The efficacy of mindfulness-based interventions and cognitive rehabilitation on emotional and executive functioning problems after Acquired Brain Injury

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Abstract

This thesis portfolio aimed to assess the effectiveness of interventions on emotional and executive functioning difficulties after brain injury; both of which can be debilitating to an individual's everyday life. The aim was to systematically review mindfulness-based literature used within the brain injury population to ascertain its effectiveness on emotional difficulties, especially anxiety and depression. Along with a meta-analytic review to assess the effectiveness of cognitive rehabilitation on executive functioning difficulties after brain injury. Databases were searched, and risk of bias and methodological quality was rated for all included papers. After inclusion and exclusion criteria were applied, 11 individual papers and five reviews were included in the systematic review, and 26 in the meta-analysis.

Overall findings from the systematic review suggest that there is insufficient methodologically robust evidence from the reviewed studies to make confident conclusions about the effectiveness of mindfulness-based interventions reducing anxiety and/or depression symptoms after brain injury. Findings from the meta-analysis show small significant effect sizes across the majority of analyses which is suggestive of the heterogenous nature of brain injury literature. Methodological quality also varied across studies reviewed.

Taking the findings from both reviews, whilst further methodologically robust research in both areas may be argued, the variation between participants and the interventions presented in both papers will create difficulty in concluding effectiveness confidently.

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Chapter 1: Thesis Portfolio Introduction

According to the British Society of Rehabilitation Medicine guidelines (BSRM;2003) an acquired brain injury (ABI) is when the brain becomes injured through any means after birth, for example after a stroke, trauma, an infection or tumour. The BSRM report stroke and traumatic brain injury (TBI) as being the most widely seen ABI in the UK. A TBI is any injury to the brain that is traumatic; for example, damage after a road traffic accident, a fall, an assault (Bruns Jr & Hauser, 2003). The United Kingdom Acquired Brain Injury Forum (UKABIF, 2018) suggest that 50% of TBI's are due to road traffic accidents and the type of injury is related to age; for example, a fall related injury is more common in the elderly. This is supported by Lawrence, Helmy, Bouamra, Woodford, Lecky and Hutchinson (2016). Headway (2018) report that, in the UK in 2013/2014, 348,934 people acquired a brain injury, with 130,551 being a stroke.

Tennant (2005) reports that approximately 6.6% of individuals attending A&E in a year do so with a head injury and in 2001/2, approximately 229 per 100,000 needed admitting to hospital in England. It has been reported that a head injury is the most common type of trauma that individual's present to A&E with; amounting to 10% of all admissions (National Institute for Health and Care Excellence Costing Report, 2014). Roozenbeek, Maas and Menon (2013) state that over 7.7 million people in the European Union have a TBI related disability. Prevalence of brain injury in the general population is high. Brain injuries can be categorised into mild, moderate and severe by examining the duration of post-traumatic amnesia (PTA) and is thought to be a good indicator of emotional and cognitive prognosis (Khan, Baguley & Cameron, 2003), along with the Glasgow Coma Scale (GCS; Teasdale & Jennet, 1974).

After brain injury individuals are reported to have difficulty across a range of domains, one of which being emotion and its impact on everyday life. Levack, Kayes and Fadyl (2010) conducted a review of the qualitative literature looking at recovery and outcome

after brain injury and found the main themes that arose was a disconnection between themselves currently and their pre-injury self, in a personal and social context. This results in a range of emotional responses, for example anxiety, fear, loneliness, anger and grief. Research suggests that anxiety and depression are prevalent after brain injury (Osborn, Mathias & Fairweather-Schmidt, 2014; Osborn, Mathias & Fairweather-Schmidt, 2016) and interventions to alleviate symptoms provide mixed outcomes; whether that be pharmacological (Tsousides, Ashman & Gordon, 2013) or psychological (Soo & Tate, 2007)

In addition, individuals face difficulties with cognition which encompasses executive functioning. Examples of executive functioning difficulties include issues with planning and problem-solving (Ylvisaker, Turkstra & Coelho, 2005), monitoring (Hart, Whyte, Kim, & Vaccaro, 2005) and attention (Mathias & Wheaton, 2007). Cognitive rehabilitation has been used to remedy issues individuals experience after brain injury, including executive dysfunction. There have been literature reviews to ascertain the effectiveness of cognitive rehabilitation on executive functioning difficulties (Cicerone et al., 2005; Cicerone et al., 2011; Rohling, Faust, Beverly & Demakis, 2009); however, these do not include more recent literature from the past ten years and focus on either specific clinical populations (Kennedy, Coelho, Turkstra, Ylvisaker, Sohlberg, Yorkston, Chiou & Kan, 2008) or interventions (Stamenova & Levine, 2018).

Literature suggests that cognition and emotion should be thought about and discussed as concepts that are joint, rather than two separate entities (Pessoa, 2008; Ochsner & Phelps, 2007). Despite literature proposing that the frontal lobes are mainly concerned with higher cognitive processes, for example executive functioning, Pessoa (2008) argues that regions of the brain considered to be just 'cognition' or 'emotion' are inherently linked. A model proposed by Stuss (2011) puts forward that the frontal area of the brain encompasses not just executive functions, but also wider cognitive functions. The model

details different areas of the brain are related to specific cognitive functions; including metacognition, monitoring, setting tasks and behavioural, emotional self-regulation. Linking emotional processing and cognition together, Teper, Segal and Inzlicht (2013) propose that mindfulness can have a positive impact on executive control; linking mindfulness to cognitive flexibility and being able to accept emotions in a non-judgemental way.

Aiming to investigate potential effectiveness of interventions within these areas, firstly a systematic review focussing on the effectiveness of mindfulness-based interventions on anxiety and depression after ABI is described. Following on from this, a meta-analysis is reported concerned with interventions for another common and debilitating issue after brain injury, that of executive dysfunction.

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Chapter 2: Systematic review for submission to Neuropsychological Rehabilitation

Evidence for the effectiveness of mindfulness-based interventions on emotional outcome after ABI: A Systematic Review

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Abstract

Background: Emotional difficulties after brain injury can be debilitating, long-standing and impact on an individual's daily life. Anxiety and depression in the brain injury population is highly prevalent, with a range of interventions showing mixed outcomes. 'Third wave' interventions, specifically mindfulness-based interventions, have been used within this population; however, the effectiveness of interventions is unclear. ***Design:*** A systematic review approach was adopted to evaluate the effectiveness of such interventions after acquired brain injury. ***Method:*** Databases were systematically searched in which, after inclusion and exclusion criteria were applied, yielded 16 papers to review; 11 individual papers and five reviews. Risk of bias and methodological quality rating of the papers were also completed. ***Results:*** Findings overall suggest that, in general, methodological quality of the articles included in the review was weak, with only one RCT being included. ***Conclusion:*** Therefore, there is not sufficient high quality evidence to make firm conclusions about the effectiveness of mindfulness-based interventions reducing symptomology of anxiety and/or depression after brain injury.

Keywords: *brain injury, anxiety, depression, mindfulness, third wave, intervention, effectiveness*

<u>**Introduction**</u>

Difficulties after Acquired Brain Injury

Langlois, Rutland-Brown and Wald (2006) suggest that suffering a TBI can be a lifelong or long-term injury, which can lead to other health conditions. Thus, after sustaining a brain injury, an individual may encounter a range of difficulties and or deficits that can impact on their daily life and functioning. Emotional difficulties after brain injury are common and can be debilitating to an individual's everyday life; with 38% of TBI survivors being diagnosed with depression (Osborn, Mathias & Fairweather-Schmidt, 2014) and 37% reporting clinical symptoms of anxiety (Osborn, Mathias & Fairweather-Schmidt, 2016).

Mood and Emotion Difficulties after Acquired Brain Injury

Emotional difficulties that people can struggle with are: controlling their emotions (Cicerone, Levin, Malec, Stuss & Whyte, 2006), lack of insight (Milders, Fuchs & Crawford, 2003), impulsivity (Rao & Lyketsos, 2000) and most commonly anxiety (Gould, Ponsford & Schönberger, 2011) and depression (Kreutzer, Seel & Gourley, 2001; Jorge, Robinson, Moser, Tateno, Crespo-Facorro & Arndt, 2004). Koponen, Taiminen, Hiekkanen & Tenovuo (2011) report that at twelve months post-injury, of 38 participants, 47.4% had mental health difficulties with depression being the most prevalent, compared to a rate of 6.5% seen in the general Finnish population. These results are supported by Fann, Uomoto and Katon (2001) who conclude that 77% of those with a TBI suffer from depression.

Literature suggests that emotional issues after brain injury may develop due to difficulty adjusting to a different view of themselves and their life. Gracey, Evans and Malley (2009) proposed a model which describes a discrepancy between an individual's view of their pre-injury self and how they currently perceive themselves. This can lead to

difficulties in a range of areas, one being with emotions and psychological well-being which can continue to be experienced several years after injury (Hoofien, Gilboa, Vakil & Donovick, 2001). In relation to stroke specifically, Broomfield, Laidlaw, Hickabottom, Murray, Pendrey, Whittick and Gillespie (2011) suggest four key areas which may predict the onset of depression. One of these areas is in relation to a negative view of themselves and the future; which is consistent with the model proposed above. This is also apparent in anxiety literature as it has been postulated that one may experience negative feelings as a threat, which may lead to individuals developing an unhelpful avoidant coping style (Riley, Dennis & Powell, 2010).

'Third Wave' Interventions

It has been over a decade in which a new concept of 'third wave' cognitive behavioural therapy was introduced (Hayes & Hoffman, 2017). Some examples of 'third wave' therapies include acceptance and commitment therapy (ACT), mindfulness-based cognitive therapy (MBCT) and compassionate mind training (Churchill et al, 2010). A recent review by Hunot et al (2013) compared 'third wave' CBT therapies with traditional CBT in the treatment of depression in non-ABI population. They conclude that outcomes were comparable; however, only three studies were included in the review.

Mindfulness-Based Interventions and Mental Health

Mindfulness meditation, has been defined by Kabat-Zinn (1990) as a present moment awareness and non-judgmental acceptance of mental events. Mindfulness-based interventions have been shown to reduce stress (Brown & Ryan 2003), increase psychological well-being (Bränström, Kvillemo, Brandberg & Moskowitz, 2010; Eberth & Sedlmeier, 2012) and reduce mood symptoms (Piet & Hougaard, 2011; Baer, 2003; Hofmann, Sawyer, Witt & Oh, 2010; Cash & Whittingham, 2010). Literature has shown

that mindfulness meditation can help change the relationship that individuals have with their emotions (Teper, Segal & Inzlicht, 2013).

Completion of mindfulness-based interventions have been shown to reduce anxiety and depression symptoms and diagnosis (Grossman, Niemann, Schmidt & Walach, 2004; Vollestad, Sivertsen & Nielsen, 2011). Toneatto and Nguyen (2007) reviewed papers looking at the effectiveness of MBSR on anxiety and depression in individuals with differing physical health conditions. The authors concluded that outcomes varied considerably, and the best outcomes appeared to be when there was not a control group to compare with; therefore, it is difficult to decipher whether the results were due to the MBSR intervention or other variables. Mindfulness has also been shown to be effective in the treatment of generalized anxiety disorder by reducing symptomology of anxiety and depression (Evans, Ferrando, Findler, Stowell, Smart & Haglin, 2008). Literature also suggests that mindfulness is linked to greater cognitive flexibility (Moore & Malinowski, 2009), improved attentional processing (Chambers, Lo & Allen, 2008) and the inhibition of specific emotional responses (Teper & Inzlicht, 2013). However, Chiesa, Calati and Serretti (2011) conducted a review of mindfulness meditation on cognitive outcomes and concluded that whilst results from studies may appear promising, overall results must be concluded tentatively due to issues such as methodological quality and differences in sample size.

Mindfulness and ABI

'Third wave' therapies have been considered beneficial in the treatment of psychological difficulties, especially depression after brain injury (Hunot et al, 2013). In addition to this, these therapies have been used to ameliorate psychological and emotional difficulties typically seen after brain injury. Kangas and McDonald (2011) discuss the potential effectiveness of ACT and mindfulness-based therapies after brain injury and report that not only are positive outcomes found in the treatment of depression, but also

wider psychological processes. For example, reducing rumination after injury and bringing the individual into the present moment. Mindfulness has also been investigated with regards to its effectiveness in remediating difficulties after brain injury that are not related to emotions, for example attention and mental fatigue, with mixed outcomes (McMillian, Robertson, Brock and Chorlton, 2002; Johansson, Bjuhr & Ronnback, 2012).

Previous Mindfulness Reviews

The popularity of using mindfulness-based interventions after brain injury to remediate difficulties has increased over several years, leading to researchers conducting reviews of the literature to ascertain their effectiveness. The majority of studies focus on stroke survivors and general physical health conditions (Lawrence, Booth, Mercer & Crawford, 2013; Lazaridou, Philbrook & Tzika, 2013), with there being limited research on traumatic brain injury and mindfulness (Kenuk & Porter, 2017). Another aspect to previous reviews is the broad interpretations of what mindfulness-based interventions entail; this, has an impact on search terms that have been used and the identifying of appropriate studies. For example, Kenuk and Porter include yoga and Tai Chi as being a mindfulness-based intervention, whereas Toivonen et al (2017) do not use these terms. Therefore, a disparity between studies that may or may not have been included in the reviews could be apparent. Lawrence et al (2013) discuss the issue of heterogeneity within mindfulness-based interventions; however, this is also an aspect to consider with ABI literature in general.

Currently, there are a limited number of systematic reviews that investigate the use of mindfulness after ABI and the number of studies included within the reviews are also relatively small. When looking specifically at the effect of using mindfulness to remediate emotional difficulties after ABI, this number reduces even further; for example, out of ten studies, only 3 in the Lazaridou et al (2013) review included an emotional outcome and the ABI paper contained in the Toivonen et al (2017) review focussed on mental fatigue with

emotional outcome being secondary outcomes. Kenuk and Porter (2017) also focus on a range of outcomes rather than focusing on emotion.

Rationale

Therefore, there is a theoretical rationale for the benefits of mindfulness given the challenges of adjustment to life post ABI, and evidence of potential effectiveness in reducing stress, depression, and anxiety in non-ABI population. There is growing interest in mindfulness-based interventions; with a range of systematic reviews of the brain injury literature (Lawrence et al, 2013; Toivonen et al, 2017; Kenuk & Porter, 2017) showing promising results. The purpose of the current review is to provide a synthesis of findings from ABI data, including stroke, TBI and other types of ABI, along with a critique of methodological quality to aid current understanding of the benefits of mindfulness-based interventions after brain injury. It is therefore felt an appropriate time to conduct a systematic review to gain a better understanding of the mindfulness-based literature in relation to its effectiveness on emotional outcome after ABI; discussing both individual studies along with a review of previous reviews.

Reviewing the current literature to decipher the rigour and quality of the research, along with how frequently mindfulness-based interventions are used within the brain injury population, will be beneficial to add to the 'third wave' therapy literature. Furthermore, it would be useful for clinicians to have an overview of other treatments that can be used with brain injury patients that may be struggling emotionally; along with whether adaptations to the conventional mindfulness-based interventions have been successful. The current review aims to capture up-to-date mindfulness and ABI literature, along with a critique of previous reviews and their findings.

Therefore, the main question of the review is whether, after brain injury, mindfulness-based interventions are effective in aiding emotional outcome. Secondary questions of the review are whether the quality of mindfulness-based literature, including previous reviews,

are robust enough to make firm conclusions of effectiveness and to summarise the types of adaptations used within the interventions for the ABI population, along with their possible usefulness for this clinical population.

Method

Search Strategy

Studies were searched according to the participant, intervention, comparison and outcome (PICO) principle; considering MeSH terms to ensure pertinent terms are included. Boolean modifiers (AND, OR) and truncation (*) were used to ensure effective searching of databases. For population the following terms were used: cerebrovascular accident, cerebrovascular disease, brain accident, brain attack, brain insult, CVA, cerebral vascular accident, ischaemic cerebral attack, ischemic cerebral attack, ischaemic seizure, ischemic seizure, brain disease*, acute brain injury, brain injur*, brain injury, chronic cerebral injury, injury brain, acquired brain injur*, acquired head injur*, head injur*, traumatic brain injur*, traumatic head injur*, diffuse brain injur*, encephalitis, meningitis, stroke. For intervention, the following terms were used: breathing therapy, mindfulness, mindfulness meditation, meditation, mindful*, MBSR, MBCT. Due to the heterogenous nature of the studies being searched for, no limits were set for comparison or outcome. No terms were used for 'outcome' but the eligibility criteria of reporting emotional or psychosocial was applied manually when screening title and abstract, and full text review.

Eligibility Criteria

The databases searched on 20th September 2018 were Medline Pubmed, PsychINFO, EMBASE, CINAHL, PsycARTICLES and OpenGrey. There were no limits on publication year. Additional papers were searched for using the reference lists of the identified papers. Searches were limited to human participants, English language articles and limiting age of participants to adults only. For papers to be included in the review there must be evidence

of a head or brain injury, participants must be 18 years or older, of English language, contain valid and reliable measures of emotion appropriate to population as primary outcome and there must be evidence of a mindfulness-based intervention. Specific designs of papers (RCT, non-RCT, pre-post, single-case experimental designs and reviews) will be included to allow broader discussion of outcomes. Papers were excluded if they were descriptive papers only, case studies/descriptions or conference presentations.

Data Extraction

Duplicate papers were removed and identified papers were either included or excluded by reading title and abstract to assess appropriateness. The primary investigator contacted authors of papers in which full papers could not be obtained; two papers were received, and the remaining papers were either not published or completed, or the primary investigator (LH) did not receive a response. The outstanding eleven papers were then read, and data extracted to obtain the following information: design, sample size, participant details, outcome measures, intervention and key findings. This data can be found in table 1.

Appraisal of Selected Studies

Fifty percent of the identified papers were rated by the lead reviewer and KV for risk of bias using an adapted scale originally created by Kocsis et al (2010), along with additional scoring criteria from SIGN50 to ensure robust assessment of quality of RCT's (Appendix 1). The overall global quality rating scale for the papers can be found in the data extraction table (table 1) and the full description of risk of bias for each paper can be found in appendix 2. The Single-Case Experimental Design (SCED) scale (Tate, McDonald, Perdices, Togher, Schultz & Savage, 2008) was used to assess the quality of single case designs. The systematic reviews contained within the current review were rated using the AMSTAR-2 tool (Shea et al.,2017) to assess the quality of the paper. PRISMA guidance

(Moher, Liberati, Tetzlaff & Altman, 2010) was used to inform reporting of the current review.

<u>Results</u>

The flow chart in figure 1 shows the process of paper selection. The initial search yielded 2270 papers, with six of these being from reading reference lists rather than the database search. After removing 115 duplicates, 2155 papers remained and papers not meeting eligibility criteria removed. The remaining 50 papers were read in full. Additional papers identified through reading of references missed in the initial search were added. After final removal of papers not meeting eligibility, 16 papers were selected for final review; 11 individual studies and five reviews. Tables 1 and 2 show the data extracted from the reviewed papers and systematic reviews respectively, along with key findings. Table 2 shows the quality ratings from the AMSTAR-2 of the previous systematic reviews.
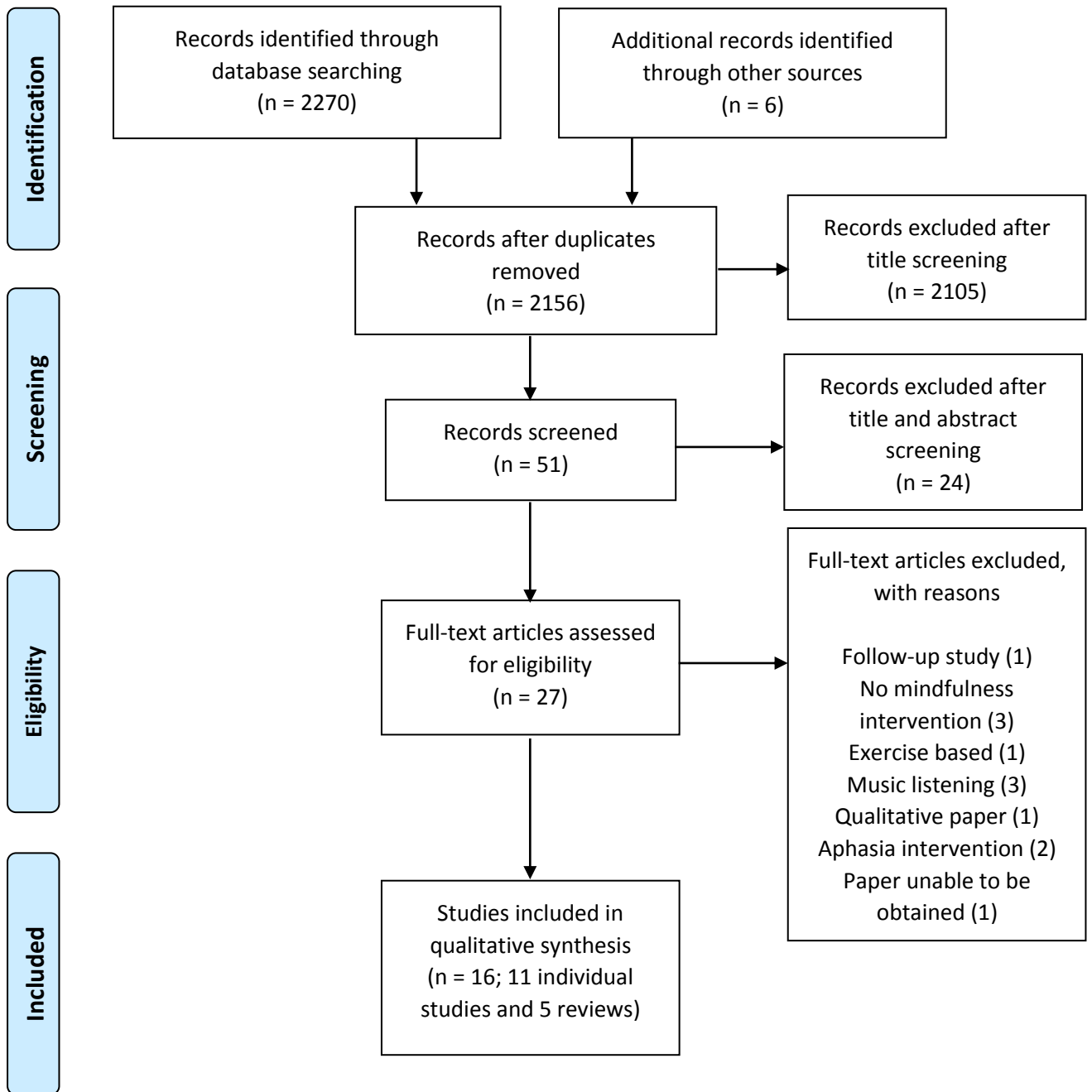
Figure 1. PRISMA style flow chart setting out paper identification and selection.

Table 1

Systematic review data extraction table (Denotes papers that are included in previous systematic reviews)*

Author and Date	Design	Participants (n, injury details, mean age)	Outcome measures	Intervention	Key Findings	Global Rating Scale
*Bedard et al. (2012).	Pre-post design	n = 20, mean age = 47.1 years. 45% of the sample were Female.	BDI-II, HADS, PHQ-9, Visual analogue scales on subjective difficulties e.g. pin, Mayo-Portland Adaptability Inventory (MPAI-4; assessing function), SCL-90-R.	90 minute session to introduce intervention. 8 weeks of 90 minute MBCT sessions - topics included awareness of thoughts, staying in present and awareness. Practice meditation, breathing and gentle yoga.	All depression measures showed a reduction post intervention. A large proportion of participants no longer met the threshold of clinical or major depression. However, there was no control group or follow-up.	Moderately poor 9 points
Dickinson, Friary & McCann (2017).	Single case design	59 year old Female. 3 years post left middle cerebral infarct - Severe non-fluent aphasia and apraxia of speech.	BAI, Comprehensive Aphasia test, Object and Action Naming Battery	Intervention included a 1:1, 4 week, 90-120 minute MBSR programme conducted by a clinical psychologist who was trained and practiced in administering the programme.	Lower anxiety and better language processing. Participant reported an improvement in emotional wellbeing. Showed reductions in distress e.g. crying less.	Met 6/11 requirements on SCED scale

Author and Date	Design	Participants (n, injury details, mean age)	Outcome measures	Intervention	Key Findings	Global Rating Scale
*Azulay, Smart, Mott & Cicerone (2012).	Pilot pre-post design	n = 22, mean age = 48.9%, 50% Female. All participants had mild TBI / post concussive syndrome	Perceived quality of life scale, Perceived self-efficacy scale (PSES), neurobehavioural symptom inventory (NSI), Neuropsychological measures, Social problem solving inventory and mindful attention awareness scale.	Ten weekly 120 minute group sessions, consisting of a modified MBSR programme.	Near significant pre-post intervention changes on NSI (p = .07; $d = 0.32$). Significant pre-post changes seen on the PSES (p = .001; $d = 0.50$).	Very poor 7 points
Kristofersson (2012).	Mixed methods within group design	n = 22 TBI participants recruited with a history of substance abuse. Mean age = 52 years, mean sobriety = <4 years, 4 females and 8 males (all dropouts were male).	Barrett Impulsivity Scale, SF-36 (QoL), State Trait Anxiety Inventory (STAI), Center for Epidemiological Studies Depression Scale (CES-D), Qualitative interviews based on participants experience, Practice logs, Weekly telephone calls.	Eight 60 minute sessions following the MBSR program. A four hour meditation retreat was discussed in the method; however, it is unclear whether this was actioned.	Non-significant reduction in both state and trait anxiety reported (p = .42 and .91 respectively). No change in depression scores (p = .79).	Moderately poor 9 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome measures	Intervention	Key Findings	Global Rating Scale
*Bedard et al. (2003).	Pre-post design	**Treatment:** n = 7, mean age = 43 years, 7/10 female, mean meds = 3.10. **Control:** n = 3, mean age = 39 years, 0/3 female.	Demographic information, quality of life (Short form health survey - SF-36), psychological processes (BDI-II, SCL-90-R, Perceived Stress Scale - PSS, Multidimensional Health Locus of Control scale - MHLC, the Global Severity Index - GSI and the Positive Symptom Distress Index - PSDI) and function.	Twelve week group intervention based on Kabat-Zinn's MBST programme and Kolb's experiential learning cycle. A manual was developed and followed throughout the intervention.	Intervention group scores on the mental health components of the SF-36 improved significantly when compared to control group (p = .036). This was also seen for the cognitive-affective domains of the BDI-II (p = .029), but not the somatic domain (p = .374).	Moderately poor 9 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome measures	Intervention	Key Findings	Global Rating Scale
*Bedard et al. (2014)	RCT	**Treatment Arm**: n = 38 TBI participants, mean age = 47.10 years, 19/38 male, 4.5 years post injury. **Control Arm**: n = 38 TBI participants, mean age = 45.81 years, 23/38 male, 4 years post injury.	Demographic information, BDI-II, Patient Health Questionnaire (PHQ-9), SCL-90-R: All for emotional outcome. Philadelphia Mindfulness Scale (PHLMS) and Toronto Mindfulness Scale (TMS): All for rating mindfulness.	Based on MBCT program by Segal et al - was standardised across all sites. Ten weekly 90 minute sessions, including 20-30 minutes of individual meditation practice.	Reduction in depression scores greater for intervention group on BDI-II but not PHQ-9 and SCL-90-R.	Moderately good 15 points
Combs et al (2018)	Pilot pre-post design.	n = 19 TBI participants, mean age = 32.8 years, 89.5% male. Type of injury: mild TBI = 3, severe TBI = 12, other ABI (stroke or anoxic) = 4.	Psychological functioning, sleep and TBI questions in one non-validated questionnaire.	Thirty-two weeks of 60 minute MBSR group.	No significant difference between severity of depression or anxiety on pre-post measures.	Very poor 7 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome measures	Intervention	Key Findings	Global Rating Scale
Mavaddat et al. (2017)	Pre-post design.	n = 10 stroke participants, mean age = 64.5 years, 8/10 Female.	Positive and Negative Affect Scale (PANAS), HADS or Depression Intensity Scales Circles (DISCS).	Positive Mental Training (PosMT) in which participants are asked to listen to guided exercise tracks on a CD. The CD contained 12 tracks; one to be listened to everyday for a week. Asked to adhere to the intervention for a minimum of four weeks.	No pre-post means or standard deviations are reported, but the authors state that three stroke participants moved severity on both the anxiety and depression scales on the HADS.	Average 13 points
Canade (2014)	Pre-post design	n = 22 participants, mean age = 51.45 years, 19/22 Female. Type of injury: ABI = 4, MS = 12, Parkinson's = 4, other neuro = 2.	**Primary** - Freiburg mindfulness inventory (FMI), Mindful attention awareness scale (MAAS), **Secondary** - Mindfulness-based self-efficacy scale (revised) (MSES-R), Perceived QoL scale (PQoL),	Four consecutive 60 minute sessions facilitated by clinical psychologist experienced in mindfulness. Measures given at 3/4 timepoints. 1 + 2 baseline measurements and 3 + 4 post intervention.	Significant difference on FMI between intervention and control scores (p = 0.021; d = 1.21). On the MSRS-R, significant difference found for the subscale 'emotion regulation' (p = 0.013; d = 1.42).	Moderately poor 10 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome measures	Intervention	Key Findings	Global Rating Scale
*Joo et al (2010)	Pre-post design	11 subarachnoid haemorrhage participants (5 male) who had all undergone surgery to treat an aneurysm. **Mean age** – 53 years.	BDI (Korean version), State-Trait Anxiety Inventory and heart rate variability.	MBSR programme was conducted. Eight weekly sessions. Unsure of length of session; authors state 2.5 times each, but unclear what this means.	BDI significantly reduced statistically (p = .013). The State and Trait measures indicated near significant reductions after the intervention (p = .09 and p = .056 respectively).	Very poor 5 points
Azulay & Mott (2016)	Pre-post design	25 participants (13 male); 5 TBI, 10 stroke, 7 autoimmune and 3 other.	Difficulties in Emotion Regulation Scale (DERS), The Freiberg mindfulness inventory, Perceived Quality of Life (PQOL), Perceived Self-Efficacy (PSE), Neurobehavioural Symptom Inventory (NSI), Neuropsychological measures, Social Problem-Solving Inventory-Revised Short Form (SPSIRS)	A modified MBSR programme called "mindfulness attention programme (MAP)" that consisted of 10 weekly 120 minute group sessions. Over time, the sessions were divided into 45 minutes of meditation and then 45 minutes of introducing a new meditation practice.	A significant difference was found on the DERS in relation to emotion regulation (p = 0.001).	Average 11 points

Table 2

Previous systematic review data extraction table

Author and Date	Primary Research Question	Number of Studies and Number of Participants	Type of Review	Main Findings
Kenuk & Porter (2017)	To ascertain whether there is sufficient evidence for mindfulness to be included within brain injury rehabilitation / therapy for TBI population.	16 studies; N = not specified	Systematic review	Mixed findings found overall; however, the authors conclude that mindfulness-based interventions show "potential" for alleviating difficulties after sustaining a TBI. No detailed information regarding methodological quality of the studies reviewed is detailed. Outcomes discussed include cognitive symptoms, physical health and psychosocial outcomes. The authors discuss the limitations of the mindfulness literature with regards to small samples sizes, lack of control groups and limited follow-up measures.
Lawrence et al (2013)	To investigate the benefit of mindfulness interventions after stroke.	4 studies; N = 107	Systematic review	From the four studies reviewed, the authors conclude that mindfulness-based interventions show potential benefits for individuals after stroke to alleviate a range of outcomes. However, further conclusions discuss the need for more methodologically sound studies investigating this topic area.

Author and Date	Primary Research Question	Number of Studies and Number of Participants	Type of Review	Main Findings
Lazaridou et al (2013)	Review to evaluate the effectiveness of yoga for individuals after stroke.	10 studies; N = 292	Systematic review	The authors conclude that using yoga as part of rehabilitation after stroke may be beneficial; however, interventions should be person-centered to account for individual differences after stroke. The authors briefly discuss the weak methodological quality of included studies and the need for more research in this area.
Toivonen et al (2017)	To investigate the effectiveness of web-based mindfulness interventions for individuals with physical health conditions.	19 studies. 1 ABI paper; N = 34.	Systematic review	Found the majority of primary outcomes improved for participants; however, discuss that findings are mixed due to the low number of control participants. Psychological outcomes did not appear to change over the course of the interventions. Specific to ABI, the primary outcome of mental fatigue improved after the MBSR intervention compare to controls.
Tsaousides et al (2013)	To review literature on interventions for post-TBI depression; with focus being on types of interventions, eligibility criteria of studies and outcome measures.	Number of studies not detailed. 3 mindfulness papers included.	Narrative review	No firm conclusions detailed with regards to outcomes from mindfulness-based interventions; however, suggest further research is required in the area of treatment of depression after TBI.

Table 3

Adaptations to mindfulness-based interventions

Author and Date	Adaptations
Bedard et al. (2012)	The intervention was adapted to take into account difficulties encountered by brain injury population. These included attention, memory and concentration difficulties. The modifications included shortening meditation sessions, repetition, using memory aids and completing reviews.
Dickinson, Friary & McCann (2017)	The programme administered was adapted from the original eight week MBSR programme into a four week individualised program. A supportive communication programme was also created by a SLT to assist completion of the MBSR intervention.
Azulay, Smart, Mott & Cicerone (2012)	Modifications included increased modelling and practicing of techniques, providing worksheets, increasing amount of sessions provided from eight to ten and reducing group size. This was to account for cognitive difficulties such as reduced recall, attentional difficulties and disorganisation. All topics were written in log books to account for difficulties with memory.
Kristofersson (2012)	Eight week adapted MBSR course delivered by experienced trainer. Adaptations were made to duration and content of sessions; however, author does not specifically state what the adaptations were apart from exercises and homework were shortened.
Bedard et al. (2003)	No adaptations to original MBSR programme apparent.
Bedard et al. (2014)	Customised the intervention to take into account population. Used simplified language, repetition and visual aids. Emphasised the learning environment. Given handouts and a book that contained a mindfulness CD - not required to read the book but asked to listen to the CD.

Author and Date	Adaptations
Combs et al (2018)	Authors modified MBSR programme to consider difficulties faced by clinical population. These adaptations included reducing amount of paperwork given, adapting language, increasing repetition, modifying environment to account for physical disabilities, using techniques to account for disinhibition and encouraging participation in sessions.
Mavaddat et al. (2017)	Recorded instructions were given with the intervention CD which was a recommendation from a psychologist specialised in working with stroke survivors.
Canade (2014)	Modified MBSR program in which participants complete four 60 minute sessions rather than the conventional eight sessions.
Joo et al (2010)	No adaptations to the original MBSR program made.
Azulay & Mott (2016)	Dispersed throughout the sessions, participants were introduced to modified yoga and relaxation exercises that were completed on chairs rather than on the floor to take into account physical difficulties after brain injury. A memory notebook was given to participants to enable them to support their meditation practice at home.

Description of studies

Participants

Two-hundred and twenty-nine participants took part in the reviewed studies; with only 41 being controls. Of the reviewed papers, six included participants that had sustained a TBI, two included stroke participants, two included participants that had mixed etiologies including TBI, auto-immune difficulties or other neurological conditions and the single case experimental design recruited a female stroke survivor. This resulted in there being 161 TBI participants, 32 stroke, eight other ABI and 28 other neurological conditions (Multiple Scleroses = 12, Parkinson's disease = 4, auto-immune = 7, other = 5). One of the TBI papers (Kristofersson, 2012) included participants that also had historical substance abuse difficulties. The mean age of the participants was 52.32 years and 113 of the 229 participants (49%) were Female.

Design

The majority of the papers analysed (9/11) were pre-post design, with two having a control group to compare outcome. A randomised control trial and single case design were also included in the analysis. Bedard et al (2014) used a randomised control trial for their study, with treatment and control arms being well matched for age, years post-injury and the number taking anti-depressant medication. The control group were a wait-list control group. Bedard and colleagues also completed previous studies in 2012 and 2003; however, these were pre-post design and not RCT. Bedard et al (2003) did not recruit a control group in the first instance but used participant dropout data to make comparisons. Therefore, the groups were not thoroughly matched for size or gender as the three participants that withdrew from the intervention, out of the ten initially recruited, were all male and the remaining seven participants that completed the study were all female. Moreover, Bedard et al (2012) also did not recruit a control group and did not use any dropout data to act as a

control despite three participants not completing the intervention due to personal reasons. This was discussed by the authors as a limitation to the study.

Canade (2014) adopted a randomly generated pre-post design, with participants being randomly assigned to one of three groups making up two intervention groups and one control. The control group was classed as a wait-list control group and offered the intervention two weeks after the second group had completed their intervention; however, as the controls had not completed the intervention at the time of the study write-up, their results were not included. It is noteworthy that not all participants had an ABI; participants were recruited from a neurological rehabilitation service so therefore had other conditions such as Parkinson's disease or Multiple Sclerosis. It is not clear what the breakdown of conditions per group was. Kristofersson (2012) described their design as a mixed methods within group design, which indicates there was no randomisation to a treatment or intervention, and therefore no control group. The author did give rationale for not randomising due to small sample size. There was substantial demographic data obtained; however, the participants did not appear to be well matched with time post-injury ranging from four to 40 years and sobriety from drugs and/or alcohol ranging from six months to nine years. Therefore, participants may have been on a different recovery trajectory which may have impacted on results. The rationale for using some dropout data and not others was not made clear in the paper and could be considered a risk of bias.

The remaining five studies (Azulay et al, 2012; Combs et al, 2018; Joo et al, 2010; Mavaddat et al, 2017; Azulay & Mott, 2016) all conducted pre-post designs. Both studies by Azulay and colleagues (2012; 2016) recruited participants over a two year period. It must be noted that as the above studies are all pre-post design, there were no control groups to compare outcomes. Furthermore, three of the papers (Azulay et al, 2012; Mavaddat et al, 2017; Combs et al, 2018) were either a pilot study or acceptability study, which may have impacted on the number of participants recruited and thus, results obtained.

Intervention

The type of intervention used within many of the papers was an adaptation of other manualised mindfulness training; either Kabat-Zinn's Mindfulness-Based Stress Reduction (MBSR; 2010) programme or Segal, Teasdale and Williams' (2004) Mindfulness-Based Cognitive Therapy (MBCT). A core aspect of both programmes is to help people develop skills in self-awareness and focussing one's attention; along with acceptance and non-judgement of mental events. All papers describe an adaptation of their programme to fit the needs of their participants; taking into account common difficulties individuals face after a brain injury (see table 3 for summary of intervention adaptations). The RCT conducted by Bedard et al (2014) used the Segal et al's (2004) MBCT program which the authors standardised across all intervention sites and was customised to consider the population, for example fatigue and memory difficulties. Furthermore, when devising materials for the intervention, the authors used simplified language, repetition and visual aids, for example a handout, to aid participants' participation. The intervention comprised of ten 90-minute weekly sessions, which included some time to have individual meditation practice. As part of the RCT process, practitioners were trained for 1 year prior to the study starting and a pair of practitioners were chosen for each site to deliver the intervention.

Bedard et al (2003) adopted and adapted the Kabat-Zinn (1994) MBSR program and incorporated Kolb's (1984) learning cycle into their intervention. A manual for their intervention was created that was followed by the group facilitators. The authors do not state whether the facilitators were specifically trained or their profession. The intervention consisted of a 12-week group programme that encouraged participants to develop a different way of thinking about disability and acceptance. Bedard et al (2012) combined Kabat-Zinn's (1994) MBSR and Segal et al's (2004) MBCT to develop their intervention, but it is unclear whether they created their own manual for the intervention. The intervention consisted of 90-minute sessions over an eight-week period, focussing on

awareness of thoughts, acceptance and being present; whilst introducing participants to meditation, breathing techniques and yoga. As in Bedard et al's 2014 study, intervention materials and techniques were adapted to consider participant difficulties e.g. attention and memory deficits, by shortening sessions and using repetition. The authors describe the group facilitator as having completed specific MBCT training and having experience in facilitating mindfulness sessions.

Canade (2014) used an adapted version of Kabat-Zinn's (1994) MBSR programme, which consisted of 60-minute sessions conducted over a four-week period and practice in-between session was encouraged. The hour sessions encompassed different mindfulness exercises, reflections on these and how to incorporate these into everyday life. The sessions were facilitated by a Clinical Psychologist who was experienced in mindfulness practice and authors state that the intervention was non-manualised.

Kristofersson (2012) described an adapted manualised MBSR programme that is based on Kabat-Zinn's (1994) programme. The intervention consisted of 60-minute sessions over an eight-week timeframe, which was delivered by an experienced trainer who had received training from the university that created the MBSR programme. The authors note a range of mindfulness techniques to be used within the intervention, for example body scan meditation exercise, yoga and other meditation exercise that can be used in everyday life. Participants were encouraged to use these techniques outside of the sessions and a telephone call was made weekly to participants to assess adherence and to gather qualitative data. There are inconsistences within this paper's description of their intervention. The authors were inconsistent in their report of the inclusion of a four-hour meditation retreat which is a common aspect of MBSR programmes. A 2.5-hour retreat is described in the participant information sheet but not described in detail, so lacks rationale and information on how this was adapted to suit people with ABI.

Dickinson, Friary and McCann (2017) describe a four-week intervention that consists of 90-120 minute sessions that are facilitated by a Clinical Psychologist trained and experienced in administering the MBSR programme. The MBSR programme was based on Kabat-Zinn's (1994) programme, but adapted to the participant's specific needs. The modified programme contained different mindfulness / meditation techniques and space for discussion in relation to acceptance and self-compassion.

Azulay et al (2012) and Azulay and Mott (2016) both describe a ten week mindfulness-based intervention that focussed on increasing attention to help with adjustment and acceptance to current challenges and experiences associated with their brain injury. Azulay et al (2012) adapted the original MBSR by having an increase of sessions, from eight to ten, and the authors state a decrease in the number of participants within the group from 26 to six. Rather than using a MBSR programme, Azulay and Mott (2016) appraised a 'Mindfulness Attention Program' (MAP) to focus on acceptance and adjustment to challenges such as physical and emotional pain.

Combs et al (2018) conducted a 32 week, 60 minute per week, modified MBSR group that was a component of a wider rehabilitation programme. Participation in the group was encouraged; however, participants did not attend all sessions for a variety of reasons. These included leaving the rehabilitation programme or a clashing of their other rehabilitation sessions. The authors state that the mindful breathing element of their intervention was completed in every session, which suggests this was an important component of the intervention itself. The group was led by a psychology postdoctoral fellow and a yoga instructor.

The intervention described by Mavaddat et al (2017), called Positive Mental Training (PosMT) training which includes aspects of mindfulness, for example body scan, consisted of participants being given an audio CD containing 12 training tracks. Participants were asked to listen to one track per day per week, and presumably complete the exercises or

actively listen to the track; however, this is not explicitly stated in the article. Therefore, the intervention could be up to 12 weeks. The authors told participants they could stop listening to the CD after four weeks; suggesting this is the therapeutic dose, but they could continue listening to the remaining tracks if they wish. Questionnaires were repeated at the time of interview; however, it is unclear whether this was at the end of four or 12 weeks. It also varied as to how long participants listened to the audio tracks.

Joo et al (2010) described a conventional MBSR program, consisting of eight 150 minute sessions that gave participants the opportunity to share their experiences through group discussion. As a conventional MBSR programme was being followed, it could be assumed that a manual was being used; however, this was not explicit in the study and there were no details of who facilitated the group. Participants completed activities such as yoga, body scan and sitting meditation, along with a mindfulness CD to support the intervention.

Adaptations

All the studies, except Bedard et al (2003) and Joo et al (2010), made some adaptations to their intervention when comparing it to the conventional MBCT or MBSR programmes. The adaptations tended to fall into two categories; either in relation to content and materials or length of intervention. Several studies discuss having shorter session length, for example 1-1 ½ hour sessions rather than 2-2 ½ hours; however, Azulay et al (2012) and Azulay and Mott (2016) continued to have 2 hour sessions. Bedard et al (2012), Bedard et al (2014), Azulay et al (2012) and Combs et al (2018) report using simplified language, visual aids, repetition and reviewing of sessions to consider attention, concentration and memory difficulties. Furthermore, Dickinson et al (2017) and Kristoffersson (2012) created personalised and specific exercises that were appropriate for the individual, in the case of Dickinson et al (2017), or the client group.

With regards to length of intervention, there was some inconsistency with the papers; with one suggesting an increased amount of sessions compared to the traditional MBCT

programme and the remainder suggesting a reduced number. Bedard et al (2014), Azulay et al (2012) and Azulay and Mott (2016) completed 10 sessions rather than the traditional eight; whereas Canade (2014) and Dickinson et al (2017) completed 4 sessions with their participants. Kristofersson (2013) does not report making any adaptations to their current study; however, makes some reference to a previous intervention group that was reviewed to help produce the outline for their current study in which only four sessions were completed. Mavaddat et al (2017) did not use a traditional mindfulness-based intervention, choosing instead to use a CD based intervention in which written instructions were given to participants for support.

Outcome Measures

The outcome measures used across the majority of the papers were valid and appropriate for use with the population. Four out of the 11 studies reviewed used the Beck Depression Inventory (BDI-II) and the Symptom Checklist 90 Revised (SCL-90-R) as their primary outcome measures for depression and self-report distress (Bedard et al, 2003; Bedard et al, 2012; Bedard et al, 2014). The Patient Health Questionnaire (PHQ-9) is a self-report measure of depression and was used as a primary outcome measure by two studies (Bedard et al, 2012; Bedard et al, 2014). The BDI was also used by Joo et al (2010) and was translated into Korean for the study population, along with the State-Trait Anxiety Inventory (STAI). Azulay et al (2012) used the Perceived Self-Efficacy Scale to measure emotional outcome after brain injury in their participants.

Dickinson et al (2017) was the only study to use the Beck Anxiety Inventory (BAI) to measure participant anxiety and Bedard et al (2012), along with Mavaddat et al (2017) were the only studies to use the Hospital Anxiety and Depression Scale (HADS). Interestingly, Mavaddat et al (2017) discussed using the Depression Intensity Scales Circles (DISCS), a pictorial depression measure, in place of the HADS; however, this was not necessary for the participants recruited to the study. The Positive and Negative Affect Scale (PANAS)

was also used in one study (Mavaddat et al, 2017). Kristofersson (2012) chose to use the STAI and the Center for Epidemiological Depression Scale (CES-D) to measure anxiety and depression in their study participants. Azulay and Mott (2016) used the Difficulties in Emotion Regulation Scale (DERS); a self-reported emotion regulation questionnaire. Combs et al (2018) did not use any validated measures in their study; choosing to use a combined measure to ask questions on pain, psychological functioning and sleep after TBI. This questionnaire was based on a validated measure that the authors state has "adequate psychometric properties".

Methodological Quality and Risk of Bias

All appropriate papers were rated for quality and risk of bias using an adapted scale by Kocsis et al (2010); with six papers being rated by a second reviewer (KV). Dickinson et al's (2017) study was rated using the Single-Case Experimental Design rating scale (Tate, McDonald, Perdices, Togher, Schultz & Savage, 2008). The overall quality rating for the papers can be found in the data extraction table (table 1) and the full description of risk of bias and quality rating can be found in appendix 1. Overall, the papers tended to fall into the moderately poor (Bedard et al, 2012; Bedard et al, 2003; Canade, 2014; Kristofersson, 2012) or very poor (Azulay et al, 2012; Combs et al, 2018; Joo et al, 2010) range due to not having a control group (selection bias), or an adequate control group (other bias). This in turn effected the ability to conceal allocation (selection bias), blinding of participants (performance bias) and outcome (detection bias). Bedard et al (2014), Mavaddat et al (2017) and Azulay and Mott (2016) were rated as being average; however, scored lowest in relation to allocation concealment and blinding. It must also be noted that despite Azulay and Mott (2016) achieving a rating of average, this was borderline with moderately poor.

All but one of the reviewed papers (Joo et al, 2010) contained either a manual or protocol that ensured consistency across all facilitated sessions and/or had a facilitator that had training in undertaking the intervention, which reduces fidelity bias. This suggests that

within the individual studies, all participants received the same intervention and training; however, none of the studies report recording sessions for rating of consistency or supervision, which would reduce fidelity bias further. The screening of participants was also adequate across the majority of the papers; thorough inclusion and exclusion criteria were given and in some cases examples of exactly how the participants were screened. Therefore, the opportunity for selection bias is reduced. However, to achieve the highest rating for quality with regards to screening there should be a clear outline of numbers screened and then included or excluded. This was only achieved by the RCT conducted by Bedard et al (2013). Positively, the papers tended to score well in relation to reliable and valid outcome measures used; which were appropriate to use within the brain injury population and reduces detection bias. Canade (2014) and Combs et al (2018) were the only papers that used measures that are not commonly used within the brain injury literature.

As stated above, the SCED scale was used to rate quality of Dickinson et al's (2017) single case study. The paper scored well in relation to clinical history, measures used, whether raw data points were recorded, statistical analysis and whether results can be generalised. However, it appears that measures were only given once at baseline and not over the course of the treatment, and no other data collection was conducted; thus, there was insufficient sampling. Tate et al. (2016) would therefore describe this design as not being sufficient to meet the criteria of a single-case experimental design, due to not taking multiple measurements during the different phases. There was also not enough information to score in relation to inter-rater reliability or independence of assessors; it is not clear who completed the measures with the participant and how these were then scored.

Results of Studies

Key Findings

The key findings of the reviewed papers indicate that whilst there may be potential benefits of using mindfulness-based interventions to support individuals after brain injury,

the current evidence lacks the methodological rigor to make firm conclusions. The RCT with the lowest risk of bias by Bedard et al (2014) report a reduction in scores on the BDI-II were greater for the intervention group who completed ten sessions of MBCT. Although they did not test for statistical significance, they report a medium effect size was obtained for the impact of mindfulness on reduction of depression symptoms on the BDI-II. This reduction in scores was not found for the PHQ-9 or the SCL-90-R.

The remaining studies were categorised as being moderately poor with regards to risk of bias; thus, findings cannot be interpreted confidently. Kristofersson (2012) did report a decrease of state and trait anxiety after their 8 session MBSR intervention; however, at follow-up the state anxiety scores increased, whereas the trait scores continued to decrease. This reduction was not statistically significant. There was no change for depression scores and all participants, except one, continued to have scores that placed them in the clinically depressed range. Bedard and colleagues (2003) found that change over time on the BDI-II was near significant, and depression symptoms were halved in the MBST intervention group. When looking at the different constructs of the BDI-II, the cognitive-affective domain reached significance. It must be noted however, that this study used three participant drop-outs as a control that were not adequately matched, which may have had an effect on the overall outcome. The authors do discuss the issue of statistical power and how they overcome this with appropriate statistical analysis; however, it may have been beneficial to look at clinically significant change due to the small sample size.

Bedard et al (2012) also found that participant scores on the BDI-II, PHQ-9 and HADS (all) significantly reduced compared to their baseline scores after 8 sessions of MBCT; however, scores on the anxiety domain of the HADS were not significantly different after intervention. The number of participants who met diagnostic threshold of clinical depression on the BDI-II reduced after intervention. The study authors developed a cut-off score of 29 which is categorised as severe depression (Beck, Steer & Garbin, 1988), and six

out of the nine participants at the end of the intervention achieved scores below the cut-off. In addition, 59% of the participants scores on the PHQ-9 fell below the study cut-off of ten which indicated a statistically significant change. On the SCL-90-R, there was a significant reduction of participant distress compared to baseline scores. This study did not contain a control group in which outcomes from the intervention group can be compared to allow a comparison; this was a limitation also discussed by the authors.

Canade (2014) did not collect data specific to anxiety or depression but found that the change on the emotion regulation domain on the MSES-R was statistically different after the intervention. In addition, they found that there was a significant different post-intervention on the FMI and MAAS measures of mindfulness. It must be noted that the overall intervention data analysed was a combination of the two intervention groups due to small sample sizes. This may have had an impact on the outcome of the study and it does not appear that this was in the authors original plan to do this. The single-case experimental design study by Dickinson et al (2017), based on 4 sessions of MBSR, reports a significant decrease in anxiety scores; with the participant's scores reducing from moderate anxiety of 25 points to low anxiety of three points. However, the authors did not take multiple measures across baseline or intervention; thus, it is difficult to confidently ascertain whether it was the intervention that impacted on the outcome.

Mavaddat et al's (2017) study comprising of participants actively listening to an audio CD and following guided exercises was rated borderline average for methodological quality; however, did not report means or standard deviations of the HADS or PANAS. The authors stated that four participants showed an increase in their positive scores and decrease in negative scores on the PANAS. Furthermore, two participants' scores on the HADS improved to being either in the normal or mild range for anxiety and depression, from moderate. Nevertheless, once again, it is not stated how many audio recordings participants listened to; thus, some caution should be taken with results. Azulay and Mott's (2016) main

findings from using an adapted MBSR intervention showed a significant change on the DERS scores, with results suggesting an effect size of .67. The authors report the subscales in which there was most change was in relation to the acceptance of emotions and the impulses around these.

The remaining three papers (Azulay et al, 2012; Combs et al, 2010; Joo et al, 2010) were rated as very poor on methodological quality. The findings from Azulay et al (2012) suggest that, although no specific emotional outcome measure was used, on both the perceived self-efficacy scale and PQOL the areas that showed most improvement were for the management of cognitive and emotional symptoms. This was also seen on the NSI, in which participants self-reported a reduction in emotional and cognitive symptoms. The authors report the findings suggest participants were more able to manage their emotional difficulties after the intervention of ten sessions of MBSR.

Combs et al (2010) report results as showing no significant difference on anxiety and depression scores post-intervention (32 MBSR sessions). However, it should be noted that as the measure used was adapted from a validated measure and not a validated measure in its own right, these results should be interpreted with care. There also appeared to be a significant relationship between the amount of sessions attended and participants belief about the benefit of mindfulness or yoga on mood. The results reported by Joo et al (2010) indicate that after their intervention of 8 MBSR sessions, depression scores on the BDI significantly reduced; with the standard deviation also reducing. For anxiety, trait scores on the STAI reduced to near significance; however, this was not the case for state anxiety.

Previous Systematic Reviews

Five systematic reviews covering 52 studies were reviewed, with a range of patient populations being investigated; for example, stroke, TBI, cancer and fibromyalgia. Six studies are included in the current review that are not contained in the previous reviews.

Description of Reviews

Toivonen et al (2017) conducted a review investigating whether web-based mindfulness was beneficial for individuals with physical health conditions including ABI. Mindfulness interventions were broad in this review; ranging from MBSR and Mindfulness-Based Cognitive Therapy, to general mindfulness. Data extraction was comprehensive and methodological quality of the papers reviewed were assessed using Cochrane tools. Out of 19 papers reviewed, only one included ABI population (Johansson, Bjuhr, Karlsson & Ronnback, 2015) and the primary outcome from that study was based on mental fatigue. Lazaridou et al (2013) investigated the effectiveness of yoga and mindfulness for stroke rehabilitation. Ten studies met their inclusion criteria; with five RCT's, four single case and one qualitative paper. It appears that a poster presentation was also included; therefore, the authors may not have been able to ascertain the methodological quality of this paper if the full paper could not be obtained.

Lawrence et al (2013) conducted a review of four papers investigating the benefits of mindfulness after stroke; with perceived stress being the primary outcome and other psychological outcomes being secondary. Kenuk and Porter (2017) conducted a systematic review on 16 papers to investigate the benefits of using mindfulness within TBI therapy on a range of outcomes. The authors searched a range of databases, using specific terms; however, when comparing the yielded papers with other reviews, the number of papers appears smaller (n = 56). Tsaousides, Ashman and Gordon (2013) conducted a review to discuss interventions for post-TBI depression. The main focus of the review was to synthesize information based on types of interventions, eligibility criteria contained in studies and outcome measures. The authors searched two databases; however, did not state terms used or number of studies included in the review.

Methodological Quality Rating

The methodological quality of the systematic reviews varied, from meeting nine out of 16 criteria to one out of 16. It must be noted that the AMSTAR-2 tool contains questions related to meta-analysis; therefore, all the above systematic reviews did not satisfy these questions so lost points for this. The questions contained in the tool are related to specific components of conducting a review; for example, how the research question is posed, details on the search strategy, how data is extracted and then assessed and how results are then presented. Heterogeneity was eluded to in two papers (Lawrence et al, 2013; Toivonen et al, 2017), but there was not specific discussion of whether this impacted on results.

Lawrence et al (2013) had the strongest methodological quality overall; with points not being awarded for amount of detail related to assessment of risk of bias and not including a list of excluded papers. It must be noted that none of the reviews reported which papers were excluded, as well as not reporting whether any funding was received. Toivonen et al (2017) met seven criteria and had a very comprehensive description of the risk of bias assessment conducted on their paper selection, which was not found in any other review. However, the authors lost points for not discussing specific study designs and only having the lead author selecting and extracting data.

The three remaining papers (Kenuk & Porter, 2017; Lazaridou et al, 2013; Tsaousides et al, 2013) met few criteria over all; four, three and one respectively. The main areas not met were in relation to not meeting the full PICO criteria when posing their question, not having clear descriptions of whether risk of bias was assessed, and if it was, then how this was assessed. Paper selection and data extraction were not conducted by two or more individuals. Furthermore, these papers did not report any sources of conflict. The only criteria met by Tsaousides et al (2013) was their question contained elements of PICO when structuring their question.

Key Findings

One only ABI paper was contained in the Toivonen et al (2017) review; comparing walking sessions with web-based MBSR and results suggest that depression and anxiety scores improved in the MBSR group, but these appear to be secondary measures and not related to the primary question. Toivonen et al (2017) rated this paper as having poor methodological quality. Lawrence and colleagues (2013) state that mindfulness interventions are varied and touch upon heterogeneity; suggesting there will be variations within the studies reviewed. The results from the review indicated positive benefits of using mindfulness-based interventions on psychological and other outcomes. Tsaousides et al (2013) did not state overall findings with regards to mindfulness-based interventions and their effect of remediating depression after TBI; however, the mindfulness studies within the review state that depression symptoms reduced after completing the mindfulness-based interventions.

Kenuk and Porter (2017) state a range of outcome measures were used within the papers reviewed, along with a variation of how the interventions were delivered; for example, 1:1 sessions Vs. a group. The authors discuss significant results from strongest to weakest findings; with mental fatigue appearing to show the strongest results and self-efficacy and energy levels the weakest. There appeared to be mixed results for depression outcomes; with some papers showing a significant effect. This review paper, along with the others discussed, includes 'other' MBI's than the conventional MBSR and MBCT programs, for example yoga and tai chi. However, it is unclear how much emphasis the 'other' interventions place on mindfulness, and not other variables such as the physical movements of exercise.

Discussion

Findings overall from the 11 individual papers reviewed suggest that mindfulness-based interventions may be beneficial in reducing emotional difficulties after brain injury.

However, as the methodological quality ratings of the reviewed papers are generally weak, there is not sufficient robust evidence to confidently conclude that the interventions being investigated are effective. Of the papers being reviewed, two focused purely on changes in depression pre-post (Bedard et al, 2003; Bedard et al, 2014), one on anxiety (Dickinson et al, 2017), four incorporated both anxiety and depression changes (Bedard et al, 2012; Kristofersson, 2012; Joo et al, 2010; Mavaddat et al, 2017), and three investigated a range of symptoms including emotional outcome (Azulay et al, 2012; Combs et al, 2018; Azulay & Mott, 2016). It is noteworthy that Canade (2014) did not explicitly measure anxiety or depression; however, the emotion regulation domain of the MSES-R is reported to have a valid relationship with the Depression Anxiety and Stress-Short From measure. The authors also suggest that there was a change in participants' mindfulness, which impacted on emotional based outcomes.

The mixed findings and weak methodology from the 11 individually reviewed papers make it difficult to draw confident conclusions about the effectiveness of mindfulness for the ABI population. Bedard et al. (2014) conducted a good quality study which concluded a positive outcome; however, as this was a pilot study, effects for significance were not tested and authors discussed replication with a full trial being warranted. The findings from the review suggest that anxiety can be reduced to below clinical levels in some cases; however, methodological quality is not robust for all papers and there was not always a control group to compare outcomes. Despite this, findings of Evans et al (2008) who conducted an RCT looking at whether mindfulness was a useful treatment for people with generalised anxiety disorder are tentatively supported. They concluded that change in participants' scores on anxiety and depression measures were statistically significant; with approximately half of participants also showing clinically significant reductions in anxiety and depression symptoms. The effectiveness of mindfulness-based interventions at reducing anxiety has

also been investigated by Vollestad et al (2011) with comparable outcomes to the papers in this review.

Hofmann et al (2010) completed a meta-analysis investigating the effectiveness of mindfulness-based interventions on anxiety and depression in non-brain injury populations. Their results show that mindfulness interventions produce a moderate effect on reducing individuals' ratings of anxiety (Hedges g = 0.63) and depression (Hedges g = 0.59). Mindfulness-based cognitive therapy as a prevention to relapse of depression has also been the subject of a systematic review and meta-analysis, with results suggesting that it is effective but only in those who have had several pervious episodes (Piet & Hougaard, 2011). This perhaps speaks to potential learning effects and how applicable this is to the ABI population when literature suggests that wider cognitive deficits are also prevalent (Draper & Ponsford, 2008).

As stated previously, the reviewed papers were rated for quality and ranged from moderately poor to moderately good. The main critique of many of the papers is they did not contain a control group which makes it problematic for the reader to confidently know that the outcome was due to the intervention and not other variables. Only one RCT was reviewed (Bedard et al, 2013), which was rated as moderately good; however, the authors did not report enough information to know if allocations were concealed and whether participants and personnel were blind, which could have improved their quality rating and reduced risk of bias.

The main theme from the five previous systematic reviews is that mindfulness-based interventions show promise at alleviating a range of outcomes after stroke or TBI; however, all discuss the limitations of this area of research, including methodologically weak studies. Lawrence et al (2013) was the highest quality rated review and suggest that mindfulness is beneficial after stroke; however, conclude that more research is required. It must be noted that this review contained only four papers. This conclusion is also mirrored by Lazaridou

et al (2013). Toivonen et al (2017) reviewed 19 articles and concluded that outcomes were improved on some measures, but no improvement was seen on the psychological outcomes. The authors concluded that main findings in general were mixed due to small sample sizes. Kenuk and Porter (2017) discuss mixed findings with regards to the benefits of using mindfulness after TBI; however, conclude that there is "potential" for mindfulness-based interventions to alleviate common difficulties expressed after brain injury. The authors also conclude that further research is warranted due to the current article sample having a lack of control groups, limited follow-up measures and small sample sizes.

There are limitations to the current systematic review which are important to discuss. One of the main limitations is there was only one researcher conducting the application of eligibility criteria, although reliability of rating of risk of bias was improved by having a second reviewer rate 50% of papers. The AMSTAR tool recommends that a minimum of 80% of papers should be second rated; thus, the rigor of rating could be improved. Comparing this to the four reviews contained in this paper, two did not second rate any of their included studies (Toivonen et al, 2017; Lazaridou et al, 2013) and two second rated 100% of their included studies (Lawrence et al, 2013; Kenuk & Porter, 2017). In relation to rating risk of bias in the individually reviewed papers, there was variation in the degree of information reported within them. This subsequently meant that some aspects of the rating tool could not be answered. Attempting to obtain this information from study authors may have enhanced the rigour of the risk of bias rating process.

The review contains a small number of papers which could be due to mindfulness-based interventions within the brain injury population being relatively novel; however, is comparable to previous systematic reviews of a similar topic area. Another limitation of the current study is not being able to obtain one paper that was reviewed in Lawrence et al (2013), despite attempts to contact the author and obtain the paper; therefore, it has not been included. However, Lawrence et al (2013) report that the study showed significant

reductions of anxiety and depression on the BDI-II, BAI and HADS after completion of a MBSR intervention. The single-case experimental design study conducted by Dickinson et al (2017) was rated using the SCED scale (Tate et al, 2008); however, the RoBIN-T would have been preferable to use as this is the more updated n-of-1study quality rating scale. The authors discuss the differences between the two measures, with more robust psychometrics being concluded (Tate, Perdices, Rosenkoetter, Wakim, Godbee, Togher & McDonald, 2013).

Many of the studies that were included in the review were group based which suggests that a larger number of individuals can be included in an intervention compared to 1:1 therapy. This has positive implications with regards to cost effectiveness, with minimal staff needing to be involved in delivering an effective intervention and is recommended by the INCOG guidelines. Explicit investigation into cost effectiveness of mindfulness-based interventions after brain injury is not adequately explored within brain injury literature. The cost effectiveness of mindfulness within other clinical populations has been investigated, however, with mixed outcomes. Kuyken et al (2015) found no significant differences between an MBCT + antidepressant reduction group and a maintenance antidepressant group on factors such as total health care and societal costs at 2-year follow-up. This may be an interesting area to investigate further; with a recommendation for future research looking at health economics with regards to interventions after brain injury and also whether group therapy in general aids effectiveness. This is supported by Kuyken et al (2008).

As previously stated, the majority of the studies reviewed made adaptations to their interventions to take into account the common difficulties faced by the ABI population. The most common adaptations were those to session and/or intervention length; with there being differentiation between studies increasing or decreasing the length. This is discussed by Gallagher, McLeod and McMillan (2019) in their systematic review of adaptations to

CBT after brain injury. More discussion and research needs to be conducted to understand which adaptations specifically are beneficial; the reviewed studies did not give evidence as to whether their adaptations contributed positively to their outcomes. This would be an interesting area to gain more information, as Kenuk and Porter (2017) found positive outcomes in studies that varied considerably in relation to session length, for example.

As only one RCT was included in the review, a recommendation for future research would be to complete further controlled trials to confidently assess the effectiveness of mindfulness-based interventions within an ABI population. In their review, Kenuk and Porter (2017) concluded that more RCT's and long-term follow-up studies need to be conducted to validate this. Moreover, further research is needed to establish whether there is any difference in outcome depending on the clinical population being investigated.

In conclusion, the studies contained in the current review have relatively weak methodological quality; therefore, despite individual studies concluding mindfulness-based interventions are effective after ABI, there is insufficient evidence to support this. The current reviewed literature contains only one RCT, which offers the most robust methodological quality; thus, completion of more RCT research is required to explore the findings of the current review further.

Disclosure of Interest

There are no reports of conflict of interest by the primary investigator.

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Chapter 3: Bridging Chapter

The previous chapter described a systematic review that focussed on investigating the effectiveness of mindfulness-based interventions on alleviating emotional difficulties, specifically anxiety and depression, after an acquired brain injury (ABI). As stated in a preceding chapter, previous literature suggests that after ABI the types of emotional challenges that individuals face are being able to control their emotions (Cicerone, Levin, Malec, Stuss & Whyte, 2006), impulsivity (Rao & Lyketsos, 2000), anxiety (Gould, Ponsford & Schönberger, 2011) and depression (Kreutzer, Seel & Gourley, 2001; Jorge, Robinson, Moser, Tateno, Crespo-Facorro & Arndt, 2004). Depression is common within TBI literature, with one study concluding that 77% of individuals with a TBI receive a diagnosis (Fann, Uomoto & Katon, 2001).

There are several theories and models that aim to describe how, after ABI, one may come to develop emotional issues. One view is there is a discrepancy with how an individual views themselves after injury compared to their pre-injury self; leading to unhelpful coping styles (Gracey, Evans & Malley, 2009), which impacts on their psychological well-being. This is partially supported by Riley, Dennis and Powell (2010) who found that experiencing negative feelings as a threat creates an unhelpful avoidant coping style in those with low self-esteem. Within stroke literature, Broomfield, Laidlaw, Hickabottom, Murray, Pendrey, Whittick and Gillespie (2011) suggest that depression manifests after stroke due to individuals having a negative view of themselves and the future.

The systematic review presented in chapter 2 aimed to provide a current overview of literature focussing on the investigation of mindfulness-based interventions and detailing the effectiveness of these interventions after ABI. The main finding from the systematic review suggests that there is insufficient good quality research to draw firm conclusions on effectiveness of mindfulness-based interventions after brain injury, as methodological

quality ratings of the reviewed papers are generally weak. Therefore, making confident conclusions regarding effectiveness is challenging as there is not adequate robust evidence. In conjunction with this outcome, within the reviewed papers, overall outcomes from studies were mixed.

As emotional difficulties are prevalent after brain injury (Koponen, Taiminen, Hiekkanen & Tenovuo, 2011) the impact that this has on an individual can be widespread; from the perspective of the self (Gracey et al, 2009) to everyday life (Konrad et al, 2010; Ponsford, Draper & Schonberger, 2008). The impact on the self has been described above with regards to discrepancy to pre and post-injury self; however, in relation to everyday life struggles, literature proposes this may be due to individuals having additional cognitive difficulties (Ochsner & Phelps, 2007). Kennedy & Coelho (2005) discuss concepts such as monitoring, working memory and problem-solving / decision making, and the relation these have with executive functioning. The authors detail a framework proposed by Stuss (cited in Kennedy & Coelho, 2005) in which executive functions are centralised and receive information from lower and higher metacognitive domains. An example given of a lower level domain is memory for specific information, whereas higher metacognitive domains include values and beliefs, especially regarding the self.

Literature documenting the relationship between emotion and cognition, historically, has been mixed; however, consensus currently is that the two concepts are inherently linked theoretically and physically through imaging studies (Khan-Bourne & Brown, 2003; Fernandez-Duque, Baird & Posner, 2000). Pessoa (2008) argues that cognition and emotion should not be considered as two separate entities and their interaction has an impact on an individuals behaviour. The main discussion point of the paper is that the regions of the brain considered to be just 'cognition' or 'emotion' are fundamentally linked. For example, the amygdala being linked to attention. Furthermore, Pessoa (2008) also argues that executive control and emotion must be linked as the same

neural pathways are required; proposing a specific circuit that involves the regions of the brain thought to be linked to cognition and emotion.

Focussing on executive functioning specifically, Gyurak et al (2012) argue that intact executive functions are important in regulating emotion and behaviour; with executive functioning being required in the monitoring of behaviours and for goal-directed behaviour. The authors conducted a study that found that individuals with higher verbal fluency scores could regulate their emotion more effectively than those with lower scores. Ownsworth, Fleming, Strong, Radel, Chan & Clare (2007) describe the association between executive functioning and deficits with self-awareness. They discuss the difficulty of individuals being able to self-monitor, and therefore achieve goals, when they have executive dysfunction.

Hoffmann, Schmeichel & Baddeley (2012) discuss that self-regulation requires three components that include concepts such as monitoring, reducing discrepancy between ones actual behaviour and that required to achieve goals and lastly, the drive to achieve goals despite any difficulties that may arise. Also discussed are the mechanisms Hoffman et al (2012) propose come under the definition of executive functions: that of "updating", "inhibition" and "shifting". The authors review four concepts that describe the relationship between self-regulation and executive functions. Self-regulation, of both emotion and cognition, has also been argued as being required within social contexts (Rochat, Ammann, Mayer, Annoni & Van der Linden, 2009; Cayyran, Oddy & Wood, 2011; Wood & Worthington, 2017).

It has been suggested that mindfulness-based interventions have an impact on both cognition and emotions. Teper, Segal & Inzlicht (2013) propose that mindfulness can have a positive impact on executive control; arguing that when an individual experiences conflict between their present behaviour and their goal, this causes a need to control the situation. Thus, there is a disparity between how they are behaving and how they want to behave.

Teper et al (2013) suggest that mindfulness enables the individual to ground themselves to the present moment, and link this to cognitive flexibility; with the ability to accept emotions in a non-judgmental way being completed by executive control. A review conducted by Chiesa, Calati and Serretti (2011) concluded that mindfulness meditation may be beneficial for cognitive outcomes; however, noted that there were discrepancies between studies reviewed with regards to issues such as methodological quality.

The synthesising of the information detailed above provides evidence of a rationale to incorporate both emotional and cognitive concepts when thinking about remediating challenges after ABI. Thus, a systematic review of a specific intervention for emotional difficulties has been presented in chapter 2, and the following chapter details a meta-analysis focussing on cognitive rehabilitation and its effectiveness for individuals with executive function difficulties, which may in turn have a positive impact on another prominent difficulty after brain injury; that of mood and emotions.

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Chapter 4: Meta-analysis prepared for submission to Neuropsychological

Rehabilitation

Evidence for the effectiveness of cognitive rehabilitation on executive functioning after ABI: A Meta-Analysis

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Abstract

Background: Executive functioning difficulties are one area in which an individual can experience difficulty after brain injury. Difficulties can be seen in areas such as planning, monitoring and attention. Cognitive rehabilitation is widely used and there are several types of cognitive interventions that aim to remediate or provide strategies to alleviate these difficulties. Previous literature reviews suggest that, in general, cognitive rehabilitation is effective; however, these do not include up-to-date studies and have tended to focus on specific intervention types. *Design:* A meta-analysis approach was conducted to evaluate the effectiveness of cognitive rehabilitation on executive function difficulties. *Method:* Twenty-six papers were reviewed, with risk of bias and methodological quality being considered. *Findings:* Small significant effect sizes were found across the majority of domains analysed which speaks to the heterogenous nature of brain injury literature. Studies varied with regards to methodological quality, and there was variability between outcome measures used. *Conclusions:* Whilst further RCT research in this area may be warranted, differences between participants and interventions will continue to make comparisons and conclusions on effectiveness difficult to conclude.

Keywords: *brain injury, executive function, cognitive rehabilitation, intervention, impairment, participation*

Introduction

Difficulties after Acquired Brain Injury

After a brain injury an individual can encounter a range of difficulties or deficits that can span across areas of functioning and is considered a life-long condition (Langlois, Rutland-Brown & Wald, 2006). The World Health Organisation (WHO) created a framework that aims to help clinicians understand the difficulties that affect an individual's life across a variety of domains. The WHO International Classification of Functioning, Disability and Health (WHO, 2001 [ICF]) categorise domains into impairments of body functions and structure, participation and activity difficulties, environmental factors and general health information. Within the body functions domain, functioning in relation to attention, emotions and higher-level cognitive functions are discussed.

Cognitive Challenges after ABI

Common cognitive difficulties that are present after brain injury include problems with attention and concentration, memory, processing information, planning, reasoning and problem-solving (Model Systems Knowledge Translation Center, MSKTC, 2018). Draper and Ponsford (2008) found that cognitive impairments continue to be present ten years post-injury which suggests a chronic difficulty (Langlois et al, 2006). After brain injury individuals often need to use compensatory strategies to help them complete activities of daily living, especially in relation to memory and attention (Christiansen et al, 2008). ABI literature focussing on cognitive deficits after stroke and TBI suggest that executive dysfunction is prominent (Tatemichi, Desmond, Stern, Paik, Sano & Bagiella, 1994; Zinn, Bosworth, Hoenig & Swaitzwelder, 2007; Krpan, Levine, Stuss & Dawson, 2007) and prevalent (Patel, Coshell, Rudd & Wolfe, 2002; Nys et al, 2007; Fish et al, 2007). Pohjasvaara et al (2002) discuss the impact post-stoke executive dysfunction can have on feelings of depression.

Executive Functioning and Regions of the Brain

Diamond (2013) discusses executive functions as encompassing skills such as inhibition, interference control and cognitive flexibility. Embedded in these skills is the need for attention. Executive functions can be negatively affected after sustaining an ABI and are thought to be controlled by the frontal region of the brain and can be used for self-monitoring and regulation (Hart, Whyte, Kim, & Vaccaro, 2005). However, Nys et al (2007) discuss evidence for executive function deficits being seen after more diffuse damage after stroke. This is supported by Stuss (2011) who describes different areas of the frontal lobes being related to specific functions; including metacognition, monitoring, setting tasks and behavioural, emotional self-regulation. Moreover, Cicerone (2006) discusses executive functions in terms of four domains; executive cognitive functions, behavioural self-regulatory functions, activation regulating functions and metacognitive processes. Therefore, given the multiplicity of functions of the frontal lobes, and different models of these functions, there are a range of interventions that aim to target these different functions. This raises questions as to what type of intervention strategy, for example remediating or compensatory, is the preferred approach.

Attentional Difficulties after ABI

Literature proposes there are differing models of attention; for example, the Supervisory Attentional System (Norman & Shallice, 1986), visual attention spotlight model (Posner, Synder & Davidson 1980) and Broadbent's filter model (Broadbent, 1958). These models propose that there are differing components (e.g. selective, sustained, divided attention) that create the term 'attention' and after brain injury an individual can have difficulty with one or more component. Mathias and Wheaton (2007) conducted a meta-analysis of 41 studies detailing selective, sustained, divided attention and supervisory attentional control as being problematic after a TBI. Moreover, Robertson, Manly, Andrade, Baddeley and Yiend

(1997) surmise that after TBI individuals are more likely to make attentional errors due to difficulty sustaining attention.

Guidelines and Recommendations for Interventions

An international group of clinical researchers (INCOG) created guidelines and recommendations for interventions to address problems with attention (Ponsford et al., 2014) and executive functioning (Tate et al., 2014) difficulties after brain injury. There are several recommendations proposed in relation to attentional difficulties that include: using metacognitive strategies, using dual task interventions and making specific adaptations to reduce load on attention. Furthermore, computer-based attention training and alerting not pertaining to everyday life are not recommended. The use of mindfulness is also not recommended. Overall, INCOG conclude that there is not sufficient strong evidence of rehabilitation programs showing remediation of attention difficulties; with research needing to have more focus on everyday life.

In relation to executive dysfunction, there are four main recommendations that are proposed by INCOG that include: using remediating problem-solving and planning in everyday life via metacognitive strategies, using strategies to help reasoning skills, providing immediate feedback to avoid errors and improve self-awareness, and for interventions to be delivered via a group. INCOG also provided broad recommendations for future research with regards to improving methodological quality and more investigation of specific intervention programmes.

Previous Literature on Cognitive Interventions

There are a range of interventions that aim to reduce executive function difficulties. Previous authors in this field highlight the importance of focussing on overcoming difficulties in an everyday life context, regardless of the specific executive domain being targeted, is required (Fleming & Ownsworth, 2006; Kennedy et al, 2008). Strategy based

interventions aiming to remediate difficulties are beneficial, with Cicerone (2002) concluding this after investigating processes in attention problems. Goal Management Training (GMT; Robertson, 1996) is a comprehensive programme that focusses on training individuals with executive functioning deficits using a range approaches; for example, self-monitoring of behaviour, planning and organising in relation to goal directed behaviour and everyday life goals. Krasny-Pacini, Chevignard and Evans (2014) conducted a meta-analysis investigating the effectiveness of GMT after brain injury and surmised that GMT is most effective when used alongside another intervention, rather than in isolation. Attention Process Training (APT; Sohlberg & Mateer, 1986) is a programme specifically used to improve issues one may have with attention via tasks related to different domains of attention. Sohlberg, McLaughlin, Pavase, Heidrich and Posner (2000) found that participants on the APT arm of their study had better outcomes than control participants.

Whilst there have been systematic reviews and meta-analyses that focus on this topic area, these do not include most recent literature and have tended to focus on either specific populations (TBI; Kennedy et al, 2008) or interventions (GMT; Krasny-Pacini et al, 2014; Stamenova & Levine, 2018). Cicerone and colleagues have completed two systematic reviews (2005; 2011) investigating the effectiveness of cognitive rehabilitation after brain injury; finding that cognitive rehabilitation is effective in the majority of the studies reviewed. Moreover, Rohling, Faust, Beverly and Demakis (2009) concluded in their meta-analysis that cognitive rehabilitation is effective in general after brain injury but do discuss that as small effect sizes were found, this result may be "limited". The authors do not appear to discuss outcomes with regards to everyday life or impairment focussed outcomes.

Poulin, Kirner-Bitensky, Dawson and Bherer (2012) conducted a systematic review investigating the effectiveness of executive function interventions after stroke. Their conclusions suggest that whilst executive function interventions are beneficial in remediating difficulties after stroke, additional research is required to encompass

participants across a wider recovery trajectory. However, it must be noted that the authors excluded attentional based interventions. Boelen, Spikman and Fasotti (2011) have also conducted a systematic review investigating intervention effectiveness on executive functioning after brain injury. They discussed outcomes in relation to compensatory internal and external strategies, along with interventions aiming to 'restore' skills. They conclude that whilst outcomes indicate promising results, further research is required in this area, especially research that contains control groups and good methodological quality. In addition, Stamenova and Levine (2018) completed a meta-analysis of the effectiveness of GMT in any adult population and found positive effects for its usefulness in alleviating executive functioning difficulties.

Rationale

The challenge of investigating how best to overcome executive functioning difficulties after acquiring a brain injury has been the subject of previous reviews; however, these have been focussed on either intervention type (GMT only; Stamenova & Levine, 2018; Krasny-Pacini et al, 2014), population (TBI only; Kennedy et al, 2008), or are now relatively out of date as several studies have been completed in recent years. A previous meta-analysis completed by Rohling et al (2009) found small effect sizes; however, did not include commentary on impairment focussed or everyday life outcomes. Furthermore, the current review aims to add to the findings of Poulin et al (2012) and Boelen et al (2001) by encompassing additional ABI literature into the review and conducting a meta-analysis to investigate effectiveness of cognitive rehabilitation interventions on executive functions.

Given the growth in rehabilitation trials looking at this topic, especially with regards to retraining and GMT type interventions, a meta-analysis is appropriate to investigate type of intervention and the effect this has on outcome. This is pertinent as previous reviews have tended to focus on specific intervention type (Krasny-Pacini et al, 2014; Stamenova & Levine, 2018) or one clinical population (Kennedy et al, 2008). Therefore, the main

question of the current study is: are cognitive rehabilitation interventions effective in reducing executive function impairments following an ABI in adulthood? Secondary questions are related to whether there are any differences between: 1. intervention type on impairment, everyday life or subjective focussed outcomes, 2. impairment, everyday life or subjective focussed outcomes in general, and 3. study type (RCT vs. non-RCT).

Method

Search Strategy

Studies were searched according to the participant, intervention, comparison and outcome (PICO) principle; with MeSH terms being considered to ensure all pertinent terms are used. Boolean modifiers (AND, OR) and truncation (*) were used to ensure effective searching of databases. For population the following terms were used: cerebrovascular accident, cerebrovascular disease, brain accident, brain attack, brain insult, CVA, cerebral vascular accident, ischaemic cerebral attack, ischemic cerebral attack, ischaemic seizure, ischemic seizure, brain disease*, acute brain injury, brain injur*, brain injury, chronic cerebral injury, injury brain, acquired brain injur*, acquired head injur*, head injur*, traumatic brain injur*, traumatic head injur*, diffuse brain injur*, encephalitis, meningitis, stroke. For intervention, attention, executive function*, working memory, goal management training, GMT, problem solving, executive plus group and for study design the following terms were used: randomised control trial, randomized control trial, RCT, control* trial, clinical trial. The databases searched on the 12th March 2019 were Medline Pubmed, PsychINFO, EMBASE, CINAHL and PsycARTICLES. Additional papers were searched for using the reference lists of the identified papers.

Eligibility Criteria

Searches were limited to human participants, English language articles and adults only. Inclusion criteria for the articles were: evidence of a head or brain injury, aged over 18

years, evidence of an intervention that addresses executive function impairment and the use of valid measures of executive functioning appropriate to the population. Papers were excluded if they were descriptive papers only, case studies/descriptions or conference presentations. The Cochrane Handbook was consulted to ascertain definition of RCT to ensure studies were categorised appropriately. Guidance suggests a study should be classed as a RCT if there is evidence of randomisation (Higgins & Green, 2011)

Data Extraction

Duplicate papers were removed and identified papers were either included or excluded by reading title and abstract to assess appropriateness. Eligibility of papers was checked by a second researcher (FG) to ensure rigor of the selection process. The primary investigator contacted authors of papers and conducted lending requests when full papers could not be obtained. Twenty-six papers were then read, and data extracted to obtain the following information: design, sample size, participant details, control condition, outcome measures, inclusion and exclusion criteria, intervention, key findings and effect size.

Appraisal of Selected Studies

Papers were rated by the primary investigator for risk of bias using an adapted scale created by Kocsis et al (2010) to assess the quality of randomised control trial's (RCT's) (Appendix 1). The overall global quality rating scale for the papers can be found in the data extraction table (table 1) and the full description of risk of bias for each paper can be found in appendix 4.

Data Analysis

Means and standard deviations of post intervention scores for both intervention and control group were used to calculate effect sizes. Where this data was not available, other appropriate statistics presented in the paper were used and primary authors were contacted to ascertain whether this data could be obtained. As there were different directions of

effects, all effects were assigned + for improvement and − for deterioration. Analyses were run on the MAVIS: Meta-analysis via shiny software (Hamilton, 2018). Data was analysed four-fold; investigating intervention type, impairment focussed outcomes, everyday life or ecologically valid outcomes and subjective outcomes (Kennedy et al, 2008; Stamenova & Levine, 2018). Comparisons between RCT and non-RCT studies were also investigated. Average effect sizes were computed where multiple outcome measures were used in single studies (Stamenova & Levine, 2018; Belanger, Curtiss, Demery, Lebowitx & Vanderploeg, 2005) for example WCST, Stroop and Trails being used within one study. Forest and funnel plots were produced to show heterogeneity and pooled results, and publication bias respectively.

Results

The flow chart in figure 1 shows the process of paper selection. The initial number of papers sourced was 982, with a further 46 being from reading reference lists. After removing duplicates 937 papers remained in which title and abstract were read and papers not meeting eligibility criteria removed. The remaining 69 papers were read in full and 26 papers selected for final review. Table 1 shows the data extracted from the papers and describes information such as outcome measures, inclusion and exclusion criteria, intervention and key findings. One paper (Cuberos-Urbano, Caracuel, Valls-Serrano, Garcia- Mochon, Gracey & Verdejo-Garcia, 2016) was included and then later excluded due to the question being investigated in the paper not sufficiently addressing the question of the current meta-analysis.

Records identified through
database searching
(n = 982)

Additional records identified
through other sources
(n = 46)

Records after duplicates removed
(n = 937)

Records screened
(n = 937)

Records excluded
(n = 868)

Full-text articles assessed
for eligibility
(n = 69)

Full-text articles excluded,
with reasons
(n = 43)

Statistics not appropriate
for MA = 7
No cognitive rehab /
intervention = 12
No executive function
measures / main outcome
= 15
Non clinical population = 1
Single case = 1
Reused data = 4
Protocol = 2
No pre-post outcomes = 1

Studies included in quantitative
synthesis
(n = 26; 24 – RCT, 2 – non RCT)

Identification

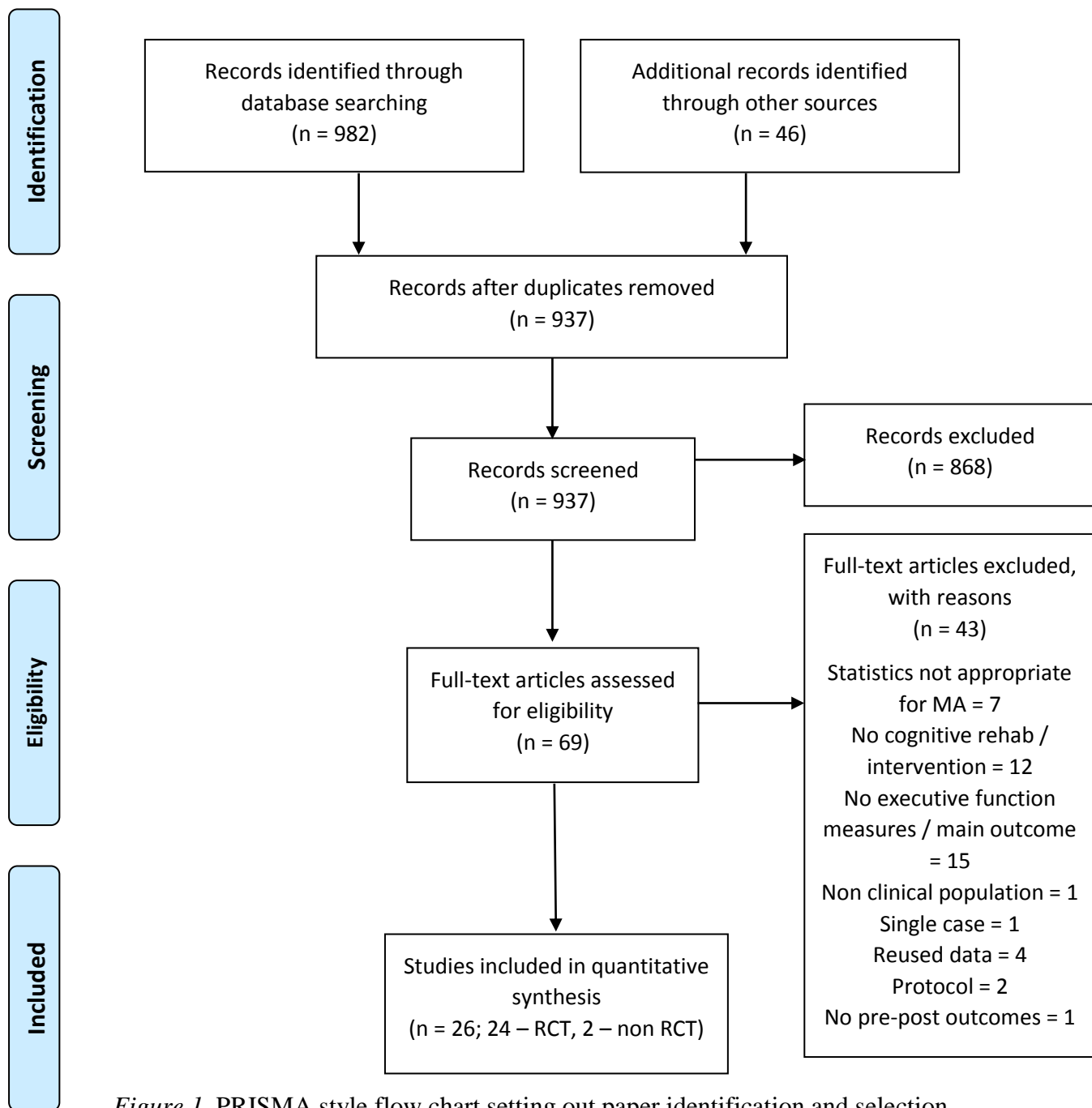**Screening**

Eligibility

Included

Figure 1. PRISMA style flow chart setting out paper identification and selection.

Table 1

Meta-analysis data extraction table

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating (Max score = 24)
Akerlund, Esbjornsson, Sunnerhagen & Bjorkdahl (2013)	RCT	**Intervention** – 13 males and 12 females, mean age = 51 years, mean time post injury = 32 weeks. 68% stroke, 16% trauma, 16% other. **Control** – 10 male and 10 female, mean age = 53 years, mean time post injury = 22.5 weeks. 75% stroke, 15% trauma, 10% other.	Digit span, DEX, HADS.	Five, 30-40 minute Cogmed training sessions over 5 weeks. Control group offered intervention.	No significant difference on the DEX between groups. DEX significantly correlated with HADS for all participants	**DEX:** 0.38	Moderately good, 16 points
Bertens, Kessels, Fiorenzato, Boelen & Fasotti (2015)	RCT	**Intervention** – 16 males, mean age = 49.7 years, mean time post injury = 52.7 months, 16 TBI, 13 stroke and 1 other. **Control** – 20 males, mean age = 46.8, mean time post injury = 52.1 months, 10 TBI, 19 stroke, 1 other.	Everyday task performance, Goal attainment scaling, verbal fluency, modified six elements, zoo map, Brixton, CFQ, DEX	GMT+ errorless learning. 8 X 60-minute individual sessions; 2 per week. Sessions 1-4 delivered at rehabilitation centre and 5-8 delivered at home / work.	Participants perform better on everyday tasks when combination of errorless learning and GMT. No significant difference between groups on DEX.	**Verbal fluency:** 0.12, **DEX:** 0.03, **MSE:** 0.43, **CFQ:** 0.31	Very good, 19 points
Cantor, et al. (2014)	RCT	**Intervention** – 14 male and 35 female, mean age = 46.7 years, mean time post injury = 10.7 years, 30 mild, 8 moderate, 11 severe. **Control** – 23 males and 26 females, mean age = 43.9 years, mean time post injury = 14.4 years, 19 mild, 11 moderate, 19 severe.	**Primary** – Problem solving inventory (PSI), FrSBe, BADS and self-awareness of deficits interview. **Secondary** – Stroop, COWAT, Animal naming, matrix reasoning and similarities, short category test and trail making	STEP program. 2 X 45-minute sessions on emotion regulation and problem solving and 1 X 60-minute session on attention training and external aids per day. 3 days per week for 12 weeks; total of 108 sessions.	ITT analysis – significant treatment effect for executive function measure. No significant differences on emotion regulation scale or attention scale. Significant treatment effects on FrSBe and PSI.	**PSI:** 0.41, **FrSBe:** 0.32 **BADS:** 0.03 **Stroop:** 0.06 **Trails:** 0	Very good, 19 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Couillet et al. (2010)	Randomised Crossover Design	**Intervention:** n = 5, mean age = 26.7 years, mean time post injury = 16.1 months. **Control:** n = 7, mean age = 23.8 years, mean time post injury = 6.3 months.	Test for Attentional Performance (TAP; divided attention and flexibility), trail making, Stroop, speed of processing, go/no-go and digit span.	2 X 6-week divided attention training; consisting of 4 X 60-minute individual sessions per week. Training in 2 everyday life tasks one at a time. Control group training did not contain aspects of divided attention.	No significant differences of main effect of group for all outcome measures.	**TAP:** 1.01, **Stroop:** 2.84 **Go/No-Go:** 0.81 **Trail making:** 0.31 **Digit span:** 0.74, **Brown-Peterson:** 0	Moderately good, 16 points
Gracey et al. (2016)	Randomized controlled, parallel crossover design	**Intervention** – 21 male and 8 female, mean age = 47.79, mean time post injury = 5 years, 10 CVA, 2 infection, 13 TBI, 4 tumour. **Control** – 21 male and 9 female, mean age = 49.76, mean time post injury = 9.15, 11 CVA, 1 infection, 14 TBI.	**Primary** – mean daily intentions completed. **Secondary** – Goal attainment, The Hotel Task, verbal fluency	Brief GMT in participants home or community. 2 X 1:1 sessions lasting 90-120 minutes. Covered topics such as setting goals, checking intentions and delivery of 'STOP' SMS reminders	Greater goal attainment during intervention phase. Significant differences between TBI and other ABI participants. No significant interaction or differences found for Hotel Task or verbal fluency.	**Verbal fluency:** 0.07, **Hotel Task:** 0.15	Exceptionally good, 22 points
Miotto, Evans, Souza de Lucia & Scaff (2009)	RCT	Fifteen males and 15 females. Mean age = 41.7.16 left frontal lesions, 14 right frontal lesions. 23 had neurosurgery for removal of tumour (9 – meningioma, 14 – low grade astrocytoma) and 7 had mild TBI with frontal lobe lesion. Mean time since surgical procedure – 2.4 years.	WMS, Multiple Errands Task, FSIQ, WCST, Verbal fluency and DEX.	APS – 10 weekly 90-minute sessions.	No significant change to cognitive or executive functions but scores improved. After intervention for control groups, significant differences for WCST but not FAS.	**WCST:** 0, **Verbal fluency:** 0.24, **DEX:** 0.88, **Hotel Task:** 0 **Digit span:** 0.37	Average, 16 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Rath, Simon, Langenbahn, Sherr & Diller (2003)	RCT	23 males, 37 females. Mean age = 43.6 years. Mean time post injury = 48.2 months. 30 traffic accident, 10 fall, 6 assault, 6 sporting accident, 8 other.	Stroop, FAS, WMS, WCST, PSI.	'Innovative' training focussing on problem solving and emotional self-regulation. 1 X 120-minute sessions per week, with 24 sessions delivered in total.	Intervention group showed significant improvements on WCST. Gains still apparent at 6-month follow-up.	**WCST:** 0.88	Moderately good 15 points
Spikman, Boelen, Lamberts, Brouwer & Fasotti (2010)	RCT	**Intervention** – 68%male, mean age = 41.4 years, mean time post injury = 105.4 months. 55% TBI, 32% stroke, 13% other. **Control** – 65% male, mean age – 43.7 years, mean time post injury = 64.1 months, 32.5% TBI, 54% stroke, 13.5% other.	**Primary** – The role resumption list. Executive functions at a social participation level. Goal attainment scaling, ecologically valid task (The Executive Secretarial Task), DEX, Executive Observation Scale, quality of life, BADS, trail making, Stroop, ToL.	'Multifaceted Treatment of Executive Dysfunction' based on GMT and problem solving training. Max 24 sessions. Aimed to improve self-awareness, goal setting, planning, self-initiation, flexibility and strategic behaviour.	Improvements on executive function measures for both groups, but greater for experimental group. Decrease in executive difficulties on the DEX for both self-reported and therapist. No interaction was found for Stroop, trails, tower of London and BADS in relation to treatment effects.	**Hotel Task:** 0.63	Exceptionally good, 23 points
Tornas et al. (2016)	RCT	**Intervention** – 19 male and 14 female, mean age = 42.12 years, mean time post injury = 106.94 months, 23 TBI, 6 stroke, 2 tumour, 0 anoxic, 2 other. **Control** – 19 male and 18 female, mean age = 43.57 years, mean time post injury = 81.46 months, 22 TBI, 9 stroke, 4 tumour, 2 anoxic, 0 other.	Completed at baseline, after training and 6-month follow-up: Behaviour rating inventory of executive function, CFQ, DEX, tasks from D-KEFS, The Hotel Task.	Adaptation of Levine et al's (2011) GMT protocol. Intervention included SMS alerts / cueing. Each condition group met for 1 day every second week; 8 X 120-minute sessions over 4 days.	GMT better effect over education group. GMT group - reduction in self-reported dysexecutive symptoms from baseline to follow-up with a medium effect size. Greatest improvement seen at follow-up.	**Stroop (condition 3-1):** 0.51 **Stroop (condition 4-1):** 0.22, **Hotel Task:** 0.05, **ToL:** 0.29, **DEX:** 0.21, **CFQ:** 0.11	Exceptionally good, 22 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Twamley, Jak, Delis, Bondi &Lohr (2014)	RCT	**Intervention:** n = 16, 93.8% male, mean age = 29.4 years, mean time post most recent injury = 3.6 years. **Control:** n = 18, 94.4% male, mean age = 34.3 years, mean time post most recent injury = 5.1 years.	Completed at baseline, 3 months (completion of study), 6 and 12 months. Premorbid IQ, prospective memory, digit span, CVLT-II, D-KEFS verbal fluency, WCST	CogSMART intervention consisted of 1 60-minute session per week in addition to the standard 2 visits per week. Control group only received the standard 2 visits per week.	No significant differences on any neuropsychological outcome measures.	**WCST:** -0.3, **Digit span:** -0.45, **Verbal fluency:** 0.27	Moderately good, 14 points
Vas, Chapman, Cook, Elliott & Keebler (2011)	RCT	**Intervention** – 9 males and 5 females, mean age = 39 years, mean time post injury = 16.71 years. **Control** – 7 males and 7 females, mean age = 47 years, mean time post injury = 16.35 years.	Test of strategic learning, digit span forward from WAIS-III, Stroop, matrix reasoning, trail making, verbal fluency, community integration questionnaire.	SMART memory and reasoning training: 18 hours of training across 12 sessions over 8-week period. First 15 hours took place over 10 sessions and completed in the first 5 weeks. The remaining 3 hours took place over a 3-week period.	No significant differences between groups in relation to processing speed. Significant main effects seen for intervention group in relation to the executive function measures.	**Stroop:** 1.2, **Trail making:** 0.45, **Verbal fluency:** 0.38	Very good, 18 points
DeLuca, Leonardi, Spadaro, Russo, Aragona, Torrisi, Maggio, Bramanti, Naro, De Cola & Calabro (2018)	RCT	**Intervention:** n = 20, mean age = 43.9 years, 11 males and 9 females, mean time post injury = 3 months. Type of stroke: Ischemic = 15, haemorrhage = 5. **Control:** n = 15, mean age = 42.1 years, 7 males and 8 females, mean time post injury = 4 months. Type of stroke: Ischemic = 9, haemorrhage = 6	Category verbal fluency, Letter verbal fluency, Attention matrices, Digit span	Cognitive rehabilitation with additional PC-based training focussing on executive functioning. Six 45 minute cognitive rehabilitation sessions for 8 weeks; plus 3 X 45 minute sessions / week, for 8 weeks PC training.	No significant difference between groups from baseline to completion of intervention.	**Verbal fluency:** 0.26, **Digit span:** -0.31, **RAVENS:** 0.2	Moderately poor, 9 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Ownsworth, Fleming, Tate, Beadle, Griffin, Kendall, Schmidt, lane-Brown, Chevignard & Shum (2017)	RCT	**Intervention:** n = 27, mean age = 37.37 years, 20 males (74.1%), mean time post injury = 36.44 months. Type of injury: RTA = 11, Fall = 10, Assault = 3, Other = 3. **Control:** n = 27, mean age = 37.86 years, 23 males (85.1%), mean time post injury = 40.81 months. Type of injury: RTA = 16, Fall = 9, Assault = 2.	**Primary:** Total errors on cooking task. **Secondary:** Zoo map, Awareness Questionnaire, Patient Competency Rating Scale, Sydney Psychosocial Reintegration Scale, Care and Needs Scale, Depression Anxiety and Stress Scales	EBL, in which individuals are allowed to make errors, compared to ELL in which errors are avoided. Both approaches were 8 X 90 minute sessions based at home. First 4 sessions learning to prepare hot meal and last 4 sessions therapist developed tasks related to goals.	No significant differences on the Zoo map.	**Cooking task:** 0.64 **Zoo map:** 0.3	Exceptionally good, 22 points
Yoo, Yong, Chung & Yang (2015)	RCT	**Intervention:** n = 23, mean age = 53.2 years, 8 males and 15 females, mean time post injury = 11.8 months. **Control:** n = 23, mean age = 56.3 years, 9 males and 14 females, mean time post injury = 10.7 months.	Digit span test, verbal learning test, visual span test, visual learning test, auditory and visual continuous performance tests, trail making test, FIM.	**Intervention:** Rehabilitation, plus cognitive computer programme, RehaCom. Thirty minute sessions / day, 5 times / week for 5 weeks. **Control:** Rehabilitation only.	Experimental group showed statistically significant changes in digit span after intervention, but not for trail making.	**Trails:** 0.07, **Digit:** 0.34	Very poor, 6 points
Levine et al. (2000)	RCT	**Intervention –** 5 male, mean age = 29 years, mean time since injury = 3.7 years. **Control –** 9 male, mean age = 30.8 years, mean time since injury = 3.8 years.	Everyday paper and pencil tasks, proofreading, grouping and room layout tasks, trail making test, Stroop and digit span.	Five stages of the GMT programme were delivered in 1 60-minute session.	Intervention group slower to complete the Stroop, trail making task and digit span compared to control group. Authors suggest due to more attention being taken post-intervention.	**Stroop:** 1.15, **Trail making:** 0.77	Moderately poor, 10 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Van de ven, Buitenweg, Schmand, Veltman, Aaronson, Nijboer, Kruiper-Doesborgh, van Bennekom, rasquin, Ridderinkhof & Murre (2017)	RCT	**Intervention:** n = 38, mean age = 57 years, 63% male, mean time post injury = 34.6 months. **Active Control:** n = 35, mean age = 60.9 years, 66% male, mean time post injury = 28.3 months.	**Primary:** Number-Letter Sequencing Trail Making, Category and Letter fluency, ToL, Letter-Number Sequencing. **Secondary:** TMT A and B, PASAT and other measures investigating other cognitive functions.	**Experimental:** Cognitive flexibility training comprising of 5 X 30 minute sessions over 12 weeks. First week – 10 minutes for each task. After this, 10 tasks of 3 minutes each. Difficulty is adapted. **Active Control:** Mock training of 4 tasks that did not train executive functioning.	All groups improved significantly over time; however, the intervention group showed no bigger improvements compared to other groups.	**Trail:** 0.27, **Verbal fluency:** 0.38, **ToL:** 0.18	Very good, 18 points
Salazar, Warden, Schwab, Spector, Walter, Cole, Rosner, Martin, Ecklund & Ellenbogen (2000)	RCT	**Intervention:** n = 67, mean age = 25 years, 93% male, mean time post injury = 38 days. **Control:** n = 53, mean age = 26 years, 96% male, mean time post injury = 39 days. Type of injury in both groups: Assault and RTA; however, numbers are unclear.	**Primary:** Return and fitness to work. This includes cognitive outcomes.	**Intervention:** Standard rehabilitation modelled on Prigatano's milieu approach. Encouraged to continue with military duty. Included separate vocational aspect of programme. **Control:** TBI education and counselling. Encouraged to use strategies to enhance cognitive and organisational skills. Weekly 30 minute telephone call to review week.	No significant differences between groups on attention or general cognitive outcomes.	**WCST:** 0.27, **PASAT:** 0.04	Very good, 18 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Elbogen, Dennis, Van Voorhees, Blakey, Johnson, Johnson, Wagner, Hamer, Beckham, Manley & Belger (2018)	RCT	**Intervention:** n = 57, mean age = 36.77 years, 4 female (10%) **Control:** n = 55, mean age = 36.25 years, 5 female (10%).	Stroop, Barrett Impulsiveness Scale, Dimensions of Anger Reactions	**Intervention:** CALM – GMT psychoeducation and exercises. Created new goal every home visit (every 2 months). Used app that promotes 'executive review' to review whether on track with goal. **Active control:** Psychoeducation on TBI and trained visual memory. Also used an app called "Unotan Memory".	No significantly different change by group on D-KEFS colour-word inhibition or BIS. CALM group family / friend reported participants had fewer maladaptive behaviours after intervention.	**Stroop:** 0.19	Very good, 17 points
Jacoby, Averbuch, Scaher, Katz, Weiss & Kizony (2013)	Pilot RCT	**Intervention** – 4 males, mean age = 27.83 years, mean time post injury = 126 days. **Control** – 4 males, mean age = 30.67, mean time post injury = 100 days. 8 = RTA's, 2 = falls, 1 = military, 1 = assault.	Multiple Errands Task (MET), executive function performance test	Standard cognitive retraining for both groups, but intervention in context of virtual supermarket - 10 45-minute sessions, 3-4 times per week.	No significant differences on MET or executive performance test in relation to total scores; however, large effect size for change of participants final scores.	**Multiple Errands Task:** 0.57, **EFT:** 0.53	Moderately good, 14 points
Niemann, Ruff & Baser (1990)	Multiple baseline design	**Intervention** – mean age = 28.9, mean time post injury = 41 months. **Control** – mean age = 34.3, mean time post injury = 37.1 months.	Attention test, PASAT, divided attention test, trail making test, Rey Auditory test, Block span.	Divided attention training using visual, auditory tasks. 6 X 120-minute sessions were given for each component, with minimum training time of 30-40 minutes. 1:1 sessions given twice per week.	Intervention group performed significantly better than memory group on 4 measures of attention; with a significant difference between the groups being seen on the trail making task.	**Trail making:** 0.23, **PASAT:** -0.31	Average, 12 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Faria, Andrade, Soares & Badia (2016)	RCT	**Intervention:** n = 9, median age = 58, 55.6% Female, median time post-injury = 7 months. Type of stroke: Right lesion = 55.6%, Left = 44.4%. **Control:** n = 9, median age = 53, 55.6% Female, median time post-injury = 4 months. Type of stroke: Right = 55.6%, Left = 44.4%.	TMT-A and B, Picture Arrangement from WAIS.	Twelve X 20 minute sessions over a 4-6 week period. **Intervention:** Reh@City virtual reality simulation to train cognition as well as ADL's. Goals given a goal with additional tasks to complete in an everyday life setting. **Control:** Generic cognitive training.	No difference seen on TMT A and B seen between groups for errors. Significant differences seen within groups on picture arrangement task. "Tendency" for significant difference between groups on picture arrangement, with intervention group performing better post-intervention.	**TMT-A:** 0.49, **TMT-B:** 0.21, **Picture Arran:** 0.15	Moderately good, 14 points
Tiersky, Anselmi, Johnston, Kurtyka, Roosen, Schwartz & DeLuca (2005)	RCT	**Intervention:** n = 11, mean age = 47.55 years, 45.5% female. **Control:** n = 9, mean age = 46 years, 66.7% female. Types of injury not separated by group: Vehicle related = 13, Falling object = 3, Falls = 2, Sport related = 1, Pedestrian in RTA = 1.	PASAT, Attention Questionnaire	**Intervention:** APT + CBT. Two individual 50 minute sessions completed in same day. Total of 3 / week, for 11 weeks. Focussed on attention and information processing and memory. **Control:** Met with principal investigator for 45 minutes 2-3 times over 11 weeks. This was either face-to-face or on telephone. Treatment offered at end of experimental phase.	Improvement seen on PASAT after intervention.	**PASAT:** 0.52	Moderately good, 15 points.

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Park and Lee (2018)	Pilot RCT	**Intervention:** n = 15, median age = 54 years, 8 males (53.3%) and 7 females (46.7%). Type of stroke: Left hemisphere = 8 (53.3%), Right hemisphere = 7 (46.7%) **Control:** n = 15, median age = 52 years, 9 males (60%) and 6 females (40%). Type of stroke: Left hemisphere = 11 (73.3%), Right hemisphere = 4 (26.7%)	Trail making A and B, Stroop and Digit Span.	**Experimental:** Cognitive-Motor Dual-Tasking (CMDT) + Auditory-Motor Synchronisation Training (AMST). Thirty minute session (15 minutes per task) pressing a button when hear specific sound. **Control:** CMDT - performing cognitive task whist also doing a motor task. Three, 30 minute sessions / week for 6 weeks.	Both the experimental and control groups showed significant changes on TMT A+ B, digit span (forward and backward) and Stroop (colour and word). Significant changes between groups on TMT A, digit span (forward and backward) and Stroop (word).	**Stroop:** 0.16, **TMT-A:** 0.1, **TMT-B:** -0.22, **Digit (forward):** 0.81, **Digit (backward):** 1.31	Very good, 19 points
Poulin, Korner-Bitensky, Bherer, Lussier & Dawson (2017)	Pilot, partial RCT	**Intervention:** n = 5, mean age = 49 years, mean time post injury = 6.1 months. Type of stroke: Right haemorrhagic = 2, Left haemorrhagic = 3, Left ischemic = 1. **Control:** n = 4, mean age = 57.75 years, mean time post injury = 6.4 months. Type of stroke: Right ischemic = 2, Left ischemic = 1, Bilateral ischemic = 1.	TMT, Digit span, DEX, Social participation	**Intervention:** CO-OP intervention to help participants create and meet goals. Two, 60 minute sessions completed / week for a total of 8 weeks. **Control:** General executive functioning training.	CO-OP group performed better on TMT-B. No significant differences found between groups on any executive function measures.	**Stroop:** 0.65, **TMT-A:** 0.35, **TMT-B:** 0.54, **Digit (forward):** 0.41, **Digit (backward):** 0.17, **DEX:** -0.28	Exceptionally good, 21 points

Author and Date	Design	Participants (n, injury details, mean age)	Outcome Measures	Intervention	Key Findings	Numerical Results (Effect Size)	Global Quality Rating
Non-RCT's							
Levine et al. (2011)	Pre-post design	**Intervention** – 8 male, mean age = 48.91 years. **Control** – 6 male, mean age = 49.25	SART, D-KEFs Tower test, The Hotel Task, DEX, CFQ	7 X 120-minute sessions covering principles of GMT and mindfulness-based meditation. Session duration, length and trainer contact same for control group; sessions based on brain injury and lifestyle psychoeducation.	No significant differences between groups on the Hotel Task for number of tasks attempted. Significant main effect – number of rule violations in the tower test; maintained at follow-up for GMT group. No significant main effects for the questionnaire data.	**DEX:** 0.81, **Hotel Task:** -0.63, **ToL:** 0.12, **CFQ:** 0.89	Average, 13 points
Novakovic-Agopian et al. (2011)	Pseudorandom crossover design	**Goals-edu group:** n = 8, mean age = 49 years, Female = 3, mean time post injury = 3.9 years. Type of injury: TBI = 5, stroke or cerebral haemorrhage = 2, leukoencephalopathy = 1. **Edu-goals group:** n = 8, mean age = 51.6 years, female = 6, mean time post-injury = 2.9 years. Type of injury: TBI = 6, stroke or cerebral haemorrhage = 1, brain tumour = 1.	Executive functions measures = Stroop, D-KEFs design and verbal fluency, trails. Functional assessments = the modified errands task.	Goal training – 10 X 120-minute group based sessions, 3 X 60-minute individual training sessions and 20 hours home practice over 5 weeks. Focussed on mindfulness-based attention regulation training and goal management strategies.	Baseline – 5 weeks: goals first group showed improvement on attention and executive function measures compared to control group. Goal group had significantly lower number of failures on the Multiple Errands Task. Week 5-10: Control group significantly improved after goals intervention in the attention and executive function domain. Goals group maintained their gains.	**Stroop:** 0.93, **Trail making:** 1.52, **Verbal fluency:** 1.23	Average, 12 points

Description of Participants

Nine hundred and seventy-seven participants were recruited to the studies; with 942 recruited to the RCT studies and 35 to the non-RCT studies. Not all studies described participants type of injury; however, of those that did 116 had a TBI, 163 a stroke/CVA, two were anoxic, 34 a tumour, three an infection and four were categorised as other. One paper categorised participants with regards to severity, which showed 49 had a mild brain injury, 19 moderate and 30 severe. There were instances in which papers documented how participants sustained their injury with 78 being road traffic accident related, 33 falls, 12 assaults, seven sporting injuries and 16 categorised as other. Mean age of all participants was 45.64 years; with the mean age for the RCT papers being 41.59 years and non-RCT papers 49.69 years. Despite not all papers documenting participants gender, of those that did, 708 participants from the RCT studies were Male (66.5%) and 357 were Female (33.5%). Of the non-RCT studies, 21 were Male (70%) and 9 were Female (30%).

Methodological Quality and Risk of Bias

Papers were divided into RCT and non-RCT for evaluation of risk of bias. The area in which the RCT's performed most poorly was appropriateness of screening, as this tended to not be explicitly reported (Couillet et al, 2010; Miotto et al, 2009; Park & Lee, 2018; Van de Ven, 2017). Other areas that scored lower for the RCT's and non-RCT's were allocation concealment, blinding of participants and study investigators, blinding of outcome measures and fidelity of treatment groups. This was due to the papers not reporting this information; thus, could not be scored.

Thirteen RCT papers contained either a manual or protocol for the intervention which was followed by trained or experienced facilitators (Akerlund et al, 2013; Gracey et al, 2016; Rath et al, 2003; Cantor et al, 2014; Spikman et al, 2010; Tornas et al, 2016; Twamley et al, 2014; Vas et al, 2011; Bertens et al, 2015; Elbogen et al, 2018; Tiersky et al, 2005; Salazar et al, 2000; Bertens et al, 2015). Four of these papers also included

videotaping and supervision to ensure fidelity (Twamley et al, 2014; Cantor et al, 2014; Rath et al, 2003; Elbogen et al, 2018). Both non-RCT papers contained a manual or protocol (Levine et al, 2011; Novakovic-Agopian et al, 2011), with Novakovic-Agopian et al (2011) also using supervision to maintain fidelity. The rigour of reporting participant screening, including inclusion and exclusion varied across the studies. Papers scoring highest in this domain reported a rigorous inclusion and exclusion criteria, along with a clear outline of numbers of participants included in the study. This was achieved by nine RCT papers overall. The remaining papers either adequately covered (8) or poorly covered (9) this in their reporting of their study.

All but two RCT papers (Levine et al, 2000; Yoo et al, 2015) and all the non-RCT papers used appropriate and valid measures for their intervention. Levine et al (2000) and Yoo et al (2015) scored adequately in this area due to using outcome measures and tasks that were not robustly described.

Results of Studies

Effect Sizes

Papers were analysed initially in relation to the type of intervention in conjunction with impairment, everyday life and subjective focussed outcomes; along with comparing these in relation to RCT and non-RCT studies. A random effects model was used within the analysis due to the differences seen in the analysed studies.

Impairment Focussed Outcomes

Twenty-two papers were included in the analysis investigating impairment focussed outcomes and intervention type; with a total of 977 participants included in the studies. The analysis produced a significant effect size of $g = 0.26$ (CI $= 0.14 - 0.40$) p $< .0001$. The sample was 0% heterogenous, which suggests there is no difference between the papers. The funnel plot is somewhat symmetrical (appendix 8), which suggests there is little or no

publication bias. Intervention types, both compensatory internal strategies and impairment focussed strategies, were analysed separately which showed small significant effect sizes for both types of interventions: compensatory internal strategies yielded an effect size of g = 0.26 (CI = 0.11 – 0.40) p = 0.0007 and impairment focussed strategies produced an effect size of g = 0.29 (CI = 0.05 – 0.54) p = 0.02.

Twenty papers were included in the RCT impairment focussed analysis, with a total of 942 participants, which yielded a combined effect size of g = 0.25 (CI = 0.13 – 0.38) p < 0.001. This suggests a small, significant effect size. The sample was 0% heterogenous, which suggests that there is no difference between the studies in the analysis. The funnel plot is quite symmetrical, which suggests little publication bias (appendix 5). The same analysis investigating impairment focussed outcomes was run for the two non-RCT papers, with a total of 35 participants, which produced a non-significant medium to large effect size of g = 0.6 (CI = -0.42 – 1.63) p = 0.25. The papers showed heterogeneity of 53.72%, suggesting that the papers are quite different; however, as noted only two papers were included in this analysis.

Everyday Life Outcomes

Nine papers were included in the analysis investigating everyday life focussed outcomes and intervention type; with total of 462 participants included in the studies. The analysis produced a significant small effect size of g = 0.22 (CI = 0.03 – 0.42) p = 0.02. The sample was 6.04% heterogenous, which suggests there is very little difference between the papers. The funnel plot appears to be near symmetrical (appendix 9), which suggests there is little publication bias. Intervention types were separated and showed that both the compensatory internal strategies (g = 0.18 (CI = -0.04 – 0.39) p = 0.1) and impairment focussed strategies produced non-significant effect sizes (g = 0.47 (CI = -0.04 – 0.98) p = 0.07); small and medium effect sizes respectively. It must be noted that the impairment

focussed strategies analysis reached near significance; however, only two papers were in this category.

Eight RCT papers were analysed to look at outcomes from everyday life measures, for example the hotel task and multiple errands task. A total of 427 participants were included in the analysed studies. The combined effect size for these studies was $g = 0.26$ (CI = 0.07 − 0.45) p = 0.01; suggesting a small significant effect size. The sample was 0.07% heterogenous which suggests that studies analysed are homogenous. The funnel plot (appendix 6) appears near symmetrical suggesting no or limited publication bias. A non-RCT analysis was not conducted as all studies containing everyday life outcomes were RCT's.

Subjective Focussed Outcomes

Seven papers were included in the analysis investigating subjective focussed outcomes and intervention type; with total of 284 participants included in the studies. The analysis produced a significant combined effect size of $g = 0.29$ (CI = 0.06 − 0.52) p = 0.01. The sample was homogenous. The funnel plot appears to be asymmetrical (appendix 10), which suggests there is publication bias. Intervention types were analysed separately and showed compensatory internal strategies yielded a small significant effect size, $g = 0.28$ (CI = 0.04 − 0.53) p = 0.02; whereas the impairment focussed strategies produced a small non-significant effect size, $g = 0.37$ (CI = -0.26 − 1.0) p = 0.25.

Six RCT papers were analysed to investigate subjective outcomes, with 284 participants being included in the analysis. The combined effect size for these studies was $g = 0.26$ (CI = 0.03 − 0.5) p = 0.03, which suggests a small significant effect size. The sample was 0% heterogenous which suggests there is no difference between the studies in the analysis. The funnel plot is asymmetrical (appendix 7), which suggests there may be publication bias. As all papers were RCT studies, a separate analysis was not conducted not investigate RCT versus non-RCT.
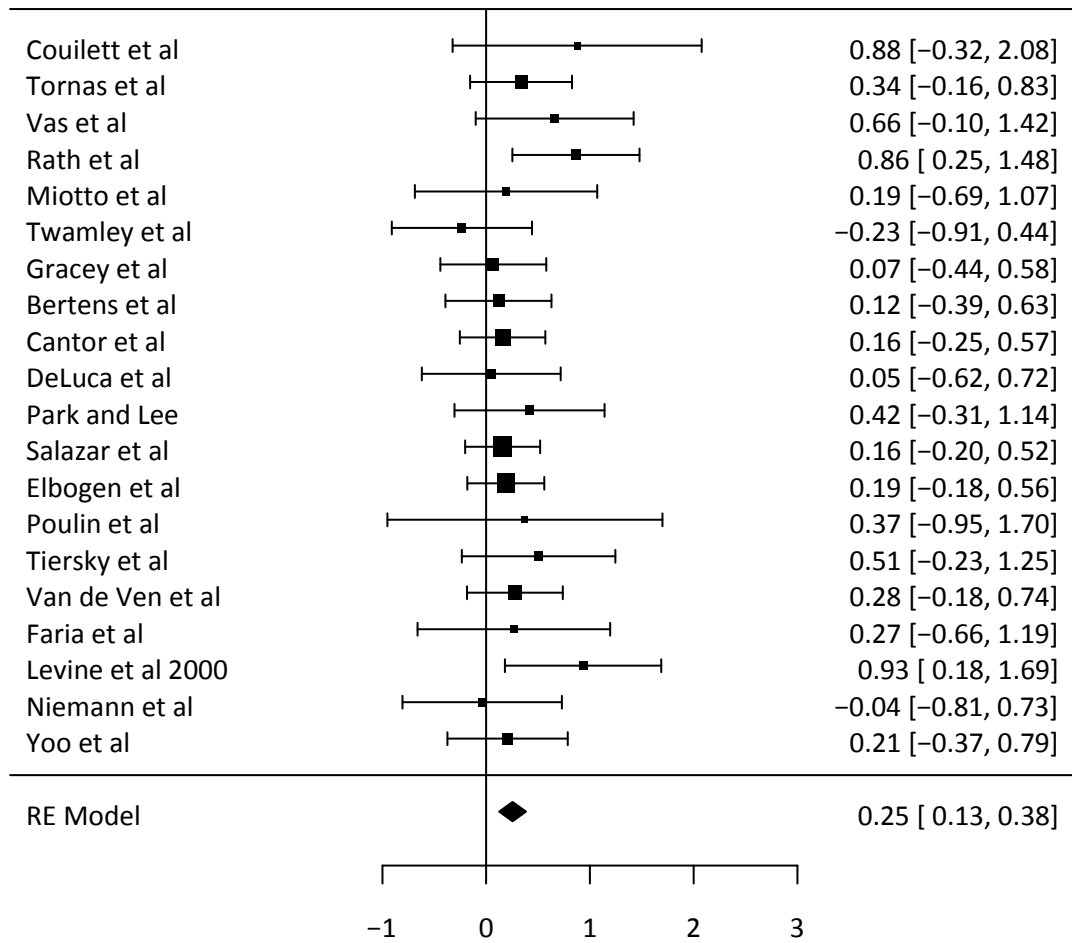
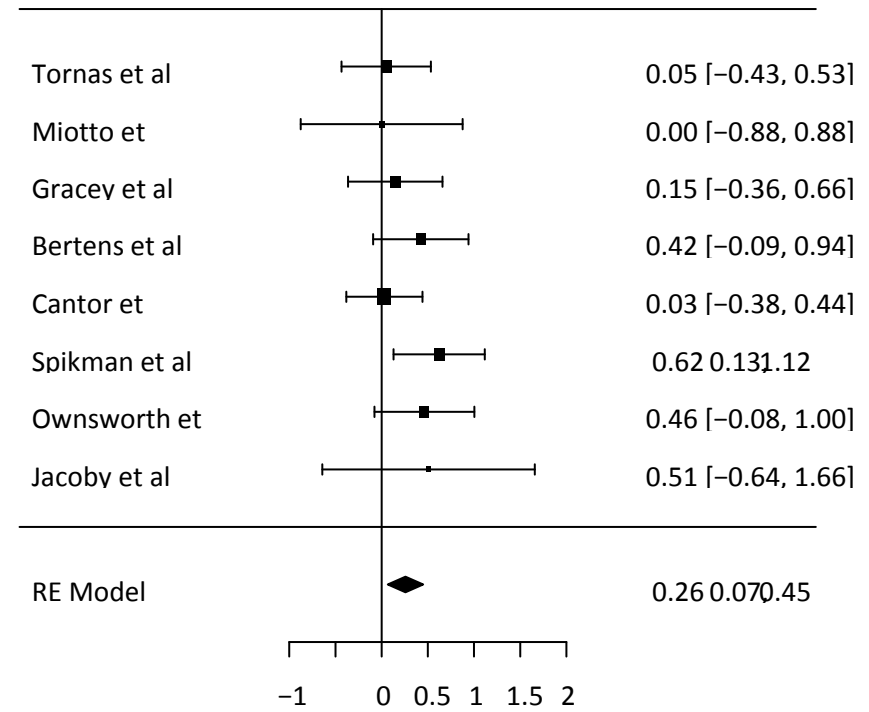*Figure 1:* Forest plot detailing RCT impairment outcomes

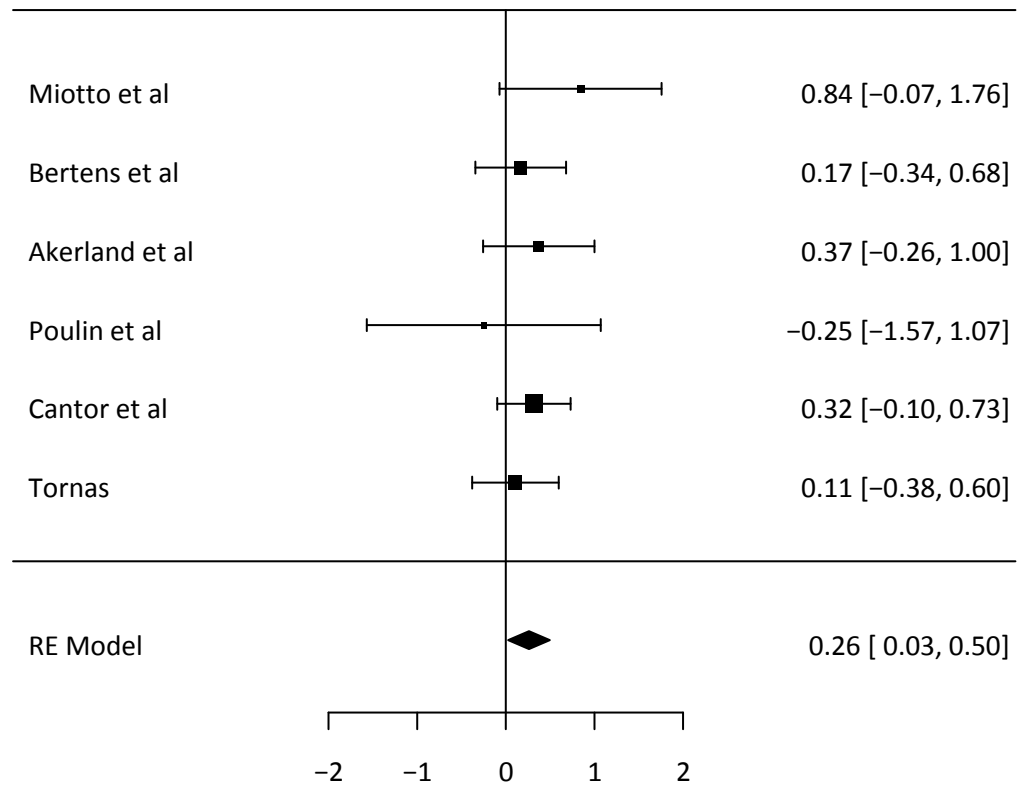
Figure 2: Forest plot detailing RCT everyday life outcomes
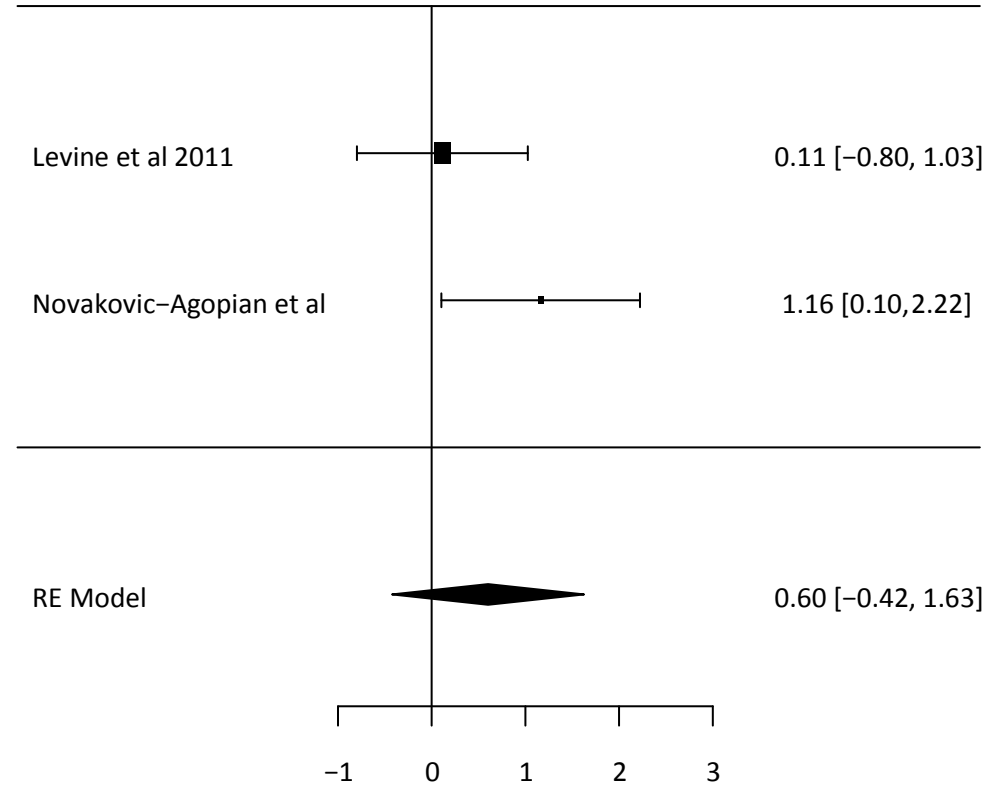
Figure 3: Forest plot detailing RCT subjective outcomes

Figure 4: Forest plot detailing non-RCT impairment data

<u>Discussion</u>

Findings overall showed small, significant effect sizes for several analyses when investigating effectiveness of cognitive rehabilitation for executive functioning difficulties after ABI. Analysis compared impairment, everyday life and subjective focussed outcomes, within RCT and non-RCT studies. The non-RCT analysis produced a small, non-significant result; however, only two papers were included. This suggests that there are small significant effects on outcomes across most domains, which is comparable to results of previous meta-analyses (Stamenova & Levine, 2018; Rohling et al 2009). The small effect sizes found by the current review may be due to the heterogenous nature of ABI literature and the range of interventions included. As stated above, previous reviews tended to focus on one etiology or intervention. Thus, reducing the heterogeneity.

Despite small effect sizes suggesting that there is minimal difference between the two groups (McLeod, 2019), within brain injury literature, this may represent a relatively big change when taking into account the heterogenous and complex nature of the brain injury population and cognitive rehabilitation. Glass, McGaw and Smith (1981, cited in Coe, 2002) suggests that despite a small effect being observed, this may produce a "significant improvement" in the area being investigated. Despite this, what also needs to be noted is that within each study, it is challenging to know whether the 'change' being seen between the two groups is clinically significant as well as statistically significant, and whether this is meaningful change for the individuals.

With regards to type of cognitive rehabilitation interventions used in the included papers, from a meta-analysis perspective, it is challenging to discuss this with confidence. The reviewed studies used a variety of interventions, from GMT programmes to computer-based programmes; consequently, differing approaches would have been taken. Interventions were categorised into compensatory internal strategies (GMT, strategy interventions and problem-solving interventions) and impairment focussed strategies

(attention training and computer training) to account for the main focus of intervention delivery. In terms of compensatory internal strategy interventions, small significant effect sizes were found for impairment and subjective outcomes; however, not everyday life outcomes. For impairment focussed strategy interventions, a small significant effect size was found for the impairment outcomes. It must be noted that the analysis of everyday life outcomes neared significance and despite the subjective outcomes analysis being non-significant, only two papers were included in the analysis.

Categorising outcome measures is challenging, as there are different ways to assess outcomes which may have had an impact on results. An example being that some impairment focussed assessments may be highly correlated to everyday life, or have high ecological validity; thus, could be included in either the impairment or everyday life groups. Chaytor and Schmitter-Edgecombe (2008) discuss the challenge of ensuring that the assessments have a clear link to everyday life situations, and the importance of assessments having a relevance to each individuals life. Furthermore, they highlight that participants may respond differently within a testing environment compared to their everyday life; using strategies when being tested but finding this more challenging day-to-day. This may be an interesting area to research further, with more emphasis being on meaningful, everyday life change for individuals rather than change on specific outcome measures.

The methodology of the included papers differ with regards to risk of bias; ranging from moderately poor to exceptionally good. The areas in which the papers either scored well or poorly tended to be similar. This supports previous literature and proposed guidelines that suggest research methodology in this area is not as robust as it can be, or produces mixed findings; consequently, it is then difficult to make firm conclusions from the results (Rohling et al, 2009; Cicerone et al, 2005; INCOG, 2014).

The papers contained in the review covered several recommendations proposed by the INCOG guidelines. The papers including GMT, problem-solving and strategy training have focussed on everyday life aspects of executive functioning (Ownsworth et al, 2017; Elbogen et al, 2018; Faria et al, 2016; Poulin et al, 2017). Vas et al (2011) used a specific memory and reasoning program and the GMT intervention conducted by Bertens et al (2015) used an errorless learning GMT approach to limit the amount of errors made by participants. Furthermore, most of the studies used group based interventions; thus, all recommendations provided by INCOG guidelines have been covered. In relation to the INCOG attention guidelines, three recommendations have been covered by the reviewed papers: using strategies that relate to participants everyday life (Twamley et al, 2014; Vas et al, 2011), using dual task interventions (Couillet et al, 2010; Park & Lee, 2018) and using computer-based interventions that related to everyday life (Faria et al, 2016; Jacoby et al, 2013). Alerting is used by Tornas et al (2016) and Gracey et al (2016); however, their findings support the INCOG guidelines that more evidence is required.

The current review found several small significant effect sizes, which includes differentiating between types of interventions. These results do support previous reviews conducted by Rohling et al (2009) and Stamenova and Levine (2018), and whilst this is promising, discussion as to why only small effect sizes were found is pertinent. As previously noted, damage to the brain after an insult can be diffuse whether that be due to a TBI or stroke (Stuss, 2011; Nys et al, 2007). Thus, despite study investigators endeavouring to match participants accordingly, there may be natural differences due to the nature of brain injury that cannot be accounted for. Furthermore, outcomes may be hindered more generally due to social and psychological factors not considered within interventions. For example, whether the participant has support outside of the intervention environment from carers or has other mental health complexities such as depression that may make motivation challenging.

The notion of selection and recruitment bias has been discussed in the literature, which may have an overall impact on results being expressed by authors and generalisability. Luoto, Tenovuo, Kataia, Brander, Ohman and Iverson (2013) highlight that studies tend to have extensive exclusion criteria to ensure minimal confounding variables are contained within each study. These criteria can include substance abuse, historical psychiatric health and employment status. In relation to recruitment bias, McCullagh and Feinstein (2002) found that the severity of an individual's injury had an impact on retention to studies. The authors propose that those with more severe injuries tended to have more health professionals involved in their care compared to more mild injuries, and are more likely to stay engaged in research studies. Therefore, there could be an argument to suggest that more participants with severe injuries are seen within the literature.

With regards to retention of participants to studies, as alluded to above, it can be challenging to keep participants involved in research. Corrigan, Harrison-Felix, Bogner, Dijkers, Terrill and Whiteneck (2003) investigated attrition within longitudinal TBI literature, with their results suggesting that approximately 42% of participants were lost to follow-up after 1 year. This number rose to between 44.9% and 48.6% after 2 years; suggesting that the biggest loss to follow-up happens within the first follow-up year. When reporting variables that appeared to significantly predict retainment or drop out of the study, the authors indicate factors such as race, education, premorbid substance use and intoxication at injury to be important.

Overall, the compensatory internal strategies appeared the most effective type of intervention with small significant effect sizes being seen in the majority of analyses, which supports previous findings (Krasny-Pacini et al, 2014; Stamenova & Levine, 2018). However, it must be noted that there were more studies using GMT as an intervention, which has an effect on the weighting when conducting a meta-analysis. The impairment focussed interventions produced a small significant effect size for outcome measures that

were based on impairment, for example neuropsychological assessments. This may be due to the types of training targeting one area, for example attention, rather than incorporating a range of strategies that can be applied to everyday life.

One of the main limitations of the current study is the included studies were not rated by a second reviewer with regards to risk of bias. Related to this, the primary investigator did not contact the primary authors of studies to gather more information before conducting the quality rating process. This might have impacted on how the primary investigator rated the specific papers overall; thus, scores may have improved with additional information.

Grey literature was not systematically searched for within the study; however, reference sections of the included papers were reviewed to ensure they did not contain additional papers not found in the initial database searches. This would suggest a degree of publication bias. It must be noted that seven papers were highlighted within the selection process that the primary investigator thought pertinent to review to determine whether they were appropriate to include within the meta-analysis. However, it was not possible to obtain these papers to review despite requesting these from authors.

Considering the findings of the current review, and in conjunction with recommendations posed by INCOG, there continues to be a debate with respects to cognitive rehabilitation and its effectiveness on executive functioning after ABI. It would be useful for future research to compare different types of ABI and the outcomes seen after cognitive rehabilitation. Despite there being participants with a range of different aetiologies of ABI included in this review, there was not enough scope to cover this question. Furthermore, it may be beneficial to gain more understanding of individuals subjective outcomes, as this was not systematically reported by studies reviewed.

It would also be interesting to understand in more detail the common elements across different interventions and whether specific components of interventions show changes in specific areas of functioning. This could be investigated with regards to the role of

moderators such as duration of treatment, addition of reminders, group vs individual interventions. Examination of this may be beneficial to add to the literature on components of cognitive rehabilitation.

In conclusion, the small significant effect sizes produced in the review suggest that cognitive rehabilitation does have a small effect on executive dysfunction after brain injury. However, as suggested by Rohling et al (2009), confident conclusions are "limited". The challenges with heterogeneity and differing sample sizes within the literature reviewed may have impacted on the overall result. Furthermore, issues with methodology, both within the current review and papers included in the review, may have also had an impact on the outcome. To add to the growing field of literature in this area, future research may want to focus on the differing components of cognitive rehabilitation, specifically for executive dysfunction, and how to improve methodological robustness of studies.

Disclosure of Interest

There are no reports of conflict of interest by the primary author; however, one of the included papers is work completed by Dr Fergus Gracey (second author).

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Chapter 5: Extended Analysis

Below is an extended narrative analysis conducted on the papers reviewed in the meta-analysis. This provides more context to the data that can be found in table 2 presented in chapter 4.

Description of studies

Design

Many of the papers analysed (24/26) were of RCT design, with the remaining two papers being either a multiple baseline or a pseudorandomised crossover design. The following studies used a RCT design and will be discussed in relation to the trial arms. Akerlund et al. (2013) used a treatment and control arm that was well matched for age and time post injury. The control condition was treatment as usual, with participants being offered the intervention after follow-up. Bertens et al. (2015) participants were relatively well matched, but the intervention group were slightly older by three years. The control group completed a conventional GMT programme, compared to the errorless learning GMT being offered to the intervention group. In Cantor et al's (2014) study, their intervention group was slightly older and injury more recent when compared to the wait-list control group. Couillet et al. (2010) used a cognitive training programme for both groups; however, the control condition did not contain aspects of divided attention. Groups were matched well for age; however, the control group were only six months post-injury compared to over 16 months for the intervention group. This may have had an impact on their results due to the different trajectory of the participants recovery journey.

Gracey et al. (2016) used well matched groups, but the control group were longer post-injury. The control condition comprised of 1:1 psychoeducation of brain injury sessions with equivalent face to face time. Miotto et al. (2009) does not distinguish between the intervention and control groups; thus, it is difficult to ascertain whether these groups were

well matched. The control condition contained two arms; an information and education arm and treatment as usual. Rath et al. (2003) does not report data specifically in relation to the two groups. The authors describe their control condition to be a conventional treatment consisting of cognitive remediation training groups. In Spikman et al's (2010) study their control group's post-injury mean was smaller than the intervention group; 64.1 months compared to 105.4 months respectively. This was also seen in Tornas et al's (2016) paper with the control group being 81.46 months post injury compared to 106.94 months. Again, this may have impacted on outcomes due to a range of issues; including recovery trajectory and whether other rehabilitation has taken place. The studies used different control conditions; computerised cognitive training programme (Spikman et al, 2010) and brain health workshop (Tornas et al, 2016).

Van de Ven et al (2017) and Vas et al (2011) all had relatively well matched intervention and control groups. Control conditions in the papers were brain health workshop (Vas et al, 2011) and mock training or wait-list (Van de Ven et al, 2017). Twamley et al's (2014) participants were relatively well matched with regards to age; however, the control group had a slightly longer time post-injury (3.6 years compared to 5.1 years). Salazar et al (2000) had well matched groups for age and time post injury; however, 14 more participants were recruited to the experimental condition. It must be noted that participants were recruited over a period of five years. Control condition for this study was TBI education and counselling. All participants in Twamley et al (2014) and Salazar et al (2000) were Veterans; therefore, it may be difficult to generalise to the general population.

Faria et al (2016) reports age and time post injury as medians, which were relatively well matched; however, means and standard deviations were not reported so the range across participants cannot be detailed. The control condition was generic cognitive training. Tiersky et al (2005) used a treatment and control arm that were well matched for age;

however, time post injury was not detailed and specific injury details were not separated into condition. The control condition was meeting with the principal investigator on two or three occasions, and then being offered the intervention once the experimental period had been completed.

Deluca et al (2018) used well matched groups for age and time post injury; however, the participants were 3 and 4 months post injury which suggests they were very early in their recovery journey. The control condition was generic cognitive rehabilitation compared to cognitive rehabilitation plus computer based training focussing on executive functioning processes. The control condition in Ownsworth et al's (2017) paper was errorless learning and the participants were well matched for age. There was a slight difference between the experimental and control groups for time post injury; 36.44 months and 40.81 months respectively.

Elbogon et al (2018) reported data that suggests the groups were well matched for age and gender; however, time post injury was not discussed and the authors included individuals with a range of injuries. The inclusion criteria specified that participants must have 1 or more symptoms from a varied list; for example, observed or self-reported confusion, impaired consciousness and dysfunction of memory after injury. This makes it challenging to decipher the extent to which participants may vary with regards to injury, and the impact this may have on results. The participants are also from a veteran only sample, so results may not be easily generalisable to non-veteran populations.

The remaining RCT papers were well matched for age and time post injury across the intervention and control groups (Levine et al, 2000; Niemann et al, 1990; Jacoby et al, 2013; Park & Lee, 2018; Yoo et al, 2015). It must be noted, however, that participants recruited in Jacoby et al (2013) are very early on in their recovery journey (< 6 months) which may have an impact on the results obtained and how they compare to other studies in the review. The mean age of the control group in Poulin et al (2017) was nine years greater

than the experimental group. The participants in the intervention and control groups described in two non-RCT papers (Levine et al, 2011; Novakovic-Agopian et al, 2011) were well matched for age and time post injury. Both used brain health education as their control condition.

Intervention

Types of intervention used within the studies varied and tended to fall within two categories of: compensatory internal strategies (Rath et al, 2003; Cantor et al, 2014; Miotto et al, 2009; Twamley et al, 2014; Vas et al, 2011; Tiersky et al, 2005; Salazar et al, 2000; Ownsworth et al, 2017; Spikman et al, 2010; Tornas et al, 2016; Gracey et al, 2016; Bertens et al, 2015; Levine et al, 2000; Levine et al, 2011; Elbogen et al, 2018; Poulin et al, 2017) and impairment focussed interventions (Van de Ven et al, 2017; Akerlund et al, 2013; DeLuca et al, 2018; Yoo et al, 2015; Faria et al, 2016; Couillet et al, 2010; Novakovic-Agopian et al, 2011; Niemann et al, 1990; Park & Lee, 2018). The compensatory internal strategies encompass interventions such as GMT, problem solving and strategy training; whereas, the impairment focussed interventions encompasses attention training and computer-based interventions.

Jacoby et al (2013) used a virtual reality concept, aiming to increase executive functioning via strategies such as planning, time management and metacognition. The intervention consisted of ten 45-minute sessions, three to four times per week; however, the authors do not explicitly state for how long, so depending on how many are completed per week depends on whether it would be over a three or four-week period. A virtual reality concept was also adopted by Faria et al (2016) who used a programme called Reh@City that aims to train cognition, as well as activities of daily living. Participants are given an everyday life related goal to complete within a virtual reality city. Twelve 20-minute sessions are administered over a four to six week period.

Compensatory Internal Strategies Interventions

Rath et al (2003) delivered 24 weekly 120-minute sessions focusing on emotional self-regulation and clear thinking; thus, 12 of each. Miotto et al (2009) required participants to complete ten weekly sessions of an Attention and Problem-Solving rehabilitation group lasting 90 minutes. This intervention consists of educating participants on attention and problem solving, along with strategies on how to manage difficulties in these areas. Cantor et al's (2014) intervention is similar to Rath et al (2003) in that it focusses on emotional regulation and problem solving, as well as attention training. Participants completed two 45-minute emotion sessions and one 60-minute attention session, three times a week for 12 weeks.

Twamley et al (2014), Vas et al (2011), Tiersky et al (2005), Salazar et al (2000) and Ownsworth et al (2017) completed interventions focused on strategy training, in which all used training protocols to target areas that may be impaired; however, studies tended to vary on amount of information described. Twamley et al (2014) combined a conventional supported employment programme with Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) which describes strategies to target deficits in a range of areas including executive functioning. The intervention consisted of one, 60-minute session per week along with two standard employment sessions with an employment specialist. Vas et al (2011) delivered a Strategic Memory and Reasoning Training program (SMART) over an eight-week period, comprising of 18 hours training in 12 group sessions. The first ten hours of training were completed over five weeks and the remaining three hours over a three-week period; however, the authors do not state a rationale for this apart from describing them as 'booster sessions'.

Tiersky et al (2000) combined attention process training (APT) with cognitive behavioural therapy (CBT), which focussed on attention and information processing and encompassed retraining and compensatory exercises. The intervention was delivered over an 11 week period, with a total of three sessions being completed per week. A session

comprised of two daily individual 50 minute sessions. The intervention described by Salazar and colleagues (2000) was rehabilitation based on the milieu approach described by Prigatano. Participants were also encouraged to continue with their military duties, as the programme also encompassed a vocational aspect. Ownsworth et al (2017) delivered an error-based learning intervention that consisted of participants being allowed to make errors whilst completing tasks; preparing a hot meal (four sessions) and an individualised goal (four sessions). The intervention consisted of eight, 90-minute sessions that were delivered at home.

Goal Management Training was used by Spikman et al (2010), Tornas et al (2016), Gracey et al (2016), Bertens et al (2015), Levine et al (2000), Levine et al (2011), Elbogen et al (2018) and Poulin et al (2017). Bertens et al (2015) compared an errorless learning GMT with conventional GMT that delivered their intervention over a four-week period, comprising of eight, 60-minute individual sessions; with sessions one to four being at a rehabilitation centre and the remaining four at the participants home or place of work. Levine et al (2000) delivered one, 60-minute session that covered the five stages of GMT. It is unclear whether the participants had undertaken previous training on goal management as the authors state that the study was part of a wider investigation. It could be argued that if it was only one, 60-minute session, perhaps participants may not have consolidated the information sufficiently to impact on the study outcome. Levine et al (2011) delivered seven, 120-minute sessions that covered GMT principles, including a mindfulness-based meditation aiming to increase awareness of present behaviour.

Spikman et al (2010) delivered an intervention that combined aspects of GMT and problem-solving training. It taught participants specific cognitive strategies that were divided into three stages: information and awareness, goal setting and planning, and initiation execution and regulation. There were no specific number of sessions reported, but a maximum of 24 was suggested. Gracey et al (2016) conducted a brief GMT programme

with participants in their home or in the community. The intervention comprised of two, 90-minute individual sessions that were no more than five days apart in their delivery. The sessions covered topics such as setting goals and checking intentions. Participants received eight text messages per day, encouraging them to review current intentions and whether they are on track with these. Tornas et al (2016) report an adaptation of Levine et al's (2011) protocol, including SMS alerts, in which the intervention group met for eight, 120-minute sessions over a four-day period.

Elbogen et al (2018) describe an intervention, Cognitive Applications for Life Management (CALM) that has several components including GMT, psychoeducation and exercises. Participants designed their own checklists, with support, working towards a GMT goal which is broken into steps. In addition, participants used an app that promotes 'executive review' to review whether they are on track with the goal. The intervention was conducted over a six month period, with home visits occurring every two months. An intervention to aid participants to create and meet goals was described by Poulin et al (2016); two 60-minute sessions were completed per week, for a total of eight weeks.

Impairment Focussed Interventions

Attention training programmes were used by Couillet et al (2010), Novakovic-Agopian et al (2011), Niemann et al (1990) and Park and Lee (2018). Couillet et al (2010) used a crossover design for a period of six weeks per condition. The intervention consisted of four 60-minute sessions per week, for 24 sessions. Participants were trained in two everyday life tasks individually that increased in difficulty when the participant's performance increased. Novakovic-Agopian et al (2011) used a crossover design in which participants took part in goal training, focusing on mindfulness-based attention regulation and goal management strategies. The intervention consisted of ten, 120-minute group sessions, followed by three, 60-minute individual training sessions and 20 hours of home practice over a five-week period. Niemann et al's (1990) intervention focussed on divided attention using both visual

and auditory tasks, in which participants underwent six, 120-minute sessions; thus, 30-40 minutes training per domain. Park and Lee's (2018) intervention consisted of Cognitive-Motor Dual-Tasking (CMDT) + Auditory-Motor Synchronisation Training (AMST), which required participants to push a button when they heard a specific sound. The intervention, and control condition, was conducted over a six-week period; three 30 minute sessions per week.

Computer training interventions were delivered by Van de Ven et al (2017), Akerlund et al (2013), DeLuca et al (2018), Yoo et al (2015) and Faria et al (2016). Van de Ven et al (2017) used a cognitive-based programme delivered via a website in which participants were required to access independently. Training sessions were 30-minutes in length and participants completed five per week, for a total of 58 sessions. Akerlund et al (2013) used the working memory program CogMed, which required participants to complete 30-40 minutes of training, five times per week for five weeks. Both groups in DeLuca et al (2018) completed conventional cognitive rehabilitation consisting of six, 45 minute sessions over an eight week period. In addition, the experimental group completed three 45-minute computer-based training focussing on executive functioning per week for eight weeks. Yoo et al (2015) used rehabilitation plus a cognitive computer programme, RehaCom, for the experimental condition. This consisted of 30-minute sessions completed five times per week for five weeks.

Outcome Measures

The main measures used by the studies appeared to be separated into impairment focussed and ecologically valid tasks. The impairment focussed measures included digit span (Akerlund et al, 2013; Couillet et al, 2010; Twamley et al, 2014; Levine et al, 2000; DeLuca et al, 2018; Park & Lee, 2018; Yoo et al, 2015; Poulin et al, 2017), verbal fluency (Bertens et al, 2015; Gracey et al, 2016; Miotto et al, 2009; Rath et al, 2003; Twamley et al, 2014; Vas et al, 2011; Novakovic-Agopian et al, 2011; DeLuca et al, 2018; Van de Ven et

al, 2017), Stroop (Cantor et al, 2014; Couillet et al, 2010; Rath et al, 2003; Spikman et al, 2010; Vas et al, 2011; Levine et al, 2000; Novakovic-Agopian et al, 2011; Elbogen et al, 2018; Park & Lee, 2018; Poulin et al, 2017), trail making (Cantor et al, 2014; Couillet et al, 2010; Spikman et al, 2010; Vas et al, 2011; Levine et al, 2000; Niemann et al, 1990; Novakovic-Agopian et al, 2011; Van de ven et al, 2017; Park & Lee, 2018; Yoo et al, 2018; Poulin et al, 2017; Faria et al, 2016), Wisconsin Card Sorting Task (Miotto et al, 2009; Rath et al, 2003; Twamley et al, 2014; Salazar et al, 2000), tower test (Spikman et al, 2010; Levine et al, 2011; Van de Ven et al, 2017). The PASAT (Salazar et al, 2000; Tiersky et al, 2005), RAVENS (DeLuca et al, 2018) and picture arrangement (Faria et al, 2016) were also used.

Ecologically valid tasks tend to relate to a person's performance in specific areas of everyday life situations. For example, managing their time to complete a range of tasks. The tasks used in the papers were the modified six elements from the BADS (Bertens et al, 2015), The Hotel Task (Gracey et al, 2016; Tornas et al, 2016; Levine et al, 2011), multiple errands task (Miotto et al, 2009; Jacoby et al, 2013; Novakovic-Agopian et al, 2011) and Spikman et al (2010) used an Executive Secretarial Task. Additional assessments that related to everyday life included: zoo map (Ownsworth et al, 2017) and independent cooking task (Ownsworth et al, 2017). Gracey et al (2016), Bertens et al (2015) and Spikman et al (2010) also reported attainment of intentions related to specific goals created during the intervention or rehabilitation. Subjective outcomes were rated using specific questionnaires, namely the Dysexecutive Syndrome questionnaire (DEX; Akerlund et al, 2013; Bertens et al, 2015; Miotto et al, 2009; Spikman et al, 2010; Tornas et al, 2016; Levine et al, 2011; Poulin et al, 2017) and the Cognitive Failures Questionnaire (Bertens et al, 2015; Tornas et al, 2016; Levine et al, 2011).

Overall it is a mixed picture with regards to findings within the reviewed papers; with some papers reporting positive outcomes and significant differences between groups, with others not showing such a notable difference. In relation to subjective focussed measures, Akerlund et al (2013) did not find any differences between the intervention and control group on the DEX questionnaire; which was supported by Bertens et al (2015), Miotto et al (2009), Poulin et al (2017) for self-reported outcome, and Levine et al (2011). However, Miotto et al (2009) do show a significant reduction in executive dysfunction reporting by carers after intervention and maintained at follow-up. Moreover, Tornas et al (2016) report that the intervention group showed a significant reduction in self-reported dysexecutive symptoms from baseline to follow-up. Spikman et al (2010) also report reductions in DEX scores for self and therapist after intervention.

When looking at assessments that focus on impairment focussed outcomes, for example Stroop, verbal fluency, tower test and WCST, there are also conflicting outcomes. Cantor et al (2014) devised a composite executive measure that incorporates subscales of standardised assessments as they suggest that these assessments just focus on specific domains of executive functioning. Their results suggest a significant treatment effect for this measure, with the intervention group performing better. However, this cannot be generalised to other study outcomes, due to the measure being a novel instrument. Tiersky et al (2005) found significant differences on the PASAT between the experimental and control group; detailing an improvement of cognitive functioning and a reduction of emotional difficulties. Faira et al (2016) reported significant differences, in favour of the experimental group, on the picture arrangement task but not the trails task. Significant differences on cognitive outcomes were also described by Park and Lee (2018). Van de Ven et al (2016) reported that all participants performance improved; however, changes did not

reach statistical significance. Poulin et al (2017) found significant differences for trails-B only and Yoo et al (2015) found significant differences for digit span only.

Other significant outcomes include Rath et al (2003) finding a significant improvement on the WCST for the intervention group that was maintained at 6-month follow-up and Novakovic-Agopian et al (2011) report that the intervention group performed significantly better than controls on executive function assessments during their intervention phase. When the participants crossed over, the control group significantly improved their scores and the intervention group maintained their gains. Levine et al (2011) found that the intervention group made fewer rule violations on the tower assessment and Levine et al (2000) hypothesise that, despite not showing significant findings, the intervention group were attending more after their intervention due to reduced completion times. Niemann et al (1990) describe the intervention group as performing better on measures of attention after intervention and report significant group differences on the trail making test. Despite these encouraging results, they are not supported by Couillet et al (2010), Gracey et al (2016), Miotto et al (2009), Spikman et al (2010), Twamley et al (2014), Salazar et al (2000), DeLuca et al (2018) and Elbogen et al (2018) who did not find significant results in relation to executive function assessments.

When looking at everyday life outcomes there is again conflicting results. Bertens et al (2015) report improved performance on everyday life tasks that require executive functions and Gracey et al (2016) found better attainment of daily intentions after the intervention phase. Ownsworth et al (2017) found significant differences on their cooking tasks, in which the experimental group made fewer errors; however, this difference was not seen on the zoo task. When exploring the everyday life outcome assessments, for example The Hotel Task, the Multiple Errands Task, there appeared to be a consensus with results suggesting that there were no significant differences found between groups after intervention (Gracey et al, 2016; Jacoby et al, 2013; Levine et al, 2011).

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Chapter 6: Overall Discussion and Critical Appraisal

This chapter will offer an overall discussion aiming to summarise key findings from the systematic review in chapter 2 and the meta-analysis in chapter 4; along with a critical appraisal. Aims for future research and final conclusions will be discussed.

Key Findings for Clinical Practice

The thesis portfolio set out to gain further knowledge of the effectiveness of different types of interventions after brain injury that can remediate difficulties with emotions and executive functioning. The systematic review contained in the portfolio aimed to address whether mindfulness is an effective intervention to reduce emotional problems, specifically anxiety and depression, after brain injury. Whereas the main empirical paper, that being a meta-analysis, investigated the effectiveness of cognitive rehabilitation for people with executive functioning problems after brain injury.

The overall findings from the systematic review indicated that mindfulness-based interventions may be beneficial in alleviating emotional difficulties after brain injury. However, methodological quality of the reviewed papers was poor in general; thus, making confident conclusions regarding effectiveness challenging. The areas in which quality rating was poorly covered was in relation to papers not containing a control group or not having an adequate control group; which impacted on concealment and blinding. Therefore, as a thorough comparison of intervention and control could not be made, it is difficult to make confident conclusions with regards to effectiveness.

The review contained a small number of studies which indicates that this topic area is relatively novel when used in conjunction with the ABI population. This is not necessarily a limitation to the review but provides evidence that more studies should be conducted to investigate this area in more detail along with more robust methodological designs. The current review contained five previous reviews that aimed to investigate the benefits of

using mindfulness-based interventions within the ABI population. Overall conclusions from these reviews suggested that whilst interventions may be beneficial, there are limitations to this area of research. These limitations tended to be with regards to methodological quality, which is also raised in the current review.

When thinking about service provision and clinical guidance, the National Institute for Health and Care Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) have created specific guidelines and recommendations for rehabilitation of emotional difficulties after brain injury. NICE suggest, after stroke, the guidance for treating depression is per the general population if there is no presence of a cognitive deficit; with recommendations being a stepped care approach using CBT in a group or individual setting. This is also the case for anxiety, with the inclusion of applied relaxation. SIGN corroborate that CBT should be offered to alleviate anxiety and depression after brain injury; however, discuss that there is limited robust outcome studies to make firm recommendations. The current review does not add to the current guidance due to the weak methodology quality of the reviewed studies.

As these recommendations do not discuss using other therapies than CBT, it is useful to think about other reviews that look at CBT and the effectiveness on alleviating emotional difficulties to compare to the findings of the current systematic review. Waldron, Casserly and O'Sullivan (2013) conducted a review investigating whether CBT for anxiety is beneficial after brain injury. Their tentative findings suggest that CBT does improve anxiety and depression in some cases, but how successfully is dependent on what the main focus of treatment is. For example, if the intervention is targeting other areas of difficulty than emotion, then anxiety and depression scores did not always change. However, when targeting these specifically the outcomes were more positive. The authors discuss other impacts for example, amount of CBT offered and the range of outcomes making firm conclusions difficult to be drawn. This is consistent with the current review in that

appropriate adaptations to interventions taking into account common difficulties faced after brain injury (attention, concentration, fatigue), may impact on the overall outcome.

Soo and Tate (2007) also conducted a review of the CBT literature on anxiety after brain injury, in which findings show its effectiveness. However, only two studies were analysed, which suggests further investigation is required in this area. Overall, this appears to be a common conclusion from the current review, previous literature and guidelines proposed by NICE and SIGN.

The systematic review contained in this portfolio investigates mindfulness-based interventions, which is thought to be a 'third wave' CBT therapy (Hayes & Hoffman, 2017; Hunot et al., 2013) and has been used within the general (Piet & Hougaard, 2011; Baer, 2003) and brain injury populations (Kangas & McDonald, 2011) to alleviate a range of difficulties. Mindfulness-based interventions are not only thought to be an effective way of alleviating a range of difficulties, for example mental fatigue (Johansson et al, 2012) and attention (McMillian et al, 2002), and maintaining positive effects, in different populations, but are also thought to be cost-effective (Teasdale, Segal, Williams, Ridgeway, Soulsby & Lau, 2000). Miller, Fletcher and Kabat-Zinn (1995) conducted an 8-week MBSR intervention on individuals with anxiety and found that scores on anxiety and depression measures reduced post-intervention and were maintained at a three-year follow-up. Furthermore, a substantial proportion of participants were still engaging in mindful practice. Moreover, mindfulness practice and mindfulness-based interventions have been found to prevent relapse in individuals with depression (Williams, 2008); however, Ma and Teasdale (2004) suggest that this depends on the number of depressive episodes an individual has encountered previously.

The overall findings from the meta-analysis investigating the effectiveness of cognitive rehabilitation for individuals with executive functioning difficulties after brain injury suggest that there is little effect overall due to small effect sizes being found. A range of

effect sizes were seen, mostly small to medium; however, the disparity seen appeared to depend on study quality and intervention type. Narratively the results indicate that for some studies, their findings produced significant differences between the intervention and control groups; however, other studies did not. When looking at the outcomes in relation to impairment vs everyday life, there tended to be a reduction in executive dysfunction symptoms seen on the DEX for the studies that used that questionnaire; however, the other measures produced varied outcomes. There were also conflicting outcomes for the everyday measures; with better attainment of daily intentions being seen, but there appeared to be a consensus that assessments measuring the everyday level did not provide any differences between intervention and control groups. This suggests that providing an intervention to benefit outcomes in an individual's everyday life yields better outcomes and this is in line with INCOG guidelines.

There are several guidelines that have been created to provide recommendations not only for cognitive rehabilitation in general, but also in relation to executive functioning. NICE guidelines for stroke rehabilitation specifically related to attention difficulties suggests that attention training should be offered with relevance to everyday life. NICE also suggests that managing one's environment and providing prompts is needed to help attention deficits. Two papers in the review used prompting (Gracey et al. 2016; Tornas et al. 2016) which adheres to this recommendation. SIGN guidance suggests using attention training to combat attention difficulties and metacognitive strategies to overcome executive functioning difficulties; which has been seen in five papers in this review (Couillet et al, 2010; Novakovic-Agopian et al, 2011; Niemann et al, 1990; Barker-Collo et al, 2009 ; Park et al, 1999).

Recommendations proposed by INCOG (Ponsford et al., 2014) in relation to attention difficulties suggest that metacognitive strategies, dual tasking and computer-based attention training should be used in interventions. The studies in the review that aim to reduce

attention difficulties specifically, adhere to these recommendations by using programmes that either used a dual task component (Couillet et al, 2010; Park & Lee, 2018) or computer-based attention training (Spikman et al., 2010; Barker-Collo et al, 2009; Park et al, 1999). This is also seen in the INCOG recommendations for executive functioning (Tate et al., 2014) that suggest interventions should tackle problem-solving and planning in an everyday life context, provide immediate feedback to limit errors and be group based. All papers in the review used a group based intervention and the paper by Bertens and colleagues (2015) used an errorless learning GMT approach to combat errors being made. However, both INCOG guidelines suggest that more evidence is needed to investigate these areas that have a focus on everyday life.

Whilst previous findings have suggested that cognitive rehabilitation is efficacious in remediating executive dysfunction (Cicerone et al. 2005; Cicerone et al., 2011; Rohling et al., 2009), the current review supports the view that interventions based on compensatory internal strategies have a small effect on alleviating executive functioning difficulties for impairment and subjective focussed outcomes. Small effect sizes were also found for impairment focussed interventions on impairment focussed outcome measures. Previous reviews have concluded that further investigation into this area is required to ensure firm conclusions can be drawn and the current review would support further analysis of individual intervention types.

Critical Appraisal

The current systematic review brings together TBI, stroke and other ABI literature, along with reviewing previous reviews; however, there are some limitations that need to be taken into account. With regards to the systematic review, there were a small number of studies included that ranged in methodological quality. Only one RCT was included and the remaining studies varied in their quality and design. The current findings corroborate overall results and conclusions from previous reviews that have also been systematically

reviewed for this portfolio, which suggest that more robust methodologically designed studies are required. A key strength of the current review is that it contains additional papers to those already encompassed in the previous reviews.

One limitation to the systematic review is that despite the primary author endeavouring to include all papers that were identified in the initial searching process, not all papers could be accessed. The primary author attempted to gain access through contacting authors directly and making interlibrary requests. Therefore, it is possible that there are additional studies that would have met inclusion criteria that should have been included in the review but were not. This has implications with regards to making full and informed conclusions. A strength to the current systematic review, though, is that half of the papers included were second rated for quality. The results from this showed that the raters were only one point out with their total ratings, suggesting good inter-rater reliability with regards to quality. However, rigor of rating could be improved as the AMSTAR tool suggests 80% of studies should be rated.

The meta-analysis topic area of executive functioning and cognitive rehabilitation is vast to examine and make firm conclusions, especially when thinking about the range of interventions that can be adopted and the array of outcome measures that can be used. Therefore, completing the meta-analysis was challenging. It is helpful to understand the areas interventions tended to fall into, to ascertain how these fit with guidelines set out by NICE and INCOG; however, the meta-analysis falls short of describing in detail the effectiveness of each intervention type.

The range of outcome measures used within the reviewed papers made the process of analysing challenging. The primary investigator used average effect sizes from each individual paper to provide one overall effect size from each domain (impairment, everyday life or subjective) to use within the analysis. This procedure has been used within previous

meta-analyses to overcome the challenge of multiple outcome measures (Stamenova & Levine, 2018; Belanger et al, 2005).

Future Research

Taking the findings from the current systematic review and meta-analysis, along with recommendations from NICE and INCOG, there are several future research ideas that would be appropriate to investigate. These will be discussed independently for the systematic review and meta-analysis.

The first area of future research that would be useful to consider for the mindfulness-based intervention literature is further RCT studies to expand on current findings, with more robust methodology. This addition to the growing field of mindfulness-based interventions may enable it to be more prominent in clinical practice, and perhaps become a recommended intervention to use after brain injury. The findings of current and previous literature do suggest mindfulness is effective at alleviating emotional difficulties after brain injury; however, to become common practice, more robustly designed studies need to be completed.

Another interesting area that would benefit from further investigation is how effective mindfulness is in relation to different clinical populations. The current systematic review focussed on ABI, with some other presentations being included (MS and Parkinson's disease); however, it would be interesting to see whether there are any explicit differences between ABI and other neurological disorders to ascertain whether this type of intervention can be generalised. In addition, a review looking at the effectiveness of mindfulness and time post-injury would be useful for clinical practice to learn whether there is a more beneficial time to introduce the concept of mindfulness, or whether it can be useful even in the acute phase.

As alluded to above, the area of future research that would be beneficial with regards to the effectiveness of cognitive rehabilitation of executive functioning difficulties is in relation to types and components of interventions. It was not possible for the current meta-analysis to adequately answer this question, which requires more in-depth analysis of the range of measures used with the studies. This could be an area for future investigation that the current study hoped to do.

Cost-effectiveness was discussed in chapter 2 with regards to mindfulness-based interventions after brain injury, with Kuyken et al (2008) concluding that more research is required in this area. Within neurorehabilitation, studies have shown that specialist input can produce cost-benefits across a range of outcomes including employment, amount of support required and residential status (Oddy & de Silva Ramos, 2013); along with individuals being able to make positive contributions to the economy (Turner-Stokes, 2008).

Overall Conclusion

With regards to the systematic review, the conclusions that can be drawn are that mindfulness-based interventions may be advantageous in alleviating emotional difficulties after brain injury. However, as methodological quality across the papers is generally weak, confident conclusions are difficult draw. Suggestions for future research include the undertaking of robust RCT studies to allow a fair comparison of intervention vs control groups, to investigate effectiveness. In addition, the generic mindfulness-based programmes, for example MBSR and MBCT, that were adapted to suit the brain injury population appear to offer positive findings but may require further investigation as adaptations varied across the studies reviewed.

The main conclusion from the meta-analysis is that cognitive rehabilitation has a small effect on executive dysfunction after brain injury; producing small, significant effect

sizes across many of the analyses. The interventions focussed on compensatory internal strategies appeared to yield the most significant small effect sizes across impairment and subjective outcomes. Whereas, the impairment focussed interventions yielded a small significant effect size for impairment outcomes only.

One final conclusion, synthesising both reviews, is that emotion and cognition should be considered as being intrinsically linked (Khan-Bourne & Brown, 2003; Fernandez-Duque et al, 2000), with the interaction between the two having an impact on behaviour (Pessoa, 2008). These concepts have been touched upon with cognitive adaptations being addressed within the mindfulness-based intervention literature, and emotional based issues being used within executive functioning interventions (Tornas et al, 2016). Therefore, there is the basis to investigate the two concepts together.

An example of future research encompassing both emotional and cognitive difficulties after brain injury is proposed by the primary investigator by trialling a mindfulness-based exercise intervention with tailored daily text messages. The aim being to provide a 'mindful interruption' of daily goals for participants to evaluate their current emotional state. As previous research shows that supporting individuals with text messages helps them to complete tasks (Gracey et al, 2016; Tornas et al, 2016) and mindfulness helps people to cope with emotional responses (Bedard et al, 2014; Bedard et al, 2003), delivering an intervention comprising content-free cueing as a 'mindful interruption' for participants to evaluate their present emotional state in relation to goal attainment may be merited.

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Quality Ratings

adapted from Kocsis, Gerber, Milrod, Roose, Barber, Thase, Perkins and Leon (2010)

Bias domain	Source of bias	Rating criteria/ points to discuss
Selection bias	Appropriate and representative sample	*Does the sample diagnostic method and inclusion and exclusion criteria ensure that the study's sample is representative of the neurodisability investigated?* Well covered (2 points) = There is a full description of and appropriate method and criteria. Participants were recruited from a representative sample and were a good representative of the neurodisability investigated. Adequately addressed (1 point) = Recruitment sample or inclusion and exclusion criteria applied may limit the generalisability of results. Or the description of diagnostic method or criteria is not complete. Poorly addressed (0 points) = Poor description of method and inclusion and exclusion criteria and inappropriate method and criteria.
	Appropriate screening of sample	*Does the study detail the screening process? Is this appropriate?* Well covered = Full description of appropriate screening process. Numbers of participants screened, included and excluded are reported. There is a detailed description of the screening procedure (e.g. a person conducted the screening assessments). Adequately addressed = Brief description of numbers screened, included and excluded.

		Poorly addressed = Poor or no description of numbers screened, included and excluded.
	Random sequence generation (randomisation to groups)	*Has the method used to generate the allocation sequence produced comparable groups? (In SR describe the method in sufficient detail when assessing bias). Is there selection bias due to inadequate generation of randomised sequence?* Well covered = Subject assignment to groups is randomised and methodology is appropriate. Differences on key variables between groups are assessed at baseline and they are sufficiently alike at baseline. Otherwise, differences on 80-100% of these variables are controlled for in the analysis. Adequately addressed = Participants are randomised into groups, but there may be some flaws in methodology or insufficient detail about methodology is given in the paper. Differences on some key variables are assessed at baseline and are sufficiently alike or 60-79% of cofounders were controlled for in the analysis Poorly addressed = Subjects are not randomised to groups or assignment is not adequately described. Or the randomisation method was not appropriate. No comparison between groups at baseline on key variable and/or less than 60% of cofounders are controlled for in the analysis.
	Allocation concealment	*Does the method used to conceal the allocation sequence so that intervention allocations could not have been foreseen before or during enrolment? Is there selection bias due to inadequate concealment of allocations before assignment?* Well covered = participants were unaware of whether they were assigned to an experimental or control condition.

		Adequately addressed = participants were made as blind as possible to which condition they were assigned, but there may be some knowledge of the research question
		Poorly addressed/ not addressed = participants were aware of the research question and/or whether they were allocated to a controlled or experimental condition. Or not sufficient detail in the paper to determine.
Performance bias	Blinding of participants and personnel	*What methods were used to blind trial participants and researchers from knowledge of which intervention a participant received? Was the intended blinding effective? Is there performance bias due to knowledge of the allocated interventions by participants and personnel during the study?*
		Well covered = Personnel and participants were unaware of which intervention participants received.
		Adequately addressed = There was an attempt at blinding personnel and participants from which intervention participants received and blinding of condition to those scoring the study, but this was not completely effective.
		Poorly addressed = Researchers and/or participants were aware of which intervention participants received. Or insufficient detail included in paper.
Detection bias	Blinding of outcome assessment	*Which measures were used to blind outcome assessment from knowledge of which intervention a participant received? Was the intended blinding effective? Is there any detection bias due to the knowledge of allocated interventions by outcome assessment?*
		Well covered = Researchers scoring and analysing data were blind to treatment condition.

		Adequately addressed = There was an attempt to blind researchers scoring and analysing the results to treatment condition, but this was not completely effective. Poorly addressed = Researchers scoring and analysing results were not blinded to group allocation. Or insufficient detail in paper.
	Reliable, valid and standardised outcome measures	*Are cognition outcome measures reliable, valid and standardised on relevant population?* Well covered = Standardised outcome measure(s) used that have good psychometric properties in the specific neurodisability population involved in the study (both valid and reliable). Adequately addressed = Standardised outcome measure(s) have been used that have adequate psychometric properties but there is little or no evidence of reliability and validity in the relevant neurodisability population. Poorly addressed = Poor validation of outcome measures or non-standardised measures used.
Attrition bias	Incomplete outcome data	*Does the study report: attrition, exclusions, numbers in each intervention group (compared to total randomised participants), reasons for attrition or exclusions and any re-inclusions in the analysis? Is there any attrition bias due to the amount, nature, or handling of incomplete data?* Well covered = Appropriate inclusion/ exclusion criteria were applied and 70% or more of those eligible to participate did so. Approximately equal number of participants in each group. The paper states attrition rates for all groups from pre- to post-intervention and they are similar for each group (rates within 10% of each other and 20% of total participants). Reasons for drop-outs are given. Appropriate statistical analysis was used for

		missing data (e.g. ITT with baseline score carried forward in order to minimise bias).
		Adequately addressed = Adequate inclusion/ exclusion criteria. Between 60-69% of those eligible to participate in the study do so. Somewhat equal number of participants in each group. Attrition rate stated pre- to post-intervention and somewhat alike between groups (within 20% of each other and less than 30% of total participants). Reasons for drop-out rates may or may not be given. There may not be statistical management of missing data but proportion of participants excluded is reported and less than 20%.
		Poorly addressed = High dropout rate in general (more than 40%) and/or uneven attrition. Reasons for drop-outs not given. Poor method used to deal with missing data and participants excluded is more than 20% or not reported at all.
		Not addressed = attrition rate not reported and there was no mention of missing data or participants who have been excluded.
Reporting bias	Selective reporting	*How selective was outcome reporting? Is there any reporting bias? Were appropriate statistical tests used (e.g. use of Bonferroni correction, longitudinal data analysis, adjustment for cofounders)?*
		Well covered = Analysis was appropriate to the design used. All outcome data was analysed and reported on.
		Adequately addressed = Analysis was appropriate to design, but not all outcomes are reported or some bias with regards to analysis used.
		Poorly addressed = Analysis is not appropriate or there is a high level of reporting bias.
	Conclusions	*Are conclusions of the study justified by the*

	reported	*sample, measures and data analysis? (Note – useful to look at conclusions stated in the abstract).* Well covered = All conclusions of the study justified. Adequately addressed = Some conclusions of the study justified. Poorly addressed = Poor or no justification of conclusions from results as presented, or insufficient information to evaluate (e.g. sample or treatment insufficiently documented, data analysis does not support conclusions, or number of withdrawals or dropouts makes findings unsupportable).
Other bias	Fidelity of treatment groups	*Does the study demonstrate that the treatment being studied is the treatment being delivered?* Well covered = Full adherence reporting for intervention with a standardised measure (must be quantitative and completed by an independent rater). And there is a full description of the therapist delivering the intervention and their training and they are suitably qualified. Adequately addressed = There is brief adherence reporting with a standardised measure or full adherence reporting with non-standardised measure. Or there is a suitably qualified therapist (or they have adequate supervision). Poorly addressed = There is poor or no adherence reporting. There are underqualified therapists who have inadequate therapist supervision. Or no information given in paper.
	Confounding variables - suitability of control group	*Is the comparison group from the same population and time frame as experimental group?* Well covered = Control group is from the same population and time frame Adequately addressed = Control group is from a

		moderately different population and/or time frame
		Poorly addressed = Control group is from a significantly different population and/or time frame
Global quality rating		12 items in total – so maximum score of 24
		1 = exceptionally poor 0-4
		2 = very poor 5-7
		3 = moderately poor 8-10
		4 = average 11-13
		5 = moderately good 14-16
		6 = very good 17-19
		7 = exceptionally good 20-24

Appendix 2 – Risk of bias and quality ratings for systematic review

Author & date	Selection bias				Performance bias	Detection bias		Attrition bias	Reporting bias		Other bias			Global quality rating (Total score = 24)
	Appropriate and representative sample	Appropriate screening of sample	Random sequence generation	Allocation concealment	Binding of participants and personnel	Blinding of outcome assessment	Reliable, valid and standardised outcome measures	Incomplete outcome data	Selective reporting	Conclusions reported	Fidelity of treatment groups	Confounding variables – suitability of control group		
Bedard et al (2003)	2 points	1 point	0 points	0 points	Not addressed	0 points	2 points	0 points	1 point	1 point	1 point	1 point		Moderately poor 9 points
Bedard et al (2014)	2 points	2 points	point	0 points	0 points	1 point	2 points	1 point	2 points	1 point	1 point	1 point		Moderately good 15 points
Canade (2014)	2 points	1 point	1 point	0 points	1 point	0 points	1 point	0 points	1 point	1 point	1 point	1 point		Moderately poor 10 points
Kristofersson (2012)	1 point	1 point	0 points	0 points	0 points	0 points	2 points	0 points	2 points	2 points	1 point	0 points		Moderately poor 9 points
Bedard et al (2012)	1 point	1 point	0 points	0 points	0 points	0 points	2 points	1 point	2 points	1 point	1 point	0 points		Moderately poor 9 points
Azulay et al (2012)	1 point	0 points	0 points	0 points	0 points	0 points	1 point	1 point	2 points	1 point	1 point	0 points		Very poor 7 points
Combs et al (2018)	2 points	0 points	0 points	0 points	0 points	0 points	0 points	0 points	2 points	2 points	1 point	0 points		Very poor 7 points
Mavaddat et al	2 points	2 points	0 points	0 points	0 points	0 points	2 points	1 point	1 point	2 points	1 point	0 points		Average 11 points

(2017)													
Joo et al (2010)	1 point	0 points	0 points	0 points	0 points	0 points	1 point	0 points	2 points	1 point	0 points	0 points		Very poor 5 points
Azulay & Mott (2016)	2 points	0 points	0 points	0 points	0 points	0 points	2 points	2 points	2 points	1 point	2 points	0 points		Average 11 points
SCED Scale	**Clinical History Specified**	**Target Behav – repeatable measures**	**Design 1 – ABA or multiple baseline**	**Design 2 – Baseline. Sufficient sampling**	**Design 3 – Treatment. Sufficient sampling**	**Design 4 – Raw data points recorded**	**Observer bias – inter rater reliability**	**Independence of assessors**	**Statistical analysis**	**Replication – either across subs, therapy or settings**	**Generalisation?**		
Dickinson et al 2017	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No	Yes		

Appendix 3 – AMSTAR-2 Quality Ratings of Previous Systematic Reviews

Author and Date	Lawrence et al (2013)	Lazaridou et al (2013)	Toivonen et al (2017)	Kenuk & Porter (2017)	Tsaousides et al (2013)
1. Question contain elements of PICO	Yes	No. Not enough detail to satisfy a yes or partial yes	Yes	No. Not enough detail to satisfy PICO.	Yes
2. Established protocol prior to conducting review	Partial yes	No. Do not detail any risk of bias assessment	Partial yes	Partial Yes. However, not a great detail on risk of bias.	No
3. Selection of study designs stated	Yes	No	No actual explanation	No	No
4. Comprehensive literature search strategy	Partial yes. Very comprehensive description but not enough to satisfy a full yes	Yes	Partial yes. Quite comprehensive. Missed information such as speaking to leaders in field	Partial yes. States English only papers; however, no full justification.	No
5. Study selection conducted with another	Yes	Yes	No. Only one researcher – lead investigator. Used a "predetermined form" but didn't state any other information.	Yes	No
6. Data extraction completed with another	Yes	No. Not enough information	No. Only one researcher – lead investigator. Used a "predetermined form" but didn't state any other information.	Implies yes, but not clear.	No
7. List of excluded studies and justifications	No	No	No	No	No
8. Included studies described in detail	Partial yes – no timeframe stated and not always a control group	Partial yes	Partial yes. Very comprehensive. Didn't include study setting and follow-up timeframe.	No. No full description of population.	No. Studies not easily distinguishable in paper
9. Assessed risk of bias adequately	No. Potentially did do this adequately, but not	No. Not enough information to satisfy a	Yes, both RCTs and non-RCTs. Very comprehensive	No. There is a brief mention, but not clear	No

	described in enough detail to qualify for a partial or full yes	yes or partial yes	description of biases assessed.	how this was assessed.	
10. Sources of funding from individual papers reported	No	No	No	No.	No
11. If meta-analysis: were appropriate methods of combining stats used	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted
12. If meta-analysis: was impact of risk of bias in results considered	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted
13. Was risk of bias discussed in results of review	Yes	No	Yes	No. There is no reference to risk of bias in results	No
14. Heterogeneity observed in results discussed	No; however, there was a brief mention of this	No	No. Eluded to this very briefly and why results should be taken with caution.	No	No
15. If meta-analysis, was adequate investigation of publication bias performed	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted	No meta-analysis conducted
16. Sources of conflict, or funding, was reported by authors	Yes	No	Yes	No	No
	9 / 16	3 / 16	7 / 16	4 / 16	1/16

Appendix 4 – Risk of bias and quality ratings for meta-analysis

Author & date	Selection bias				Performance bias	Detection bias		Attrition bias	Reporting bias		Other bias		Global quality rating (Total score possible, 24)
	Appropriate and representative sample	Appropriate screening of sample	Random sequence generation	Allocation concealment	Binding of participants and personnel	Blinding of outcome assessment	Reliable, valid and standardised outcome measures	Incomplete outcome data	Selective reporting	Conclusions reported	Fidelity of treatment groups	Confounding variables – suitability of control group	
Rath et al (2003)	2 points	1 point	1 point	0 points	0 points	0 points	2 points	1 point	2 points	2 points	2 points	2 points	Moderately good 15 points
Cantor et al (2014)	2 points	1 point	1 point	0 points	1 point	2 points	2 points	2 points	2 points	2 points	2 points	2 points	Very good 19 points
Couillet et al (2010)	2 points	0 points	2 points	1 point	1 point	1 point	2 points	2 points	2 points	1 point	0 points	2 points	Moderately good 16 points
Miotto et al (2009)	2 points	0 points	1 point	0 points	0 points	0 points	2 points	1 point	2 points	2 points	0 points	2 points	Average 12 points
Tornas et al (2016)	2 points	2 points	2 points	2 points	1 point	2 points	2 points	2 points	2 points	2 points	1 point	2 points	Exceptionally good 22 points
Twamley et al (2014)	1 point	0 points	1 point	2 points	0 points	1 point	2 points	1 point	1 point	2 points	1 point	2 points	Moderately good 14 points
Elbogen et al	1 point	2 points	1 point	2 points	1 point	2 points	2 points	1 point	1 point	2 points	2 points	0 points	Very good 17 points

(2018)												
Vas et al (2011)	2 points	0 points	1 point	1 point	2 points	2 points	2 points	1 point	2 points	2 points	1 point	2 points	Very good 18 points
Akerlund et al (2013)	2 points	1 point	1 point	1 point	0 points	0 points	2 points	1 point	2 points	2 points	2 points	2 points	Moderately good 16 points
Spikman et al (2010)	2 points	2 points	1 point	2 points	2 points	2 points	2 points	2 points	2 points	2 points	2 points	2 points	Exceptionally good 23 points
Gracey et al (2016)	2 points	2 points	2 points	2 points	1 point	2 points	2 points	2 points	2 points	2 points	1 point	2 points	Exceptionally good 22 points
Bertens et al (2015)	2 points	1 point	2 points	2 points	2 points	0 points	2 points	Not addressed as no drop out data	2 points	2 points	2 points	2 points	Very good 19 points
Poulin et al (2017)	2 points	2 points	2 points	2 points	2 points	0 points	2 points	2 points	2 points	2 points	0 points	2 points	Exceptionally good 20 points
DeLuca et al (2018)	2 points	2 points	1 point	0 points	0 points	0 points	2 points	Not addressed	2 points	0 points	Not addressed	2 points	Moderately poor 9 points
Park and Lee (2018)	2 points	0 points	2 points	2 points	2 points	2 points	2 points	2 points	2 points	1 point	0 points	2 points	Very good 19 points
Van de Ven (2017)	2 points	1 point	2 points	2 points	1 point	0 points	2 points	2 points	2 points	2 points	0 points	2 points	Very good 18 points
Salazar et al (2000)	2 points	2 points	2 points	Not addressed	1 point	2 points	2 points	1 point	2 points	1 point	1 point	2 points	Very good 18 points

Tiersky et al (2005)	2 points	2 points	2 points	0 points	0 points	0 points	2 points	1 point	1 point	2 points	1 point	2 points	Moderately good 15 points
Faria et al (2016)	2 points	0 points	2 points	0 points	0 points	0 points	2 points	2 points	2 points	2 points	0 points	2 points	Moderately good 14 points
Bertens et al (2015)	1 point	1 point	1 point	0 points	0 points	0 points	2 points	1 point	2 points	2 points	1 point	2 points	Average 13 points
Jacoby et al (2013)	1 point	1 point	1 point	1 point	0 points	2 points	2 points	Not addressed as no drop out data	2 points	2 points	0 points	2 points	Moderately good 14 points
Levine et al (2000)	2 points	1 point	1 point	0 points	0 points	0 points	1 point	Not addressed as no drop out data	2 points	1 point	0 points	2 points	Moderately poor 10 points
Niemann et al (1990)	2 points	2 points	1 point	1 point	0 points	0 points	2 points	Not addressed	2 points	1 point	0 points	2 points	Average 13 points
Yoo et al (2015)	0 points	0 points	1 points	0 points	0 points	0 points	1 point	Not addressed	2 points	1 point	0 points	2 points	Very poor 7 points
Non-RCT													
Novakovic-Agopian et al (2011)	1 point	0 points	0 points	1 point	0 points	1 point	2 points	1 point	2 points	2 points	2 points	0 points	Average 12 points

Levine et al (2011)	2 points	0 points	1 point	0 points	0 points	2 points	2 points	0 points	2 points	2 points	0 points	2 points	Average 13 points

Key

0 points = poorly addressed

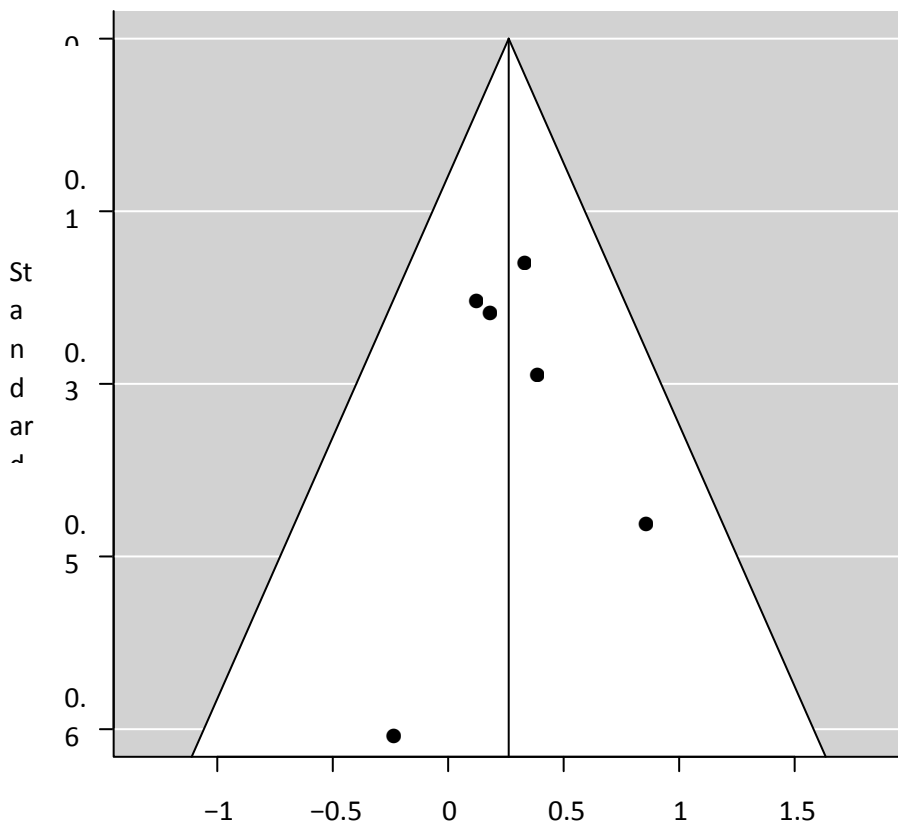1 point = adequately addressed

2 points = well addressed
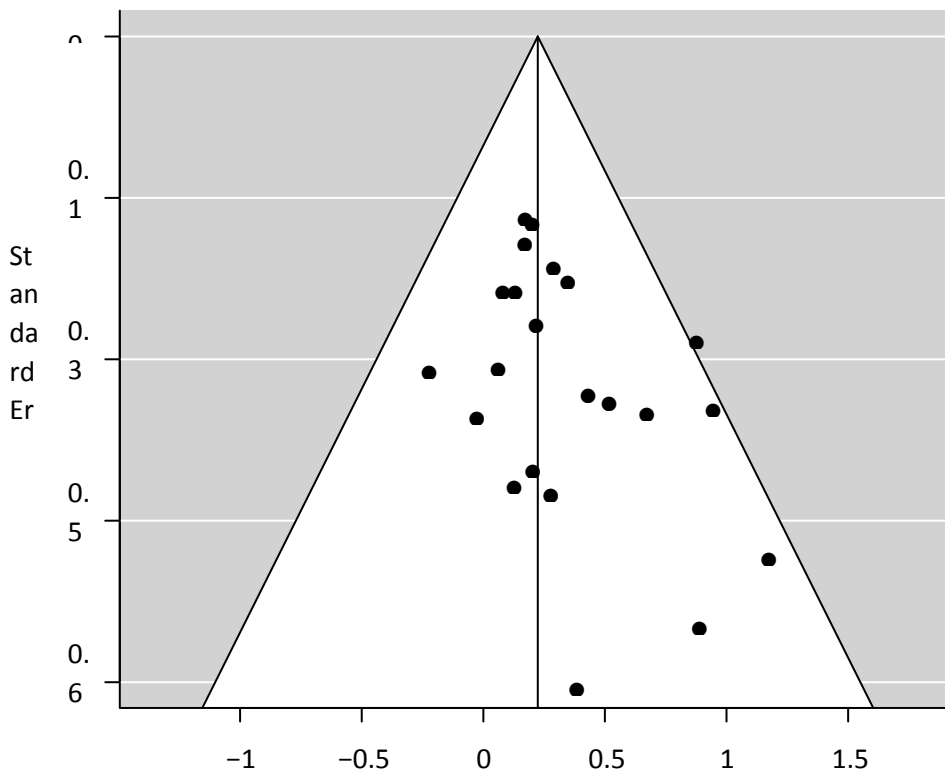
Appendix 5: Funnel plot for RCT impairment outcomes
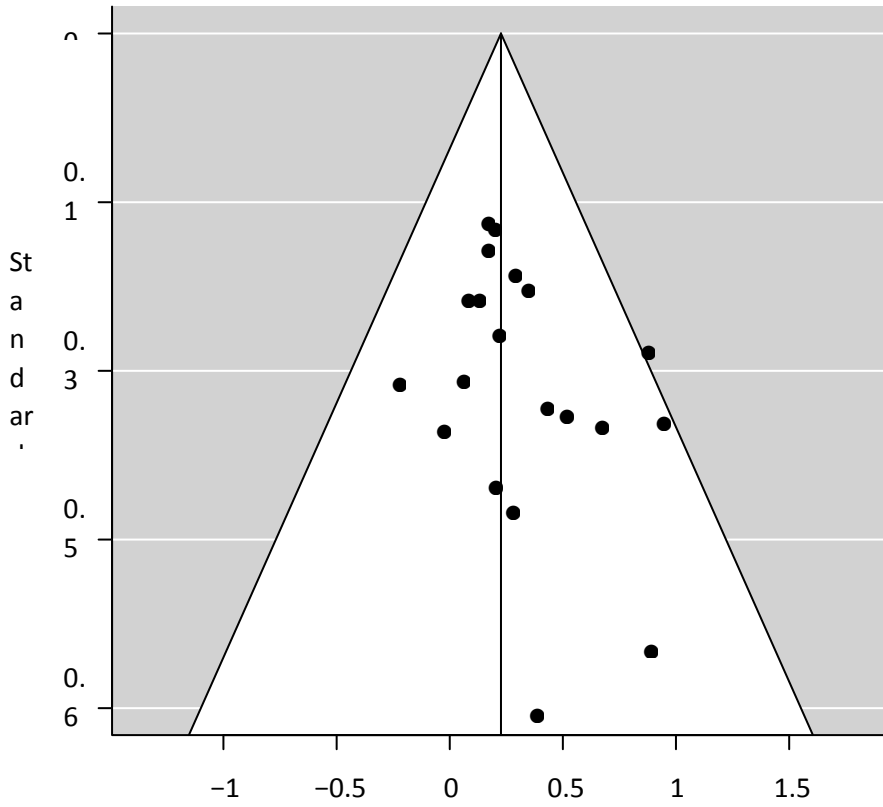
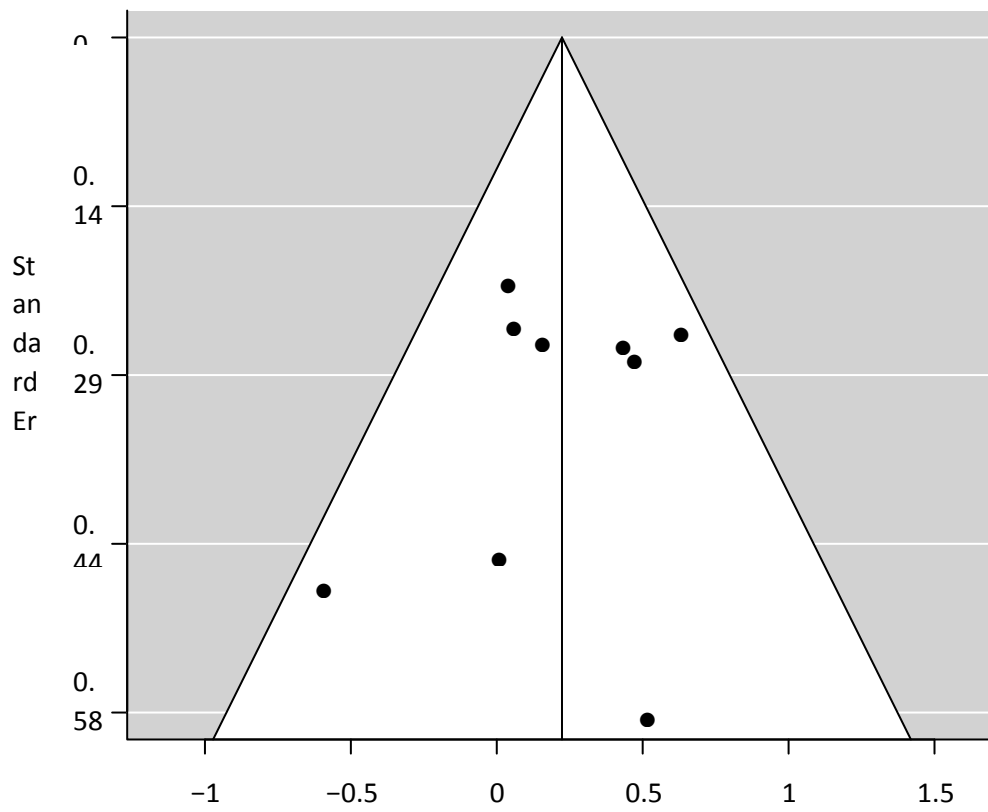## Appendix 6: Funnel plot for RCT everyday life outcomes
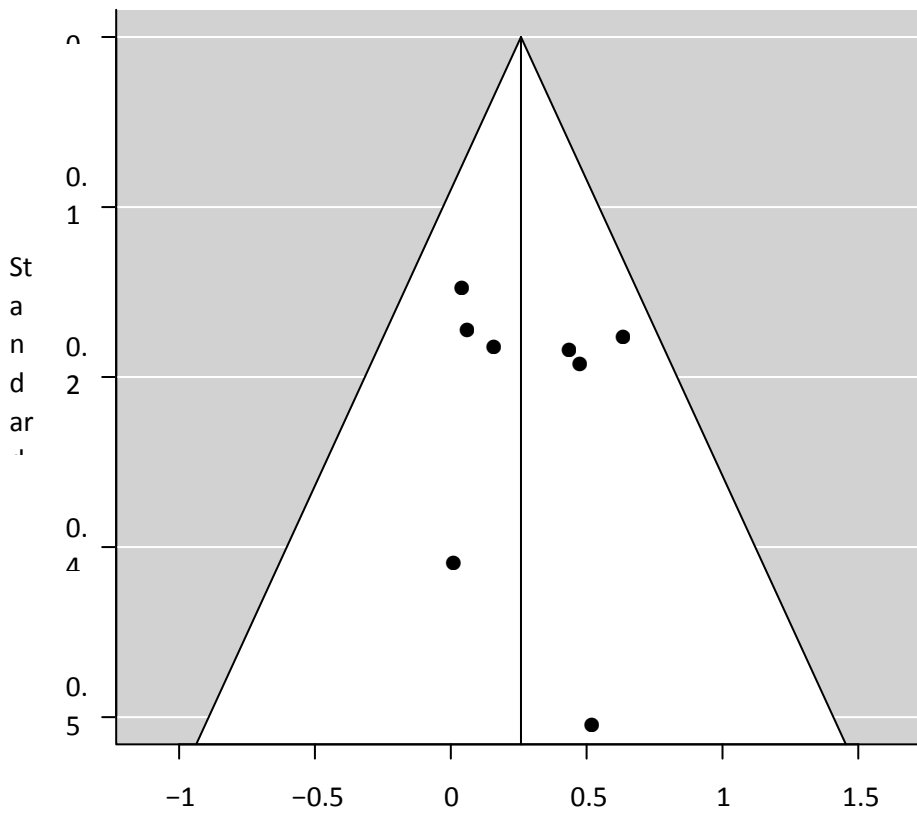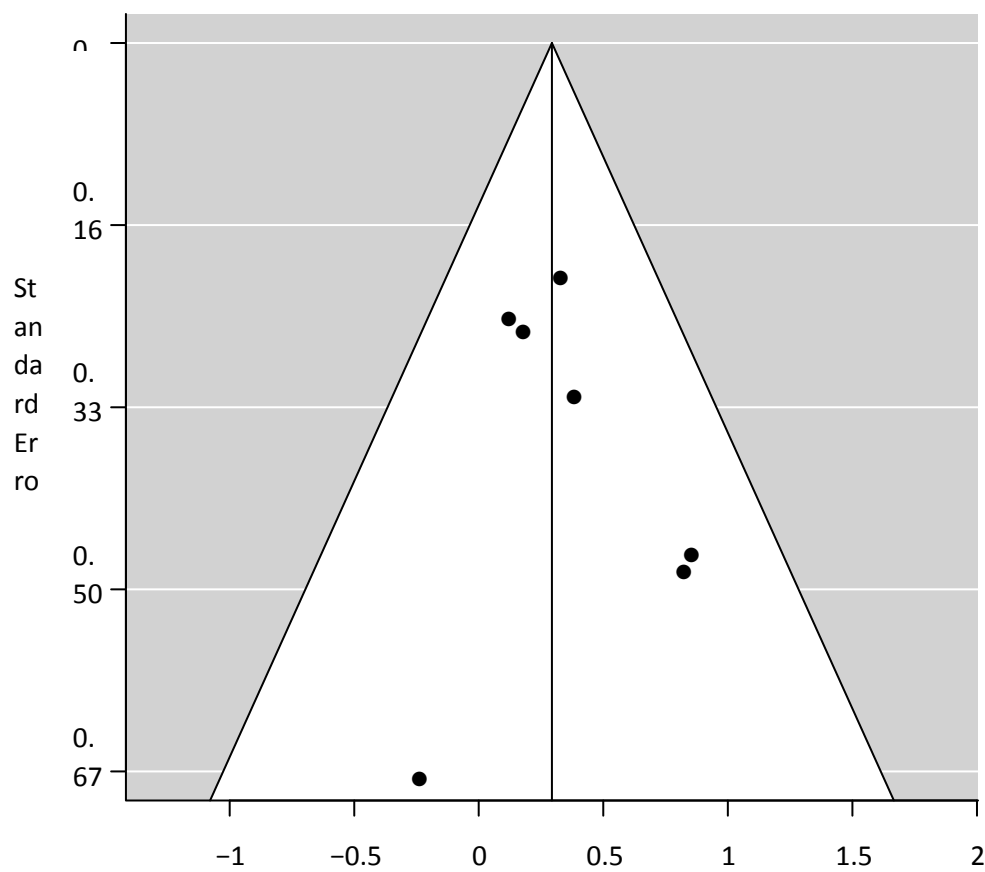
Appendix 7: Funnel plot for RCT subjective outcomes

Appendix 8: Funnel plot for impairment outcomes when interventions grouped

Appendix 9: Funnel plot for everyday life outcomes when interventions grouped

Appendix 10: Funnel plot for subjective outcomes when interventions grouped

Appendix 11: Journal submission guidelines for preparing paper

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