper J, Defina P. Dextromethorphan/quinidine leading to remission of 39 years of compulsive behaviour following traumatic brain injury (TBI). Brain Inj. 2016;30(5-6):814

40. Khanna S, Narayanan HS, Sharma SD, Mukundan CR. Post traumatic obessive compulsive disorder-a case report. Indian J Psychiatry. 1985;27(4):337.

41. Khouzam HR, Donnelly NJ. Remission of traumatic brain injury-induced compulsions during venlafaxine treatment. Gen Hosp Psychiatry. 1998; 20(1):62-63.

42. Jenike MA, Brandon AD. Obsessive-compulsive disorder and head trauma: a rare association. J Anxiety Disord. 1988;2(4):353-359.

43. Drummond LM, Gravestock S. Delayed Emergence of Obsessive–Compulsive Neurosis Following Head Injury: Case Report and Review of its Theoretical Implications. Br J Psychiatry. 1988;153(6):839-842.

44. Hofer H, Frigerio S, Frischknecht E, Gassmann D, Gutbrod K, Müri RM. Diagnosis and treatment of an obsessive–compulsive disorder following traumatic brain injury: A single case and review of the literature. Neurocase. 2013;19(4):390-400.

45. Arco L. Neurobehavioural treatment for obsessive-compulsive disorder in an adult with traumatic brain injury. Neuropsychol Rehabil. 2008;18(1):109-124.

46. Williams WH, Evans JJ, Fleminger S. Neurorehabilitation and cognitive-behaviour therapy of anxiety disorders after brain injury: An overview and a case illustration of obsessive-compulsive disorder. Neuropsychol Rehabil. 2003;13(1-2):133-148.

47. Harlow JM. Passage of an iron rod through the head. Boston Med Surg. 1848;39(20):1.

48. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011;64(4):383-394.

49. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D. The CARE guidelines: consensus-based clinical case reporting guideline development. BMJ Case Rep. 2013;23.

50. Coetzer B, Stein DJ. Obsessive-compulsive disorder following traumatic brain injury: Clinical issues. J Cogn Rehabil. 2003;21(4).