

**The impact of executive functioning on attention to threat in an adult traumatic brain injury population: an experimental group design**

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### **Overall Abstract for Thesis Portfolio**

**Objective:** to explore the impact of executive function (EF) on emotional distress in an adult traumatic brain injury (TBI) population.

**Methods:** A systematic review of the literature was conducted using electronic databases and the reference section of relevant papers to determine whether impaired EF acts as a vulnerability factor to emotional distress. Alongside this an experimental group design was utilised to explore whether selective attention to threat differs between a TBI group (n = 18, impaired EF) and a comparison group (n = 34, EF intact). Participants completed measures of EF, emotional distress and the dot-probe task.

**Results:** The systematic review found 10 studies which met the inclusion criteria, of which, eight studies were rated as methodologically 'poor' and two were rated as 'fair' in response to the review aims. Seven of the studies reported associations between EF and emotional distress but none of the studies addressed the question directly and were unable to provide evidence of EF as a vulnerability factor. After analysis, the research paper found no significant differences between the reaction times to the threat stimuli in EF intact (comparison group) versus the EF impaired (TBI group). Therefore the hypotheses were not supported.

**Conclusions:** The research contained in the thesis portfolio has highlighted the need for more research to be carried out into EF processes and the particular impact these deficits have on emotional outcomes in a TBI sample. Previous research has suggested an association between EF and emotional distress, and the current systematic review only provided weak evidence to support this. The processes behind this are still not fully understood. By gaining a deeper understanding of these processes, it is hoped that this could inform the development of potential interventions to best suit the needs of the TBI population.

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## **Introduction to the thesis portfolio**

This thesis portfolio consists of two main papers: a systematic review and an empirical paper, both exploring executive function (EF) and emotional distress in an adult traumatic brain injury (TBI) population. There is a bridging chapter and a final discussion chapter, bringing together the findings from both studies and discussing them in the context of the current available literature.

The research within this portfolio focuses on TBI, a specific type of brain injury, which is a direct result of an external force, and can often be sustained during a fall, assault or road traffic incident (Simpson, Simons & McFadyen, 2002). TBI can have a significant impact on a person's ability to function on a daily basis (Warriner & Velikonja, 2006) and a consequence of TBI is often frontal lobe damage, which can result in difficulties with EF (Roussel, Dujardin, Henon, & Godefroy, 2012). EF is involved in a range of complex processes including: attention, planning and working memory (Arciniegas, Held, & Wagner, 2002; Frencham, Fox, & Maybery, 2005; Stuss, 2011). EF difficulties can have a substantial impact on the individual's life and adjusting to these changes can be distressing (Hoofien, Gilboa, Vakils & Donovik, 2000). Research suggests that individuals who have sustained a TBI also report significant emotional change (Albrecht et al., 2014; Bay & Donders, 2008; Jorge et al., 2004) and major depression has been associated with impairment of EF skills in a TBI population (Himanen et al., 2009).

The systemic review sets out to evaluate the current available evidence to ascertain whether EF impairment acts as a vulnerability factor to poor emotional outcomes after sustaining a TBI. Following on from this, the empirical paper seeks to test the hypothesis that EF impairment in an adult TBI population results in individuals being quicker to respond to threat when compared to a comparison group of participants without a TBI and intact EF.

## **Chapter 1.**

**Systematic review prepared for submission to: Journal of Experimental and Clinical  
Neuropsychology**

# **A Systematic Review of the Strength of the Evidence that Low Executive Functioning in a Traumatic Brain Injury Population is a Vulnerability Factor for Increased Emotional Distress**

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## **Abstract**

**Introduction:** Traumatic brain injury (TBI) can cause severe cognitive, emotional, behavioral and interpersonal difficulties that impact on an individual's everyday functioning. One common difficulty post-TBI is impaired executive functioning (EF). Associations between EF impairment and emotional distress have been seen across different populations. The main objective was to review the quantitative research findings concerning the role of impaired EF as a vulnerability factor to increased emotional distress in adults post-TBI.

**Methods:** A systematic review of the literature was conducted using five electronic databases: PsycINFO, EMBASE, Medline, Allied and Complementary Medicine and Cumulative Index to Nursing and Allied Health Literature and manual searches of the reference section of relevant papers.

**Results:** After applying the inclusion criteria 10 studies were deemed appropriate to include and the data from each study was collated. Eight of the studies were rated as 'weak' and two were rated as 'fair' using the Quality Assessment Tool for Observational Cohort and Cross-sectional Studies. All but one study used cross-sectional designs and none of the studies specifically explored EF as a vulnerability factor for emotional distress. However, seven of the studies reported significant associations between the two factors.

**Conclusions:** Despite all studies measuring EF and emotional distress, none of the studies indicates that EF is a vulnerability factor for emotional distress. Nonetheless there are reported associations between EF and emotional distress which suggest that more research is needed on the specific EF processes and key aspects of emotional distress to improve our understanding of these relationships. It is important to consider the psychosocial consequences that impaired EF can have on an individual e.g. reduced community access

etc., which may impact upon an individual's emotional distress rather than the EF impairment itself. These findings have clinical implications with regard to rehabilitation and the development of current and future interventions.

**Keywords:** executive function, traumatic brain injury, emotional distress, adult,

## **Introduction**

Traumatic brain injury (TBI) is a type of acquired brain injury that is caused by an external force as a consequence of events such as an assault, a road traffic incident, a fall or gunshot (Simpson, Simons & McFadyen, 2002). TBI has been referred to as a “hidden disability” as often there may be no physical marker that the individual has sustained such an injury (Simpson et al., 2002). However, TBI can cause severe cognitive, emotional, behavioral and interpersonal difficulties which impact on how an individual functions day to day (Warriner & Velikonja, 2006). These difficulties can affect all aspects of an individual’s life and adjusting to these changes can be a significant challenge and distressing to the individual, and also to those around them (Hoofien, Gilboa, Vakils & Donovan, 2000).

Frontal lobe damage is frequently a consequence of TBI and can result in executive functioning (EF) impairment, as this area of the brain is said to be responsible for much of the EF processes (Godefroy, 2012; Roussel, Dujardin, Henon & Godefroy, 2012; Salas et al., 2014). For the majority of individuals who have suffered a mild TBI, most of these cognitive deficits are reported to be resolved after around three months (Ruff, 2001). However, individuals who suffer a moderate to severe TBI may have difficulty with tasks involving EF (Pare, Rabin, Fogel, & Pepin, 2009), which create difficulties in their daily functioning for a longer duration after their injury (Rabinowitz & Levin, 2014) and which are associated with high levels of emotional distress (Erickson, Karlsson, Borrell, & Tham, 2007).

It is important to acknowledge the complexity of the EF and the lack of clarity and consensus around the concept of what this encompasses (Mueller & Dollaghan, 2013). Early research that conceptualized EF was conducted by Atkinson and Shrifin (1971) who produced a model of short-term memory. This model proposed that central control

processes within the short-term memory system assist with the regulation of information. The concept of EF was later suggested to include complex processes such as goal-setting, inhibition, planning and shifting (Lezak, 1982). Baddeley (1986) proposed the Working Memory model, which added to Atkinson's and Schiffrin's work, suggesting that the regulation of these processes was controlled by a 'central executive' component. It was suggested that the 'central executive' was responsible for selecting, initiating and ending processing tasks such as the encoding, storing and retrieval of information. Baddeley and Wilson (1988) went on to create the term 'dysexecutive syndrome' to describe three areas of impairment: cognitive, emotional and behavioral, commonly observed after frontal damage. However, Stuss and Alexander (2007) challenged this concept and proposed that their findings do not suggest the presence of a central or supervisory executive system but that impairments are better explained as a collection of independent anatomical and functional attentional control processes which are interrelated. These early models have evolved and developed, and EF is now postulated to involve a range of cognitive processes including planning, impulse control, attention, processing speed and working memory (Arciniegas, Held, & Wagner, 2002; Frencham, Fox, & Maybery, 2005; Stuss, 2011). These EF processes are essential to successful functioning in everyday life and in particular for self-regulation (Hofmann, Friese, Gschwender, Wiers & Schmitt, 2008).

As well as extensive cognitive impairments, survivors of TBI report significant emotional changes, in particular depressed mood (Albrecht et al., 2014; Bay & Donders, 2008; Jorge et al., 2004;) and anxiety (Gould et al., 2014). Indeed, individuals who have sustained a brain injury are reported to be at greater risk of developing a depressive disorder (Kreutzer, Seel & Gourley, 2001). A significantly higher prevalence of psychiatric disorders and suicide attempts has also been recorded for individuals who have sustained a head injury alongside a generally poorer quality of life (Silver, Kramer, Greenwald & Weissman, 2009).. There are many possible routes to poor emotional outcome that have

been identified within the TBI population including: the effects of loss and changes to life due to acquired deficits across a range of domains (Gracey & Ownsworth, 2008), coping style or appraisal (Riley et al., 2010), or changes psychosocial circumstances (Hoofien et al., 2000).

Emotional disturbances have been suggested to be the most socially and vocationally disruptive sequelae of TBI (Mauri, Paletta, Colasanti, Misericocchi & Altamura, 2014). It has been clinically observed that mood can dramatically deteriorate once the recovery curve plateaus and the survivor perhaps gains more awareness and understanding of what life with a TBI might be like (Bowen, Neumann, Tennant, & Chamberlain, 1998). However, research has also shown that individuals with poorer self-awareness post-TBI reported greater emotional distress and experienced poorer social outcomes than those with greater self-awareness (Ownsworth et al., 2007). Research focusing on adjustment post-TBI has identified possible cognitive processes related to identity that are thought to impact upon emotional outcomes (Gracey & Ownsworth, 2008). These include threat appraisal (Riley et al., 2010), and loss and grief (Carroll & Coetzer, 2011). A case study described that EF impairment was found to impact emotional reactivity and emotional regulation (Salas et al., 2014). These reported difficulties were understood in terms of difficulty with cognitive flexibility and thinking processes. The individual's EF impairment compromised their ability to reappraise negative events and also led to increased rumination on negative experiences and a struggle to disengage from these, resulting in greater emotional distress. This suggests that survivors of TBI may go on to suffer emotional difficulties due to a variety of reasons including their changed circumstances and the difficulties that they may have adjusting.

The links between EF difficulties and emotional distress have been seen in various populations. EF problems were found to be important predictors of depression in adults

with ADHD, specifically difficulty with problem solving, holding information in mind and goal-directed behavior, which in turn has been found to have a negative impact on daily functioning (Knouse, Barkley & Murphy, 2013). Bredemeier and Miller (2015) carried out a systematic review of 43 published articles and found tentative support for a link between EF deficits and suicidality. Their results suggested that these deficits could not be completely explained by psychological distress and more research on this topic is needed to better understand the relationship between EF and suicidality. Watkins and Brown (2002) found links between major depression and EF deficits and proposed that these deficits are perhaps due to rumination occupying an individual's ability to utilize their EF resources. More recent research has supported this idea and found that individuals with major depressive disorder require more cognitive effort to perform tasks involving EF such as those involving inhibitory control (Cotrena, Branco, Shansis & Fonseca, 2016).

Major depression has been associated with impairment of attention and memory in individuals who have experienced a mild to moderate TBI (Rapoport, McCullagh, Shammi, & Feinstein 2005). Bailey, Seagrave, Hoy, Maller, and Fitzgerald (2014) compared four groups of individuals: TBI only; major depressive disorder (MDD) only; TBI and MDD; and a 'healthy' control group to explore the differences in working memory deficits. Their results suggested that inhibitory deficits may account for working memory impairment in MDD and TBI-MDD. For those with TBI and MDD, they postulated that it was perhaps the depression, rather than the TBI, that impaired working memory.

Krpan, Levine, Stuss & Dawson (2007) explored the relationship between EF and coping styles one year post-TBI compared to a matched control group. They found that, in the TBI sample, lower EF performance was related to the use of emotion-focused coping (EFC) compared to those with higher EF performance who were more likely to use

problem-focused coping. Problem-focused coping is described as managing stress by actively attempting to resolve the problem, whereas EFC is said to involve managing stress through emotion such as avoidance. It was suggested that individuals who have EF impairment post-TBI may not have the cognitive abilities to use problem solving focused coping strategies. This could perhaps contribute to the level of distress an individual experiences if they are unable to use adaptive coping strategies. However, they only looked at EF and coping, rather than a focus on emotional distress and were unable to infer the direction of causality. Shields, Ownsworth, O'Donovan and Flemming (2015) adopted a transdiagnostic approach to understanding the predictors of emotional distress post-TBI. 'Threats to self' and 'emotional dysregulation' emerged as the two significant factors associated with general emotional outcomes. The findings suggest that emotional dysregulation could be seen a result of EF impairment. However, it is important to note that their study utilized rating based measures rather than neuropsychological assessment. This highlights the need for further exploration of the impact of impaired EF post-TBI on emotional regulation and for conducting research that allows causality to be inferred. By understanding the nature of this relationship, interventions can be developed to target the difficulties experienced by these individuals and resources can be better allocated to reduce the economic burden of TBI.

Unlike previous research, Gyurak et al., (2009) sought to determine if acquired EF deficits resulted in individuals being less able to regulate their emotional reactions. They compared frontotemporal lobar degeneration patients, Alzheimer's patients and 'normal controls' in their responses to an acoustic startle stimulus. The results indicated that higher levels of verbal fluency scores, which are used as a standardized measure of EF, were related to greater emotional regulation. However, no relationships were found between emotion regulation and the other EF measures. They concluded that verbal fluency best indexes the complex processes of monitoring, evaluation and control needed for emotion

regulation. This adds further evidence to suggest that EF deficits might act as a vulnerability factor to emotional regulation difficulties, rather than previous research where the direction of causality has been difficult to determine.

While some more general reviews have been published exploring the area of EF and emotional distress, no review to date has specifically focused on EF impairment as a vulnerability factor to emotional distress in an adult TBI population. One systematic review explored EF and the possible relationship with suicidality, which provided tentative support for a relationship between the two constructs (Bredemeier & Miller, 2015). It is important to consider the impact of both cognitive and emotional functioning after TBI as it is proposed that untreated emotional difficulties can have a serious long-term effect on the rehabilitation process and that such resources are not utilized effectively (Morton & Wehman, 1995).

The main objective of the current review is to establish the nature and quality of the evidence regarding the role of EF as a vulnerability factor to emotional outcome following TBI. Vulnerability factor refers to whether a factor (in this case EF) can impact the likelihood of developing a condition or problem (in this case emotional disorder), as defined by Nugent (2013).

The systematic review question posed for the current review is “To what extent does impairment of EF act as a vulnerability factor to emotional distress in adults who have suffered a moderate to severe TBI”? It is anticipated that there will be a large degree of heterogeneity in the studies included and therefore a narrative synthesis (rather than a quantitative meta-analysis) will enable a full capture and integration of the data. Reviewing the research on this specific sample (moderate – very severe TBI) should help clarify the nature and quality of evidence of associations between EF and emotional distress in this population where EF difficulties are common. By focusing on this specific sample, this



review aims to synthesize the available evidence and draw conclusions on the possible links between EF and emotional distress. By further understanding these underlying EF processes as potential vulnerability factors to emotional distress, it is hoped that possible areas for future study may be high-lighted and perhaps areas where existing interventions can be refined or new interventions developed.

## **Method**

### **Search Strategy**

Systematic searches were conducted using five electronic databases: PsycINFO, EMBASE, Medline, Allied and Complementary Medicine (AMED) and Cumulative Index to Nursing and Allied Health Literature (CINAHL). The search was conducted combining the search terms “brain injur\*; head injur\*; ABI; TBI; concussion; head trauma; brain damage; closed head injury” with “executive func\*; cognitive func\*; cognitive control; neurocognitive deficits; metacognition; awareness; self-awareness; planning; problem solving; self-monitoring; self-control; self-regulation and metamemory” and “emotional distress; anxiety; depression”. To ensure comprehensiveness, the reference lists of all the included papers were hand searched for any other potentially relevant articles. The final literature search was conducted on the 8<sup>th</sup> January 2017; therefore only research published up to this point was included in the review.

### **Eligibility Criteria**

The current review focuses on individuals who have sustained a moderate to severe brain injury. There will be no restriction as to how this was classified. Severity of injury is commonly classified by duration of post-traumatic amnesia (PTA): <1 hour = mild, 1–24 hours = moderate, 1–7 days = severe and 7>days = very severe (Malec et al., 2007). Severity of injury is also classified by the Glasgow coma scale (GCS, Teasdale et al.,

2014); score between 13 and 15 are defined as mild, between 9 and 12, moderate and between 3 and 8 severe. The eligibility criteria are presented below.

### *Inclusion*

- Peer reviewed journal, published in English
- Adult (majority of participants 18 years and older)
- Majority of participants had moderate to severe TBI ( >50% there were no restrictions on how the severity of the TBI was defined or the time since injury)
- Use of quantitative methodology
- Reports the use of a reliable and valid measure of EF with established psychometric properties (e.g. Delis-Kaplan Executive Function System, D-KEFS, Delis et al., 2001)
- Reports the use of a reliable and valid measures of emotional distress with established psychometric properties (e.g. Hospital Anxiety and Depression Scale, HADS, Zigmond & Snaith, 1983)

### *Exclusion*

- Qualitative methodology
- Literature reviews
- Case studies
- Articles that did not explicitly report measures used and the methodology employed or did not use measures designed to measure EF or emotional distress
- Focused on ABI or neurodegenerative disorders e.g. stroke, dementia, etc.

### **Search results**

The electronic search identified 705 records, and a further 24 articles through manual searches of the reference lists of the 17 short-listed relevant papers were identified.

Details of the process of paper selection is provided in Figure 1, which was completed under the guidance of the PRISMA statement (2009). Studies which met the inclusion criteria were evaluated initially by their title and abstract, and then by obtaining the full text if they appeared to meet the selection criteria. After duplicates were removed and an initial screening, 17 potentially relevant articles were identified and the full text was obtained to consider against the inclusion and exclusion criteria. A total of 10 articles were included in the review.

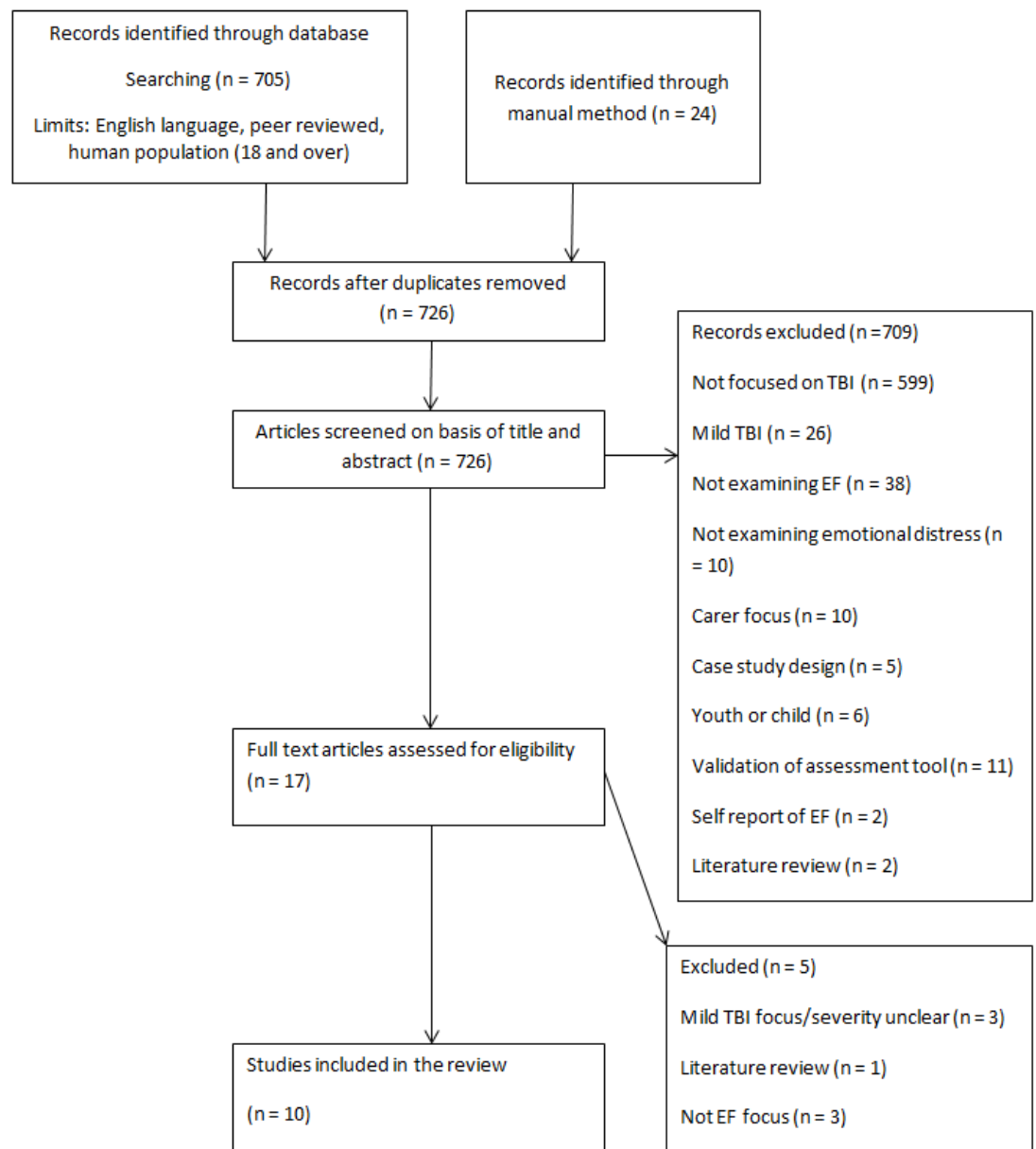


Figure 1. Prisma flow diagram detailing the selection of papers for review.

## **Data synthesis and quality assessment**

Each of the 10 articles was reviewed against the aims of the systematic review and relevant data was extracted from each study (see table 1). This included the main aims of the study relating to EF and emotional distress, details of the sample, the measures used to quantify EF and emotional distress, and the results and main conclusions related to the aim of the systematic review.

All articles included in the review were critically appraised in terms of their methodological strengths and weaknesses using the Quality Assessment Tool for Observational Cohort and Cross-sectional Studies (QATOCCS; National Heart, Lung and Blood Institute, NHLBI, 2014), alongside the accompanying ‘dictionary’ which aims to assist the assessor with the process of rating each of the studies (NHLBI, 2014). This tool was deemed most appropriate due to its application to quantitative studies. It considers the quality of each study based on different domains; research question, selection bias, study design, blinding, confounders, data collection methods, and withdrawals and drop-outs. The tool is in the form of 14 questions which are to be rated ‘yes’, ‘no’, ‘cannot determine’, ‘not applicable’ or ‘not reported’, alongside the guidance from the provided dictionary. Rating the quality and risk of bias in a study using scales only is discouraged by the Cochrane guidance (Higgins & Green, 2011). However, they advocate for the use of a domain-based evaluation tool. The QATOCCS allows the rater to summarize and critically appraise the studies based on the responses to the questions and then to provide an overall rating of ‘good’, ‘fair’ or ‘poor’. No studies were excluded based on the grounds of quality. However, quality ratings are reported and discussed in relation to interpretation of the study findings.

Due to the varied methodological design of the studies included, a meta-analysis was not deemed appropriate. Therefore, the results of the 10 studies included were

synthesized and the key findings summarized in the context of grading of methodological quality and strength of the evidence.

Table 1.

*Summary of studies included in the systematic review*

Authors	Hypotheses and study aims	Sample	Cognitive measure(s)	Emotional distress measure(s)	Significant findings (in relation to SR question)
Bowen, Neumann, Conner, Tennant and Chamberlain (1998)	What is the rate of mood disorders 6 months post injury? What risk factors would allow early identification? Is there an association between specific impairments and mood disorders?	n = 99, Mild-very severe TBI (mod-very severe 85%), 6 months post, acute admissions hospital.	Logical Memory 1 & 2 subtests from the Wechsler Memory Scale - Revised, Rey-Osterreith Complex Figure test, Trails A & B from the Trail making test and Verbal fluency using the 'FAS' test.	The Wimbledon Self Report Scale (WSRS)	38% of the sample showed some clinically significant mood disorder Significant correlations between the WSRS scores on all but one cognitive test. Associations were found between emotional state, cognitive and everyday functioning 6 months post injury.
Fordyce, Roueche & Prigatano (1983)	What is the difference in emotional distress between individuals with chronic and acute head injury? Hypothesis: individuals 6 + months post injury will exhibit greater emotional distress than those tested less than 6 months.	Case files of acute (n = 17) and chronic head injury (n = 35). (mean duration of coma 15.5 days = very severe) 15+ years post injury. Department of neurosurgery.	WAIS verbal and performance IQs and the Wechsler Memory Scale Quotient. The Trail making test, Digit symbol, block design, subtests of the WAIS, the total number of paired-associates learned over the three trials of the WMS associated learning sub-test.	Minnesota Multiphasic Personality Inventory (MMPI) self report measure	Participants 6+ months post injury (chronic) were more emotionally distressed than participants with acute head injury (less than 6 months). No significant group differences on neuropsychological measures. The results show those with chronic head injury have greater emotional distress than those with acute head injury.

Gould, Ponsford & Spitz (2014)	Having an anxiety disorders will be associated with greater impaired attention, processing speed, EF, and verbal memory.	n = 66, moderate - severe TBI, 12 months post injury, rehabilitation hospital	The Controlled Oral Word Association Test (COWAT), Hayling Sentence Completion Test, The Trail Making Test	Structured Clinical Interview for the DSM-IV-TR	12 months post TBI 27.3% had a diagnosis of an anxiety disorder. Those with post-TBI anxiety disorders had significantly slower information processing speed, reduced working memory and impaired EF. EF best differentiated those with and without post-TBI anxiety.
Himanen, Portin, Tenovuo, Taimen, Koponen, Hiellanen, & Helenius (2009)	To compare the cognitive profiles of TBI patients with a depressive symptoms to patients without a mood disorder and healthy controls. To describe attention profiles that may differentiate these groups.	mild - very severe TBI (71% moderate to very severe) with depressive symptoms n=32, TBI without depressive symptoms n = 29 and healthy controls n = 31. University Hospital	The Trail-making- test, The Modified Wisconsin Card Sorting test, The Verbal fluency tests (VT), The CogniSpeed software - simple reaction time (SRT).	The short form of the Beck depression scale and the Schedules for Clinical Assessment in Neuropsychiatry (version 2.1) (SCAN)	TBI with depressive symptoms were slower on the SRT and had poorer performances on the VT than non-depressed TBI. The non-depressed TBI performed more poorly on cognitive flexibility, attention and speed related tests than the controls. TBI with depression did not differ from the other TBI in any cognitive methods.
Hoofien, Gilboa, Vakils & Donovick (2000)	To investigate long-term mental and psychosocial outcomes for individuals with a severe TBI	n = 76, severe TBI, average 14.1 years post injury. Neuropsychological rehabilitation center	WAIS-R; Hebrew version, Rey Auditory Verbal Learning Scale, WMS-R and Purdue Peg Board Test.	The Symptom Check List 90 Revised (SCL-90-R)	The SCL-90-R showed high level of psychiatric distress in the TBI group compared with normative data. There were difficulties in verbal learning when compared with aged matched controls. The most common psychiatric symptoms were hostility, depression and anxiety. Most cognitive deficits were related to slower psychomotor reaction and processing speed

Jorge et al. 2004	To determine the clinical, neuropsychological and structural neuroimaging correlates of major depression occurring after TBI	n = 91, mild-severe TBI (55.7% moderate –severe), and control group n = 27 multiple traumas, no central nervous system injury. Hospital or a medical center	Rey Auditory Verbal Learning test, Rey complex figure test, Trail making test, Stroop color-word interference test, Wisconsin Card sorting test.	Modified version of Present State Examination, the structured clinical interview for the DSM-IV diagnoses, Hamilton Depression rating scale and the Hamilton Anxiety scale.	Major depressive disorder was significantly associated with anxiety disorders following TBI. Compared with the non-depressed group those who were depressed had lower scores on all EF tasks. Participants with major depression showed significantly greater impairment in problem solving and cognitive flexibility when compared to the non-depressed group. Major depressive and mood disorder were significantly more frequent in TBI than the control group. Participants with depression and TBI were significantly impaired in EF when compared to those with TBI only.
Mauri, Paletta, Colasanti, Miserocchi & Altamura (2014)	To explore the prevalence of psychiatric disorders in a TBI sample, to characterize neuropsychological deficits and clinical symptoms post-TBI. To compare the differences between post-TBI and primary MDD.	n = 16, mild-severe TBI (62.5% moderate – severe), control group n = 6 with MDD, Neurosurgery Department	Raven's colored matrices, prose memory, digit span and Corsi's span, verbal fluency, trail making A & B, attentive matrices, the Wisconsin card sorting test, the Tower of London test.	Hamilton rating scale for depression (HRS-D), the Beck depression inventory scale (BDI) and the Hamilton rating scale for anxiety (HRS-A), brief psychiatric rating scale (BPRS)	One month after discharge 62.5% of the TBI group were diagnosed with MDD, 50% after 3 months and 43.75% after 6 months. Controls scored significantly higher in total BDI and HRS-D but no significant difference in HRS-A. TBI-MDD group showed significantly greater impairment in trail making A, Digit span, Corsi's span, verbal fluency and token test. The main findings are that MDD and total mood disorders were significantly more frequent in TBI compared to controls.



Ponsford, Draper & Schoneberger (2008)	To explore the association of injury severity, demographic factors, cognitive and psychiatric functioning with functional outcomes 10 years post mild-severe TBI. Hypothesis: poorer functional outcome will be associated with poorer performance on tests of information processing, attention memory and EF and higher levels of emotional distress compared to controls.	n = 60, mild - severe TBI Mean PTA indicates TBI severity = very severe average 10.38 years post-injury, control group n = 43, hospital	Digit span and digit symbol (subtests from the WAIS - III), Trail making task, Sustained Attention to Response Task, Hayling and Brixton test, Porteus Maze Test - Vineland revision and Controlled oral word association test	The Hospital Anxiety and Depression Scale (HADS)	There were significant differences in performances on tests of information processing speed, attention, memory and EF. There was a strong relationship between cognitive status and functional outcome - slow processing speed was the most strongly associated with poorer outcomes. The presence of anxiety on the HADS was strongly associated with poorer outcomes. TBI participants had lower scores on the cognitive tests and more emotional distress than the healthy controls.
Spitz et al 2013	Hypothesis: cognitive impairment would have a direct effect on psychosocial outcome—by restricting occupational and social activities—as well as an indirect effect—by restricting the utilization of coping strategies and accurate appraisal of stressful situations.	n = 97, mild - severe TBI (89% moderate – severe), average 19.29 months post injury, outpatient	BIRT Memory and Information Processing Battery-List Learning subtest, The Hayling Sentence Completion test from the Hayling and Brixton tests, Controlled Oral Word Association Test, Trail Making Test A & B, Digit Span subtest from the WMS-III, Symbol Digit Modalities Test-Oral Version	The Hospital Anxiety and Depression Scale (HADS)	Scores on the HADS did not differ significantly based on injury severity. Less frequent use of adaptive coping strategies and greater use of non-productive strategies predicted higher depression. Greater use of non-productive strategies predicted higher anxiety. Poorer performance on Total Recall, Recognition Memory, Trails B, and the SDMT directly predicted higher depression. Performance in Recognition Memory, the Hayling B, Trails A, Trails B, and the SDMT predicted higher anxiety.

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Wood and Rutterford (2006)	To explore the relationships between psychosocial, neurological and cognitive functioning at the very late stages of recovery after TBI.	n = 131, mild-severe TBI (85.5% moderate-severe), 10+ years post-injury. Clinical archives at a regional neurotrauma center and psychology assessment service.	Vocabulary, Similarities, Digit Symbol, Block design, Matrix reasoning and digit span subtests of the WAIS-III. Hayling and Brixton, Trail making tests, SCOLP, Brixton Spatial Anticipation test	The Hospital Anxiety and Depression Scale (HADS)	Community integration, satisfaction with life, depression and employment were significantly predicted by cognitive domains. Working memory was the only significant contributor. Participants with working memory difficulties seemed to have a low perception of their ability to deal with situations effectively, which leads to low mood and dissatisfaction with life. A causal relationship between low mood and memory cannot be inferred.
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Table 2.

## Summary of QATOCES Rating

Criteria	Bowen et al.	Fordyce et al.	Gould et al.	Himanen et al.	Hoofien et al.	Jorge et al.	Mauri et al.	Ponsford et al.	Spitz et al.	Wood et al.
Clear research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Study population defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Participation rate above 50%?	Yes	No	CD	Yes	Yes	Yes	Yes	Yes	NR	Yes
Inclusion and exclusion criteria prespecified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sample size justification?	No	No	No	No	No	No	No	No	No	Yes
Exposure of interest measured prior to outcome?	No	No	No	No	No	No	No	No	No	Yes
Timeframe between measures sufficient?	No	No	No	NA	No	Yes	Yes	No	No	NR
Different categories of exposure?	Yes	NA	NA	Yes	NA	NA	NA	No	Yes	Yes
Exposure measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Exposure assessed more than once?	No	No	No	No	No	Yes	Yes	No	No	Yes
Outcome measures clearly defined?	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Outcome assessors blinded?	NA	Yes	CD	CD	CD	CD	NR	NR	NR	NA
Follow-up loss under 20%?	NA	NA	NA	NA	NA	NR	No	NA	NA	NR
Measurement of confounding variables?	No	NR	Yes	Yes	NR	Yes	NR	NR	Yes	Yes
Overall quality rating	Poor	Poor	Poor	Fair	Poor	Fair	Poor	Poor	Fair	Fair
Overall quality rating in relation to answering the SR question	Poor	Poor	Poor	Fair	Poor	Fair	Poor	Poor	Poor	Poor

## Results

Review of the literature identified a total of 10 peer-reviewed articles which are included in the current review. Each study measured both the cognitive processes involved in EF and emotional outcomes in an adult TBI sample, the majority of whose injury was deemed to range from moderate to very severe. Only two of the studies were published prior to 2000 and the remaining eight studies were published between 2000 and 2014. Table 1 presents the main characteristics of each study: hypotheses and aims, sample, EF measure, emotional distress measure and the main finding and conclusions Table 2 presents the overall classification of quality in accordance with QATOCCS and a second rating of quality in relation to answering the review question . It is clear that, from the 10 studies reviewed, none specifically aimed to explore the links between EF and emotional distress as their main focus. Five out of the 10 sought to explore outcomes after TBI across a number of domains: psychosocial functioning, neurological and cognitive (Bowen et al., 1998; Hoofien et al., 2000; Ponsford, Draper & Schoneberger, 2008; Spitz, Schoneberger & Ponsford, 2013; and Wood & Rutterford, 2006). In comparison, the remaining five studies had a more specific focus on cognitive functioning (including EF processes) and emotional distress (Fordyce, Roueche & Prigatano, 1983; Gould, Ponsford & Spitz, 2014; Himanen et al., 2009; Jorge et al., 2004 and Mauri et al., 2014).

### Description of the Study Characteristics

All studies used more than one measure of EF, the most commonly administered measures included the Trail Making Test (9 studies), Haying and Brixton Sentence Completion (4 studies), The Controlled Oral Word Association Test (3 studies) and Verbal Fluency (3 studies). Subtests from the Wechsler Adult Intelligence Scale, both the revised and fourth edition (WAIS, Wechsler, 1981) were used by five studies. These subtests included: block design and digit span, which measure a number of cognitive processes

including: working memory, attention, cognitive flexibility and perceptual reasoning. All studies used standardized measures of EF, or measures of the cognitive processes associated with EF.

The most commonly used measure of emotional outcome was the HADS (Zigmond & Snaith, 1983) which was employed by three studies. All studies used both the anxiety and depression scale of the HADS, which consists of 14 self-report items. The Symptom Check List 90 Revised (SCL-90-R, Derogatis, 1977) was used by one study and this, like the HADS, is a self-report measure but also encompasses other psychiatric domains including interpersonal sensitivity and paranoid ideation, as well as anxiety and depression. Two of the studies used the Hamilton Rating Scale for Depression (HRS-D, Hamilton, 1960), and the Hamilton Rating Scale for Anxiety (HRS-A, Hamilton, 1959) which, unlike the previous measures, are clinician rated rather than self-report. The structured clinical interview for the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association, 2000) was used in two studies to measure emotional distress and this is also clinician rated. The less commonly used measures of emotional distress used are detailed in table 1.

### **Sample Descriptives**

Across the 10 studies a total of 749 participants with TBI were included ranging in age from >15 years (Fordyce, et al., 1983), 16-65 years (Bowen et al., 1998) or more typically >18 years. One study did not provide the age range for the complete sample and only provided the mean age of participants, 36, (Jorge et al., 2004). Another key inclusion criteria for the systematic review was that the majority of participants were required to have sustained a TBI that was moderate or above in severity. All included studies met this criteria. However, seven of the ten studies stated that the range of TBI severity was from mild to severe with the majority of the participants being rated as moderate to severe (see

table 1). One study included moderate to severe TBI, and one study only recruited individuals with severe TBI. One study did not state the severity of the TBI but reported that accurate coma data was only available for 22 out of the 37 participants, and the mean duration of coma was 15.5 days which places them in the very severe category of TBI (Fordyce et al., 1983). A common strength identified in all of the included studies was a clear description of the TBI participant sample and the measures used. However, a weakness identified across all studies was that there was no justification of sample size or evidence of a power calculation.

### **Study Designs**

Information on study design was extracted in order to inform conclusions regarding the nature and strength of the evidence for the role of EF in emotional distress. Nine studies used a cross-sectional design to explore their study aims and hypotheses, and one study used a prospective case-controlled surveillance design. Four studies included a control group as part of their design: healthy controls (Himanen et al., 2009; Ponsford et al., 2008), individuals who had experienced trauma but no TBI (Jorge et al., 2004) and individuals with major depressive disorder (MDD, Mauri et al., 2014).

Only three of the 10 studies assessed their participants on more than one occasion, measuring over several time points which added to the methodological strength when rating the overall quality of these studies. If EF difficulties are a vulnerability factor, they should be present prior to the onset of emotional distress rather than EF difficulties being a consequence of emotional distress. Mauri et al. (2014) compared two groups over several different time points. They assessed the TBI group at baseline, three months and six months, and the control group who had a diagnosis of major depressive disorder (MDD) at baseline, one month, three months and six months. Their results showed that MDD was diagnosed in the TBI sample 62.5% after one month, 50% after three months and 43.75%

after six months. The post-TBI MDD participants displayed significantly greater deficits in trail making A, Digit span, Corsi's span, verbal fluency and token test, when the scores were averaged over the three time points, when compared with the MDD group. The main finding from this study was that total mood disorders occurred significantly more frequently in the TBI group compared to the control group. Mauri et al. (2014) suggested that this could be explained by neuropathological processes which are linked to TBI and a risk factor to developing mood disorders. It is important to note that, although the quality of this study was strengthened by the use of a control group, only 16 TBI participants were included and only six included in the comparison group. It was unclear whether this sample was large enough to power the chosen analysis. The quality of this study was rated as 'poor' using the QATOCCS and therefore the findings reported within this study must be interpreted with caution. It is important to note, that the QATOCCS was used to rate the quality of the studies when considered alongside the systematic review question, rather than the overall quality of the study.

The second study to use multiple assessment points was Jorge et al. (2004), who compared a TBI group and control group, who had suffered trauma but not one that resulted in a TBI, across four time points: baseline, three months, six months and 12 months. Assessment was obtained for 80% of the TBI group at the 12 month follow-up. Their aim was to explore the clinical, neuropsychological, neuroimaging correlates of MDD following TBI. They found that 33% of the 91 TBI participants experienced an MDD in the first year post injury and those with MDD were more likely to have comorbid anxiety disorders. EF and memory was measured at the three month follow-up and those with MDD had significantly more impaired EF. In line with previous research, they also suggested that MDD and EF impairment may be related to the same pathophysiological mechanism (changes to the fronto-striatal-thalamic circuits), and certain changes in the volume of the left pre-frontal cortex seen in MDD seem to add to these cognitive deficits.

However, only an association is demonstrated and the direction of causality between EF and MDD is unclear. The use of assessment at multiple time points, and a control group of individuals who had experienced trauma but unrelated to TBI, are key methodological strengths. However, it seems that EF and depression were only analyzed at 3 months, rather than across the multiple time-points which would have increased the strength of this study further with regard to answering the systematic review question. The sample of participants was also larger than the previously mentioned study and therefore adds weight to the presented evidence.

### **Evaluation of Methodological Quality**

Eight studies were rated as methodologically ‘poor’ and two were rated as ‘fair’. All studies had strength in clearly stating the objective of the paper, having a clearly specified study population and having reliable and valid measures which were clearly described. The two studies that were rated as ‘fair’ (Himanen et al., 2009; Jorge et al., 2004) had specific areas of strength in a number of areas including; implementing a control group, larger sample size and measuring and making adjustment for confounding variables. They also focused on aspects of EF and emotional distress, rather than overall outcome, which added strength to their quality in reference to answering the systematic review question. The remaining eight studies overall had a greater number of weaknesses including: low sample size, no clear reporting or adjustment of confounding variables, not measuring over multiple time point and no control group implemented.

Nine studies used a cross-sectional design and one study used a case-control design. A particular weakness of this is that causality cannot be inferred. None of the study aims or hypotheses set out to explore EF as a vulnerability factor to emotional distress and therefore do not set out to specifically answer the systematic review question: does EF impairment act as a vulnerability factor to emotional distress after a TBI? For this



reason, all of the studies were rated as either ‘poor’ or ‘fair’ using the QATOCCS when considered alongside the systematic review question.

### **Study Findings**

It is important to note that, due to the cross-sectional design used, the studies are only able to state whether there was an association between EF and emotional distress, and not the direction of this association. Seven out of the ten studies reported a significant association between aspects of EF and emotional distress (Bowen et al., 1998; Gould et al., 2014; Himanen et al., 2009; Jorge et al., 2004; Mauri et al., 2014; Spitz et al., 2013; and Wood & Rutterford, 2006). The remaining three studies found no association between EF and emotional distress (Fordyce, et al., 1983; Hoofien et al., 2000; Ponsford et al., 2008).

Of the studies that found a significant association between EF and emotional distress, Himanen et al. (2009) and Jorge et al. (2004) were the only two studies where the methodological quality was rated as fair using the QATOCCS in relation to the current review’s research question. The other eight studies included in the review were given a rating of ‘poor’. Both of these studies had a stronger focus on the relationship between EF and emotional distress rather than the approach taken by the majority of the reviewed studies, which was to measure a wide variety of variables in order to assess general functional outcome. Both studies demonstrated methodological rigor and employed a control group as part of their research design, which added strength to the findings reported. Although the study sample was not justified, the sample sizes for both were larger than some of the other studies  $n = 118$  (Jorge et al., 2004) and  $n = 92$  (Himanen et al., 2009). Both studies concluded that there was a significant association between emotional distress and the more demanding processing and cognitive flexibility tasks. Despite the ‘fair’ rating, the findings of these two studies must be interpreted with caution due to the cross-sectional design employed. Himanen et al. (2009) stated that there was a

significant difference between the TBI groups with and without depressive symptoms on three computerized tests: simple reaction time, visual recognition speed of letters, and the total hit rate on a vigilance test. They reported that the effect of depressive symptoms seemed to be limited to attentional functions. Specifically, on the simple reaction time task, there was a significant difference between the TBI groups with and without depressive symptoms. However, there was no difference between the TBI group without a mood disorder compared to the control group. They proposed that this supports the possibility of a prefrontal-subcortical circuit being linked with depression and that depressive symptoms seem to have an impact on simple processing or vigilance tasks, while complex cognitive tasks, which require more flexibility are more specific to TBI itself.

Jorge et al., (2004) acknowledge some of their study limitations including a potentially biased sample where the majority were young, male and Caucasian. A strength of this study was the measurement over several time points but they state that they were unable to complete the longitudinal data sets for 16 (21.6%) of the 74 participants. As well as assessment measures, this study also utilized neuroimaging in their methodology. They compared two TBI groups, one with depressive symptoms and one without. They found no differences between the non-depressed versus depressed group in total brain volume, grey matter or white matter, or in temporal, parietal and occipital lobe grey matter between the two groups. However, those with depression had significantly decreased frontal grey matter volumes and smaller left frontal grey matter volume compared to the non-depressed group. They stated that it was unclear if this reduced prefrontal volume in the group with depressive symptoms was the result of pathophysiological mechanisms as a result of the TBI or of a pre-existing vulnerability to developing a mood disorder prior to the TBI. They carried out further analyses and found no significant differences in psychiatric histories between the two groups. They concluded that differences in frontal lobe volume did not appear to be present prior to the TBI and they hypothesized that the decreased frontal lobe

volume in the left frontal lobe three months post injury was due to resolving traumatic lesions. This is an important finding in relation to the systematic review question as from their findings they conclude that neuropathological processes associated with TBI may also be a contributing factor to the development of mood disorders. They also suggested that EF impairment and depression may be related to the same pathophysiological mechanism. These two studies provide interesting and tentative evidence for an association between EF and emotional distress and also point to an underlying mechanism that might account for any such association and possible evidence of causality.

The remaining five studies which reported a significant association between aspects of EF and emotional distress were rated as methodologically ‘poor’ with regard to the aim of the current systematic review. Three of them focused on ‘functional outcomes’ across a variety of different domains and cognitive processes, and emotional distress was one of many variables explored (Bowen et al., 1998; Spitz et al., 2013 and Wood & Rutterford, 2006). The main focus of these studies was looking at broader outcomes post-TBI: neuropsychological assessment, employment status, quality of life, everyday functioning, life satisfaction, community integration and emotional distress, rather than a focus on EF and emotional distress.

Bowen et al. (1998) focused on the risk factors for mood disorders six months post TBI. One of their main findings was that those unoccupied (not in full-time work, study or with caring responsibilities) pre-injury were more likely to report emotional distress post injury. Associations were found between emotional state, and cognitive and everyday functioning, perhaps suggesting that better cognitive functioning in general, including EF ability, may be associated with a better emotional state. However, as with previous studies, there is a lack of predictive power due to the cross-sectional nature of the design and the direction of causality cannot be determined. Spitz et al. (2012) aimed to examine

the relationships among cognition, coping strategies and emotional adjustment on average 19 months post TBI. Their findings stated that greater impairments in cognition directly predicted higher levels of anxiety and depression. They also found that EF was the only cognitive measure related to coping, with poorer EF skills being associated with the use of less adaptive coping strategies. This study was limited due to not meeting statistical power and the lack of a control group. Wood and Rutterford (2006) explored the later stages of recovery post-TBI using a range of measures. An indirect relationship was observed between working memory, life satisfaction and depression. They proposed that individuals with working memory deficits may have a low perception of their coping abilities, which in turn could perhaps result in dissatisfaction with life and subsequently low mood. There appears to be some association between working memory and depression but a causal relationship between the two cannot be inferred, and it does not suggest that EF impairment is a vulnerability factor to emotional distress. These four studies show some evidence of an association between EF and emotional distress. However, this was not the main focus of the studies and part of a much wider aim of exploring outcome after TBI. Wood and Rutterford (2006) did explore a particular aim relating to cognitive impairment, but hypothesized that cognitive impairment would indirectly influence the multidimensional outcome by mediation of appraisal and coping, rather than cognitive impairment itself being a vulnerability factor to poorer outcomes. Their analyses found that depression was significantly predicted by working memory. However, mediation analyses revealed that the association between working memory and depression was mediated by self-efficacy. The evidence it provides regarding impaired EF as a vulnerability factor to emotional distress is extremely limited. There was a broad focus for the outcome variables rather than a specific focus of emotional outcome and therefore, the quality rating for these studies was rated as 'poor'. Gould et al., (2014) found an association between EF and emotional distress and carried out further analysis using akaike weights and akaike

information criterion for each cognitive model. They found that the EF model was the best approximating model, followed by attention and working memory, and then the information processing speed model. However, this study was exploratory in nature and the design meant that the direction of causality could not be inferred.

Three studies found no association between EF and emotional distress and these were rated as methodologically ‘poor’ (Fordyce et al., 1983; Hoofien et al., 2000; Ponsford et al. 2008). Hoofien et al., (2000) focused on a range of long term outcomes post-TBI: psychiatric symptomology, cognitive abilities, vocational status, family integration, social functioning and independence in daily routines. Again, due to the cross-sectional design and the lack of clearly stated hypotheses related to EF and emotional outcome, this study was rated as ‘poor’ in its methodological quality. The study indicated a high level of psychiatric distress in the TBI participants when compared with the normative data. Although this study measures aspects of EF and emotional distress, it does not explore or report an association between the two, and therefore provides no evidence to support the main aim of this systematic review.

Ponsford et al., (2008) explored functional outcomes 10 years post-TBI and focused on a number of domains: functional, disability, demographic variables, cognitive abilities and emotional distress. A healthy control group was utilized in this study to identify whether the cognitive abilities and functional outcomes were related to TBI. They found significant differences in EF between the groups and a strong relationship between cognitive status and functional outcome, with slow processing speed being the most strongly associated with poorer outcomes. The presence of anxiety was also strongly associated with poorer outcomes. The main focus of the data exploration was to determine the predictors of functional outcome, rather than whether EF impairment predicted greater

emotional distress, and therefore they did not explore the association between the two and the direction of causality cannot be inferred.

In comparison to the previously mentioned studies, Fordyce et al. (1983) focused mainly on emotional distress and neuropsychological impairment rather than overall functional outcome post-TBI. Their results showed that participants more than six months post injury were more emotionally distressed than those less than six months post injury. However, they found no significant group differences on neuropsychological measures between the chronic TBI group (>6 months post injury) and the acute TBI group (<6 months post injury). One of the key limitations of this study is the small sample size ( $n = 52$ ) and therefore this must be taken into account when considering the findings.

## **Discussion**

### **Summary of the systematic review main findings**

This systematic review sought to evaluate the quality of the evidence regarding the potential contribution of EF to vulnerability to poorer emotional outcomes after TBI by evaluating the methods and findings of 10 studies. Seven studies reported a significant association between aspects of EF and emotional distress, and three reported no such association. Eight were rated as ‘poor’, when considered against the aim of the current review, due to methodological weaknesses including: no clear focus on EF and emotional outcome, small sample size, no control group and no inclusion of power analyses. Two studies were rated as ‘fair’ quality. The findings of the ‘fair’ quality studies indicated that there is an association between emotional distress and the more complex cognitive processing tasks. All but one study used a cross-sectional design, which, as discussed, meant limiting the extent to which a causal relationship could be inferred. Only one study

(Wood and Rutterford, 2006) attempted to infer the direction of causality between EF and emotional distress with the use of moderation analyses. However, the results did not support a direct link between EF and emotional distress as the relationship was mediated by self-efficacy. It is therefore concluded that there is currently insufficient evidence to affirm that EF is a specific vulnerability factor for emotional outcomes post-TBI, but that there is weak-moderate evidence of an association between EF and poorer emotional outcome.

### **Key findings in relation to the literature**

One of the key findings from this review was the lack of literature exploring specific EF processes and the impact they have on emotional distress in an adult TBI population. It is therefore difficult to build a model based on the available evidence on the impact of impaired EF as a vulnerability factor to emotional distress. There is a clear lack of consensus around the concept of EF and what it encompasses (Mueller & Dollaghan, 2013). This was evident in the current review due to the diverse range of assessments used to measure EF processes. No two studies used exactly the same measures. Therefore, what is lacking is a specific hypothesis about which aspects of EF, or model of EF, might infer an association with emotional distress.

Outcomes in TBI are highly variable and can involve multiple different brain areas and consequently very different profiles of strengths and difficulties across the varied EF measures. The majority of studies set out to look at predictors of outcome and selected key areas to measure that are likely to be implicated. It seems that they mostly selected measures typically used in clinical practice. It is perhaps for this reason that the majority of studies reviewed tended to focus on outcomes across multiple domains rather than specifically focusing on EF or emotional outcome. This approach does provide us with a

broad view of outcomes post TBI but perhaps, as this review has described, they overlook the finer detail of what is going on in specific processes.

As well as variability in the profiles of strengths and difficulties, there was also variability in the sample location, which could have possibly influenced the findings and comparability across studies. First, the studies reviewed were carried out in various countries including; Australia, Italy, Israel and United Kingdom and, therefore, it is possible that the findings presented in each of these studies may be difficult to generalize to a wider population. The location of recruitment also varied from inpatient services to outpatient clinics and psychology assessment centers. Another area of great variability within recruitment of the sample was the variability in time since injury some were six months post injury and other studies included participants 15 years post-injury. It is important to be mindful that the conclusions drawn from each study may only be relevant to the specific population they describe and any further interpretation of these results must be treated with caution.

All but one study used a cross-sectional design. Cross-sectional designs have strengths and provide a natural view of the research focus without the researcher influencing what happens and, therefore, the measurement of the variables should be unbiased by the presence of the researcher (Field, 2009) .. However, a limiting factor is that by using a cross-sectional design a causal relationship cannot be inferred. The study design make it difficult to conclude the direction of the association and whether it relates to: general impairment severity or the effects of impairment on psychosocial factors and therefore mood, or specific vulnerability relating to EF.

The two studies that were rated as methodologically stronger ('fair') both had a greater focus on EF processes and emotional distress, rather than looking at general outcomes post-TBI. They both used a control group and used validated measures of EF



rather than only using measures of cognitive abilities associated with EF e.g. sub-tests from the WAIS (Himanen et al., 2009; Jorge et al., 2004). Jorge et al., (2004) strengthened the quality of their study design by recruiting a control group that had experienced similar trauma to the TBI group but had not sustained a TBI. This design helps us to understand whether the differences seen are associated with the experience of trauma or are more to do with sustaining a TBI and the associated cognitive deficits. Their results suggested that mood disorders occurred more frequently in those who had sustained a TBI in comparison to those who had experienced another form of trauma. Further studies would benefit from employing a similar design to ascertain what might be the underlying reasons for the individual experiencing increased emotional distress. As no clear causal link can be inferred between emotional distress and impaired EF from the literature reviewed, it could suggest that increased emotional distress may not be as a direct result of EF impairment. The poorer emotional outcomes reported by the reviewed studies may be more of a reflection on the individual's level of overall impairment and their general reduced ability, which may have resulted in: loss of employment, reduced social support, limited physical capabilities, etc., and subsequently it may be these factors which result in the individual becoming more depressed. It also might be cognition in general that is associated with emotional outcome via the person's experience of loss and change post-TBI, rather than specific EF processes.

Previous research has explored the relationship between EF and coping. Some research has shown an interaction between EF impairment and the use of less adaptive coping styles (Krpan et al., 2007). In the current review, Gould et al., (2014) stated that individuals who have experienced a TBI may be more likely to develop anxiety disorders because they are using all their cognitive resources to cope with everyday life, and any additional stressors may cause them to become more anxious and experience emotional distress as a result. In line with this, Spitz et al., (2013) also found that the use of adaptive

coping skills had a greater impact on depression for individuals with poor processing speed. Wood and Rutterford (2006) found self-efficacy to be a mediator in the relationship between EF and emotional distress, which also suggests that it is perhaps an individual's ability to utilize their coping skills that has a greater impact on emotional distress rather than EF itself (see figure 2). Although these studies were rated as 'poor', these findings suggest the importance of considering the influence coping can have on emotional distress in a TBI population. This research could suggest it is the negative impact the EF has on an individual's ability to function on a daily basis, rather than the EF itself, that causes emotional distress (Knouse et al., 2013).

Two of the studies within this review looked at common underlying neuroanatomical networks in EF and depression (Jorge et al., 2004; Mauri et al, 2014) that perhaps suggest that acquired EF deficits involving certain frontal systems might lead to exacerbation of, or vulnerability to, depressive symptoms. It is suggested that increased risk of emotional distress post-TBI is likely to be due to the frontal systems being most vulnerable to damage and also the systems that are known to be associated with psychiatric disorders (Mauri et al., 2014).

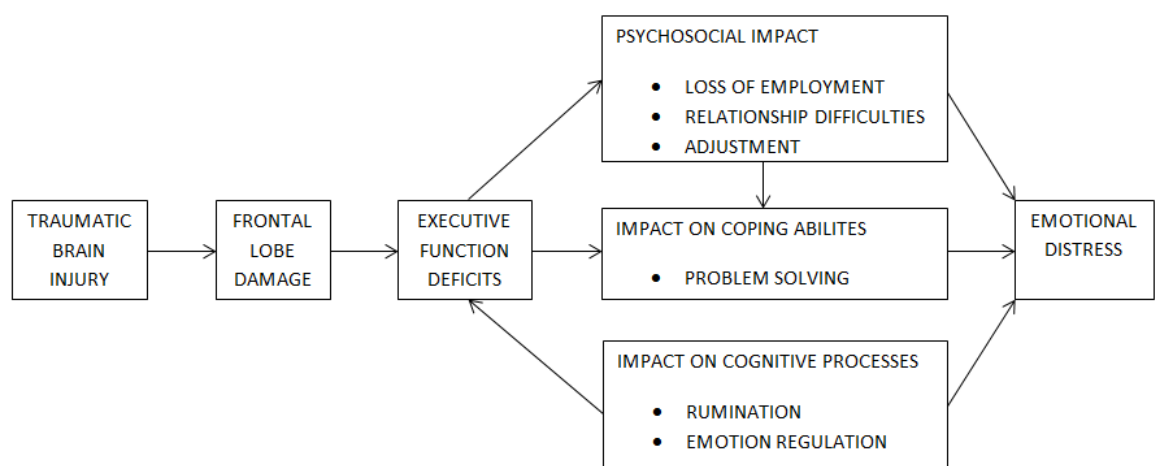


Figure 2. Summary of the different pathways by which EF is hypothesized to impact emotional distress

## **Study Limitations and methodological issues**

A limit of the current review is that there was a low threshold for inclusion which meant that studies that did not directly answer the question were included due to measuring the variables of interest (emotional distress and EF). The systematic review is therefore more accurately described as a review of studies looking at the association between EF and emotional outcome. One limitation of the current review is that it was undertaken by one individual when, ideally, it is suggested that studies would be reviewed by at least two reviewers (Thomas, Ciliska, Dobbins, & Micucci, 2004). The QATOCCS tool used to assess the quality of the studies also implies the need for a second rater to reduce possible bias. The raters are advised to evaluate the study using the guiding questions and then come to a mutual quality rating for each study. However, in the current review, the quality rating of the studies is based on the interpretation of one individual, so possible bias must be acknowledged. It would be more robust to have a second rater validating the paper selection and quality rating. However, due to the constraints of the current study, review by multiple individuals was not possible and, despite the systematic approach utilized, it must be acknowledged that the findings and conclusions drawn from this literature review are from the perspective of one individual.

A second potential limitation is the exclusion of unpublished literature and studies not published in English. By excluding these studies, there may be publication bias which may decrease the generalizability of the findings of the systematic review (Hopewell, McDonald, Clarke & Egger, 2007). Although a range of search terms were used to capture all relevant studies, it is possible that the search terms included may not have captured all the diverse ways that EF might be conceptualized and thereby potentially excluding papers that are focused on different areas of EF.

## **Conclusion and future implications for research and clinical practice**

The present study evaluates the current evidence on impairment of EF as a vulnerability factor to emotional distress in a TBI population. From this review it seems that there is currently no research that has specifically explored EF as a vulnerability factor to emotional distress post-TBI and, consequently, there are several potential directions for future research. First, it is recommended that more consensus is needed on robust measures of EF and what the key processes which require measuring are when we are exploring the impact of EF on other variables. Secondly, it is recommended that more experimental research is needed looking at specific EF processes, rather than overall cognitive functioning, to determine if there are specific EF processes, that act as a vulnerability factor. It would also be beneficial to look at specific areas of emotional distress rather than looking at this in general terms, such as rumination or selective attention to threat. Thirdly, there is a need for more robust methodological designs, such as the use of longitudinal studies and control groups, in order to strengthen the quality of the evidence. These areas of future study would enable a better understanding of the underlying processes that may impact upon an individual's well-being after they have experienced a TBI and thus guide the development of rehabilitation services to ensure the best quality treatments are being provided to meet all the needs of the service-users.

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## **Chapter 2. Bridging Chapter**

The systematic review focussed on reviewing the literature to ascertain whether EF impairment is a vulnerability factor to emotional distress in a TBI population. Having completed the review it is clear that there is no current research that specifically answers this question. The majority of the research reviewed demonstrated evidence of an association between EF and emotional outcome but the lack of focus to possible specific underlying mechanisms linking specific EF processes with particular emotional processes was not present, and therefore it was not possible to infer causality.

The reviewed studies outlined a number of possible hypotheses that might account for these associations such as: specific areas of the brain that are associated with emotional outcome and also EF difficulty (Jorge et al., 2004; Mauri et al, 2014): EF difficulties relating to overall impairment and emotional outcome being associated with psychosocial outcome (Hoofien et al., 2000; Ponsford et al., 2008) and EF having an impact on how an individual is able to implement effective coping strategies (Gould et al., 2014; Spitz et al., 2014; Wood & Rutterford, 2006). These findings demonstrate the need for research to take a more focused look at specific EF processes that might be involved in vulnerability to threat response and possible emotional distress post- TBI. Therefore, the current research project aims to explore specific aspects of EF impairment and the impact these deficits have on attention to threat in a TBI sample.

### **Chapter 3.**

**Empirical paper prepared for submission to: Journal of Experimental and Clinical  
Neuropsychology**

**The impact of executive functioning on attention to threat in an adult traumatic brain injury population: an experimental group design**

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## Abstract

**Objective:** To test the contribution of executive function (EF) to selective attention to threat by exploring the difference between a healthy comparison group and individuals who have sustained a traumatic brain injury (TBI) with EF difficulties.

**Method:** 18 TBI and 34 healthy participants were recruited from inpatient behavioral rehabilitation units and community settings, and completed measures of general intellectual functioning, EF, emotional symptoms and the dot-probe task of selective attention to threat.

**Results:** There was no significant difference on selective attention to threat, nor was there an interaction between group and condition as predicted, indicating that the presence of EF difficulties did not significantly contribute to selective attention to threat. However, the pattern of results was contrary to the predicted direction and suggested a possible difficulty to disengage from threat for the TBI group. Small effect sizes were noted suggesting the study was underpowered to detect this effect.

**Conclusions:** The pattern of results suggested a possible difficulty with disengaging from threat in the TBI group, however effect sizes were small and analyses did not detect significant effects and the study hypotheses were not supported. This suggests further investigation of EF processes and selective attention to threat is essential. Larger samples or more sensitive paradigms may be required. Attention to the role of EF in emotional disorders may be clinically warranted for some.

**Keywords:** Traumatic Brain Injury, Executive Function, Attention to Threat, Dot Probe

## **Introduction**

Impairment of executive functioning (EF) is commonly reported after an individual has suffered a traumatic brain injury (TBI) (Pare, Rabin, Fogel, & Pepin, 2009). EF encompasses a set of complex processes including working memory, planning, attention, self-regulation and cognitive flexibility (Stuss, 2011). Dysfunction in these areas is associated with frontal lobe damage (Roussel, Dujardin, Henon, & Godefroy, 2012). EF impairment can have a significant impact on an individual's everyday functioning (Ponsford, 2013) and their coping mechanisms (Krpan, Levine, Stuss & Dawson, 2007). EF is also reported to be associated with psychosocial outcome (Ponsford et al., 2008).

Lezak (1982) described EF as including the following capabilities: planning, goal-setting, inhibition and shifting attention. Baddeley's (1986) Working Memory model described there being a 'central executive' component to working memory which regulates the other subsystems and it is described as being responsible for selecting, initiating and process routines such as encoding, storing and retrieval. Baddeley and Wilson (1988) extended this describing the term 'dysexecutive syndrome' which related to three categories of observed symptoms after frontal damage: cognitive, emotional and behavioral. The 'dysexecutive syndrome' suggests a link between the central executive of the working memory and the behavioral patterns observed in 'frontal patients'. They state that these difficulties are attributable to underlying deficits in performance of the central executive and therefore individuals can have difficulty with tasks such as sustaining attention and a lack of flexibility, particularly with novel information.

EF impairment has been associated with poorer outcomes following brain injury and this is perhaps due to difficulties highlighted thus far, such as problems in working memory, planning and attention, for example. However, it has also been noticed that EF impairment might impact indirectly on emotional outcomes via coping. When comparing a

TBI group with healthy controls, Krpan et al. (2007) found that, in the TBI group, variation in coping styles was related to the variation in EF. More specifically, emotionally focused coping skills were more likely to be used by those with impaired EF than problem focused coping skills. Wolters-Gregorio et al., (2016) found some association between changes in coping and self-reported EF but not through neuropsychological testing. Wood and Rutterford (2006) found a possible interaction between coping and depression and, in particular, self-efficacy as a mediator between EF difficulties and poorer emotional outcome. In line with Krpan's work, this may be partly explained by deficits in problem solving, a process associated with EF, overlapping with the difficulty in using problem orientated coping, which requires problem solving ability.

Some research has argued that EF difficulties are associated with impaired attention regulation and that the whole concept of EF is often conceptualized in terms of attentional processes (Bessel, Watkins & Williams, 2008; Cicerone, Levin, Malec, Stuss, & Whyte, 2006; Gyurak et al., 2009; Hofmann, Friese, Gschwender, Wiers & Schmitt, 2008). Attentional control has been described as the ability to direct attention or inhibit responses (Derryberry & Reed, 2002) and being able to do this is said to be indicative of intact EF (Miyake et al., 2000). Impaired attentional control can interfere with goal directed behavior (Eysenck, 1992) and thus, have an impact on an individual's daily functioning. Posner, Sheese, Odludas and Tang (2006) proposed a model of attention, stating that specific neural areas are involved in attention functions. One particular attentional process described was the 'executive attention network' and they proposed it regulates the activity in other brain networks involved in thought and emotion. They reported that strong connectivity to the frontal and parietal brain areas and higher levels of executive attention were related to emotional regulation. However, the interaction of selective attention to threat and EF has not been examined in any great detail.

## **Selective Attention to Threat and Anxiety Disorders**

Selective attention towards threat is an adaptive evolutionary function (Richards, Benson, Donnelly, & Hadwin, 2014) and involves prioritizing one's attention towards the threatening stimuli, a response particularly pertinent if the stimuli are survival related (Dolan & Vuilleumier, 2003). The brain has a limited processing capacity and this can be a major cognitive difficulty when faced with a substantial amount of sensory information (Hutton, 2008). The brain is able to cope with these demands by selectively attending to stimuli that are deemed important (Vuilleumier, 2005). However, this can become maladaptive if an individual becomes excessively sensitive to threat (Yiend & Mathews, 2001) as is commonly seen in anxiety disorders.

Richards et al., (2014) explored theoretical frameworks and key empirical studies of selective attention to threat in anxiety disorders and identified evidence for the existence of this process in anxiety disorders. There is evidence of this across anxiety disorder including: generalized anxiety disorders (Daghighi et al. 2003), panic disorder (Teachman, Smith-Janik & Sapority, 2007), post-traumatic stress disorder (PTSD, Bardeen & Orcutt, 2011), obsessive compulsive disorder (OCD, Cisler & Olatunji, 2010), and social phobia (Becker, Rinck, Margraf & Roth, 2001). Evidence shows individuals with specific anxiety disorders are more reactive to threat stimuli which are directly related to the specific concern associated with their anxiety disorder (Bradley, Mogg, White, Groom & De Bono, 1999).

An established experimental paradigm that is used to determine whether individuals display an attentional bias towards threat is the visual dot probe task (MacLeod, Mathews, & Tata, 1986). This task records reaction times to threatening and non-threatening stimuli to detect threat sensitivity. It is suggested that the emotional meaning of a word can affect an individual's reaction to the stimuli. Individuals with high trait anxiety have a tendency

to selectively attend to threat (Koster, Crombez, Verschere, & De Houwer, 2004).

Although typically interpreted as indicating vigilance for threat, Koster et al., (2004) argue that performance could be interpreted in terms of, either vigilance for, or disengagement from, threat stimuli. Findings from studies with anxious participants appear to confirm this (Taylor, Cross & Amir, 2016). Similar findings in anxious populations have supported this concept and found that anxious individuals may have a difficulty to disengage from threat once detected, rather than a vigilance for threat (Fox et al., 2002; Salemink, van der Hout, & Kindt, 2007). Consequently it must be considered that the dot-probe paradigm results could be interpreted as a difficulty to disengage from threatening stimuli or a selective attention to threat when comparing the response times between trial conditions. Koster suggested that measurement of reaction time differences between the congruent and incongruent location does not take into account the differences between congruent, incongruent and neutral stimuli. It was suggested that faster reaction times for congruent versus neutral stimuli indicate a selective attention to threat and slower reaction times for incongruent versus neutral stimuli indicate a difficulty to disengage attention with threat. This suggests that threat sensitivity and emotional processes are affected by cognitive processes. Control of attention is considered an EF process, but currently there is limited research testing the hypothesis regarding a specific relationship between attentional control or EF and selective attention to threat.

### **The role of Executive Function and Selective Attention to Threat**

A heightened vigilance for threat could be partially understood as a failure of EF (Hutton, 2008). Research involving healthy participants found that EF was a predictive factor for threat response, and individuals with poorer EF were more vulnerable to stressors and showed a greater physiological reactivity to them (Williams, Suchy and Rau, 2009). There is evidence indicating that EF impairment in individuals with PTSD may

lead to difficulty completing tasks that involve divided attention, cognitive flexibility, working memory and planning (Kanagaratman & Asbjørnsen, 2007; Koso & Hasen, 2006). Based on Posner et al's., (2006) model of attention, and the hypothesized presence of an 'executive attention network' regulating attention in both 'cold' cognitive tasks as well as emotionally 'hot' tasks, it seems that we could predict that the presence of acquired deficits in aspects of EF would result in poorer attentional control and difficulty with emotional regulation. It is possible that difficulty with the allocation of attentional resources could result in a greater susceptibility to selectively attending to emotionally threatening stimuli. After suffering a TBI, individuals can be particularly sensitive to social threats and display increased anxiety about being negatively judged by others (Riley, Brennan & Powell, 2004). Understanding such processes could help contribute to the refining and improvement of interventions for rehabilitation. Interventions such as cognitive behavioral therapy (CBT) are based on models related to processing biases (Clark & Beck, 2010), but in the context of TBI, the acquired deficits and the interaction these might have with emotional processes need to be taken into account.

## **Aims**

The current research intends to build on the aforementioned research which proposes that individual differences in EF impact selective attention to threat (Williams et al., 2009). It aims explore whether EF difficulties contribute to selective attention to threat. The research will employ the dot-probe methodology to explore threat sensitivity to socially and physically threatening stimuli. The overall aim is to explore whether individuals with impaired EF selectively attend to threat to a greater degree than individuals without EF impairment.

## **Hypotheses**

1. Individuals with impaired EF (TBI) will show a greater selective attention to physical and social threat stimuli compared to individuals without impaired EF (comparison group) whilst controlling for anxiety.
2. Individuals with impaired EF (TBI) will show a greater selective attention towards socially threatening words, followed by physically threatening words, and then neutral words whilst controlling for anxiety, compared to the comparison group.

## **Method**

### **Design**

This study utilized an experimental between-within group (comparison and TBI) by condition (5 levels: physical threat congruent, physical threat incongruent, neutral, social threat congruent, social threat incongruent) repeated measures design. Data were collected via a computerized dot-probe task, three EF tasks, a measure of pre-morbid functioning and a measure of anxiety and depression.

### **Participants**

Two groups of participants were recruited: individuals who had sustained a TBI and a comparison group who had no history of TBI. TBI participants were recruited from three brain injury services across largely rural areas of the UK; two inpatient services for individuals with acquired brain injury ( $n = 17$ ) and one community brain injury day center ( $n = 5$ ). The comparison group were staff members at the same sites. In total 22 TBI participants completed the study (22 male) all aged between 18 and 65 years ( $M = 36$ ,  $SD$

= 10.56) and 34 healthy participants completed the study (6 male) all aged between 21 and 60 ( $M = 31.7$ ,  $SD = 8.94$ ). The TBI group were all male and the majority reported their average number of years in education as between 11 and 14 years (83.3%) compared to the comparison group which was mostly female (82.4%) and the majority of participants had been in education for 17 years and over (85.3%). Further demographic information is reported in table 1.

All participants met the following inclusion criteria: individuals in the TBI group were required to have sustained a TBI and be at least six months post injury. The TBI severity was required to be from the moderate to severe range as classified by either the Glasgow coma scale (GCS, Teasdale et al., 2014) or by duration of post traumatic amnesia (Malec et al., 2007). If this information was unavailable, the historical records and clinicians within the team were consulted to ascertain the severity of the TBI from the available information. Individuals were required to show evidence of acquired executive functioning (EF) difficulties as indicated by the individual's score falling one or more standard deviations below the norm on a measure of EF (e.g. Dysexecutive Questionnaire, Wilson, Alderman, Burgess, Emslie & Evans, 1996, letter fluency or color-word interference test, sub-tests from the D-KEFS; Delis et al., 2001). All participants, both comparison and TBI, were required to be aged between 18 and 65 and have the ability to understand and speak verbal and written English.

Exclusion criteria were: any communication or cognitive deficits of sufficient severity to preclude participation in the study tasks, significant current mental health difficulties (such as psychosis or severe depression), substance misuse, learning disability or degenerative neurological condition. In addition, potential participants for the comparison group were excluded if they had any history of sustaining a brain injury or showed EF impairment.



## **Measures**

### **Demographic information.**

Individuals were asked to report their age, gender, ethnicity, highest level of education achieved, and the type and date of brain injury (if applicable). If the severity, nature or date of injury was unknown, this information was obtained, with permission, from the individual's clinical records.

### **Wechsler Test of Adult Reading**

The Wechsler Test of Adult Reading (WTAR, Wechsler, 2001) measures estimated pre-morbid functioning and in healthy controls measures estimated IQ based on reading ability. It takes approximately 10 minutes to administer and it requires the participant to read aloud a 50-word list. The WTAR is a valid measure of pre-morbid IQ for TBI (Green et al. 2008) and has extensive clinical validity in TBI group studies (Donnell, Pliskin, Holdnack, Axelrod, & Randolph, 2007).

### **Affective distress - Hospital Anxiety and Depression Scale**

The Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983) is a 14-item self-report scale measuring anxiety and depression which can be administered in five minutes. Each item relates to symptoms experienced over the last week, and participants are required to read a statement in each subscale and rate it on a four-point Likert scale. The maximum score that can be obtained is 21 and a score ranging from 0-7 is categorized as 'normal', 8-10 is 'mild', 11-14 is 'moderate' and 15-21 is categorized as 'severe'. The HADS has been found to be reliable for a TBI population (Skillbeck, Holm, Slatyer, Thomas & Bell, 2011; Whelan-Goodinson, Ponsford & Schonberger, 2008). It has a good internal consistency with a Cronbach's alpha of 0.82 for depression and 0.82 for anxiety (Bjelland, Dahl, Haug, & Neckelmann, 2002).

### **Executive function: Dysexecutive Questionnaire**

The Dysexecutive Questionnaire (DEX, part of the Behavioural Assessment of the Dysexecutive Syndrome (BADS), Wilson et al., 1996) consists of 20-items focusing on four areas of executive dysfunction: emotional or personality changes, motivational changes, behavioral changes and cognitive changes.

The DEX takes approximately 5-10 minutes to administer and participants are required to indicate their response using a five-point Likert scale ranging from 'never' to 'very often'. There are two versions of the DEX: one that is completed by an informant who knows the participant well, and a self-rated version. The DEX has been shown to have a good internal consistency for individuals with a brain injury, with a Cronbach's coefficient reported to be 0.91 (Bennett et al., 2005). The DEX has been found to be a valid and reliable measure of executive deficits in community, psychiatric and neurological populations (Shaw, Oei & Sawang, 2015). The comparison group completed the DEX-self and an independent rater completed the DEX-Other for the participants in the TBI group. Independent ratings were used for the TBI group due to possible impaired self-awareness that is common post-TBI (McBrinn et al., 2008).

### **Executive function: The Color-Word Interference Test**

The Color-Word Interference Test (sub-test from the D-KEFS; Delis, et al., 2001) is a version of the original Stroop test (Stroop, 1935) which measures the ability of the participant to suppress their automatic response and switching. It consists of four trials. In the first trial participants read the words of the colors which are printed in black ink. Secondly the participants name the color of the printed stimuli. In the third trial the color names are printed in a discrepant ink color and participants must name the color in which they are presented, and not read the word. Finally the participants switch back and forth

between reading the word and naming the color of the ink. The tasks are timed and longer times indicate poorer inhibition. The reliability is reported to be reasonable, with test–retest correlations of 0.70 to 0.79 (Delis et al., 2001). This test is found to differentiate between healthy participants and participants with head injuries more effectively than the original Stroop test (Bohnen, Jolles, & Twijnstra, 1992).

### **Executive Functioning: The Verbal Fluency Test**

The Verbal Fluency Test (sub-test from the D–KEFS; Delis et al., 2001) includes the sub-tests; letter fluency, category fluency, and category switching. Letter fluency is purported to be a measure of EF processes such as cognitive flexibility (Gawda & Szepletowska, 2016). Participants are asked to state as many words as they can that start with a specific letter. A higher number of words generated indicates better cognitive flexibility. This test has high reported reliability and a test–retest correlation of 0.90 (Delis et al., 2001).

### **Selective Attention to Threat: The Modified Dot Probe Task**

The Modified Dot Probe Task (Ononaiye, Turpin & Reidy, 2007) was used to measure selective attention to threat. The dot-probe programme was built and run with OpenSesame (Mathôt, Schreijf, & Theeuwes, 2012) and the stimuli were displayed on a laptop to record the participants' responses. The laptop was positioned below eye-level and approximately 60cm away from the participant. The task employs 'physical threat' (e.g. violence) and 'negative evaluation' (e.g. stupid) words from the original study (Ononaiye, et al., 2007). The threat categories were chosen in accordance with previous research which found these to be important to a brain injury population e.g. 'failure', 'mocked', 'pain' and 'violence' (Riley et al., 2004). Each of the threat words were paired with a neutral word of a similar length and frequency in the English Language (Ononaiye et al.,

2007). Gilligan (2015) used the dot probe task with an ABI population and selected stimuli based on research into threat appraisals, the same stimuli from Gilligan's study was used in the current research. There were 10 practice trials and 92 further trials which were presented in a random order and counter-balanced.

Each participant was presented with the stimuli on a laptop and instructed to stare at a fixation point in the center of the screen which stayed on the screen for 500-ms. A randomly selected word pair (font size 30) then appeared on either side of the screen (left and right), after 500ms the words disappeared and a probe "X" replaced one of the words. Each trial was either a 'negative evaluation-neutral', 'physical threat-neutral' or 'neutral-neutral' word-pair combination. In line with previous research the time was 500ms to ensure an automatic response was provided (Notebaert, Clarke, Grafton, & Macleod, 2015). Participants were asked to indicate the location of the "X" as quickly and accurately as possible by pressing the "Z" key for left and "M" key for right (each had a white sticker on to make this clearer for the participants). The next trial automatically began after 1500ms.

The experiment generated reaction times to the stimuli. Comparison of the median reaction times on all trials, including neutral, were performed to test disengagement from threat (Koster et al., 2004), and reaction times on incongruent and congruent threat trials were compared to determine selective attention to threat (MacLeod et al., 1986). The dot-probe task has been found to be a reliable measure of selective attention to threat (e.g., Notebaert, et al., 2015; Ononaiye et al., 2007).

## **Procedure**

Guidelines from the British Psychological Society's code of human research ethics (2010) were adhered to during the development and completion of the current research and ethical approval was gained from the North West – Preston National Research Ethics

Service. Written informed consent was gained from each participant after the aims and details of the study had been fully described and all questions answered. Only participants able to provide informed consent were considered for participation in the study.

Participants were informed of their right to withdraw at any point in the study and that all data would be anonymized and not be individually identifiable.

Potential participants for the TBI group were identified and approached by the clinical care team collaborator at each recruitment site. The comparison participants were recruited from the staff at the identified recruitment sites. Recruitment posters were displayed in staff areas and the clinical care team collaborator also approached potential comparison participants. All potential participants were given the participant information sheet and any interested potential participants were asked for consent to pass on their contact details to the main researcher. Once this consent was obtained, the researcher made contact with each individual, either directly or through a member of their care team, and arranged a time and venue to meet to answer any questions, and to complete the research if the participant consented. The venue was either in a healthcare setting, day center or at the person's home depending which was most convenient for the participant.

Once written consent was obtained, demographic information was collected and participants completed the WTAR (Wechsler, 2001), HADS (Zigmond & Snaith, 1983) and the DEX (Wilson et al., 1996). Participants who scored 15 and above on the HADS, indicating severe depression, were excluded. If participants did not meet the inclusion criteria after these measures were administered, they were thanked for their time, any questions were answered and further support was provided if required ( $n = 1$ ). Following this, those participants that were included in the study completed the dot-probe task (Ononaiye, et al., 2007), the color-word interference test (Delis, et al., 2001) and the verbal fluency test (Delis, et al., 2001). TBI participants were required to show evidence of EF

impairment as evidenced by a score on one of the EF measures falling more than one standard deviation below the norm.

The researcher was available throughout the administration of the measures to assist as required. The data collection was completed over one or two sessions which lasted between 30 and 90 minutes. Breaks were provided during the session as required. To conclude the session participants were de-briefed and thanked for their time. Participants were given the option to leave their contact details to be provided with a general summary of the study findings.

### **Data Analyses**

The statistical analyses were conducted with SPSS statistical software version 23. Hypothesis one was tested using independent samples comparisons t- tests on whether there was a significant differences between the two groups (TBI versus healthy comparisons) on 'negative evaluation' selective attention to threat and 'physical threat' selective attention to threat. To test hypothesis two, a between groups repeated measures analysis of variance (ANOVA) was conducted. The mean reaction times of the two groups (TBI/ comparison) were compared across the five dot-probe conditions (neutral, social threat congruent, social threat incongruent, physical threat congruent and physical threat incongruent) to determine whether there was a group by condition interaction (Koster et al., 2004). By comparing the differences between neutral, congruent and incongruent trials it will be possible to determine whether the results reflect a difficulty to disengage from threat (delay in reaction times of incongruent trials) or a selective attention to threat (faster response to congruent trials). If groups differed on anxiety they were entered as a covariate. If an overall significant interaction effect was found, post hoc tests were conducted to confirm where the differences occurred and to test the specific hypotheses regarding negative evaluation, physical threat and neutral stimuli.

G\*Power software (Faul, Erdfelder, Buchner & Lang, 2009) was used to complete the power calculation. For the main planned analyses of the repeated measures ANOVA an  $f$  value of 0.175 was entered (equivalent to a  $d$  of 0.35, small effect size, consistent with the results of Gilligan (2015)). This reported an estimated sample size for this analysis of 62 participants (31 TBI and 31 healthy). The power calculation for the secondary analyses, independent samples comparisons  $t$ - tests, was calculated with  $d$  set to 0.5, medium effect size and reported an estimated sample size of 102 participants (51 TBI and 51 healthy).

### **Data Preparation**

The data was inputted and explored for missing values. All of the dot-probe trials were reviewed and incorrect responses were removed from the analysis, which resulted in the removal of 41 trials (0.8% of all trials). Trials were also removed if reaction times were  $<200\text{ms}$  and assumed to be anticipatory errors, leading to one trial being removed. Reaction times which exceeded  $3000\text{ms}$  were also removed and assumed to be due to concentration difficulties, resulting in the removal of a 23 trials (0.5% of all trials). These cut-offs were used by Gilligan (2015), based on previous research (Koster et al., 2004), but with a higher upper reaction time limit given the possible slower processing speeds due to brain injury. The same approach was adopted in the current study. The data of one TBI participant was excluded from the study due to a high level of errors in the dot-probe task (22.82%) and one TBI participant was excluded due to not demonstrating significant EF impairment in any of the EF tasks.

## **Results**

Data were analyzed for normality and to check that assumptions for parametric tests were met. This was done via visual inspection of the histogram. This resulted in the

removal of two outliers, two TBI participants whose reaction time on the dot-probe task was much slower in comparison to other group members. This was thought to be due to difficulty with processing speed and motor function and therefore the data were removed leaving 18 participants in the TBI group and 34 in the comparison group for analysis. This resulted in the key variables for testing the hypotheses meeting the assumptions for the planned analyses. Demographic information is presented in table 1.

Table 1.

*Participant Demographic Information (TBI group n = 18, comparison group n = 34)*

		TBI – n	TBI – Sample Percentage	Comparison – n	Comparison – Sample Percentage
<b>Gender</b>	Male	18	100%	6	17.6%
	Female	0	0%	28	82.4%
<b>Number of years in education</b>					
	17 and over	1	5.6%	29	85.3%
	15-16 years	2	11.1%	2	5.9%
	12-14 years	8	44.4%	3	8.8%
	Up to 11 years	7	38.9%	0	0
		Mean	SD	Mean	SD
<b>Age at Assessment</b>		34.4	8.90	31.7	8.94
<b>Time since injury (years)</b>		18.06	9.43	-	-
<b>WTAR scaled score</b>		92.28	15.35	109.88	7.67
<b>DEX-Self</b>		-	-	9.53	6.23
<b>DEX-Other</b>		42	11.33	-	-



Independent samples t-tests were performed to evaluate whether there were significant differences between the two groups on the demographic variables. There was a significant difference in the WTAR scores for the comparison group ( $M=109.88$ ,  $SD=7.67$ ) and the TBI group ( $M=92.28$ ,  $SD=15.35$ );  $t(50) = -5.54$ ,  $p < .001$ . There was also a significant difference on the HADS-D score for the comparison group ( $M=1.5$ ,  $SD=2.22$ ) and the TBI group ( $M=4.61$ ,  $SD=3.09$ );  $t(50)=4.19$ ,  $p < .001$ .

### **Standardized Tests of Executive Functioning**

The mean and range of the scores obtained from the letter fluency test and the color-word inhibition test are displayed in table 2. This table shows that there were a range of EF scores across both samples, with as expected the mean EF score for the TBI group being lower than the comparison group on both the color-word inhibition test and the letter fluency test.

Table 2.

*Mean for the verbal fluency and color-word interference test.*

	TBI - Mean (SD)	Comparison - Mean (SD)
CW Inhibition	5.3 (3.96)	11.5 (2.80)
Letter Fluency	6.2 (3.28)	10.5 (3.28)

Independent samples t-tests were conducted to evaluate whether there were significant differences between the groups on the EF measures. As expected, there was a significant difference in the scores for color-word inhibition between the comparison group ( $M=11.5$ ,  $SD=2.81$ ) and the TBI group ( $M=5.33$ ,  $SD=4$ );  $t(50)=-6.52$ ,  $p < .001$ . There was also a significant difference in the letter fluency scores between the comparison group ( $M=10.59$ ,  $SD=3.28$ ) and the TBI group ( $M=6.12$ ,  $SD=3.07$ );  $t(50)=-4.73$ ,  $p < .001$ .

### Measures of attentional bias: Dot probe paradigm.

In accordance with previous studies, each participant's average reaction time for each trial category was calculated using the median to help control for possible outliers and avoid skew in the data (Horry & Wright, 2009). From this data the overall mean and standard deviations for each group for the different trial categories were then calculated and are presented in table 3 and figure 1.

Table 3.

*Average mean reaction time data/standard deviation across dot probe trials*

Dot Probe Trial Type	TBI	Comparison
	Mean (SD)	Mean (SD)
Neutral – Neutral Trial	606.861 (132.917)	457.044 (113.893)
Negative Evaluation – Incongruent Trial	619.556 (172.830)	460.118 (105.174)
Negative Evaluation – Congruent Trial	607.778 (135.043)	459.706 (113.830)
Physical Threat – Incongruent Trial	630.222 (193.638)	461.206 (104.922)
Physical Threat – Congruent Trial	610.000 (134.977)	455.059 (110.236)

### Hypothesis testing

1. Individuals with EF impairment (TBI) will show a greater attentional bias to both physical and social threat compared to individuals without EF impairment (healthy comparisons) whilst controlling for anxiety.

The mean attentional bias score for the 'physical threat' condition for the comparison group was 6.15 and 20.22 for the TBI group. The mean score for the 'negative evaluation' condition for the comparison group was 0.41 and 11.78 for the TBI group. A positive score indicates selective attention to threat, whereas a negative score indicates avoidance of threat. This suggests a small attentional bias to 'negative evaluation' stimuli in the

predicted direction. There was no statistically significant difference in the HADS-A scores between groups and therefore this was not added as a covariable  $t(50)=1.76, p = .09$ .

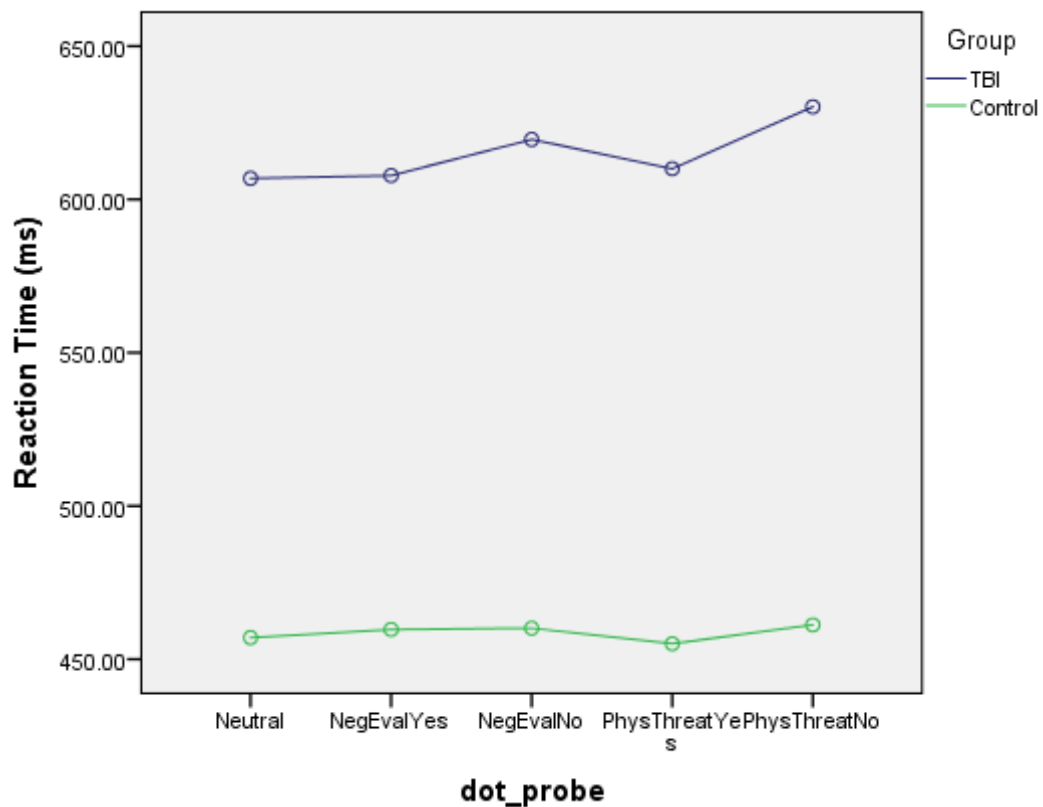
Years of education was added as a covariable and therefore an ANCOVA was conducted to evaluate whether there were significant differences between the two groups on 'negative evaluation' selective attention to threat and the 'physical threat' selective attention to threat whilst controlling for years in education. The difference between groups was not significant for either the 'negative evaluation' condition,  $F(1, 49) = 0.534, p = .468, \eta_p^2 = 0.011$ , indicating small effect. or the 'physical threat' condition,  $F(1, 49) = 0.786, p = .380, \eta_p^2 = 0.016$ , indicating negligible effect.. Therefore, hypothesis one is not supported. Consistent with this, the Cohen's  $d$  for 'physical threat' is 0.12 and 0.11 for 'negative evaluation' indicating a negligible effect size.

2. Individuals with EF impairment (TBI) will show a greater attentional bias towards socially threatening words, followed by physical threat words, and then neutral words, whilst controlling for anxiety, compared to the healthy comparison group.

To test whether the TBI group has significantly faster reaction times towards the 'negative evaluation' condition, followed by the 'physical threat' condition (i.e. indicating increased vigilance to threat), and then the 'neutral' condition, compared to the comparison group, a between-within group repeated measures ANCOVA was conducted on the reaction times from the five different dot probe conditions (neutral, physical threat congruent, physical threat incongruent, negative evaluation congruent and negative evaluation incongruent), see table 3 for average median reaction times for each trial condition. There was no statistically significant difference in the HADS-A scores between groups and therefore this was not added as a covariable, as stated previously. Years in education was added as a covariable due to the difference between groups. Mauchley's test

of sphericity indicated that the assumption of sphericity had been violated,  $\chi^2(9) = 135.57$ ,  $p < .001$  and therefore the Greenhouse-Geisser was reported. The results show that there was no significant main effect of dot probe condition,  $F(1.744, 85.448) = 0.936$ ,  $p = .385$ ,  $\eta_p^2 = 0.014$ , indicating small effect. There was no interaction effect between group and dot probe condition whilst controlling for years in education,  $F(1.744, 85.448) = 0.85.448$ ,  $p = .437$ .  $\eta_p^2 = 0.035$ , indicating small effect. As the main effect was not significant, post-hoc tests examining reaction time between trial types were not undertaken.

Figure 1. Average median reaction times and standard error scores across dot probe trials



## Discussion

The aim of the present study was to explore the relationship between EF and selective attention to threat. It was hypothesized that TBI participants would show greater attention to threatening stimuli versus neutral stimuli, compared to the comparison group. It was also hypothesized that the TBI participants would have a greater attentional bias for

socially threatening words, followed by physically threatening words, when compared to the healthy comparison group. Neither hypothesis was supported by the research findings.

Both groups demonstrated marginally faster median reaction times to the congruent threat trials for both ‘negative evaluation’ and ‘physical threat’ trials when compared to the incongruent trials, consistent with a pattern of results which indicates selective attention towards threat stimuli. There was a larger difference between the congruent and incongruent threat trial reaction times for the TBI group, perhaps suggesting a greater attentional bias towards the threat words compared to the comparison group. However, this difference was not significant and therefore hypothesis one was not supported. The two groups did not significantly differ in how they responded to the different types of threat versus neutral trials, and therefore hypothesis two was not supported.

However, although not significant, the largest difference between reaction times on the trial types for the TBI group was between the neutral trials and the incongruent trials. TBI participants responded more slowly to the incongruent trials when compared to the neutral trials. This pattern and direction of results could suggest a difficulty with disengagement from threatening stimuli, and in particular, physical threat, which is in line with the findings proposed by Koster et al., (2004). These findings, although not significant, suggest that EF difficulties may in fact impair an individual’s ability to disengage from threat rather than selectively attend to threat as was hypothesized in the current study.

Although there were no significant findings, the trend in the data was consistent with the previous research that argues that attention and EF are associated with emotional regulation (Bessel, et al., 2008; Cicerone et al., 2006; Gyurak et al., 2009; Hofmann et al., 2008). The current study was concerned with the specific idea about aspects of attentional control and the phenomenon of selective attention to threat as described in the anxiety

disorder literature, and thus attempted to answer the question – do deficits in the control of attention impact upon emotional processes of selective attention to threat in a TBI sample. Although the TBI group responded marginally quicker to the congruent threat trials in comparison to the incongruent trials, suggesting a selective attention to threat, when taking into account neutral trial performance (Koster et al., 2007) differences appear to be attributable to slower reaction times for incongruent compared with neutral, rather than faster reaction times for congruent compared with neutral and incongruent. This suggests that perhaps there might be two processes to consider: a possible selective attention to threat but also a difficulty to disengage from threat.

There were several methodological limitations in the current study that must be acknowledged. First, the two groups were not comparable so there is risk of bias in attributing the differences in dependent variables to the presence or absence of EF deficits. The main group differences were gender and education level. The TBI group were all male with a lower number of years in education and the comparison group were mostly female with a higher number of years in education. Thus, the comparisons made between the TBI and comparison group within this study must be treated with caution. Another limitation was the small sample size. Although every effort was made to recruit the required sample size, this was not achieved and, therefore, both hypotheses and all related analyses were underpowered, thus any findings must be interpreted with this in mind. However, a particular strength of this study was the focus on only recruiting from a TBI sample, rather than all acquired brain injury, as the TBI population is reported to display more extensive EF impairment. This was the primary focus of the research. Twenty-two participants were recruited to the TBI group but due to slow processing speed or difficulties with motor coordination, the data of three participants was removed, and another TBI participant's data was removed due to not displaying EF impairment on the assessment measures. The majority of the TBI group was also recruited from inpatient services, perhaps suggesting

that they may have a higher level of impairment specifically relating to behavioral issues following their TBI than perhaps those recruited from day services. This must also be considered when attempting to generalize findings to a wider population. Given what we know about EF impairment in the TBI population, it could also be that impaired processing speed (Denney et al., 2005; Hutton, 2008) has an impact on how an individual responds to stimuli rather than selective attention to threat. The results of the WTAR could perhaps also suggest a deficit in verbal comprehension that might confound the dot-probe results which to a certain extent rely on the ability to identify words relatively automatically. Future studies in TBI should attempt to control for this by screening out individuals with significant difficulties with verbal comprehension that may impact upon reaction times or by using pictorial stimuli.

Another consideration is the reliability of the dot-probe paradigm in measuring the selective attention to threat hypothesis and, as this study showed, the results could be interpreted as a difficulty to disengage from threatening stimuli (Koster et al., 2004; Booth, 2014). It is also important to consider the utility of the visual dot-probe task with a brain injury population, as although an established paradigm, to the authors knowledge it has only been used once previously with this population (Gilligan, 2015). A strength of the dot-probe paradigm was that the TBI participants were capable of understanding and completing the task due to its simple and easy to follow procedure. However, a weakness of this methodology is that TBI participants may have slower processing speed and psycho-motor functioning and therefore the task may not be measuring attention to threat in the same way it is utilized with other populations. Without robust checks for external validity, we cannot be sure of the equivalence of using the dot-probe in a TBI sample. This is something that needs further exploration.

### **Clinical Implications**

A key clinical implication from the current study is the need for consideration of EF impairment and its impact upon an individual's ability to engage with therapeutic approaches. Selective attention to threat is a key process in cognitive behavioral models of emotional disorders. The current study indicates that although individuals with TBI responded more quickly to congruent stimuli, suggesting a slight selective attention to threat, the main difference in reaction times was seen between the neutral and incongruent trials suggesting a small tendency for individuals with EF impairment to struggle to disengage from threat stimuli. Therefore, in addition to attending to the cognitive content (such as appraisals of threat to self, negative self-evaluations) and making general adaptations due to deficits in memory or attention, it may be necessary to focus on skills that aid cognitive control in emotionally demanding situations. In particular, approaches such as mindfulness, attention control techniques and other skills for down-regulating negative affect or altering capacity for metacognition should be considered (Gracey, Longworth & Psaila, 2015).

### **Future Directions for research**

This study highlights the need for further research into how the specific aspects of EF may influence selective attention to threat. Future studies should attend to some of the methodological weaknesses of the current study, in particular, by ensuring the sample size is large enough to power the appropriate analyses and detect whether EF has a significant influence on attending to threat. Employing matched control groups would help reduce confounding of group differences on EF with demographic variables which limits comparison of the groups.

### **Conclusion**

The hypothesized effects of deficits in EF on dot probe performance were not found, however methodological weaknesses render the results difficult to interpret. Non-



significant small effects in the analysis tentatively suggest attention to threat processes should be decomposed into vigilance and disengagement, and that more sensitive or reliable paradigms for measuring attention to threat processes should be used, and TBI participants with EF difficulties who are not too impaired in other domains recruited.

### **Disclosure of interest**

The author reports no conflict of interest. This research was supported by the University of East Anglia as fulfilment of the Doctoral Programme in Clinical Psychology.

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## **Chapter 4. Overall discussion and critical appraisal**

### **4.1 Overview of the chapter**

This chapter will synthesise and critically evaluate the findings from both the systematic review and the empirical paper, and consider how they sit together in the context of the wider literature.

### **4.2 Main findings**

The current thesis portfolio set out to explore the impact of executive function (EF) on emotional responses in an adult traumatic brain injury (TBI) population. First, by systematically reviewing the available literature and by evaluating the strength of the evidence to support the hypothesis that EF impairment is a vulnerability factor to emotional distress, and secondly by conducting research looking specifically at the impact of impaired EF on selective attention to threat.

It became clear from the systematic review that limited research exists that explicitly focuses on specific processes of EF as a vulnerability factor for emotional distress. All of the studies reviewed were only able to find a significant association with aspects of EF on emotional distress in a TBI population. The majority of the research sets out to identify general predictors of emotional distress and is cross-sectional in design consequently, it is not possible to infer causality. Research suggests that there is a potential association between impaired EF and heightened emotional distress but the nature of this association is still not well understood due to the limited evidence base. Some of the research suggested that the association between EF and emotional outcome is due to the impact of the impairment following TBI on psychosocial factors and an individual's ability to engage in daily activities which then causes them to become emotionally distressed. Other research has suggested that it is perhaps an individual's coping abilities (or

difficulties in this area) that can mediate the relationship between EF impairment and emotional distress, perhaps due to the overlapping domain of problem solving that is implicated by EF impairment. Others have suggested that the association may be as result of a lowered threshold for threat sensitivity due to altered physiological reactivity post-TBI. Finally, and consistent with the current study's pattern of results, it is potentially due to difficulties from disengaging with threat once it has been attended to, as might be predicted by working memory models. The Working Memory model (Baddeley, 1986), and in particular the 'central executive', is suggested to be responsible for selecting, initiating and ending processing tasks and thus, may be implicated in an individual's ability to disengage from threat. This status of research exploring these different possible mechanisms by which EF might be implicated in emotional outcomes suggests that there is no clear consensus for the explanation of the association between emotional distress and EF processes. Accordingly, further research into specific EF processes, and the impact on elements of emotional distress, would be beneficial.

The research paper within this portfolio aimed to provide further insight into whether particular EF processes impact how an individual responds to threatening stimuli or whether EF deficits interfere with allocation of attentional resources when faced with affective stimuli using the dot-probe paradigm. The main hypotheses were that individuals with EF difficulties (TBI group) would respond more quickly to threatening stimuli when compared to a healthy comparison group, thus showing an attentional bias towards threat. The stimuli were in the form of word categories, 'physical threat', 'negative evaluation' and 'neutral'. It was hypothesised that individuals with EF difficulties would have a selective attention bias towards 'negative evaluation', followed by 'physical threat', and then 'neutral', when compared to the healthy comparison group. Although the findings did show a marginal trend for the TBI group to demonstrate an attentional bias towards threatening stimuli, when compared to the comparison group, this was not found to be

significant and therefore the findings did not support the hypothesis. After further analysis there was also no significant difference between the dot-probe conditions (neutral, physical threat congruent, physical threat incongruent, negative evaluation congruent, negative evaluation incongruent) and therefore neither hypotheses was supported. When reaction times were compared across all five conditions the largest difference, for the TBI group, appeared to be between neutral and incongruent trials. This pattern of results could suggest a possible difficulty with disengagement from threat, although, the findings did not reach significance. The dot-probe paradigm will be discussed in further detail in relation to the results of the current study and the possible interpretations of the data that need to be considered. Strengths and limitations of the thesis portfolio will be discussed later in this chapter.

### **4.3 The Dot-Probe Paradigm: Selective Attention or Difficulty to Disengage**

The current research study utilised the dot-probe paradigm to detect selective attention to threat. However, there is a body of research exploring whether the measurement of attentional control can, in fact, be interpreted as both a selective attention to threat *and* a difficulty to disengage from threat. Attentional control has been defined as an individual's ability to purposefully direct their attention and inhibit their automatic response (Derryberry & Reed, 2002). Being able to deliberately and flexibly direct attention is said to be indicative of intact EF (Miyake et al., 2000). If an individual finds it difficult to direct their attention, it may be that threat stimuli occupy their attention and they find it difficult to disengage from this, which can significantly interfere with goal directed behaviour (Eysenck, 1992).

Koster et al., (2004) stated that the dot-probe paradigm may not, in fact, be measuring selective attention to threat but, rather, the results could be interpreted as a difficulty to disengage from threatening stimuli. Research was carried out with 44

psychology students using the dot-probe paradigm and their findings suggested that the congruency effect was caused by a delayed response to the incongruent threatening trials. This suggests that the findings cannot be interpreted solely as individuals having a selective attention to threat, and this difficulty to disengage from threat may itself result in prolonged anxiety. It was reported that having problems in shifting attention away from threat may leave the individual feeling that they are not in control of the situation and thus heighten anxiety. Their results suggest that through further exploration of the dot-probe paradigm, difficulty in regulation of attention to emotional stimuli and also the possibility of the selective attention to threat hypothesis cannot be eliminated. As stated, results from the current study indicated that TBI participants reacted marginally more quickly to congruent trials than incongruent trials, which is in keeping with the selective to attention to threat hypothesis. However, interestingly although not reaching significance the TBI group responded more slowly to the incongruent trials when compared to the neutral trials for both physical and socially threatening stimuli. This trend in the data is consistent with explanations proposed by Koster and, it was observed that the reaction times of the TBI group to the incongruent threat trials were slower when compared to the neutral trials. The reaction time for the physical threat trials was the slowest suggesting disengagement from physical threat was the most difficult for this population. As stated previously, the majority of the TBI participants were recruited from inpatient behavioural rehabilitations units and it is possible that physical threat is more frequently observed in these settings, and perhaps with the EF difficulties these participants demonstrated, it makes it more difficult to disengage from the threats around them.

Taylor et al., (2016) also conducted research using the dot-probe paradigm in a student population. Findings suggested that attentional control moderated the association between social anxiety and attentional disengagement from, but not engagement with, social threat stimuli. This finding is compatible with the trend in the data in current study

which suggests that attentional control impacts on the ability to disengage from, but not sensitivity to be captured by, threat stimuli, again high-lighting the importance of considering the components of the attentional control processes.

Similarly research suggests that anxious individuals do not have a vigilance to threat, but they have difficulty in disengaging from threat once they have detected it (Fox et al., 2002; Salemink, van der Hout, & Kindt, 2007; Yiend & Mathews, 2001). It has been found that, once threat has become the focus of the individual's attention, it is much harder for those reporting high levels of anxiety to disengage from it (Gole, Köchel, Schäfer & Schienle, 2012). Research has also shown that individuals higher in attentional control were able to inhibit attentional biases to threat compared to those low in attentional control demonstrating that being skilled in attentional control may enable an individual to limit the effect the threatening stimuli has on them (Derryberry & Reed, 2002). Similarly, Bardeen and Orcutt (2011) reported that attentional control moderated the relationship between posttraumatic stress symptoms and selective attention to threat suggesting that the ability to purposefully direct attention may act as a buffer to prolonged engagement with threat stimuli and associated emotional distress. Similarly other studies have found that attentional control moderated the relationship between anxiety and selective attention to threat (Hou et al., 2014; Schoorl, Putman, Van Der Werff, & Van Der Does, 2014). More research is needed to explore the EF processes involved in attentional regulation to emotional stimuli in order to better understand the underlying processes impacting on the difficulties experienced by individuals post-TBI. Further research in this area may also assist with the development of paradigms to reliably assess attentional bias to threat (Kappenman, Farrens, Luck & Proudfit, 2014) and also investigate the differences between selective attention to threat and difficulty to disengage from threat.

#### **4.4 Executive Functioning and its association with emotion**

As stated, the main aim of this thesis portfolio was to explore whether underlying EF impairment impacts negatively upon emotional responses in a TBI population. From the systematic review it was clear that, although there is a lack of literature on the impact of specific EF processes on emotional distress in people with TBI, research has demonstrated associations between emotional distress and EF (Bowen et al., 1998; Gould, Ponsford & Spitz, 2014; Himanen et al., 2009; Jorge et al., 2004; Mauri et al., 2014; Spitz et al., 2013; and Wood & Rutterford, 2006). However, findings were mixed and not all of the reviewed research found an association (Fordyce, Roueche & Prigatano, 1983; Hoofien et al., 2000; Ponsford, Draper & Schoneberger, 2008). Two of the studies focused on long-term outcomes after TBI and predictors of functional outcome (Hoofien et al., 2000; Ponsford, Draper & Schoneberger, 2008) and although they assessed EF and emotional distress they did not conduct analyses to explore any presence of association between the two. Fordyce et al., (1983) compared two groups of TBI participants, one group were less than six months post-TBI (acute) and the second group were more than six months post-TBI (chronic). It is suggested that the lack of association could be explained by a sampling issue as acute patients may not have been referred for a neuropsychological assessment if they had demonstrated emotional adjustment, suggesting that individuals in the acute group who had completed a neuropsychological assessment were likely to display greater cognitive impairments. This is perhaps also reflected in the sample size as more chronic patients were included ( $n = 35$ ) than acute ( $n = 17$ ). It is important to acknowledge that, although most studies found an association between EF and emotional distress, due to the nature of the study designs causality cannot be inferred.

Research has also suggested that emotional distress post-TBI is perhaps as a result of poorer psychosocial outcomes e.g. loss of employment, reduced social support, limited



physical capabilities, etc. (Knouse, Barkley & Murphy, 2013), rather than as a direct effect of EF impairment. Individuals who have sustained a TBI often find it more cognitively demanding to function and cope in everyday life and therefore any additional stressors may cause them to experience increased emotional distress (Gould et al., 2014). It has been suggested that poorer EF post-TBI has an impact on how an individual utilises coping strategies, with these individuals utilising more emotionally focussed, rather than problem focussed coping strategies (Krpan, Levine, Stuss & Dawson, 2007). These findings propose that deficits in EF and, in particular, problem solving might interact with coping style and subsequently the emotional distress experienced by the individual. However, the study by Krpan et al., (2007) did not measure mood and therefore we are unable to show an interaction between coping EF and mood. This is vital when developing interventions and resources for the TBI population who have EF impairment and experience emotional distress.

Previous research has also suggested that it was perhaps slower psychomotor reaction and slower processing speed that has impacted on individual performance in tasks that were time-dependent (Hoofien et al., 2000) and that slower processing speed was associated with functional outcomes (Ponsford et al., 2008). This suggests that it is important to consider the impact processing speed has on an individual's performance on timed tasks post-TBI and how this may impact the assessment of overall EF. In the current research study the data of 3 out of the 22 participants in the TBI group had to be removed due to either a high number of errors or significantly longer response times on the dot-probe task. This was thought to be the result of poorer processing speed and difficulty with psychomotor ability due to observed difficulties during assessment. The impact of this must be acknowledged, as it may have affected the results on the dot-probe trials for some of the TBI participants who experienced these difficulties. These difficulties may have resulted in slower reaction times to the dot-probe trials.

#### **4.5 Strengths and Limitations of the Thesis Portfolio**

This thesis portfolio aimed to explore EF and emotional distress in a TBI population, and although no significant findings were observed, there are both strengths and limitations that need to be considered within this project. The empirical study aimed to investigate the contribution of EF to selective attention to threat. The inclusion of a TBI population only allowed sufficient levels of EF impairment to be present in order to test the study hypotheses, although this did create challenges with regard to recruitment of participants. In addition, it also resulted in a less varied sample than may have been present if other types of brain injuries were included, such as stroke or encephalitis. Another key strength, was in the empirical study all the measures used had been previously validated in a brain injury population and therefore, the findings can be generalised to a similar population. The HADS has previously been used as a measure of emotional distress with a brain injury population (Ponsford et al., 2008; Spitz et al., 2013). However, some researchers have suggested that several of the questions related to ‘feeling slowed down’, ‘having difficulty with activities’, ‘enjoying a good book’, these are common symptoms experienced as a result of TBI rather than emotional distress and which can lead to a false positive response (Bowen et al 1998).

The visual dot-probe task, although an established paradigm, to the authors knowledge, has only once previously been used in a brain injury population (Gilligan, 2015) and as such requires consideration when interpreting the findings from the current study. The paradigm was found to be feasible to use within this population and TBI participants were able to understand and complete the task. However, without robust checks for external validity, we cannot be sure of the equivalence of using the dot-probe in a TBI sample. A key strength of the current research was that, due to the majority of the

data being collected at one time point, there were very few missing data points, which was beneficial when analysing the data. As previously discussed, it has been suggested that the traditional dot-probe is not measuring selective attention to threat but difficulty to disengage from threat (Koster et al., 2004). Koster stated that it was important to consider how the analysis of reaction times is operationalised and to include a comparison between neutral, congruent and incongruent to ascertain whether an individual is selectively attending to threat or having difficulty with disengagement. Only by taking the neutral trials into account is it possible to explore these processes further. This is important in relation to the current study, as by comparing the reaction times across all trials, the pattern of results seemed consistent with individuals in the TBI group showing a difficulty to disengage from threat rather than selectively attending to it as was hypothesised, although this did not reach significance. The systematic review found that there is a lack of research exploring impaired EF as a vulnerability factor to emotional distress. This provided a strong rationale for hypotheses regarding specific aspects of EF and emotional processes to be targeted in future studies and designs that allow causation to be inferred.

A weakness of the research study was the small sample size and, whilst every effort was made to recruit the required sample size, this was not achieved and therefore both hypotheses and all analyses were underpowered. This must be considered as the study did not have the power to detect the effects and it is possible that, given the appropriate sample, the results may have been different. There is also the consideration that the reaction time measure of selective attention to threat in the traditional dot-probe (the difference between reaction times on threat incongruent and threat congruent trials) has poor internal reliability and does not reliably measure attentional bias to threat (Kappenman, Farrens, Luck & Proudfit, 2014; Schmukle, 2005). There were key differences between the comparison group and the TBI group that may have caused bias in the data, most notably gender differences; the TBI group were all male and 82.4% of the

comparison group were female. It is more common for TBIs to be seen in the male population and therefore this is perhaps why the sample in the current study reflects this difference. There was an initial plan for a wider recruitment strategy by including relatives of the TBI participants in the hope of better control of possible between group systematic biases. However, it was recognised that this would not be possible due to the majority of the TBI participants currently being cared for at inpatient units with limited contact with family members. In the general population, Pfabigan et al., (2014) suggested that the higher prevalence of anxiety disorders seen in women compared to men suggests a difference in attentional biases in the general population. The implications of which are, possible gender differences in attentional control which must be considered in relation to the current study. Previous research has suggested gender differences in the dot-probe task, in particular, a study by Pintzinger et al., (2016) based on healthy participants, showed that men were more likely to be avoidant of negative stimuli than women. In the current empirical study the trend in data for the TBI group suggested difficulties disengaging with threat rather than selectively attending to it. There was significant difference in educational level and WTAR scores between the two samples, with the majority of the comparison group having significantly more years in education and higher WTAR scores compared with the TBI group. Although all participants were deemed to have suitable verbal comprehension skills to complete the tasks, it is possible that the difference in abilities may have impacted the TBI group's ability to complete the dot-probe task which relies on verbal comprehension. This may have caused bias, perhaps also resulting in increased reaction times on the dot probe task, thus conclusions drawn on the basis of the current comparison group must be treated with caution.

A key limitation of the current research was, due to the time and budget limitations of the Doctoral programme, a full EF assessment was not able to be completed and only two subtests were used (letter fluency and color-word interference test). There is a lack of

clarity around exactly what EF encompasses (Mueller & Dollaghan, 2013) and, as discussed in the systematic review, this has resulted in a lack of consensus with regard to its assessment and a difficulty in comparing the findings of different research papers. The QATOCCS rating scale used for the systematic review also suggested a second rater. However, the ratings were only completed by one rater and therefore findings and interpretation of the results are from the perspective of one individual.

#### **4.6 Future implications for research and clinical practice**

The findings from this thesis portfolio have both research and clinical implications in identifying future directions for research and to consider potential developments that could contribute to clinical practice. By improving our knowledge of the underlying processes involved in EF we may be better able to develop treatment programmes and interventions for individuals who have sustained a TBI and are experiencing emotional distress by adapting them to suit the needs of the individual. TBI survivors can be left with a diverse range of difficulties and changes to their lives to which they have to adjust, and this can be distressing. The current project has highlighted the need for more experimental research to explore whether specific aspects of EF difficulties (e.g. working memory) act as a vulnerability factor for increased emotional distress or whether emotional distress may be a result of changes to the individual's life, and the difficulty in adjusting to these which may cause emotional distress. The current research suggests the need for further experimental studies to explore this possible relationship between EF and emotional distress by recruiting larger samples ensuring the sample size is sufficient to power the required analyses and by employing a matched control group to reduce bias and enable comparison between groups. Only by understanding the impact of EF impairment post-TBI will we be in a better position to consider how to develop interventions and where best to

target resources so that the individual can engage fully with their rehabilitation and achieve the best outcomes.

#### **4.6.1 Therapeutic Interventions after TBI**

TBI is complex and requires life-long management (Cicca & Threats, 2014) and anxiety is reportedly common post-TBI (Gould, Ponsford, Johnston, & Schonberger, 2011). Poor emotional adjustment can often be undetected (Kangas & McDonald, 2011), and this can result in behavioural difficulties and the development of more severe mood disorders. It is important to consider the impact that EF difficulties may have on an individual's ability to engage with the therapeutic interventions available. For example cognitive behaviour therapy (CBT) interventions are based on models of processing biases (Clark & Beck, 2010) and research has found that post-TBI individuals can display biases to social threat and being negatively judged by others (Riley, Brennan & Powell, 2004). CBT requires also requires complex cognitive skills such as; keeping track of conversations, completing homework, generating ideas, self-monitoring and use evaluation skills and EF skills are needed for all of these tasks (Hsieh, Ponsford, Wong & McKay, 2012). It is important to acknowledge the impact this will have on the individuals ability to engage and benefit from these interventions and to consider possible adjustments.

Waldron, Cassidy & O'Sullivan (2012) reviewed studies of treatment outcomes on CBT for depression and anxiety post-ABI. Their review found that when CBT treatments were targeted specifically at anxiety and depression, they were better able to produce therapeutic effects on anxiety and depression rather than if they had a broader focus e.g. coping skills. The review also highlighted that, whilst CBT shows pre to post treatment change for depression and anxiety difficulties in those that receive CBT compared to control groups, in terms of clinical significance, studies often only report partial reduction in symptoms and, in some cases, no improvement. Gracey, Longworth and Psaila (2015)

proposed a transdiagnostic model of emotional distress for individuals post-ABI considering that there are substantial challenges to working therapeutically with individuals post-ABI due to a wide range of factors including acquired deficits that can impact on emotional responses. The changes post-ABI can have a significant impact on the individual's life and it is important to consider the meaning of these changes to the individual. Within the cognitive behavioural models increased sensitivity to concern engages emotionally driven processing biases such as selective attention to threat and, in particular, the sensitivity of "threat to self". Gracey et al., (2015) hypothesised that EF can also have a direct impact on emotional outcome and may increase an individual's vulnerability to specific cognitive-affective processes e.g. rumination and therefore it is vital to consider EF deficits when working with someone therapeutically.

Treatment options for the brain injury population, although improving, are still limited. Case reports of individual work (Lu, Krellman, & Dijkers, 2016; McIlvain, Walter & Chard, 2012) and group programmes (Backhaus et al., 2010; Bradbury, Christensen, Lau, Ruttan, Arudine & Green, 2008) have found good results for the use of CBT. However, in a non-TBI population, CBT has been found to have a higher drop-out rate than other psychological input, seemingly due to the requirement of active participation (Cuijpers, van Straten, Andersson, & van Oppen, 2008). Interestingly, there have been promising results, from a case report design, for the use of a combined motivational interviewing (MI) and CBT approach post-TBI, with a view to developing the individual's self-efficacy to cope with their anxiety, and also to help with the development of more realistic goals (Hsieh et al., 2012). This particular research showed significant reductions in anxiety and improvement in reductions in subjective units of distress, suggesting that the use of MI followed by CBT is effective with a TBI population. A further review of the efficacy of CBT with preparatory MI sessions was completed (Ponsford et al., 2016). The individuals that received CBT and MI, and those who received CBT and non-directive counselling,

both showed a significant reduction in anxiety and depression symptoms compared with the ‘treatment as usual’ group. However there were no significant differences between the CBT and MI group, and the CBT and non-directive counselling group. This is important in relation to the current study findings, as it suggests the need to better understand the underlying processes that can contribute to engagement with therapy and how these can be addressed. Despite the mixed findings, it seems that providing MI input prior to CBT may be a helpful resource to some and should be considered in future therapeutic approaches.

Third wave CBT approaches have also been used with individuals post-TBI, such as, Compassion Focussed Therapy (CFT) have also been found to have benefits post TBI, and can have a focus on the regulation of threat-focused emotions (Ashworth, Gracey & Gilbert, 2011). Mindfulness based cognitive therapy has also been found to have some benefit (Bedard et al., 2014) and has been shown to have clinically significant impact in improving depressive symptoms in 50% of individuals with TBI who received the intervention (Ozen et al., 2016). More recently, there appears to be more focus on third wave models of CBT which attend to processes such as how we respond to emotions and what we do with our attention. Thus, interventions that address attentional processes in response to threat in this way would be appropriate for addressing issues with disengagement from threat. This is in line with the current study findings as, although not significant, the pattern of results seemed to suggest a pattern indicative of a difficulty to disengage from threat and thus interventions that address this may be beneficial for this population.

#### **4.7 Conclusion**

As highlighted throughout this discussion, future studies should attend to some of the methodological weaknesses of the current research by ensuring the sample size is of sufficient size to power the required analyses and perhaps by employing a matched control



group to help with the comparison of EF impairment across two groups with fewer potentially confounding variables. From both the empirical paper and the systematic review it seems that there is an association between EF and emotional distress. However, the nature of this association is not yet fully understood. Future research should aim to investigate specific EF processes and whether they are a vulnerability factor for particular aspects of emotional distress e.g. selective attention to threat, rumination, processing biases etc. By further understanding these underlying processes, we will be in a better position to provide effective and more targeted treatment to individuals from the TBI population, taking into consideration the variability in cognitive profile of those who have difficulty with EF and may be experiencing varying levels of emotional distress.

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## Appendix A

### Ethical approval conformation letter

Page 1



#### **Health Research Authority** North West - Preston Research Ethics Committee

Barlow House  
3rd Floor  
4 Minshull Street  
Manchester  
M1 3DZ

Telephone: 020 71048008

11 April 2016

Miss Stephanie Keay  
Trainee Clinical Psychologist  
CPFT NHS Trust  
University of East Anglia  
Norwich  
NR47TJ

Dear Miss Keay

<b>Study title:</b>	<b>The impact of executive functioning on attention to threat in an adult traumatic brain injury population: an experimental group design</b>
<b>REC reference:</b>	<b>16/NW/0244</b>
<b>IRAS project ID:</b>	<b>183250</b>

Thank you for responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager Mrs Carol Ebenezer, [nrescommittee.northwest-preston@nhs.net](mailto:nrescommittee.northwest-preston@nhs.net). Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

#### **Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

#### **Conditions of the favourable opinion**

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).*

*Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, [www.hra.nhs.uk](http://www.hra.nhs.uk) or at <http://www.rdforum.nhs.uk>.*

*Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

*For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.*

*Sponsors are not required to notify the Committee of management permissions from host organisations.*

#### Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publicly accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact [hra.studyregistration@nhs.net](mailto:hra.studyregistration@nhs.net). The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

#### **Ethical review of research sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

#### **Approved documents**

The documents reviewed and approved by the Committee are:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Copies of advertisement materials for research participants [poster for control group]	1	10 November 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [UEA insurance letter]	1	17 March 2016
Letters of invitation to participant [consent to contact form]	1	20 August 2015
Non-validated questionnaire [Demographic info]	1	14 March 2016



Other [CV for MO academic]	1	03 November 2015
Other [Covering letter for amendments]	1	04 April 2016
Participant consent form [consent form]	4	04 April 2016
Participant information sheet (PIS) [PIS TBI group]	4	04 April 2016
Participant information sheet (PIS) [PIS control group]	4	04 April 2016
REC Application Form [REC_Form_16032016]		16 March 2016
Research protocol or project proposal [Proposal]	1	10 November 2015
Summary CV for Chief Investigator (CI) [Chief investigator CV]	1	20 August 2015
Summary CV for supervisor (student research) [CV fergus gracey]	1	02 November 2015
Validated questionnaire [DKEFS COLOUR AND VERBAL]	1	21 March 2016
Validated questionnaire [HADS]	1	21 March 2016
Validated questionnaire [DEX]	1	21 March 2016
Validated questionnaire [WTAR]	1	21 March 2016
Validated questionnaire [DOT PROBE]	1	21 March 2016
Validated questionnaire [GCS RATING CUT OFFS]	1	21 March 2016

### Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

### After ethical review

#### Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

#### Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: <http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance>

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

16/NW/0244	Please quote this number on all correspondence
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With the Committee's best wishes for the success of this project.

Yours sincerely



Dr Rob Monks  
Chair

Email: [nrescommittee.northwest-preston@nhs.net](mailto:nrescommittee.northwest-preston@nhs.net)

Enclosures: "After ethical review – guidance for researchers"

Copy to: Mrs Yvonne Kirkham

Ms Vivienne Shaw, NHS Cambridgeshire and Peterborough CCG

## Appendix B

### Confirmation email of category C minor amendment

Sweep
Move to
Categories
...
Undo

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**From:** AMENDMENTS, Hra (HEALTH RESEARCH AUTHORITY)  
**Sent:** 30 January 2017 10:27  
**To:** Stephanie Keay (MED)  
**Cc:** Sian Coker (MED); Fergus Gracey (MED); [y.kirkham@uea.ac.uk](mailto:y.kirkham@uea.ac.uk); SHAW, Vivienne (NHS CAMBRIDGESHIRE AND PETERBOROUGH CCG)  
**Subject:** IRAS 183250. Confirmation of Amendment Categorisation as Category C

Dear Stephanie Keay,

<b>IRAS Project ID:</b>	183250
<b>Short Study Title:</b>	The impact of executive functioning on attention to threat
<b>Date complete amendment submission received:</b>	20/01/2017
<b>Amendment No./ Sponsor Ref:</b>	1
<b>Amendment Date:</b>	30/11/2016
<b>Amendment Type:</b>	Non-substantial

Thank you for submitting the above referenced amendment. In line with the [UK Process for Handling UK Study Amendments](#) I can confirm that this amendment has been categorised as:

**Category C** - An amendment that has no implications that require management or oversight by the participating NHS organisations

As such, the sponsor may implement this amendment **as soon as any relevant regulatory approvals are in place** (for participating organisations in England, please see 'Confirmation of Assessment Arrangements' below).

As Chief Investigator/Sponsor, it remains your responsibility to ensure that the research management offices and local research teams (if applicable) at each of your participating organisations are informed of this amendment.

**Note:** you may only implement changes described in the amendment notice or letter.

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**Participating NHS Organisations in England – Confirmation of Assessment Arrangements**

Further to the details above, I can confirm that no HRA assessment of this amendment is needed.

- If this study has HRA Approval, this amendment may be implemented at participating NHS organisations in England once the conditions detailed in the categorisation section above have been met
- If this study is a pre-HRA Approval study, this amendment may be implemented at participating NHS organisations in England that have NHS Permission, once the conditions detailed in the categorisation section above have been met. For participating NHS organisations in England that do not have NHS Permission, these sites should be covered by HRA Approval before the amendment is implemented at them, please see below;
- If this study is awaiting HRA Approval, I have passed your amendment to my colleague in the assessment team and you should receive separate notification that the study has received HRA Approval, incorporating approval for this amendment.

Please do not hesitate to contact me if you require further information.

Kind regards

Laura Greenfield



Laura Greenfield | Amendments Coordinator  
**Health Research Authority**  
**Research Ethics Service (RES)**  
HRA, The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS  
E: [hra-amendments@nhs.net](mailto:hra-amendments@nhs.net)  
T: 020 7104 8096  
[www.hra.nhs.uk](http://www.hra.nhs.uk)

## Appendix C

### Submission guidelines for Journal of Clinical and Experimental Neuropsychology

#### Instructions for authors

Thank you for choosing to submit your paper to us. These instructions will ensure we have everything required so your paper can move through peer review, production and publication smoothly. Please take the time to read and follow them as closely as possible, as doing so will ensure your paper matches the journal's requirements. For general guidance on the publication process at Taylor & Francis please visit our [Author Services website](#).



This journal uses ScholarOne Manuscripts (previously Manuscript Central) to peer review manuscript submissions. Please read the [guide for ScholarOne authors](#) before making a submission. Complete guidelines for preparing and submitting your manuscript to this journal are provided below.

#### About the journal

*Journal of Clinical and Experimental Neuropsychology* is an international, peer reviewed journal, publishing high-quality, original research. Please see the journal's [Aims & Scope](#) for information about its focus and peer-review policy.

Please note that this journal only publishes manuscripts in English. This journal accepts the following article types: regular (Original) Articles, Review Articles and Critiques.

#### Peer review

Taylor & Francis is committed to peer-review integrity and upholding the highest standards of review. Once your paper has been assessed for suitability by the editor, it will then be double blind peer-reviewed by independent, anonymous expert referees. Find out more about [what to expect during peer review](#) and read our guidance on [publishing ethics](#).

#### Preparing your paper

All authors submitting to medicine, biomedicine, health sciences, allied and public health journals should conform to the [Uniform Requirements for Manuscripts Submitted to Biomedical Journals](#), prepared by the International Committee of Medical Journal Editors (ICMJE).

We also refer authors to the community standards explicit in the [American Psychological Association's \(APA\) Ethical Principles of Psychologists and Code of Conduct](#).

#### Structure

Your paper should be compiled in the following order: title page; abstract; keywords; main text; acknowledgements; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figure caption(s) (as a list).

#### Word limits

Please include a word count for your paper.  
There are no word limits for articles in this journal.

## Style guidelines

Please refer to these [style guidelines](#) when preparing your paper, rather than any published articles or a sample copy.

Please use American spelling style consistently throughout your manuscript.

Please use double quotation marks, except where "a quotation is 'within' a quotation". Please note that long quotations should be indented without quotation marks.

The style and format of your paper should conform to the specifications given in the *Publication Manual of the American Psychological Association* (6th ed.).

**Abstracts:** Authors submitting papers should note that the journal offers a choice to authors to publish either ordinary abstracts, or structured abstracts of between 200-300 words. Structured abstracts have the advantage of being clearer for readers and facilitate better, appropriate indexing and citation of papers, and their essential features are below:

- **Introduction:** Describe the background to the study, hypotheses, aims, objectives, research questions, etc. **Method:** Include outline of the methodology and design of experiments; materials employed and subject/participant numbers with basic relevant demographic information; the nature of the analyses performed.
- **Results:** Outline the important and relevant results of the analyses.
- **Conclusions:** State the basic conclusions and implications of the study. State, clearly and usefully, if there are implications for management, treatment or service delivery.

Note: Any clinical implications should be clearly stated. Avoid abbreviations, diagrams, and references to the text in the abstract.

## Formatting and templates

Papers may be submitted in any standard format, including Word and LaTeX. Figures should be saved separately from the text. To assist you in preparing your paper, we provide formatting templates. A [LaTeX template](#) is available for this journal. [Word templates](#) are available for this journal. Please save the template to your hard drive, ready for use. If you are not able to use the templates via the links (or if you have any other template queries) please contact [authortemplate@tandf.co.uk](mailto:authortemplate@tandf.co.uk). If any assistance is needed with uploading files to our submission system, please feel free to email the [Editorial Assistant](#).

**References:** Please use this [reference style guide](#) when preparing your paper. An [EndNote output style](#) is also available to assist you.

## Checklist: what to include

1. **Author details.** Please ensure everyone meeting the International Committee of Medical Journal Editors (ICMJE) [requirements for authorship](#) is included as an author of your paper. Please include all authors' full names, affiliations, postal addresses, telephone numbers and email addresses on the title page. Where available, please also include [ORCID identifiers](#) and social media handles (Facebook, Twitter or LinkedIn). One author will need to be identified as the corresponding author, with their email address normally displayed in the article PDF (depending on the journal) and the online article. Authors' affiliations are the affiliations where the research was conducted. If any of the named co-authors moves affiliation during the peer-review process, the new affiliation can be given as a footnote. Please note that no changes to affiliation can be made after your paper is accepted. [Read more on authorship](#).
2. A structured or unstructured **abstract** of more than 200 and no more than 300 words. A structured abstract should cover (in the following order): Introduction, Results and Conclusions. Read tips on [writing your abstract](#).
3. **Graphical abstract** (Optional). This is an image to give readers a clear idea of the content of your article. It should be a maximum width of 525 pixels. If your image is narrower than 525

pixels, please place it on a white background 525 pixels wide to ensure the dimensions are maintained. Save the graphical abstract as a .jpg, .png, or .gif. Please do not embed it in the manuscript file but save it as a separate file, labelled GraphicalAbstract1.

4. You can opt to include a **video abstract** with your article. [Find out how these can help your work reach a wider audience, and what to think about when filming.](#)
5. Up to five **keywords**. Read [making your article more discoverable](#), including information on choosing a title and search engine optimization.
6. **Funding details**. Please supply all details required by your funding and grant-awarding bodies as follows:  
*For single agency grants:* This work was supported by the [Funding Agency] under Grant [number xxxx].  
*For multiple agency grants:* This work was supported by the [funding Agency 1]; under Grant [number xxxx]; [Funding Agency 2] under Grant [number xxxx]; and [Funding Agency 3] under Grant [number xxxx].
7. **Disclosure statement**. This is to acknowledge any financial interest or benefit that has arisen from the direct applications of your research. [Further guidance on what is a conflict of interest and how to disclose it.](#)
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## Appendix D

### Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			
<b>Quality Rating (Good, Fair, or Poor) (see guidance)</b>			
Rater #1 initials:			
Rater #2 initials:			
Additional Comments (If POOR, please state why):			

\*CD, cannot determine; NA, not applicable; NR, not reported

## Appendix E

### Participant information sheet for TBI group

<b>PIS - TBI - Version 5. 29/11/16</b>
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 Fax: +44 (0) 1603 591132  
 Web: www.uea.ac.uk

#### Study title

The impact of executive functioning and anxiety on attention to threat in an adult traumatic brain injury population: an experimental group design

#### Invitation

We would like to invite you to take part in our research study. Before you decide if you would like to take part it is important for you to read this information sheet that explains what the study is about and how you will be involved. A member of the research team will go through this information sheet with you and answer any questions you may have.

Please take your time to read the information sheet carefully and ask if you have any questions or there is anything you are not sure about.

#### What is the purpose of this study?

The purpose of this study is to look into the effect that anxiety and difficulties with executive functioning may have on how a person looks at threat. 'Executive functioning' is a phrase used to describe lots of different things that our brain does e.g. planning, attention, control and problem solving etc. Some people who have suffered a brain injury may have difficulties with some or all of these things. We are interested in finding out whether people who have suffered a brain injury with these difficulties respond to threat in different ways to people without a brain injury who do not have these difficulties. Previous studies have found that people who are anxious are quicker to notice threat than people who are less anxious. We are interested to see how anxiety and executive functioning difficulties effect how someone notices threat.

### **Do I have to take part?**

It is up to you to decide. We will provide you with information about the study and answer any questions you have. If you agree to take part you will be asked to sign a consent form. You are free to withdraw at any point without giving a reason. This will not affect the care you are receiving.

### **What would taking part involve?**

The researcher or a member of your care team (if applicable) will arrange a suitable place and time to complete the study with you. This could be at your home or a room in the healthcare setting that you are currently attending or staying. Unfortunately expenses will not be reimbursed but arrangements will be made to make participation in the study as convenient as possible.

You will be asked to meet with the researcher to complete a set of short questionnaires to ensure that you meet the criteria to participate in the study. After these are completed you will be told whether you meet the criteria to continue with the study if you do not then there will be no further information required. If you meet the criteria you will then be asked to complete a computer task that involves looking at word pairs on the screen and responding to them by clicking a button lasting approximately 15 minutes. Once you have completed this you will then have a short break before filling out a further set of questionnaires and tasks.

At the end of the questionnaires you will be given an opportunity to ask any questions. You can decide not to participate at any point. We will only meet once to complete the questionnaires and computer task.

### **What are the possible benefits of taking part?**

We cannot guarantee that the study will help you but the information we get from this study will help improve the understanding of brain injury and therefore help improve the treatment of people who have suffered a brain injury.

### **What are the possible disadvantages and risks of taking part?**

It is unlikely that distress will be caused by participating in this study, however, should you feel distressed at any point the researcher will be available to discuss any concerns you may have. If you have any further concerns about difficulties that have come to light from participating in this study you may also wish to contact your GP directly to discuss these. Remember that you have the right to withdraw at any point. Contact details will also be provided should you have any concerns at a later date.

### **What if there is a problem?**

If you have any concerns about any aspects of this study, you should speak to the researcher directly who will do their best to answer your questions (see contact details for Stephanie Keay). If you remain unhappy you can make a formal complaint by contacting either Professor Kenneth Laidlaw, [k.laidlaw@uea.ac.uk](mailto:k.laidlaw@uea.ac.uk). University of East Anglia, Norwich Medical School, Health Policy and Practice,

Elizabeth Fry Building, NR4 7TJ. Or you can contact Professor Michael Frenneaux, the Head of School in the Faculty of Medicine and Health Sciences, University of East Anglia, [m.frenneaux@uea.ac.uk](mailto:m.frenneaux@uea.ac.uk).

### **What happens if I don't want to carry on with the study?**

You are free to withdraw from the study at any point. This will not affect your rights or your care in any way. After you have completed the study you have up until the point of data analysis to request that your data is removed from the study and destroyed.

### **How will information be kept confidential?**

All information that is collected will be kept strictly confidential. Your information will be seen by the research team only. All documentation will be kept in a locked filing cabinet. The information you provide will be identified by your individual number so everything will remain anonymous and completely confidential. Your data will be held for up to 10 years after the study had ended and then destroyed. All data will be managed in line with the Data Protection Act.

There are occasions when confidentiality must be broken. If you disclose information that indicates that you or others are at risk of harm it will be necessary for me to inform the appropriate authorities.

Data will be stored on a computer database using only the individuals' participant number. All files will be password protected.

### **What will happen to the results of the study?**

We intend to publish the results of this study. There will be no identifiable information used. Once all the participants have been seen and the research has been completed we will write to you with a summary of the results.

### **Who is organising and funding this study?**

This study is being organised by Miss Stephanie Keay (Trainee Clinical Psychologist) under the supervision of Dr Fergus Gracey and Dr Sian Coker, and is being funded by the University of East Anglia.

### **Who has reviewed this study?**

The research is being supervised and monitored by the Department of Clinical Psychology at the University of East Anglia. All research in a healthcare setting is reviewed – this study was reviewed by the North West Preston Ethics Committee to protect the interests of service-users.

**Further information and contact details**

I am able to provide further information should you require it. I can be contacted via the following:

Address:

Stephanie Keay

Department of Clinical Psychology

Norwich Medical School  
Faculty of Medicine and Health Sciences  
University of East Anglia  
Norwich Research Park  
Norwich  
NR4 7TJ

Email: [S.Keay@uea.ac.uk](mailto:S.Keay@uea.ac.uk)

## Appendix F

### Participant information sheet for comparison group

<b>PIS. CONTROL - Version 5. 29/11/16</b>
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Tel: +44 (0) 1603 593076  
Fax: +44 (0) 1603 591132  
Web: [www.uea.ac.uk](http://www.uea.ac.uk)

#### Study title

The impact of executive functioning and anxiety on attention to threat in an adult traumatic brain injury population: an experimental group design

#### Invitation

We would like to invite you to take part in our research study. Before you decide if you would like to take part it is important for you to read this information sheet that explains what the study is about and how you will be involved. A member of the research team will go through this information sheet with you and answer any questions you may have.

Please take your time to read the information sheet carefully and ask if you have any questions or there is anything you are not sure about.

#### What is the purpose of this study?

The purpose of this study is to look into the effect that anxiety and difficulties with executive functioning may have on how a person looks at threat. 'Executive functioning' is a phrase used to describe lots of different things that our brain does e.g. planning, attention, control and problem solving etc. Some people who have suffered a brain injury may have difficulties with some or all of these things. We are interested in finding out whether people who have suffered a brain injury with these difficulties respond to threat in different ways to people without a brain injury who do not have these difficulties. Previous studies have found that people who are anxious are quicker to notice threat than people who are less anxious. We are interested to see how anxiety and executive functioning difficulties effect how someone notices threat.

You have been invited to participate in the study as part of the 'healthy control' group. We will be collecting data from both 'healthy controls' and individuals who

have suffered a brain injury so that we can compare the two groups and see if there are any differences in how people look at threat.

### **Do I have to take part?**

Participation in the study is purely voluntary. The study will be recruiting approximately 74 participants who may or may not have suffered a traumatic brain injury and have difficulty with executive functioning. We will provide you with information about the study and answer any questions you have. If you agree to take part you will be asked to sign a consent form. You are free to withdraw at any point without giving a reason.

### **What would taking part involve?**

The researcher will arrange a suitable place and time to complete the study with you. This will be suitable a room in your place of work or study. Unfortunately expenses will not be reimbursed but arrangements will be made to make participation in the study as convenient as possible.

You will be asked to meet with the researcher to complete a set of short questionnaires to ensure that you meet the criteria to participate in the study. After these are completed you will be told whether you meet the criteria if you do not then there will be no further information required. If you meet the criteria you will then be asked to complete a computer task that involves looking at word pairs on the screen and responding to them by clicking a button lasting approximately 15 minutes. Once you have completed this you will then have a short break before filling out a further set of questionnaires and tasks.

At the end of the questionnaires you will be given an opportunity to ask any questions. You can decide not to participate at any point. We will only meet once to complete the questionnaires and computer task.

### **What are the possible benefits of taking part?**

We cannot guarantee that the study will help you but the information we get from this study will help improve the understanding of brain injury and therefore help improve the treatment of people who have suffered a brain injury.

### **What are the possible disadvantages and risks of taking part?**

It is unlikely that distress will be caused by participating in this study, however, should you feel distressed at any point the researcher will be available to discuss any concerns you may have. If you have any further concerns about difficulties that have come to light from participating in this study you may also wish to contact your GP directly to discuss these. Remember that you have the right to withdraw at any point. Contact details will also be provided should you have any concerns at a later date.

### **What if there is a problem?**

If you have any concerns about any aspects of this study, you should speak to the researcher directly who will do their best to answer your questions (see contact details for Stephanie Keay). If you remain unhappy you can make a formal complaint by contacting either Professor Kenneth Laidlaw, [k.laidlaw@uea.ac.uk](mailto:k.laidlaw@uea.ac.uk). University of East Anglia, Norwich Medical School, Health Policy and Practice, Elizabeth Fry Building, NR4 7TJ. Or you can contact Professor Michael Frenneaux, the Head of School in the Faculty of Medicine and Health Sciences, University of East Anglia, [m.frenneaux@uea.ac.uk](mailto:m.frenneaux@uea.ac.uk).

### **What happens if I don't want to carry on with the study?**

You are free to withdraw from the study at any point. This will not affect your rights in any way. After you have completed the study you have up until the point of data analysis to request that your data is removed from the study and destroyed.

### **How will information be kept confidential?**

All information that is collected will be kept strictly confidential. Your information will be seen by the research team only. All documentation will be kept in a locked filing cabinet. The information you provide will be identified by your individual number so everything will remain anonymous and completely confidential. Your data will be held for up to 10 years after the study had ended and then destroyed. All data will be managed in line with the Data Protection Act.

There are occasions when confidentiality must be broken. If you disclose information that indicates that you or others are at risk of harm it will be necessary for me to inform the appropriate authorities.

Data will be stored on a computer database using only the individuals' participant number. All files will be password protected.

### **What will happen to the results of the study?**

We intend to publish the results of this study. There will be no identifiable information used. Once all the participants have been seen and the research has been completed we will write to you with a summary of the results.

### **Who is organising and funding this study?**

This study is being organised by Miss Stephanie Keay (Trainee Clinical Psychologist) under the supervision of Dr Fergus Gracey and Dr Sian Coker, and is being funded by the University of East Anglia.

### **Who has reviewed this study?**



The research is being supervised and monitored by the Department of Clinical Psychology at the University of East Anglia. All research in a healthcare setting is reviewed - this study was reviewed by the North West Preston Ethics Committee to protect the interests of service-users.

**Further information and contact details**

I am able to provide further information should you require it. I can be contacted via the following:

Address:

Stephanie Keay

Department of Clinical Psychology  
Norwich Medical School  
Faculty of Medicine and Health Sciences  
University of East Anglia  
Norwich Research Park  
Norwich  
NR4 7TJ

Email: [S.Keay@uea.ac.uk](mailto:S.Keay@uea.ac.uk)

## Appendix G

### Consent form

I

Version 5, 29/11/16



Norwich Medical School  
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 Norwich Research Park Norwich  
 NR4 7TJ  
 Email: clinpsyd@uea.ac.uk  
 Tel: +44 (0) 1603 593076  
 Fax: +44 (0) 1603 591132  
 Web: www.uea.ac.uk

Participant Identification Number:

#### CONSENT FORM

Title of Project: The impact of executive functioning and anxiety on attention to threat in an adult traumatic brain injury population: an experimental group design

Name of Researcher: Stephanie Keay (Trainee Clinical Psychologist)

Please  
 initial box

1. I confirm that I have read the information sheet dated 29/11/16 (version 5) for the above study. I have had the opportunity to think about the information, ask questions and have had these answered. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from within my care team or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I understand that the information held and maintained by the Health and Social Care Information Centre and other central UK NHS bodies may be used to help contact me or provide information about my health status. ☐

5. There are occasions when confidentiality must be broken. If you disclose information that indicates that you or others are at risk of harm it will be necessary for me to inform the appropriate authorities. I understand that should any member of the research team be concerned that I may be a risk to myself or another person then they will contact a member of my care team, my general practitioner or the appropriate authority.

☐

6. I agree to take part in the above study.

☐

\_\_\_\_\_  
Name of Participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of Person  
taking consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

**\*\* Your GP will only be contacted should we have any concerns about risk or the welfare of you or another person. If you do not wish to provide the details of your GP you are still able to participate in the study and will be advised to contact your GP yourself.**

**Name of GP:** \_\_\_\_\_

**Address for GP:** \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

**Telephone number:** \_\_\_\_\_

## Appendix H

### Request for results form



**Version 1. Aug 2015**

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Postgraduate Research Office 2.30  
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NR4 7TJ  
Email: clinpsyd@uea.ac.uk  
Tel: +44 (0) 1603 593076  
Fax: +44 (0) 1603 591132  
Web: www.uea.ac.uk

### Summary of Study Results Contact Details Form

Thank you for participating in the study. If you would like to be sent a copy of a summary the final results of the study then please fill in your details below.

Thank You.

Name: \_\_\_\_\_

**AND**

Email Address: \_\_\_\_\_

**OR**

Postal Address: \_\_\_\_\_

## Appendix I

### Demographic information form

**Version 1. 14/03/16**

#### Participant Demographic Questionnaire

Participant Number		Age	
Date of Assessment		Gender	

Ethnicity	White / Mixed / Indian / Pakistani / Bangladeshi / Other Asian / Black Caribbean / Black African / Other Black / Chinese / Other Ethnic
Marital Status	Single / Married / Co-habiting / Widowed / Divorced
Education	Some Secondary School / GCSEs / A-Levels / Diploma / Undergraduate / Post graduate
Cause of injury	
Date of injury	



## Appendix F

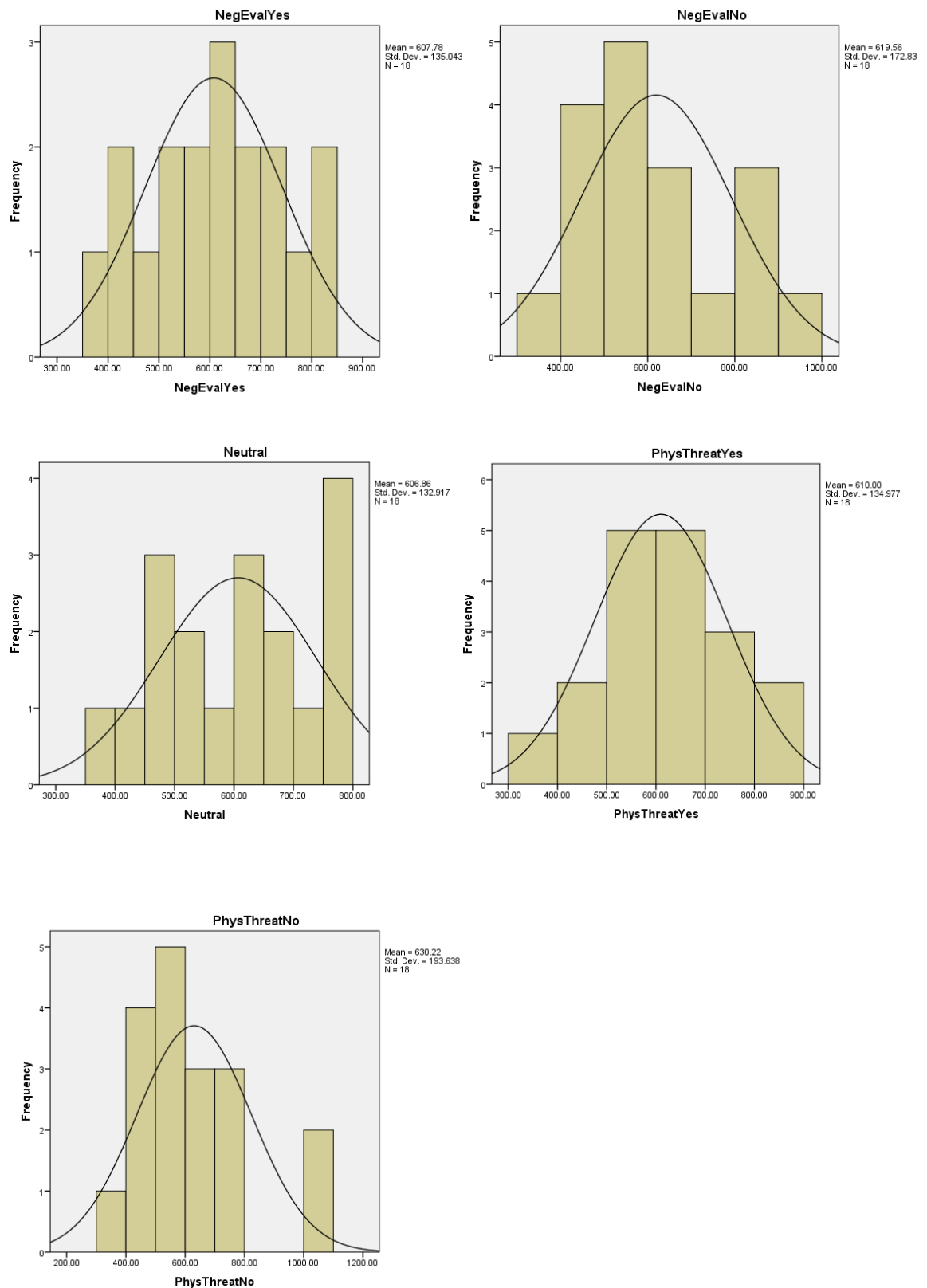
**Table Showing Dot-Probe Word Pairs by Category**

Negative Evaluation		Physical Threat		Neutral Words	
(paired neutral words)		(paired neutral words)		(paired neutral words)	
STUPID	BARREL	INJURY	SILVER	OCTOPUS	POTTING
MOCKED	BANNER	DISEASE	VERSION	AGENT	BROAD
FOOLISH	GRADUAL	LETHAL	MARROW	FLOORING	POSTCARD
EMBARRASSED	TRANSFORMED	CANCER	SADDLE	LEAFLET	OATMEAL
FAILURE	BALANCE	PAIN	BANK	GUJAR	MILLER
DISGRACED	WAREHOUSE	AMBULANCE	FLOWERING	GINGER	RUBBER
PATHETIC	EXTERIOR	DEADLY	LADDER	HOOR	MIND
INFERIOR	INVENTOR	ILLNESS	MUSTARD	INCH	TOOL
WORTHLESS	CULTIVATE	EMERGENCY	FURNITURE	SAUSAGE	PADDOCK
RIDICULED	PICTORAL	VIOLENCE	CREATION	SHAMPOO	GALLERY
INEPT	PURGE	DOCTOR	CATTLE	JUICE	VENUE
CRITICISED	INGREDIENT	COFFIN	ROCKET	CREEK	SALAD
INADEQUATE	LOCOMOTION	STROKE	STRING	FRESH	INDEX
ASHAMED	ORCHARD	FATAL	PERCH	SHEEP	SLOPE
HUMILIATED	MINIATURES	HOSPITAL	NUTSHELL	PIANO	CREST
INCOMPETENT	MANUFACTURE	CORONARY	SNAPSHOT	CARROT	DONKEY

## Appendix L

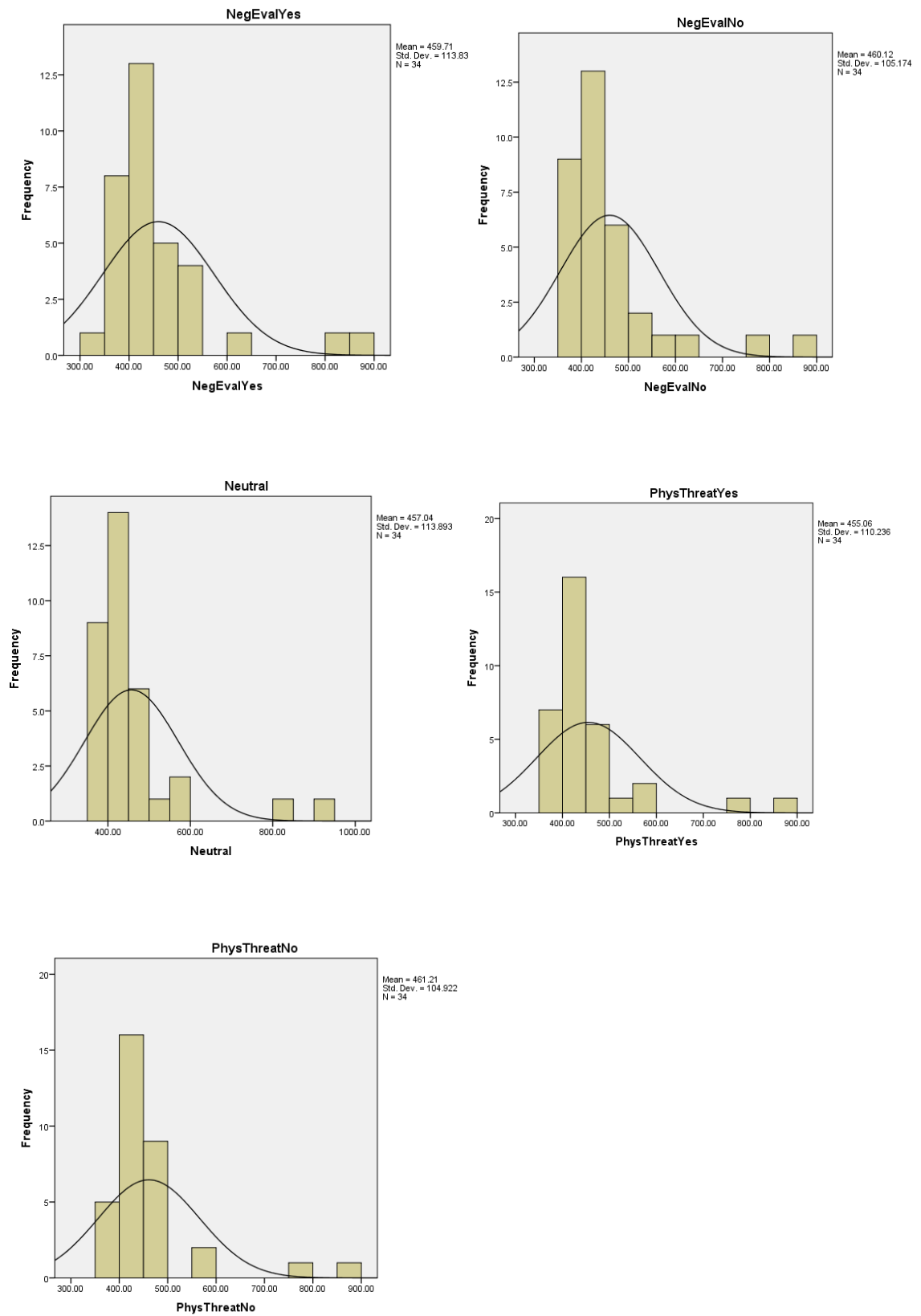
### Graphs for testing assumptions

Histograms showing distribution for TBI group with 4 outliers removed for the five dot probe conditions.

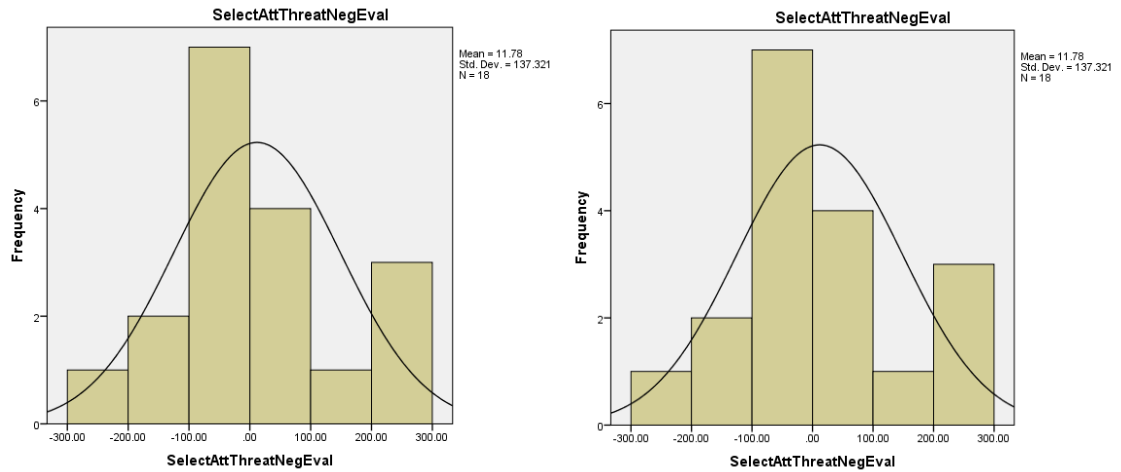




Histograms showing distribution for Healthy Comparison group for the five dot probe conditions.



Histograms showing distribution for TBI group for selective attention to threat



Histograms showing distribution for the comparison group for selective attention to threat

