Psychological interventions for treating neuropsychiatric consequences of acquired brain injury

NEUROPSYCHOLOGICAL REHABILITATION
2019, VOL. 29, NO. 10, 1509–1542
https://doi.org/10.1080/09602011.2018.1433049

Routledge
Taylor & Francis Group

Psychological interventions for treating neuropsychiatric consequences of acquired brain injury: A systematic review

Daan P. J. Verberne[a,b,c], Peggy J. J. Spauwen[a,b] and Caroline M. van Heugten[b,c,d]

[a]Department of Acquired Brain Injury, GGZ Oost Brabant, Boekel, the Netherlands; [b]Department of Psychiatry and Neuropsychology, Faculty of Health, Medicine and Neuroscience, School of Mental Health and Neurosciences (MHeNS), Maastricht University Medical Centre, Maastricht, the Netherlands; [c]Limburg Brain Injury Centre, Maastricht, the Netherlands; [d]Department of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, the Netherlands

ABSTRACT

Anxiety, aggression/agitation, apathy and disinhibition are common neuropsychiatric consequences of acquired brain injury (ABI); these consequences can cause functional impairment and lead to reduced social integration. This systematic review aims to provide an examination of the current evidence on psychological interventions for treating these consequences. Two reviewers selected potential relevant articles, retrieved from five literature databases; methodological quality was assessed and appraised. A total of 5207 studies were found, of which 43 were included: 21 studies for anxiety, 18 for aggression, two studies for apathy, and six for disinhibition. Three studies addressed multiple consequences. Four high-quality (i.e., Class I and II) studies showed significant decreases in anxiety after cognitive behavioural therapy (CBT). In total, 14 studies consistently showed significant decreases in aggression/agitation after behavioural management techniques or anger management sessions. Substantial variability existed in the examined interventions and in their effects on apathy and disinhibition. Unfortunately, firm conclusions and recommendations for clinical practice are considered premature, due to concerns about the methodology used. However, this review yielded new evidence on the effectiveness of CBT for anxiety symptoms post-ABI and there has been some response to the ongoing call for studies with high methodological quality.

ARTICLE HISTORY Received 23 June 2017; Accepted 21 January 2018

KEYWORDS Acquired brain injury; neuropsychiatric consequences; psychological interventions; effectiveness; systematic review.

Introduction

The neuropsychiatric consequences of Acquired Brain Injury (ABI) or, in other words, neuropsychiatric symptomatology (behavioural, emotional and psychiatric) due to ABI, occur frequently. As many as 65% of patients with brain injury have at least one

CONTACT Peggy J. J. Spauwen p.spauwen@ggzoostbrabant.nl Department of Acquired Brain Injury, GGZ Oost Brabant, Huize Padua, PO Box 3, Boekel 5427 ZG, the Netherlands

psychiatric disorder (Whelan-Goodinson, Ponsford, Johnston, & Grant, 2009) and 44% of the patients with brain injury have two or more psychiatric disorders (Hibbard, Uysal, Kepler, Bogdany, & Silver, 1998). The most frequently occurring psychiatric consequences of ABI are depression, anxiety, aggression/agitation, apathy and disinhibition. It is acknowledged that these neuropsychiatric consequences may arise from both internal (e.g., damaged neural systems, cognitive impairment) and external factors (i.e., environment, post-injury learning experiences), or because of an interplay between these factors (Alderman & Wood, 2013; World Health Organisation, 2001).

Depression is expressed particularly by feelings of uselessness, sadness, crying episodes, pessimism and suicidal ideas (Angelelli et al., 2004). Depression is highly prevalent and is reported in about 29% to 61% of patients with ABI (Angelelli et al., 2004; Ciurli, Formisano, Bivona, Cantagallo, & Angelelli, 2011; van Heugten et al., 2013). Anxiety includes feelings of apprehension or dread with or without autonomic signs or symptoms (Vaishnavi, Rao, & Fann, 2009) and is reported in 8% to 39% of those with ABI (Angelelli et al., 2004; Ciurli et al., 2011; van Heugten et al., 2013). Aggression/agitation is particularly expressed in restlessness, outbursts of anger and obstinacy (Ciurli et al., 2011) and is observed in 24% to 55% (Angelelli et al., 2004; Ciurli et al., 2011; van Heugten et al., 2013) of the ABI population. Apathy is characterised by a loss of motivation, reduced initiation, reduced/loss of sustained activity and concerns regarding goal-directed behaviour (Marin, 1991). Rates of apathy symptoms, secondary to ABI, range from 27% to 56% (Angelelli et al., 2004; Ciurli et al., 2011; van Heugten et al., 2013). Disinhibited behaviour is reported in 10% to 39% of ABI cases (Angelelli et al., 2004; Ciurli et al., 2011; van Heugten et al., 2013) and can be expressed by acting impulsively, speaking confidentially with unfamiliar people and being tactless or offensive. Furthermore, disinhibition can include inappropriate sexual behaviour such as inappropriate sexual talk, inappropriate touching or exhibitionism; these behaviours have been reported in 9–28% of all cases with ABI (Kelly, Brown, Todd, & Kremer, 2008; Simpson, Sabaz, & Daher, 2013).

Neuropsychiatric consequences of ABI significantly increase the likelihood of functional impairment, reduced social functioning and reduced health-related quality of life (Bryant et al., 2010; Diaz et al., 2012; Rogers & Read, 2007). Therefore, it is important to know which interventions are available and effective in decreasing these consequences. A number of reviews have been conducted in which psychological interventions for neuropsychiatric consequences of ABI were examined. In particular, depression has been extensively addressed, such as by the systematic Cochrane review of Gertler, Tate, and Cameron (2015). Other reviews, however, lack a systematic approach in their literature search (Alderman & Wood, 2013; Rao, Koliatsos, Ahmed, Lyketsos, & Kortte, 2015), limiting their focus to patients with Traumatic Brain Injury (TBI; Rao et al., 2015; Wiart, Luaute, Stefan, Plantier, & Hamonet, 2016; Ylvisaker et al., 2007), keeping their main focus on specific psychiatric consequences of ABI such as aggression (Alderman & Wood, 2013; Byrne & Coetzer, 2016), or providing treatment options based on the evidence of a single clinical trial, or non-experimental studies (Rao et al., 2015). Cattelani, Zettin, and Zoccolotti (2010) provide a well-designed systematic review, but this review can be considered outdated at this point, as the literature was gathered up until 2008. In addition, previous reviews did not use guidelines for classifying single case experimental design (SCED) studies, even though these designs are considered methodologically strong and are frequently used in this field because of the heterogeneity of the population (Perdices et al., 2006). Furthermore, these designs

can be of significant added value for practitioners/clinicians (Alderman & Wood, 2013; Ylvisaker et al., 2007).

The current systematic review therefore aimed to provide a comprehensive examination of the current evidence on psychological interventions for neuropsychiatric (anxiety, aggression, apathy and disinhibition) consequences of ABI. Depression is excluded from this review as it is an extensive topic, more suitable for a separate review, and was covered by Gertler et al. in 2015. In comparison with reviews conducted earlier, our approach to the literature search was systematic, and the perspective has been extended to ABI and the frequently occurring psychiatric consequences of ABI. Furthermore, the methodological quality of the included studies was assessed using established methods.

Methods

Study selection

This systematic review was designed according to the guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P; Moher et al., 2015). The protocol was not registered in PROSPERO. Studies were included when: (1) the study population included adults with ABI or non-progressive brain injury; (2) a psychological intervention was examined for effectiveness with quantitative outcome measures; (3) anxiety, aggression or agitation, apathy or disinhibition was specifically addressed by the intervention; and (4) the effect of the intervention was measured in patients (i.e., not the caregiver or family). Exclusion criteria were studies including (1) only patients <18 or >65 years of age; (2) patients with a premorbid diagnosis of psychiatric disorders, premorbid mental retardation or current drug/alcohol dependency; (3) patients were military personnel or veterans; (4) pharmacological interventions were in play (stable dosage of medication during the study was permitted); (5) interventions were aimed at prevention of symptom development; (6) the results of qualitative case descriptions were not quantified; or (7) the patients had neurodegenerative diseases. The rationale for excluding the above-mentioned patients was that we were specifically interested in the consequences of ABI. In the case of military personnel, it cannot be stated with certainty that post-traumatic stress disorder has evolved as a consequence of ABI, as it is likely to have evolved prior to the brain injury in these patients (e.g., due to psychological traumatic events). Therefore, this group was excluded. Interventions with the aim of preventing the development of symptoms were excluded as the focus of this review was on symptoms actually present in the studied populations (such as the presence of aggressive events for which behavioural management interventions were included in this review).

The following literature databases were searched systematically: Cochrane, CINAHL, EMBASE, PsycINFO and PubMed. These databases were searched on (the combination of) the following categories: "*population*", "*aggression*", "*agitation*", "*anxiety*", "*apathy*", "*disinhibition*" and "*therapy*". Medical subject headings (MESH and Emtree) were used for the searches, in combination with terms entered as text words. For EMBASE it was sufficient to use only Emtree terms. First, the population was selected and subsequently the different terms for "population" were combined with the different terms for the neuropsychiatric consequences. This search, with all the terms combined per consequence, was combined with "intervention". Language was limited to "English" and "Dutch", and

publication date to "2000 to 2016". The last search was conducted in June 2016. Appendix 1 outlines the search strategy for PubMed. Limiting species to "human" and population age to "18–65" was manually conducted during the selection of studies. Duplicates were removed. All potentially relevant studies were collected and managed with Endnote X4. The first step of selection was by title/abstract, assessed by two reviewers (DV and PS). Those studies about which inclusion or exclusion was unclear were read in their entirety before a decision was made. Hand searches were conducted after checking reference lists of the studies that were read full-text, and checking reviews on the topic. Reviews were examined for potential accompanying single case studies, both non-experimental and experimental. Studies describing multiple single subject designs were assessed separately for eligibility (i.e., according to specified age, premorbid psychiatric diagnosis, current alcohol dependency or medication change). When disagreement occurred regarding study eligibility, a joint discussion took place or a third reviewer (CvH) was consulted to reach a consensus.

Classification and appraisal

The full text of all included studies was read and the studies were subsequently divided into three levels of quality, according to the method of Cicerone et al. (2011). The first level was Class I evidence, which included well-designed, prospective, randomised controlled trials (RCTs). Class II evidence consisted of prospective, non-randomised cohort studies; retrospective, non-randomised case–control studies; or multiple-baseline studies, which permitted a direct comparison of treatment conditions. Studies were regarded as Class III evidence when they included a clinical series without concurrent controls; studies using a single subject design with adequate quantification and analyses; or studies that were designed as comparative effectiveness studies but lacked a direct statistical comparison of treatment conditions. SCED, which is called "N-of-1" design in the field of medicine, is a frequently used design in this field of research (Perdices et al., 2006). However, this kind of design is not separately described by the classification method of Cicerone et al. (2011). Therefore, classification of SCEDs was based on the description of Tate et al. (2017). SCEDs with randomisation can provide Class I level of evidence (Guyatt, Jaeschke, & McGinn, 2002; OCEBM, 2011) and are therefore considered as such. SCEDs without randomisation were considered as Class II level of evidence. These classifications were based on the agreement of two reviewers (DV and PS). In case of disagreement, this was resolved by a joint discussion or by consultation with a third reviewer (CvH).

Class I and II studies were considered studies of high-quality and Class III of moderate-quality. Additionally, a critical appraisal of the high-quality studies was made by assessing Class I and II studies with the use of the guidelines of Cicerone, Azulay, and Trott (2009) and Tate et al. (2013). Conclusions and recommendations were based on the quality (including appraisal) and quantity of the included studies.

Effectiveness of interventions

Interventions were considered effective in the case of a statistically significant decrease or clinically relevant decrease (i.e., from a score above the clinical cut-off to below or a change in a score that was large enough to be considered as clinically relevant) on at least one outcome measure.

Results

Characteristics of the included studies

Figure 1 depicts a flowchart that shows the results of the selection process with the number of studies according to each step. Forty-seven studies were included, of which 21 addressed anxiety, 18 addressed aggression, two addressed apathy, and six addressed disinhibition. Two studies examined two domains of interest, i.e., aggression and disinhibition (Yody et al., 2000), and anxiety and agitation (Suffoletto et al., 2013). Another study examined three domains of interest: anxiety, apathy and disinhibition (Backhaus, Ibarra, Parrott, & Malec, 2016). This adds up to 43 unique studies in total. Not all participants in (multiple) single case design studies met the criteria for inclusion of this review, i.e., they had a premorbid psychiatric diagnosis, had unstable medication use or were too old/young, and some single case design studies examined more than one kind of intervention by studying separate cases (these separate cases are considered as one study, but the results of the different kinds of interventions are described separately). The study of Arundine et al. (2012) examined the same population as Bradbury et al. (2008).

A total of 678 unique patients met the inclusion criteria. In the 43 studies, the sample size varied from 1 to 180, with a mean overall sample size of 16 patients and a median of two per study. The most studied population was TBI patients, who were examined in 25 studies. Other study populations included stroke patients (five studies), patients with subarachnoid haemorrhages (two studies) or patients with hypoxia (one study). Eleven studies examined patients with ABI or, in other words, mixed samples. Sixteen different kinds of interventions were studied, of which Cognitive Behavioural Therapy (CBT) was the focus of 14 studies and behavioural management techniques in 12 studies. Anger management sessions were addressed in four studies and multifactorial interventions were investigated in two studies. Twelve other kinds of interventions were studied once (see Tables 1–4 for more detailed descriptions of interventions). Of the 47 studies across the domains of interest (including studies examining effects on multiple neuropsychiatric consequences), 37 (78.7%) showed significant decreases or clinically relevant decreases on at least one outcome measure.

Classification and appraisal

The included studies were classified according to quality, which resulted in 10 (23.3%) Class I studies, 10 (23.3%) Class II studies and 23 (53.5%) Class III studies. Derived from this classification, 20 high-quality studies and 23 moderate-quality studies were included.

On average, 51.2% (33.3% to 81.3%) of the quality criteria were met in the high-quality studies. With regard to the RCTs (i.e., Class I; Table 5), the mean was 64.4%, whereas the only Class I SCED study met 40.0% of the quality criteria (Table 6). Of the Class II SCED studies, an average of 45.8% of the criteria was met, whereas the only prospective cohort study (Class II) met 75.0%. No RCT scored more than 81.3%, where it is notable that internal validity is of less quality or is less documented: information on possible co-interventions was lacking, outcome measurements were not blinded and intention-to-treat (ITT) analysis was performed in only one study. Descriptive criteria were in general well documented, but information on withdrawal/drop-out rates and long-term outcome measurements were missing in more than half of the RCTs. No

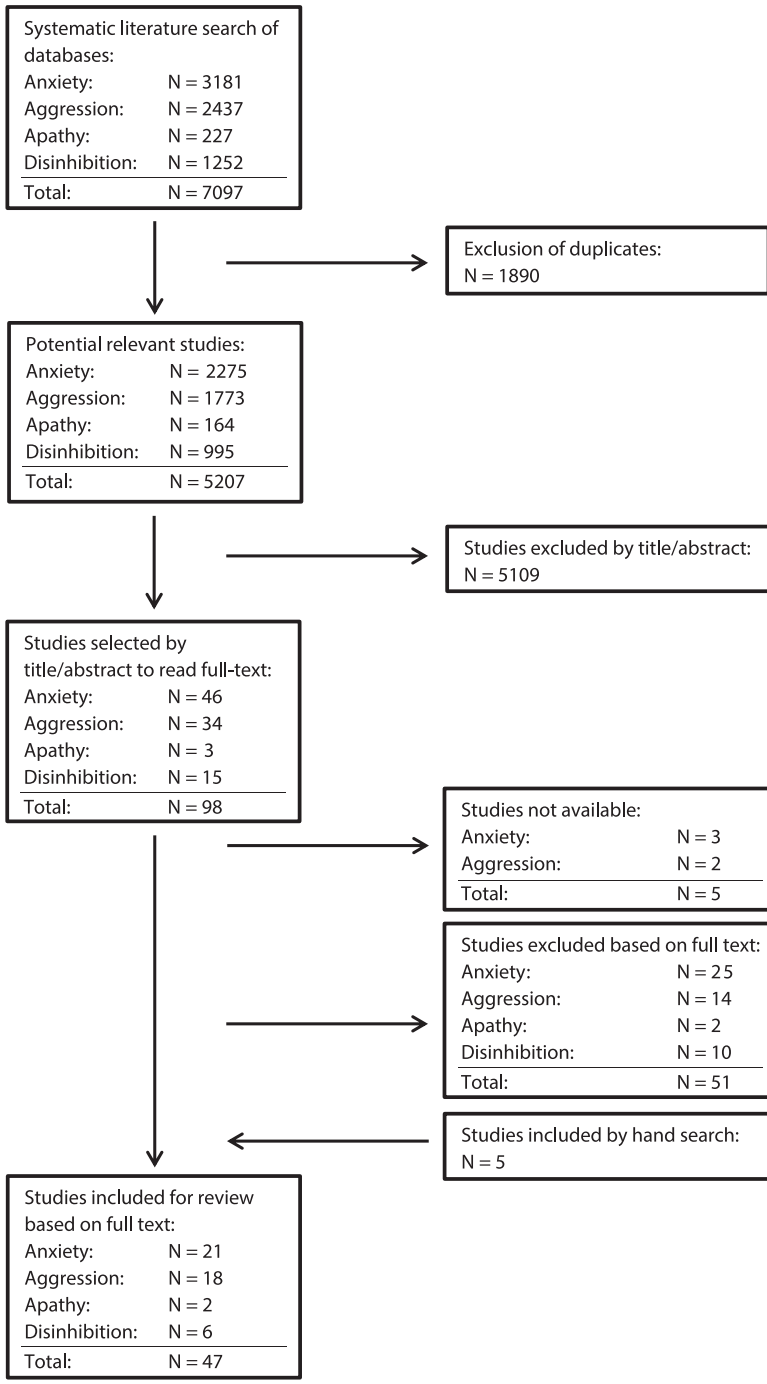

Figure 1. Flowchart displaying selection of studies.

Table 1. Evidence table with studies that examined the effectiveness of psychological interventions addressing anxiety.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Arco (2008)	SCED Changing criterion design without randomisation	Class II	TBI *N* = 1	- Multifactorial neurobehavioral treatment consisting of (1) in-home consultations, (2) self-regulation procedures (i.e., self-recording of compulsive behaviour, errorless remediation, social reinforcement) Duration: 1 hr per session, for 10 weeks, with varying frequency.	1. Self-recording of compulsive behaviour (counting & voiding) 2. Self-ratings of urges	1. Compulsive counting decreased to zero levels during intervention and remained at this level at 6 months post-intervention. Compulsive voiding decreased by 45%. 2. Urges to void decreased from pre- to post-intervention.	+
Arundine et al. (2012)	Clinical series without concurrent controls	Class III	ABI *N* = 17	1. Telephone-administered CBT 2. Group CBT Duration: 45–75 min/session, 1–2 per week, for 9 weeks	1. DASS-21 – domain anxiety	1. Significant decrease in anxiety from pre-treatment to 6-months follow-up in both groups. However, there was a significant increase in anxiety from post-treatment to 6-month follow-up.	+
Ashworth, Clarke, Jones, Jennings, and Longworth (2015)	Clinical series without concurrent controls	Class III	ABI *N* = 12	CFT including: Group therapy using the CFT approach. Duration: 4 days - Individual CFT session Duration: 1 per week, for 18 weeks	1. HADS – domain anxiety	1. Significant decrease in anxiety from pre- to post-intervention and from pre-intervention to 3 month follow-up. No differences between post-intervention and follow-up.	+
Backhaus et al. (2016)	RCT	Class I	ABI *N* = 19	1. CBT with psycho-education and instructions in stress management and problem-solving strategies. 2. Peer support group (control) Duration: 2 hr per session, 1 per week, 16×	1. BSI-18	1. No significant differences between the two groups over time. No significant improvements reported for either group.	–

(*Continued*)

Table 1. Continued.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Bradbury et al. (2008)	Prospective cohort study	Class II	ABI *N* = 20	1. Telephone-administered CBT 2. Group CBT 3. General information provided by telephone (control) 4. General information provided in group (control) Duration: 45–75 min/session, 1 or 2 per week, for 9 weeks	1. SCL-90-R, GSI scale 2. DASS-21 – domain anxiety	1. Significant decreases for both CBT groups from pre- to post-intervention and from pre-intervention to 1-month follow-up. No significant changes for either information provision control group. 2. Significant decreases for both CBT groups from pre- to post-intervention and from pre-intervention to 1-month follow-up. No significant changes for either information control group.	+
Gracey, Oldham, and Kritzinger (2007)	Single subject design	Class III	Subarachnoid haemorrhage *N* = 1	1. CBT Duration: 1 per week, for 10 weeks	1. HADS – domain anxiety 2. PRS	1. Anxiety scores increased from baseline to start of intervention but decreased to below clinical cut-off at the end of intervention. Slight increase in scores from the end of intervention to 6 months follow-up. 2. Safety-seeking behaviour due to panic attack reduced from pre-intervention to end of intervention, as well as beliefs relating to fear of a catastrophic neurological event when panicking.	+
Graham, Gillanders, Stuart, and Gouick (2015)	Single subject design	Class III	Stroke *N* = 1	1. ACT Duration: 9 sessions	1. DASS-21 – domain anxiety	1. Anxiety scores decreased steadily throughout the intervention from "extremely severe" to "mild" based on cut-off scores.	–

Hodgson et al. (2005)	RCT	Class I	ABI $N = 12$	1. Individual CBT including relaxation, cognitive strategies, graded exposure and assertiveness skills training. Duration: 1 hr per session, 1 per week, for 9–14 weeks 2. Waitlist (control)	1. SPAI 2. HADS – domain anxiety 3. POMS Tension anxiety	1. No significant group × time interaction effect for either social phobia scales. 2. Significant group × time interaction effect for anxiety. This includes a decrease in anxiety for treatment group from pre- to post-treatment, and an increase in anxiety for the waitlist control group. 3. Significant group × time interaction effect for tension anxiety. This includes a decrease for treatment group from pre- to post-treatment, and an increase in tension anxiety for waitlist group.	+
Hofer et al. (2013)	Single subject design	Class III	TBI $N = 1$	Multifactorial intervention, including - CBT phase with exposure and response prevention) Duration: 13 sessions, 4 months - Psychotherapeutic phase Duration: 15 sessions, 4 months - Cognitive therapy to restructure the dysfunctional thoughts Duration: 2 sessions	1. Y-BOCS 2. SCID-I	1. A decrease of 16% in OCD symptoms from pre- to post intervention and 31% from pre-intervention to 6 months follow-up in scores. Scores remained above clinical cut-off. 2. Decrease in intensity and frequency of symptoms. However, OCD diagnosis remained after treatment.	–
Hsieh et al. (2012a)	Single subject design	Class III	TBI $N = 1$[c]	- Supportive counselling Duration: 1 per week, 3× -CBT Duration: 1hr/session, 1 per week, 9×	1. HADS – domain anxiety 2. DASS-21 – domain anxiety	1. Scores decreased from "severe" to "moderate" and remained "moderate" at 21 weeks follow-up. 2. Scores decreased from severe to within normal range. Effects were maintained at 21 weeks follow-up.	+

(*Continued*)

Table 1. Continued.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Hsieh et al. (2012b)	Single subject design	Class III	TBI *N* = 1	1. MI Duration: 50–60 min per session, 1 per week, 3× 2.CBT Duration: 60 min per session, 1 per week, 9×	1. HADS – domain anxiety	1. Anxiety scores decreased from "moderate" at baseline to "mild" at post-MI and reduced further to "normal" post-CBT.	+
Joo, Lee, Chung, and Shin (2010)	Clinical series without concurrent controls	Class III	Subarachnoid haemorrhage *N* = 11	1. Mindfulness-based stress reduction programme Duration: 150 min per session, 1 per week, 8 weeks	1. STAI-trait/state scale anxiety	1. No significant difference from pre- to post-intervention.	–
Kneebone and Jeffries (2013)	Single subject design	Class III	Stroke *N* = 1[c]	1. CBT. Duration: 45–60 min per session, 7×, 3–4 months	1. HADS – domain anxiety	1. Anxiety scores decreased from clinical levels pre-intervention to subclinical levels post-intervention. This effect was maintained at 2 and 3 months post-intervention.	+
McDonald et al. (2008)	RCT	Class I	ABI *N* = 51	1. Social skills training with CBT components. 2. Social group with social activities. (control) Duration: 4 h/week, 12 weeks 3. Waitlist (control)	1. DASS-21 – domain anxiety	1. No significant time × group interaction effect. This is indicative of no treatment effect. No significant change in anxiety scores from pre- to post-intervention for treatment group.	–
Peng et al. (2015)	RCT	Class I	Stroke *N* = 180	1. NLP with health education Duration: 60–120 min per session, 2 per week, 2 weeks 2. Usual care (control)	1. HAM-A	1. Significantly more patients in the intervention group achieved subclinical levels of anxiety post-intervention than the control group. Anxiety scores significantly decreased from pre- to post-intervention. No significant decrease in score from pre-intervention to 6-months follow-up.	+

Ponsford et al. (2016)	RCT	Class I	TBI $N = 75$	1. MI and tailored CBT 2. NDC and tailored CBT Duration: 12 weeks + 3 "booster" sessions 3. Waitlist control	1. HADS – domain anxiety	1. Significant decrease in anxiety scores for both CBT groups. The NDC + CBT group showed significantly greater reduction in anxiety compared with MI + CBT group, relative to waitlist control. No significant differences in change scores from pre- to post- intervention between MI + CBT and NDC + CBT.	+ (CBT intervention)
Suffoletto et al. (2013)	RCT	Class I	TBI $N = 43$	1. Mobile phone text messaging with education and support 2. Text messaging without feedback (control) Duration: 3 messages per day, 2 weeks	1. SMS Anxiety/ Irritability scores 2. PHQ-Anxiety 3. PTSD-screening	1. No significant decrease in anxiety for either group. No significant differences between groups in anxiety at follow-up, 2 + 3. At 2-week follow-up no significant differences between groups in proportion of patients meeting PTSD criteria or anxiety criteria for positive diagnosis.	–
Tiersky et al. (2005)	RCT	Class I	TBI $N = 20$	1. Individual CBT and individual cognitive remediation Duration: 2 × 50 min/session, 3×/ week, 11-weeks. Plus daily half-hour homework 2. No-treatment control	1. SCL-90-R anxiety subscale	1. Treatment group showed significantly decreased anxiety scores from baseline to post-intervention. Anxiety levels reduced to within normal levels after treatment. No significant change for the control group.	+
Wall, Turner, and Clarke (2013)	Single subject design	Class III	TBI $N = 1$	1. Holistic rehabilitation (i.e., structured daily routine, neuro-rehabilitation approaches, psychotherapy, CBT) Duration: 12 months	1. HADS – domain anxiety	1. Anxiety scores decreased from "mild" at pre-intervention to within "normal" levels post-intervention.	+
Ward and Hogan (2015)	Single subject design	Class III	TBI $N = 1$	1. Client-centred, integrative therapy (including action-focused,		1. Over the first year, scores on domain Problems (which	+

(*Continued*)

Table 1. Continued.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
				rehabilitation-oriented and psycho-educational interventions) Duration: 43 sessions, 1× per week, and 22 sessions, 1× per 2 weeks.	1. CORE-OM domain Problems	includes anxiety) decreased to subclinical levels but only showing clinically reliable decreases after two years of intervention.	
Williams, Evans, and Wilson (2003)	Single subject designs	Class III	TBI *N* = 1[c]	- CBT including psycho-education, exposure, mood management. Art classes. Duration: 24 weeks, unknown times/ week	1. CAPS	1. Frequency and severity of PTSD scores decreased from "severe" to "moderate" levels from pre- to post-intervention, without a significant change from post-intervention to 6 months and 12 month follow-up.	–

ABI = Acquired Brain Injury; ACT = Acceptance and Commitment Therapy; BSI = Brief Symptom Inventory; CAPS = Clinician Administered Posttraumatic Stress Disorder Scale; CBT = Cognitive Behavioural Therapy; CFT = Compassion Focused Therapy; CORE-OM = Clinical Outcomes in Routine Evaluation Outcome Measure; DASS-21 = Depression Anxiety Stress Scales-21; HADS = Hospital Anxiety and Depression Scale; HAM-A = Hamilton Anxiety scale; IES = Impact of Events Scale; MI = Motivational Interviewing; NDC = Non-directive Counselling; NLP = Neuro-Linguistic Programming; OCD = Obsessive Compulsive Disorder; PHQ = Patient Health Questionnaire; POMS: Profile of Mood States; PRS = Panic Rating Scale; RCT = Randomized Control Trial; SCED = Single-Case Experimental Design; SCID-I = Structured Clinical Interview; SCL-90-R = Symptom Checklist-90-Revised; SPAI: Social Phobia and Anxiety Inventory; STAI = State-Trait Anxiety Inventory; TBI = Traumatic Brain Injury; Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

[a]Outcome measure used for the target behaviour.

[b] + = effective, - = not effective. Interventions were considered effective in the case of a statistically significant decrease or clinically relevant decrease (i.e., from a score above clinical cut-off to below or a change in a score that was large enough to be considered as such) on at least one outcome measure.

[c]Not all patients in the sample met criteria for inclusion – numbers of patients included for this systematic review are mentioned.

Table 2. Evidence table of studies that examined the effectiveness of psychological interventions addressing aggression/agitation.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Aboulafia-Brakha, Greber Buschbeck, Rochat, and Annoni (2013)	Clinical series without concurrent controls	Class III	TBI *N* = 10	1. Group CBT Duration: 60 min per session, 1 per week, 8 weeks	1. AQ-12	1. Significant decrease in aggression scores from pre-intervention to four months follow-up. No significant differences between pre-intervention and 1 week post-intervention.	+
Alderman (2003)	Single case design	Class III	TBI *N* = 2	1. Individual CBT Duration: 40 sessions over 22 weeks, plus daily checks 2. Behaviour modification therapy with differential reinforcement Duration: 19 weeks	1. Frequency of aggression/ irritability 2. OAS-MNR	1a. Decrease in frequency of aggression was observed from pre- to post-intervention. During the last 6 weeks of intervention, no aggression was observed. 2. Decrease in frequency of aggression was observed from pre- to post-intervention, with effects remaining up to 22 months follow-up.	+ +
Carnevale et al. (2006)	RCT	Class I	ABI *N* = 47	1. Natural community setting behavioural management by caregivers consisting of: - Assessment phase Duration: 3 weeks - Education phase Duration: 120 min per session, 1 per week, 4 weeks - Individualised behaviour plan phase Duration: 120 min per session, 1 per week, 8 weeks. 2. Waitlist (control) 3. Education only control group	1. Frequency of aggressive behaviour 2. NFI-R domain aggression	1. Frequency of aggressive behaviour did not significantly decrease more in the intervention group than in the control groups from pre- to post-intervention, but did significantly decrease from pre-intervention to 30 week follow-up. Significant difference between intervention-group and education only at 30-week follow-up. 2. No significant differences on aggression scores between groups. No significant decrease in aggression for the intervention group.	+

(*Continued*)

Table 2. Continued.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Chang et al. (2011)	RCT	Class I	Hemiplegic stroke *N* = 66	1. Knowledge and behaviour therapy including counselling, belief changes, forgiveness training and anger management. Duration: 60–120 min per session, 1 per week, 4 weeks 2. Treatment as usual (control)	1. STAXI	1. Significant time × group interaction for state anger, anger-in, anger-out and anger control. Intervention group showed significantly greater improvements from pre- to post-intervention in state anger, anger-out, and anger control than the control group. Control group showed significantly greater improvement in anger-in from pre- to post-intervention in comparison with intervention group.	+
Ebanks and Fisher (2003)	Single case design	Class III	TBI *N* = 1	1. Antecedent prompting which includes altering antecedents and consequences 2. Consequent feedback. Duration: 10 min per session, 20x	1. Destructive behaviour per minute	1a. Destructive behaviour decreased to zero levels with antecedent prompting. 1b. Low but consistent rates of destructive behaviour were shown with consequent feedback	+
Feeney and Achilich (2014)	Single case design	Class III	TBI *N* = 1[c]	1. Structured flexibility and context-sensitive behavioural support based on functional behaviour assessment Duration: 24/7, 40 days	1. Frequency of aggressive behaviour	1. Aggressive incidents decreased from 8–17 episodes per activity at pre-intervention, to zero levels post-intervention.	+

Hart et al. (2012)	Clinical series without concurrent controls	Class III	TBI *N* = 10	1. Anger self-management training including psycho-education, self-monitoring and self-evaluation Duration: 60–90 min per session, 8 sessions	1. STAXI Domain trait anger and anger-expression out 2. BAAQ	1. Both self-reported trait anger and anger-expression out significantly decreased from pre- to post-intervention, whereas significant-other ratings of only anger-expression out significantly decreased. 2. Self-reported anger significantly decreased from pre- to post-intervention. No significant decrease for significant-other ratings.	+
Hegel and Ferguson (2000)	SCED Withdrawal design without randomisation	Class II	TBI *N* = 1	1. DRO. Duration: 30 min/ session, 1 to 2 hour interval 2. No DRO in evening hours (control)	1. Frequency of aggressive acts per day	1. Aggressive acts decreased from 7.4 aggressive acts per day at baseline to 0.74 with implementation of DRO. Same effects were seen at 1-month follow-up with complete cessation of the intervention. These effects were not seen in the evening hours (control).	+
Medd and Tate (2000)	RCT	Class I	ABI *N* = 16	1. Anger management intervention including psycho-education, raising self-awareness, relaxation, self-talk, cognitive challenging, assertiveness training, distraction and time-out methods Duration 1 per week, 5–8 weeks 2. Waitlist control group	1. STAXI 2. Anger logs each day	1. There was a significant group × time interaction effect for anger-expression out. The intervention group showed a significant greater decrease in anger expression out from pre- to post-intervention than the control group. Significant change in trait anger from pre-intervention to post-intervention and 2 month follow-up scores combined for intervention group. No significant change for intervention group from post-intervention to 2-month follow-up for all domain scores. No significant interaction effects for trait anger, anger control and	+

(*Continued*)

Table 2. Continued.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
						anger-expression in. 2. Too much missing data for analyses.	
O'Leary (2000)	Single case design	Class III	ABI *N* = 3[c]	1. Coping and anger management intervention Duration: 60 min/session, 2×/week, 10 weeks	1. Frequency of aggressive incidents	1. Verbal and physical aggression decreased from pre- to post-intervention for all patients. Further decrease in aggressive incidents was observed post-intervention to 10 weeks follow-up.	+
O'Neill and Findlay (2014)	Single case design	Class III	TBI *N* = 1[c]	1. Biofeedback Duration: 10-20 min per day, 5×/week, ±20 months	1. OAS-MNR	1. No significant difference between baseline and intervention period, but the target behaviour decreased to zero levels.	+
Stewart and Alderman (2010)	SCED Alternating treatments design without randomisation	Class II	TBI *N* = 1	1. DRI Duration: ± 25 days, 24/7 2. DRL Duration: ± 25 days. 24/7 3. STO and verbal prompting Duration: ± 55 days, 24/7 4. Withdrawal of STO and re-implementation of DRI Duration: ± 20 days, 24/7 5. Re-implementation of STO intervention Duration: ±80 days, 24/7	1. Frequency of aggressive behaviour during morning hygiene routine.	1.1 Visual inspection showed no effect of DRI intervention. No significant effects. 1.2 Visual inspection showed no effect of DRL intervention. No significant effects. 1.3 Visual inspection showed a clear decrease in visual inspection in aggression with STO and verbal prompting, which showed to be significant. 1.4 Visual inspection showed a clear increase in aggressive behaviour after withdrawal of STO, which was statistically significant. Aggressive behaviour did not reach levels observed at first implementation of DRI. 1.5 Re-implementation of STO resulted in clear decrease in aggressive behaviour, i.e., to zero levels.	+

Suffoletto et al. (2013)	RCT	Class I	TBI $N = 43$	1. Mobile phone text messaging with education and support 2. Control-condition (text-messaging without feedback) Duration: 3 messages per day, 2 weeks	1. SMS Anxiety/ Irritability scores	1. No significant decrease in irritability for both groups.	–
Swan and Alderman (2004)	Single case design	Class III	TBI $N = 1$[c]	1. Behavioural management through antecedent manipulation by multidisciplinary approach. Duration: 9 weeks, 24/7	1. Frequency of aggressive behaviour.	1. During implementation, aggressive behaviour initially increased but decreased throughout, to zero levels at the end of the intervention.	+
Walker et al. (2010)	Clinical series without concurrent controls	Class III	TBI $N = 52$	1. Psycho-educational anger management group Duration: 120 min per session, 1 per week, 12 weeks, + 120 min follow-up session (at 7 months average)	1. STAXI	1. Significant decrease in trait anger, anger expression-out and significant increase in anger control from pre-intervention to post-intervention. No significant changes for anger expression-in and state anger. No significant differences between post-intervention and follow-up on any domain score.	+
Winkens et al. (2014)	SCED	Class I	ABI $N = 1$	1. ABC method focusing on Antecedent events, target Behaviour, and Consequent events Duration: 36 days 2. Baseline measurements Duration: 9 days	1. Frequency and severity of aggressive behaviour. 2. NPI 3. SOAS-R 4. SDAS -11 5. ABS	1. Significant decrease in severity and frequency of aggression from baseline to intervention phase. Visual inspection showed aggression was still present post-intervention. 2-5. No significant decreases from baseline to intervention phase.	+
Woodhead and Edelstein (2008)	Bi-phasic design	Class III	TBI $N = 1$	1. DRO Duration: 30 days, 24/7 2. Baseline measurements Duration: 60 days	1. Frequency of physical and verbal aggressive acts.	1. Visual inspection showed that physical aggression decreased while verbal aggression remained at baseline levels.	+

(*Continued*)

Table 2. Continued.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Yody et al. (2000)	Single case design	Class III	TBI *N* = 1	1. Applied behaviour management including altering antecedents and consequences of behaviour Duration: daily, ± 3 months	1. Frequency of verbal and physical aggressive acts	1. Visual inspection showed that both verbally and physically aggressive acts per day decreased from baseline to post-intervention, although with implementation, an initial increase in aggression was observed.	+

ABI = Acquired Brain injury; ABS = Agitated Behaviour Scale; AQ-12 = Buss and Perry Aggression Questionnaire; BAAQ = Brief Anger-Aggression Questionnaire; CBT = Cognitive Behavioural Therapy; DRI = Differential Reinforcement of Incompatible Behaviour; DRL = Differential Reinforcement of Low Rates of Responding; DRO = Differential Reinforcement of Other Behaviour; NFI-R = Neurobehavioural Functioning Inventory Revised; NPI = Neuropsychiatric Inventory; OAS-MNR = Overt Aggression Scale – Modified for Neurorehabilitation; RCT = Randomized Control Trial; SCED = Single-Case Experimental Design; SDAS-11 = Social Dysfunction and Aggression Scale -11; SOAS-R = Staff Observation of Aggression Scale-Revised; STAXI = State-Trait Anger Expression Inventory; STO: Situational Time Out; TBI = Traumatic Brain Injury.

[a]Outcome measure used for the target behaviour.

[b] + = effective, - = not effective. Interventions were considered effective in the case of a statistically significant decrease or clinically relevant decrease (i.e., from a score above clinical cut-off to below or a change in a score that was large enough to be considered as such) on at least one outcome measure.

[c]Not all patients in the sample met criteria for inclusion – numbers of patients included for this systematic review are mentioned.

Table 3. Evidence table with studies that examined the effectiveness of psychological interventions addressing apathy.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Backhaus et al. (2016)	RCT	Class I	ABI *N* = 19	1. CBT with psycho-education and instructions in stress management and problem-solving strategies. 2. Peer support group (control) Duration: 2 hr per session, 1 per week, 16×	1. FrSBe – Apathy Caregiver	1. No significant time × group interaction effect. No significant decreases reported for either group on apathy.	–
Lane-Brown and Tate (2010)	SCED Multiple baseline single case design without randomisation	Class II	TBI *N* = 1	- MI Duration: 60 min per session, 1 per week, 28 weeks - External compensation Duration: Daily, 3 months for each goal set (3 in total).	1. Sustained activity on goals in minutes. 2. AES (self, relative, clinician) 3. FrSBe – Apathy	1. Significant increase in sustained activity and initiation for treated goals. Effects maintained after withdrawal was limited to one goal. Effects did not generalise to non-treated goals. 2. Statistically significant and clinically relevant decrease in apathy, on self and relative ratings and a statistically, but not a clinically relevant decrease in apathy in clinician ratings. 3. Self-reports showed a statistically and clinically relevant decrease in apathy symptoms.	+

ABI = Acquired Brain Injury; AES = Apathy Evaluation Scale; CBT = Cognitive Behaviour Therapy; FrSBe = Frontal Systems Behaviour Scale; MI = Motivational Interviewing; RCT = Randomized Control Trial; SCED = Single-Case Experimental Design; TBI = Traumatic Brain Injury.

[a]Outcome measure used for the target behaviour.

[b] + = effective, - = not effective. Interventions were considered effective in the case of a statistically significant decrease or clinically relevant decrease (i.e., from a score above the clinical cut-off to below or a change in a score that was large enough to be considered as such) on at least one outcome measure.

Table 4. Evidence table of studies that examined the effectiveness of psychological interventions addressing disinhibition.

Study	Design	Quality	Population (*N*)	Intervention	Outcome measure[a]	Results	Effective intervention (+/−)[b]
Arco et al. (2004)	SCED Multiple baseline design without randomisation	Class II	ABI *N* = 4	1. Verbal self-regulation during group sessions (during role-plays, table top games and problem-solving exercises). Duration: 30 min per session, 18 sessions, 8 weeks.	1. Percentage of impulsive behaviour	1. Impulsive behaviour decreased to zero and stable levels during the intervention in 2 out of 3 patients. One patient showed remaining variable impulsive behaviour. Control patient, receiving no verbal self-regulation, showed small and gradual changes in impulsivity but the variability herein remained.	+
Backhaus et al. (2016)	RCT	Class I	ABI *N* = 19	1. CBT with psycho-education and instructions in stress management and problem-solving strategies. 2. Peer support group Duration: 2 h per session, 1 per week, 16x	1. FrSBe – Disinhibition	1. No significant group × time interaction. Significant decrease in disinhibition scores for both groups over time. Post-hoc analyses showed that the CBT group showed a significant decrease in scores from baseline to 3 months follow-up, whereas the control group showed no significant decrease.	–
Kelly and Simpson (2011)	SCED Multiple baseline single case design without randomisation	Class II	Hypoxia *N* = 1	1. DRO 2. DRO plus sex worker Total duration: ± 7 months, sex worker weekly.	1. OBS domains: exhibit, touch and talk.	1. All inappropriate sexual behaviours decreased during DRO. With the addition of a sex worker, all inappropriate sexual behaviours decreased further to zero levels.	+
Knight et al. (2002)	SCED Multiple baseline single case design without randomisation	Class II	TBI and stroke *N* = 3	1. Differential reinforcement of low rates (DRL) of behaviour with self-monitoring Duration: 36-39 weeks 2. Self-monitoring training (SMT) and DRL Duration: 57 weeks	1. Frequency of verbal comments and of functional activities.	1. DRL was shown to be effective in decreasing the target behaviour. After SMT verbal comments decreased. SMT may not be necessary but inhibits the behaviour further. SMT took more time than DRL in order to be effective but functional activities increased more than with DRL.	+
Ter Mors et al. (2012)	SCED Multiple baseline single case design	Class II	TBI *N* = 1	1. Electrical aversion therapy. Duration: 240 min per session, 3 sessions	1. SASBA	1. Significant decrease in inappropriate sexual behaviour from baseline to intervention phase and from baseline to withdrawal. No significant differences	+

	without randomisation			introduction. 16 months of application.		between intervention phase and withdrawal.	
Yody et al. (2000)	Single case design	Class III	TBI $N = 1$	1. Applied behaviour management including altering antecedents and consequences of behaviour. Duration: daily, ± 3 months	1. Frequency of elopement behaviour.	1. Visual inspection showed that the frequency of elopement behaviours per day decreased from baseline to post-intervention, although with implementation of the intervention, an initial increase in elopement behaviour was observed.	+

ABI = Acquired Brain Injury; OBS = Overt Behaviour Scale; RCT = Randomized Controlled Trial; SASBA = St. Andrew's Sexual Behaviour Assessment; SCED = Single Case Experimental Design; TBI = Traumatic Brain Injury.

[a]Outcome measure used for the target behaviour.

[b]+ = effective, - = not effective. Interventions were considered effective in the case of a statistically significant decrease or clinically relevant decrease (i.e., from a score above the clinical cut-off to below or a change in a score that was large enough to be considered as such) on at least one outcome measure.

Table 5. Appraisal of RCT and observational studies (i.e., Class I and II).

	Internal validity								Descriptive					Statistical			
Study	Eligibility criteria	Method of randomisation	Treatment allocation concealed	Similarity of baseline characteristics	Treatment/control interventions described	Co-interventions avoided or equivalent	Outcome measurement blinded	Outcome measures relevant	Withdrawal/dropout rates described	Short-term outcomes measured	Long-term outcomes measured	Timing of outcome measures equivalent	Sample size described	ITT analysis	Point estimates and variability provided	Statistical comparison of treatment effects	% criteria met (max. 16)
Class I																	
Backhaus et al. (2016)	x	x	x	x	x	–	–	x	–	x	x	x	x	–	x	x	75.0%
Hodgson et al. (2005)	x	–	–	x	x	–	–	x	–	x	–	x	x	–	x	x	56.3%
Peng et al. (2015)	x	x	x	x	x	x	–	x	–	x	x	x	x	–	x	x	81.3%
Ponsford et al. (2016)	x	x	x	x	–	–	–	x	–	x	–	x	x	x	x	x	68.8%
Suffoletto et al. (2013)	x	x	–	–	x	–	–	x	x	x	–	x	x	–	x	–	56.3%
Tiersky et al. (2005)	x	x	x	x	x	–	–	x	–	x	x	x	x	–	x	x	75.0%
Carnevale et al. (2006)	x	x	x	x	x	–	–	x	x	x	x	x	x	–	–	x	75.0%
Chang et al. (2011)	–	–	–	–	x	x	–	x	–	x	–	x	x	–	x	x	50.0%
Medd and Tate (2000)	x	–	–	–	–	–	–	x	–	x	–	x	x	–	x	x	43.8%
McDonald et al. (2008)	x	–	–	x	x	–	–	x	x	x	–	x	x	–	x	x	62.5%
Class II																	
Bradbury et al. (2008)[a]	x	o	o	x	x	–	–	x	o	x	–	x	x	o	x	x	75.0%

[a]Being an observational study, 12 out of 16 criteria were of interest. [o] = indicates "omitted".

Table 6. Appraisal of SCED studies (i.e., Class I and II).

	Internal validity							External								
Study	Design	Randomisation	Sampling	Blinding participant/therapist	Blind assessors	Inter-rater reliability	Treatment adherence	Baseline characteristics	Therapeutic setting	Target behaviour	Intervention	Raw data record	Data analysis	Replication	Generalisation	% criteria met (max. 15)
Class I																
Winkens et al. (2014)	–	–	–	–	–	–	–	x	x	x	x	x	x	–	–	40.0%
Class II																
Arco (2008)	–	–	x	–	–	–	–	x	–	x	x	x	x	–	–	40.0%
Hegel and Ferguson (2000)	–	–	x	–	–	–	–	x	x	x	x	x	–	–	–	40.0%
Stewart and Alderman (2010)	–	–	x	–	–	–	–	x	–	x	x	x	x	–	–	40.0%
Lane-Brown and Tate (2010)	–	–	x	–	–	–	–	x	–	x	x	x	x	–	x	46.7%
Arco et al. (2004)	x	–	x	–	–	x	x	x	x	x	x	x	x	x	–	73.3%
Knight et al. (2002)	–	–	x	–	–	–	–	x	–	x	x	x	x	x	–	46.7%
Kelly and Simpson (2011)	x	–	x	–	–	–	–	x	–	x	x	–	x	–	x	46.7%
Ter Mors et al. (2012)	–	–	x	–	–	–	–	x	–	–	x	x	x	–	–	33.3%

SCED study met more than 73.3% of the criteria; in particular, information on internal validity was missing or did not meet the standards (i.e., information with regard to design, randomisation, blinding, inter-rater reliability and treatment adherence).

Overall, positive points are the description of the included patient(s), which is well-documented (inclusion/exclusion criteria, baseline characteristics, target behaviour) and the adequate use of statistics (use of point estimates, statistical comparisons, visual analysis). Furthermore, interventions in SCED studies were adequately described in all studies.

Anxiety

A total of 21 studies examined interventions addressing anxiety symptoms. In total, 453 patients with ABI (i.e., TBI, stroke, cerebral anoxia/ hypoxia, anaphylaxis, encephalitis or subarachnoid haemorrhage) met the inclusion criteria. With regard to the types of interventions, 12 (57.1%) studies focused on CBT, and two (9.5%) studies used multifactorial interventions. Furthermore, Acceptance and Commitment Therapy (ACT), Compassion Focused Therapy (CFT), a mindfulness-based intervention, counselling provided via telephone, client-centred psychotherapy, a holistic rehabilitation approach and Neuro-Linguistic Programming (NLP), were all studied once (4.8% each). In total, 19 different outcome measures were used in these 19 studies; see Table 7 for further specifics.

Table 7. Overview of used outcome measures of included studies per neuropsychiatric consequence of acquired brain injury.

Frequency (#)	Anxiety ($n = 21$)	Aggression/agitation ($n = 18$)	Apathy ($n = 2$)	Disinhibition ($n = 6$)
12		Frequency of target behaviour.		
8	HADS			
5	DASS-21			
4		STAXI		
3				Frequency of target behaviour
2	SCL-90-R	OAS-MNR	FrSBe – Apathy	
1	BSI-18, SPAI, PRS, POMS tension anxiety, CAPS, PHQ, PTSD-screener, IES, STAI, SCID, Y-BOCS, HAM-A, PHQ, CORE-OM, self-rating of symptoms, frequency of target behaviour	AQ-12, BAAQ, NPI, SOAS-R, SDAS-11, ABS, NFI-R, self-rating of symptoms	Sustained activity on goals in minutes, AES	OBS, SASBA, FrSBe – Disinhibition
Total different measures (#)	19	11	3	4

ABS = Agitated Behaviour Scale; AES = Apathy Evaluation Scale; AQ-12 = Buss and Perry Aggression questionnaire; BAAQ = Brief Anger-Aggression Questionnaire; BSI = Brief Symptom Inventory; CAPS = Clinician-Administered Posttraumatic Stress Disorder Scale; CORE-OM = Clinical Outcomes in Routine Evaluation Outcome Measure; DASS-21 = Depression Anxiety Stress Scales-21; FrSBe = Frontal Systems Behaviour Scale; HADS = Hospital Anxiety and Depression Scale; HAM-A = Hamilton Anxiety scale; IES = Impact of Events Scale; NFI-R = Neurobehavioural Functioning Inventory Revised; NPI = Neuropsychiatric Inventory; OAS-MNR = Overt Aggression Scale – Modified for Neurorehabilitation; OBS = Overt Behaviour Scale; PHQ = Patient Health Questionnaire; POMS = Profile of Mood States; PRS = Panic Rating Scale; PTSD = Posttraumatic Stress Disorder; SASBA = St. Andrew's Sexual Behaviour Assessment; SCID-I = Structured Clinical Interview; SCL-90-R = Symptom Checklist-90-Revised; SDAS-11 = Social Dysfunction and Aggression Scale -11; SOAS-R = Staff Observation of Aggression Scale-Revised; SPAI: Social Phobia and Anxiety Inventory; STAI = State-Trait Anxiety Inventory; STAXI = State-Trait Anger Expression Inventory; Y-BOCS = Yale-Brown Obsessive Compulsive Scale

The included studies comprised seven Class I studies (33.3%), two Class II studies (9.5%) and 12 Class III studies (57.1%). Accordingly, there were nine high-quality studies. Fourteen (66.7%) studies showed significant decreases or clinically relevant decreases.

In four out of six high-quality studies (66.7%), CBT was shown to be effective in decreasing anxiety symptoms. In addition, a multifactorial, and an NLP intervention (both examined in high-quality studies) were shown to be effective, whereas Motivational Interviewing (MI) prior to CBT and telephone counselling were shown to be ineffective in high-quality studies. In five out of six moderate-quality studies (83.3%) CBT interventions were shown to be effective. Other interventions examined in moderate-quality studies and shown to be effective were CFT, holistic interventions and psychotherapy, whereas ACT and a mindfulness-based intervention were ineffective.

Aggression/agitation

Aggression/agitation was addressed in 18 studies, in which 258 patients with ABI met the inclusion criteria. Predominantly, patients with TBI were studied (in 13 of the 18 studies; 72.2%). The other studies included patients with varying injuries; four studies (22.2%) included patients with ABI and one included stroke patients (5.6%). Six different kinds of interventions were examined, of which behavioural management techniques was the most frequently studied (10 studies, 55.6%). Anger management sessions were examined in four studies (22.2%). CBT was the focus of two studies (11.1%); biofeedback, counselling provided by telephone and a knowledge and behaviour intervention were all studied once (5.6% each). Eleven different outcome measures were used in these 17 studies; see Table 7 for further specifics. Five of the studies (27.8%) were Class I, two (11.1%) were Class II studies, and 11 (61.1%) were Class III studies. Accordingly, there were seven high-quality studies. In four out of four high-quality studies (100%), behavioural management techniques were shown to be primarily effective in decreasing aggression symptoms. These techniques were also frequently studied in moderate-quality studies (i.e., six times) and were found to be effective in all. Anger management was shown to be effective in the one high-quality study and in the three moderate-quality studies. The knowledge and behaviour intervention is related to anger management and was shown to be effective in a high-quality study. Telephone counselling was not effective in a high-quality study, whereas CBT was ineffective in a moderate-quality study.

Apathy

Two studies examined apathy (Backhaus et al., 2016; Lane-Brown & Tate, 2010). These two studies included a total of 20 patients with ABI (TBI, stroke, subarachnoid/intracerebral haemorrhage, or encephalopathy). Three different outcome measures were used in these two studies; see Table 7 for further specifics. CBT and MI in combination with external compensation were examined in high-quality studies, i.e., a Class I and Class II study respectively. MI, in combination with external compensation, had a significant effect on apathy and resulted in clinically relevant decreases whereas CBT did not show significant effects. Table 3 presents the characteristics of the included studies for apathy.

Disinhibition

A total of six studies, in which 29 patients with ABI participated, addressed disinhibition symptoms. Three studies examined a population of TBI, patients with ABI were studied twice and patients with hypoxia were studied once. Four different kinds of interventions were examined, of which three studies (50.0%) examined behavioural management techniques. A self-management technique, CBT, and electrical aversion therapy were each studied once (16.7% each). Four different outcome measures were used in these six studies (see Table 7). The included studies comprised one Class I study (16.7%), four Class II studies (66.7%) and one Class III study (16.7%). This added up to five high-quality studies.

Five out of six studies (83.3%) showed significant decreases or clinically relevant decreases in disinhibition. Behavioural management techniques were shown to be effective in both high-quality studies and in the only moderate-quality study. The other three high-quality studies showed that a self-management technique and electrical aversion therapy were effective in decreasing disinhibition (i.e., significantly or clinically relevant) whereas CBT was not found to be effective. The CBT intervention showed a significant effect only in a post-hoc analysis, not in the main analysis (i.e., interaction effect) and was therefore not considered to be effective. Table 4 presents the characteristics of the included studies regarding disinhibition.

Discussion

The aim of this systematic review was to examine the current evidence on psychological interventions for anxiety, aggression/agitation, apathy and disinhibition as a consequence of ABI. Most studies addressed interventions for anxiety after ABI. High-quality studies showed that individual and/or tailored CBT programmes were particularly effective in decreasing anxiety in patients with ABI (Hodgson, McDonald, Tate, & Gertler, 2005; Ponsford et al., 2016; Tiersky et al., 2005). Other high-quality studies showed that the addition of MI sessions prior to tailored CBT sessions was not a valuable addition (Ponsford et al., 2016) and that an NLP programme comprised of relaxation techniques, thought conversion, self-awareness methods and meditation was effective in decreasing anxiety symptoms (Peng et al., 2015).

In other high-quality studies, behavioural management techniques were shown to be successful in decreasing aggression or agitation after ABI. The frequency by which these techniques were studied, including moderate-quality studies, gave insight into which elements are effective: behavioural strategies applied by nurses (Winkens, Ponds, Pouwels, Eilander, & van Heugten, 2014) or caregivers (Carnevale, Anselmi, Johnston, Busichio, & Walsh, 2006), extinction procedures (Hegel & Ferguson, 2000; Stewart & Alderman, 2010), differential reinforcement procedures (Alderman, 2003; Woodhead & Edelstein, 2008; Yody et al., 2000) and antecedent manipulation (Ebanks & Fisher, 2003; Swan & Alderman, 2004). Anger management sessions were effective in decreasing aggression, wherein counselling (Chang, Zhang, Xia, & Chen, 2011), psycho-education, behavioural methods and cognitive challenging seemed to be particularly effective elements (Medd & Tate, 2000). Next to these high-quality studies, moderate-quality studies supported the effectiveness of anger-management sessions (Hart, Vaccaro, Hays, & Maiuro, 2012; O'Leary, 2000; Walker et al., 2010) and increasing self-awareness might be of interest for managing aggression in community-based settings (Feeney & Achilich, 2014).

The high-quality studies that addressed apathy showed that through the implementation of an MI intervention in combination with external compensation, symptoms were successfully decreased (Lane-Brown & Tate, 2010). In contrast, a CBT group programme did not prove to be of added value to a peer-support group (Backhaus et al., 2016).

Mainly high-quality studies addressed disinhibition after ABI, but with considerable heterogeneity in interventions and symptoms of disinhibition being addressed. Despite this heterogeneity, interesting effective elements can be drawn from the high-quality studies: self-regulation to decrease impulsive behaviour (Arco, Cohen, & Geddes, 2004), differential reinforcement methods to decrease disinhibition, possibly through the addition of self-monitoring (Knight, Rutterford, Alderman, & Swan, 2002) and the combination of differential reinforcement and a sex worker (Kelly & Simpson, 2011) or electrical aversion therapy (despite being regarded as a "last-resort") to decrease inappropriate sexual behaviour (Ter Mors, van Heugten, M, & van Harten, 2012). Elopement behaviour might be effectively diminished through differential reinforcement, as shown in a moderate-quality study (Yody et al., 2000).

Added value of this review

This systematic review adds upon reviews conducted earlier in that it appraised a new integral body of evidence since the review of Cattelani et al. (2010). The body of evidence put forward here strengthens the effectiveness of CBT for anxiety symptoms, and new evidence was found for behavioural management techniques and anger management interventions for managing aggression/agitation after ABI. This review adds a systematic search, including multiple diagnoses of ABI, as well as the most frequently occurring psychiatric consequences of ABI, and discusses the interventions per consequence. The scope of this review was expanded beyond RCT studies by including SCEDs, as recommended by Cattelani et al. (2010). It was observed that SCEDs have been used more frequently (six in total) since the systematic review of Cattelani et al. (2010). This can be regarded as a positive finding, since SCEDs are suitable for the ABI population, which is very heterogeneous in clinical presentation (i.e., symptoms) (Alderman & Wood, 2013). Moreover, the SCED design enables the evaluation of highly tailored interventions, which can subsequently increase the effectiveness in comparison with generic interventions (as evaluated with RCTs) (Byrne & Coetzer, 2016).

Limitations of this review

Despite being among the most frequently occurring problem behaviours after ABI (Angelelli et al., 2004; Ciurli et al., 2011) depression/dysphoria was not selected as a target behaviour in this review. Furthermore, although the selected range of years (2000–2016) is limited, the primary aim of this study was to give an update on psychological interventions that have been studied since Cattelani et al. in 2010; this led to the decision to use the limited time-frame. Furthermore, certain studies were unclear with regard to our inclusion criteria; i.e., they did not explain sufficiently what the goal of the intervention was, whether patients with a premorbid psychiatric history were included, or whether pharmacological treatment was added/changed during the intervention; all of which made the inclusion process more difficult. Consensus was reached amongst the authors with regard to these criteria, but this may have, to some degree, influenced the objectivity of the inclusion process. Furthermore, this systematic review was not

supplemented by a meta-analysis, which could have increased objectivity in interpreting the results but would not be appropriate given the low quality of most studies, the lack of statistical analyses and because of the large heterogeneity in outcome measures and type and content of the interventions.

Limitations and strengths of included studies

The vast body of included studies used weak methodological designs. Fewer than half of the studies, i.e., 20 studies, were assessed as being of high-quality, but only 11 of these reached the highest level of evidence (i.e., Class I). Moreover, despite being of high-quality, the studies often did not meet internal validity standards or information was not documented properly. In particular, adequate descriptions of possible existing co-interventions outside the study design and the blinding of the outcome assessor were lacking. A side note should be made, as blinding participants in this field of study can be difficult; self-report measures are mostly used and patients are often aware of the intervention. Furthermore, adequate information on drop-out rates and including long-term outcome measurements should receive extra attention in future research. With regard to SCED studies, internal validity was also a point of concern, as randomisation procedures were not included, and participants and/or assessors were not blinded to the phase of intervention. However, as Tate et al. (2013) also note, blinding is a relatively new point being raised for SCED studies, and is possibly difficult to achieve in behavioural interventions. Furthermore, inter-rater reliability and treatment adherence were not addressed in the included SCED studies. Used outcome measures were often appraised as relevant but it was observed as well that a wide variety was used, making it difficult to derive common elements from the studies and/or generalise the findings. Most single case design studies (37.2%) included in this review were not experimental. Therefore, future single case design studies should use higher-quality designs, like SCED, which includes alternating designs, multiple baselines and/or changing criteria (Tate et al., 2017). All designs should include randomisation (Tate et al., 2017).

Although the vast body of included studies used weak methodological designs, there seems to be a modest increase in frequency and a tendency towards using stronger designs to examine the effectiveness of interventions in this field of research. More specifically, 28.6% of the included studies published in the last six years (2011–2016) reached Class I level of evidence, while 22.7% of the included studies published in the preceding 10 years (2000–2010) reached this level of evidence. This is only a small increase, which is not seen in the complete group of high-quality studies (i.e., Class I and II). Inclusion and exclusion criteria are often well-described, but we would like to add that information on premorbid psychiatric diagnoses or medication is less described and is needed for a better understanding of study results. Interventions were well-described, particularly in the SCED studies, but we also observed that there is a wide variety in implementation strategies, and in the operationalisation and content of interventions.

Implications

Clearly, methodological issues, particularly internal validity, should be addressed in future research. Therefore, strong conclusions with regard to, for example, intervention guidelines or standards for practice cannot be drawn. Concerns regarding

methodological weaknesses were raised by previously conducted reviews (Alderman & Wood, 2013; Cattelani et al., 2010; Ylvisaker et al., 2007); unfortunately, the importance of these concerns is stressed again here. In addition, it would be desirable to work towards a consensus on which (parts/content of) interventions to examine in future research in order to reach more conclusive and united remarks. In the debate on methodology, it must be noted that most studies are executed in clinical environments, which limits the possibility for stringent methodology, as treating the individual is of primary concern. SCED design benefits from strong methodology, yet the intervention can be personalised to serve the treatment of the individual. This is why a SCED represents an appropriate design for achieving both methodological rigour and clinical feasibility.

Conclusion

In conclusion, the quantity and quality of the studies addressing psychological interventions for psychiatric consequences of ABI are too limited at this point to make firm conclusions for clinical practice, especially with regard to apathy and disinhibition. There has been some response to the criticisms and recommendations of earlier reviews, which is reflected by studies using stronger designs to examine psychological interventions. This particularly accounts for studies on anxiety after ABI, of which CBT interventions have been shown to be the most effective in decreasing anxiety symptoms. There is considerable evidence for the effectiveness of behavioural management techniques in decreasing aggression/agitation; the value of these methods may be explored further in community-based settings. This might be achieved through the implementation of structured behaviour analyses. Future research is advised to replicate results in order to make more conclusive statements about the effectiveness of the above-mentioned interventions. There has been some response to the ongoing call for studies with high methodological quality – RCTs as well as SCEDs – but the call remains.

Disclosure Statement

No potential conflict of interest was reported by the authors.

References

Aboulafia-Brakha, T., Greber Buschbeck, C., Rochat, L., & Annoni, J. M. (2013). Feasibility and initial efficacy of a cognitive-behavioural group programme for managing anger and aggressiveness after traumatic brain injury. *Neuropsychological Rehabilitation*, *23*(2), 216–233. doi:10.1080/09602011.2012.747443

Alderman. (2003). Contemporary approaches to the management of irritability and aggression following traumatic brain injury. *Neuropsychological Rehabilitation*, *13*(1-2), 211–240. doi:10.1080/09602010244000327

Alderman, N., & Wood, R. L. (2013). Neurobehavioural approaches to the rehabilitation of challenging behaviour. *NeuroRehabilitation*, *32*(4), 761–770.

Angelelli, P., Paolucci, S., Bivona, U., Piccardi, L., Ciurli, P., Cantagallo, A., … Pizzamiglio, L. (2004). Development of neuropsychiatric symptoms in poststroke patients: A cross-sectional study. *Acta Psychiatrica Scandinavica*, *110*(1), 55–63. doi:10.1111/j.1600-0447.2004.00297.x

Arco, L. (2008). Neurobehavioural treatment for obsessive-compulsive disorder in an adult with traumatic brain injury. *Neuropsychological Rehabilitation*, *18*(1), 109–124. doi:10.1080/09602010701656706

Arco, L., Cohen, L., & Geddes, K. (2004). *Verbal self-regulation of impulsive behavior of persons with frontal lobe brain injury*. [3]. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed6&NEWS=N&AN=2005014123

Arundine, A., Bradbury, C. L., Dupuis, K., Dawson, D. R., Ruttan, L. A., & Green, R. E. (2012). Cognitive behavior therapy after acquired brain injury: Maintenance of therapeutic benefits at 6 months posttreatment. *Journal of Head Trauma Rehabilitation*, *27*(2), 104–112. doi:10.1097/HTR.0b013e3182125591

Ashworth, F., Clarke, A., Jones, L., Jennings, C., & Longworth, C. (2015). An exploration of compassion focused therapy following acquired brain injury. *Psychology and Psychotherapy: Theory, Research and Practice*, *88*(2), 143–162. doi:10.1111/papt.12037

Backhaus, S., Ibarra, S., Parrott, D., & Malec, J. (2016). Comparison of a cognitive-behavioral coping skills group to a peer support group in a brain injury population. *Archives of Physical Medicine and Rehabilitation*, *97*(2), 281–291. doi:10.1016/j.apmr.2015.10.097

Bradbury, C. L., Christensen, B. K., Lau, M. A., Ruttan, L. A., Arundine, A. L., & Green, R. E. (2008). The efficacy of cognitive behavior therapy in the treatment of emotional distress after acquired brain injury. *Archives of Physical Medicine and Rehabilitation*, *89*(12 Suppl), S61–S68. doi:10.1016/j.apmr.2008.08.210

Bryant, R. A., O'Donnell, M. L., Creamer, M., McFarlane, A. C., Clark, C. R., & Silove, D. (2010). The psychiatric sequelae of traumatic injury. *American Journal of Psychiatry*, *167*(3), 312–320. doi:10.1176/appi.ajp.2009.09050617

Byrne, C., & Coetzer, R. (2016). The effectiveness of psychological interventions for aggressive behavior following acquired brain injury: A meta-analysis and systematic review. *NeuroRehabilitation*, *39*(2), 205–221. doi:10.3233/NRE-161352

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. *Archives of Physical Medicine and Rehabilitation*, *87*(10), 1289–1297. doi:10.1016/j.apmr.2006.06.010

Cattelani, R., Zettin, M., & Zoccolotti, P. (2010). Rehabilitation treatments for adults with behavioral and psychosocial disorders following acquired brain injury: A systematic review. *Neuropsychology Review*, *20*(1), 52–85. doi:10.1007/s11065-009-9125-y

Chang, K., Zhang, H., Xia, Y., & Chen, C. (2011). Testing the effectiveness of knowledge and behavior therapy in patients of hemiplegic stroke. *Topics in Stroke Rehabilitation*, *18*(5), 525–535. doi:10.1310/tsr1805-525

Cicerone, K. D., Azulay, J., & Trott, C. (2009). Methodological quality of research on cognitive rehabilitation after traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, *90*(11), 52–59.

Cicerone, K. D., Langenbahn, D. M., Braden, C., Malec, J. F., Kalmar, K., Fraas, M., … Ashman, T. (2011). Evidence-based cognitive rehabilitation: Updated review of the literature from 2003 through 2008. *Archives of Physical Medicine and Rehabilitation*, *92*(4), 519–530. doi:10.1016/j.apmr.2010.11.015

Ciurli, P., Formisano, R., Bivona, U., Cantagallo, A., & Angelelli, P. (2011). Neuropsychiatric disorders in persons with severe traumatic brain injury: Prevalence, phenomenology, and relationship with demographic, clinical, and functional features. *The Journal of Head Trauma Rehabilitation*, *26*(2), 116–126. doi:10.1097/HTR.0b013e3181dedd0e

Diaz, A. P., Schwarzbold, M. L., Thais, M. E., Hohl, A., Bertotti, M. M., Schmoeller, R., … Guarnieri, R. (2012). Psychiatric disorders and health-related quality of life after severe traumatic brain injury: A prospective study. *Journal of Neurotrauma*, *29*(6), 1029–1037.

Ebanks, M. E., & Fisher, W. W. (2003). Altering the timing of academic prompts to treat destructive behavior maintained by escape. *Journal of Applied Behavior Analysis*, *36*(3), 355–359. doi:10.1901/jaba.2003.36-355

Feeney, T. J., & Achilich, J. (2014). Structured flexibility and context-sensitive behavioral support for the chronically cranky. *NeuroRehabilitation*, *34*(4), 709–723. doi:10.3233/nre-141088

Gertler, P., Tate, R. L., & Cameron, I. D. (2015). Non-pharmacological interventions for depression in adults and children with traumatic brain injury. *Cochrane Database of Systematic Reviews* (12), CD009871. doi:10.1002/14651858.CD009871.pub2

Gracey, F., Oldham, P., & Kritzinger, R. (2007). Finding out if "The 'me' will shut down": Successful cognitive-behavioural therapy of seizure-related panic symptoms following subarachnoid haemorrhage: A single case report. *Neuropsychological Rehabilitation*, *17*(1), 106–119.

Graham, C. D., Gillanders, D., Stuart, S., & Gouick, J. (2015). An acceptance and commitment therapy (ACT)–based intervention for an adult experiencing post-stroke anxiety and medically unexplained symptoms. *Clinical Case Studies*, *14*(2), 83–97. doi:10.1177/1534650114539386

Guyatt, G., Jaeschke, R., & McGinn, T. (2002). N of 1 randomized controlled trials. In *User's guides to the medical literature* (pp. 275–290). Chicago: AMA Press.

Hart, T., Vaccaro, M. J., Hays, C., & Maiuro, R. D. (2012). Anger self-management training for people with traumatic brain injury: A preliminary investigation. *Journal of Head Trauma Rehabilitation*, *27*(2), 113–122. doi:10.1097/HTR.0b013e31820e686c

Hegel, M. T., & Ferguson, R. J. (2000). Differential reinforcement of other behavior (DRO) to reduce aggressive behavior following traumatic brain injury. *Behavior Modification*, *24*(1), 94–101.

Hibbard, M. R., Uysal, S., Kepler, K., Bogdany, J., & Silver, J. (1998). Axis I psychopathology in individuals with traumatic brain injury. *The Journal of Head Trauma Rehabilitation*, *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 Impairment*, *6*(3), 169–180. doi:10.1375/brim.2005.6.3.169

Hofer, H., Frigerio, S., Frischknecht, E., Gassmann, D., Gutbrod, K., & Müri, R. M. (2013). Diagnosis and treatment of an obsessive-compulsive disorder following traumatic brain injury: A single case and review of the literature. *Neurocase (Psychology Press)*, *19*(4), 390–400 311p. doi:10.1080/13554794.2012.690423

Hsieh, M.-Y., Ponsford, J., Wong, D., Schönberger, M., McKay, A., & Haines, K. (2012a). A cognitive behaviour therapy (CBT) programme for anxiety following moderate-severe traumatic brain injury (TBI): Two case studies. *Brain Injury*, *26*(2), 126–138 113p. doi:10.3109/02699052.2011.635365

Hsieh, M.-Y., Ponsford, J., Wong, D., Schönberger, M., McKay, A., & Haines, K. (2012b). Development of a motivational interviewing programme as a prelude to CBT for anxiety following traumatic brain injury. *Neuropsychological Rehabilitation*, *22*(4), 563–584. doi:10.1080/09602011.2012.676284

Joo, H. M., Lee, S. J., Chung, Y. G., & Shin, I. Y. (2010). Effects of mindfulness based stress reduction program on depression, anxiety and stress in patients with aneurysmal subarachnoid hemorrhage. *Journal of Korean Neurosurgical Society*, *47*(5), 345–351. doi:10.3340/jkns.2010.47.5.345

Kelly, G., Brown, S., Todd, J., & Kremer, P. (2008). Challenging behaviour profiles of people with acquired brain injury living in community settings. *Brain Injury*, *22*(6), 457–470.

Kelly, G., & Simpson, G. (2011). *Remediating serious inappropriate sexual behavior in a male with severe acquired brain injury*. [4]. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&NEWS=N&AN=2011692934

Kneebone, I. I., & Jeffries, F. W. (2013). Treating anxiety after stroke using cognitive-behaviour therapy: Two cases. *Neuropsychological Rehabilitation*, *23*(6), 798–810. doi:10.1080/09602011.2013.820135

Knight, C., Rutterford, N. A., Alderman, N., & Swan, L. J. (2002). Is accurate self-monitoring necessary for people with acquired neurological problems to benefit from the use of differential reinforcement methods? *Brain Injury*, *16*(1), 75–87. doi:10.1080/02699050110082188

Lane-Brown, A., & Tate, R. (2010). Evaluation of an intervention for apathy after traumatic brain injury: A multiple-baseline, single-case experimental design. *Journal of Head Trauma Rehabilitation*, *25*(6), 459–469. doi:10.1097/HTR.0b013e3181d98e1d

Marin, R. S. (1991). Apathy: A neuropsychiatric syndrome. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *3*(3), 243–254. doi:10.1176/jnp.3.3.243

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. *Archives of Physical Medicine and Rehabilitation*, *89*(9), 1648–1659. doi:10.1016/j.apmr.2008.02.029

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

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., … Stewart, L. A. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, *4*(1), 1.

OCEBM. (2011). The Oxford 2011 levels of evidence: Oxford centre for evidence-based medicine Oxford, UK.

O'Leary, C. A. (2000). Reducing aggression in adults with brain injuries. *Behavioral Interventions*, *15*(3), 205–216.

O'Neill, B., & Findlay, G. (2014). Single case methodology in neurobehavioural rehabilitation: Preliminary findings on biofeedback in the treatment of challenging behaviour. *Neuropsychological Rehabilitation*, *24*(3-4), 365–381. doi:10.1080/09602011.2014.915856

Peng, Y., Lu, Y., Wei, W., Yu, J., Wang, D., Xiao, Y., … Wang, Z. (2015). The effect of a brief intervention for patients with ischemic stroke: A randomized controlled trial. *Journal of Stroke and Cerebrovascular Diseases*, *24*(8), 1793–1802. doi:10.1016/j.jstrokecerebrovasdis.2015.04.009

Perdices, M., Schultz, R., Tate, R., McDonald, S., Togher, L., Savage, S., … Smith, K. (2006). The evidence base of neuropsychological rehabilitation in acquired brain impairment (ABI): How good is the research? *Brain Impairment*, *7*(2), 119–132. doi:10.1375/brim.7.2.119

Ponsford, J., Lee, N. K., Wong, D., McKay, A., Haines, K., Alway, Y., … O'Donnell, M. L. (2016). Efficacy of motivational interviewing and cognitive behavioral therapy for anxiety and depression symptoms following traumatic brain injury. *Psychological Medicine*, *46*(5), 1079–1090. doi:10.1017/s0033291715002640

Rao, V., Koliatsos, V., Ahmed, F., Lyketsos, C., & Kortte, K. (2015). Neuropsychiatric disturbances associated with traumatic brain injury: A practical approach to evaluation and management. *Seminars in Neurology*, *35*(1), 64–82. doi:10.1055/s-0035-1544241

Rogers, J. M., & Read, C. A. (2007). Psychiatric comorbidity following traumatic brain injury. *Brain Injury*, *21* (13–14), 1321–1333. doi:10.1080/02699050701765700

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

Stewart, I., & Alderman, N. (2010). Active versus passive management of post-acquired brain injury challenging behaviour: A case study analysis of multiple operant procedures in the treatment of challenging behaviour maintained by negative reinforcement. *Brain Injury*, *24*(13-14), 1616–1627. doi:10.3109/02699052.2010.523050

Suffoletto, B., Wagner, A. K., Arenth, P. M., Calabria, J., Kingsley, E., Kristan, J., & Callaway, C. W. (2013). Mobile phone text messaging to assess symptoms after mild traumatic brain injury and provide self-care support: A pilot study. *Journal of Head Trauma Rehabilitation*, *28*(4), 302–312. doi:10.1097/HTR.0b013e3182847468

Swan, L., & Alderman, N. (2004). Measuring the relationship between overt aggression and expectations: A methodology for determining clinical outcomes. *Brain Injury*, *18*(2), 143–160. doi:10.1080/02699050310001596923

Tate, R. L., Perdices, M., Rosenkoetter, U., Shadish, W., Vohra, S., Barlow, D. H., … Wilson, B. (2017). The single-case reporting guideline In BEhavioural interventions (SCRIBE) 2016 statement. *Neuropsychological Rehabilitation*, 1–15. doi:10.1080/09602011.2016.1190533

Tate, R. L., Perdices, M., Rosenkoetter, U., Wakim, D., Godbee, K., Togher, L., & McDonald, S. (2013). Revision of a method quality rating scale for single-case experimental designs and n-of-1 trials: The 15-item risk of bias in N-of-1 trials (RoBiNT) scale. *Neuropsychological Rehabilitation*, *23*(5), 619–638.

Ter Mors, B. J., van Heugten, C. M., & van Harten, P. N. (2012). Evaluation of electrical aversion therapy for inappropriate sexual behaviour after traumatic brain injury: A single case experimental design study. *BMJ Case Reports* doi:10.1136/bcr-02-2012-5932

Tiersky, L. A., Anselmi, V., Johnston, M. V., Kurtyka, J., Roosen, E., Schwartz, T., & Deluca, J. (2005). A trial of neuropsychologic rehabilitation in mild-spectrum traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, *86*(8), 1565–1574. doi:10.1016/j.apmr.2005.03.013

Vaishnavi, S., Rao, V., & Fann, J. R. (2009). Neuropsychiatric problems after traumatic brain injury: Unraveling the silent epidemic. *Psychosomatics*, *50*(3), 198–205. doi:10.1176/appi.psy.50.3.198

van Heugten, C. M., Janssen, E. P., Visscher, A. J., Wolters Gregorio, G., Smeets, S., Berkers, R. M., & Ponds, R. W. (2013). Patients with brain injury in a psychiatric setting; assessment of health care needs and received care. *Tijdschrift voor Psychiatrie*, *55*(9), 665–675.

Walker, A. J., Nott, M. T., Doyle, M., Onus, M., McCarthy, K., & Baguley, I. J. (2010). Effectiveness of a group anger management programme after severe traumatic brain injury. *Brain Injury*, *24*(3), 517–524. doi:10.3109/02699051003601721

Wall, G., Turner, A., & Clarke, R. (2013). Evaluation of neuropsychological rehabilitation following severe traumatic brain injury: A case report. *Neurocase*, *19*(6), 530–541. doi:10.1080/13554794.2012.701642

Ward, T., & Hogan, K. (2015). Using client-centered psychotherapy embedded within a pluralistic integrative approach to help a client with executive dysfunction: The case of "Judith.". *Pragmatic Case Studies in Psychotherapy*, *11*(1), 1–20. doi:10.14713/pcsp.v11i1.1883

Whelan-Goodinson, R., Ponsford, J., Johnston, L., & Grant, F. (2009). Psychiatric disorders following traumatic brain injury: Their nature and frequency. *Journal of Head Trauma Rehabilitation*, *24*(5), 324–332. doi:10.1097/HTR.0b013e3181a712aa

Wiart, L., Luaute, J., Stefan, A., Plantier, D., & Hamonet, J. (2016). Non pharmacological treatments for psychological and behavioural disorders following traumatic brain injury (TBI). A systematic literature review and expert opinion leading to recommendations. *Annals of Physical and Rehabilitation Medicine*, *59*(1), 31–41. doi:10.1016/j.rehab.2015.12.001

Williams, W. H., Evans, J. J., & Wilson, B. A. (2003). *Neurorehabilitation for two cases of post-traumatic stress disorder following traumatic brain injury*. [1]. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed6&NEWS=N&AN=2003064139

Winkens, I., Ponds, R., Pouwels, C., Eilander, H., & van Heugten, C. (2014). Using single-case experimental design methodology to evaluate the effects of the ABC method for nursing staff on verbal aggressive behaviour after acquired brain injury. *Neuropsychological Rehabilitation*, *24*(3–4), 349–364. doi:10.1080/09602011.2014.901229

Woodhead, E. L., & Edelstein, B. A. (2008). *Decreasing physical aggression and verbal abuse in a brain-injured nursing home resident*. [4]. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed8&NEWS=N&AN=2008313810

World Health Organization. (2001). *International classification of functioning, disability and health: ICF*. Geneva: WHO.

Ylvisaker, M., Turkstra, L., Coehlo, C., Yorkston, K., Kennedy, M., Sohlberg, M. M., & Avery, J. (2007). Behavioural interventions for children and adults with behaviour disorders after TBI: A systematic review of the evidence. *Brain Injury*, *21*(8), 769–805. doi:10.1080/02699050701482470

Yody, B. B., Schaub, C., Conway, J., Peters, S., Strauss, D., & Helsinger, S. (2000). Applied behavior management and acquired brain injury: Approaches and assessment. *The Journal of Head Trauma Rehabilitation*, *15*(4), 1041–1060.

Appendix 1. Search strategy PubMed.

Population

(brain injuries [Mesh Terms] OR stroke [MeSH Terms] or brain neoplasms [MeSH Terms] or hypoxia [MeSH Terms] or encephalitis [Mesh Terms] or hydrocephalus [Mesh Terms] or meningitis [MeSH Terms] Or Traumatic brain injur* [text word] OR TBI [text word] OR CVA [text word] OR cerebrovascular accident* [text word] OR stroke* [text word] OR encephalitis [text word] OR meningitis [text word] OR hydrocephalus [text word] OR head-injur* [text word] OR head injur* [text word] OR brain disease* [text word] OR ABI [text word])

Intervention

(psychotherapy [MeSH Terms] OR rehabilitation [MeSH Terms] OR behavior control [MeSH Terms] OR counseling [Mesh Terms] OR motivational interviewing [Mesh Terms] or education, nonprofessional [MeSH Terms] OR problem solving [Mesh Terms] or psychological intervention [text word] or psychological therapy [text word] or cognitive intervention [text word] or cognitive therapy [text word] or behavioral intervention [text word] or behavioural intervention [text word] or behavior intervention [text word] or behaviour intervention [text word] or behavioral therapy [text word] or behavioural therapy [text word] or behavior therapy [text word] or behaviour therapy [text word] or supportive intervention [text word] or supportive therapy [text word] or problem solving intervention [text word] or problem solving therapy [text word] or counseling [text word] or motivational interviewing [text word] or psychotherap* [text word] or mindfulness [text word] or psychoeducat* [text word] OR rehabilit* [text word] or behaviour control [text word] or behavior control [text word] or behavioral control [text word] or behavioural control [text word])

Symptoms

Anxiety

(Anxiety [MeSH Terms] OR anxiety disorders [MeSH Terms] OR anxiet* [text word] or anxious [text word] or post traumatic stress [text word] or post-traumatic stress [text word] or PTSD [text word] or feeling apprehension [text word] or feeling apprehensive [text word] or feelings apprehension [text word] or feelings apprehensive [text word] or manifest anxiety scale [text word])

Aggression/agitation

(Aggression [MeSH Terms] or psychomotor agitation [MeSH Terms] or violence [MeSH Terms] or negativism [MeSH Terms] or hostility [MeSH Terms] or anger [MeSH Terms] or rage [MeSH Terms] or irritable mood [MeSH Terms] or aggress* [text word] or psychomotor agitation [text word] or violen* [text word] or negativism [text word] or hostility [text word] or anger [text word] or angry [text word] or rage* [text word] or agitat* [text word] or restlessness [text word] or irritability [text word] or irritable mood [text word] or combative behavio* [text word] or destructive behavio* [text word] or explosive behavio* [text word] or escalating temper [text word] or verbally abusive [text word] or assault* [text word] or catastrophic reaction [text word] or Behavioral disorder [text word] or behavioural disorder [text word] or behavioral dysfunction [text word] or behavioural dysfunction [text word])

Apathy

(Apathy [MeSH Terms] OR apath* [Text Word] OR avolition [Text Word] OR bradyphren* [text word] OR "lack of initiative" [text word] OR "loss of initiative" [text word] OR motivational disorder [text word])

Disinhibition

("Disruptive, Impulse Control, and Conduct Disorders" [MeSH Terms] or conduct disorder [Mesh Terms] or self-control [Mesh Terms] or impulsive behavior [Mesh Terms] or sexual behavior [MeSH Terms] or impulsive* [text word] or disinhibited behavio* [text word] or lack of restraint [text word] or loss of restraint [text word] or unrestrained behavio* [text word] or inappropriate sexual behavio* [text word] or inappropriate behavior* [text word] or conduct disorder [text word] or emotional control [text word] or self regulation [text word] or self-control [text word] or impulse control disorder* [text word] or impulsive behavio* [text word] or episodic discontrol [text word] or disinhibit* [text word] or hypersexual* [text word] or sexual disinhibit* [text word] or sexual disorder [text word] or sexual behavio* [text word] or kleptomania* [text word] or pyromania* [text word])

Limiters

NOT dementia [MeSH Terms] NOT neurodegenerative diseases [MeSH Terms] NOT military personnel [MeSH Terms] NOT veterans [MeSH Terms]

Publication year: "2000/01/01–2016/06/31".

Language: "English" and "Dutch".