The Self and Self-Knowledge after Frontal Lobe Neurosurgical lesions

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Systematic Literature Review and Empirical Research Project

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Systematic Literature Review

The Self and Self-Knowledge after Frontal Lobe Neurosurgical lesions

Supervised by Professor Robin Morris and Dr Jessica Fish,
Discussant: Dr Daniel Mograbi

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List of abbreviations and key references

AI-A - Awareness Interview-Adapted (Anderson & Tranel, 1989)

AQ - Awareness Questionnaire (Sherer et al, 1998)

BRIEF-A - Behaviour Rating Inventory of Executive Function-Adult (Rabin et al, 2006)

CAPM - Comprehensive Assessment of Prospective Memory (Roche, 2002)

CFQ - Cognitive Failures Questionnaire (Broadbent et al, 1982)

CHART - The Craig Handicap Assessment and Reporting Technique (Hall et al, 1998)

CIQ - Community Integration Questionnaire (Willer, Rosenthal et al, 1993)

DEX - Dysexecutive Questionnaire (Wilson et al, 1998)

EBIQ - European Brain Injury Questionnaire (Teasdale et al, 1997)

FrSBe - Frontal Systems Behaviour Scale (Grace & Malloy, 2001)

KAS - Katz Adjustment Scale (Katz & Lyerly, 1963)

KBCI - Key Behaviours Change Inventory (Kolitz, Vanderploeg & Curtiss, 2003)

MFIS - Modified Fatigue Impact Scale (Fisk et al, 1994)

MPAI/MPAI-4 - Mayo-Portland Adaptability Inventory (Malec et al, 1997; Bohac et al, 1997)

NSI - Neurobehavioural Symptom Inventory (Cicerone & Kalmar, 1995).

NFI - Neurobehavioural Functioning Inventory (Kreutzer et al, 1996)

NBRS - Neurobehavioural Rating Scale (Levin et al, 1987; McCauley et al, 2001)

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PCRS - Patient Competency Rating Scale (Prigatano et al, 1990)
SADI - Self-Awareness of Deficits Interview (Fleming, Strong & Ashton, 1996)
SCSQ-A - The Social Communication Skills Questionnaire-Adapted (McGann, Werven & Douglas, 1997)
SIP - Sickness Impact Profile (Bergner et al, 1976).
TBIFI - TBI Follow-Up Interview (Malouf, Langon & Taylor, 2014)

1. Abstract

Background: Measurement of awareness plays an important role in adjustment following a brain injury and is noted to impact on engagement with and outcome of rehabilitation.
Aim: To systematically review all instruments used to assess intellectual awareness of deficits following TBI and evaluate study design, instrument properties and methods adopted and explore associated factors.
Results: Thirty-four studies, all rated as fair to good quality, were identified and within these twenty-three different assessment tools were adopted. The most common method of assessment was patient-proxy discrepancy with the AQ, PCRS and FrSBe instruments being most frequently employed. However, variability was noted regarding the type of assessment method dependent on various sample demographics (e.g. age of sample) and injury characteristics (e.g. time post injury). Exploration of the association between non-cognitive factors and awareness was more common than cognitive factors and awareness. Cognitive functioning appeared to be worse when there was increased unawareness. By comparison greater variation was found in non-cognitive associates.
Conclusions: The findings reveal that there still lacks a consensus about the preferred instrument to assess intellectual awareness of deficits after TBI specifically. Recommendations for future research to aid comparability across studies and continued tool development ideas are discussed.

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Self-awareness following Traumatic Brain Injury: a systematic review of current methods of assessment, their properties and their correlates

2. Introduction

Traumatic Brain Injury (TBI) is a very complex phenomenon having dramatically varied effects. TBI can result in cognitive, physical, emotional and behavioural impairments that lead to permanent or temporary changes in functioning. Unawareness of a range of cognitive, emotional, psychosocial and behavioural deficits after TBI is often reported in the clinic. Epidemiological data has estimated awareness deficits affect approximately 45% of people with TBI (Flashman & McAllister, 2002). Professionals working in rehabilitation for people with TBI generally agree that impaired self-awareness significantly complicates both the rehabilitation and community reintegration process (Robertson et al, 2015; Winson et al, 2017). In addition to rehabilitation engagement and outcome, awareness deficits have been adversely linked to caregiver distress and patient quality of life (Sherer et al, 1998; Wise et al, 2005).

The potential impact reduced self-awareness can have on a patient's recovery and rehabilitation sparked an interest in developing methods of exploring unawareness, so that its effect on patient outcome can be studied and efficacy of treatments aimed at

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improving self-awareness can be assessed. However, variability exists in the assessment methods chosen, the perspectives sourced and indeed how awareness is defined.

Awareness is difficult to conceptualise as it can be interpreted in different ways. Several researchers consider self-awareness to be a complex construct with multiple aspects. It has further been suggested that different aspects of self-awareness may impact outcome uniquely. Awareness models typically incorporate several 'types' of awareness[1]. Crosson et al (1989) proposed the pyramid model, which was the first multi-dimensional model of self-awareness. This model conceptualised awareness by proposing three hierarchical levels: intellectual, emergent and anticipatory awareness, and this framework is still prevalent in the literature. Intellectual awareness involves the recognition of deficits and an intellectual understanding of these deficits in everyday life. Emergent awareness refers to 'in-the-moment' awareness, whereby individuals can recognise their difficulties as they occur (e.g. error monitoring). Anticipatory awareness refers to an individual's ability to anticipate when activities and routines may be adversely affected by the injury and cause them to experience difficulties in the future. Studies suggest strong correlation between emergent and anticipatory, but not with intellectual awareness, highlighting these as two separate constructs (O'Keeffe, et al, 2007). Irrespective of the model of awareness, there appears general consensus that at least two separate constructs exist: off-line (intellectual) awareness and on-line (emergent and anticipatory) awareness.

When awareness after brain injury is discussed people typically refer to a person's knowledge and appreciation of his or her difficulties (Winson et al, 2017). In line with this, most studies have focused on intellectual awareness, as does the present review.

From the literature (Smeets et al, 2012; Lloyd et al, 2015), three common approaches to assessing intellectual awareness appear to exist. Two involve comparing patient self-ratings on questionnaires of functional abilities to another standard, typically informant ratings (family or clinician-report), or objective task performance. The other common method of assessment involves clinician-lead semi-structured interviews, following which the professional rates the awareness of the patient using their clinical judgment. For each of these methods a range of measures exists; however, some of these awareness measures

[1] A full review of all models of awareness is beyond the scope of this review. However, Abreu et al (1997) and Clare (2004) provide concise and detailed overviews of the theoretical frameworks proposed to explain deficits in self-awareness.

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have only been used in one published study. This is particularly the case for adapted measures designed to focus more specifically on particular areas of deficit (e.g. Awareness of Theory of Mind, Bach et al, 2006 or fatigue awareness, Chiou et al, 2016). To date, investigation into the comparability of different methods of assessing awareness and their properties has been relatively limited.

Previous reviews concerning acquired brain injury have not been systematic in nature (Fleming et al, 1996), have focused only on child TBI populations (Lloyd et al, 2015) or have focused on the effectiveness of interventions targeting awareness (Schmidt et al, 2011) as opposed to the assessment measures specifically. The most recent previous review (Smeets et al, 2012) exploring the instruments used to measure awareness in adults with ABI imposed strict exclusion criteria that potentially eliminated a number of instruments frequently used clinically and that allow a measure of insight to be obtained (e.g. discrepancy measures), either because they were not specifically designed to measure awareness or because they focused solely on one domain. Additionally, this paper also described its sample population broadly as individuals with an ABI. However, this was not further defined, so ambiguity remains as to the cause of injury (e.g. traumatic versus non-traumatic), constraining the conclusions that can be made for either population specifically. This is of note as although the effects of non-traumatic ABI and TBI are often noted to have similarities, clinically there are key differences that make treating and coping with non-traumatic ABI quite different to TBI, suggesting a benefit to exploring these separately. Furthermore, Bach & David (2006) suggest that self-awareness deficits in TBI may be different from other conditions. For example, non-traumatic ABI (e.g. brain tumours) and neurodegenerative diseases often include brain disturbances that tend to involve the slow progression of symptoms. Comparatively, in TBI, symptom onset is acute, commonly due to RTAs, assaults or falls, for example. This may impact awareness ratings as people with TBI may have little or no time for adjustment to changes in the self in comparison to the potentially longer adjustment period found in a number of non-traumatic ABI conditions. The current review expanded upon Smeets et al's (2012) review findings by focusing on TBI samples specifically and including instruments for which a measure of awareness was the intended focus, as well as those which due to design allowed a measure of awareness to be obtained. The current review, therefore, appears novel and warranted to provide a more comprehensive overview of the methods commonly used to assess unawareness following TBI specifically.

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A number of factors have been posited to impact on the degree of awareness deficits. Longer duration of time since injury is associated with less awareness deficits, with greater impairments typically noted in the post-acute stage (Ownsworth et al, 2006). Lower intelligence (Bogod et al, 2003) and weaker executive functioning skills (Dockree et al, 2015; Morton et al, 2010) have also been shown to correlate with less post-injury awareness. A number of studies have explored the association between emotional state, specifically anxiety and depression, and degree of awareness (Fleming et al, 1998; Chiou et al, 2016). However, variability exists in the consistency of these findings; often, it appears dependent on the awareness assessment measure adopted.

Although various tools exist for detecting impaired self-awareness, there appears to be limited and variable information as to whether and how these relate to other neuropsychological measures (Bogod et al, 2003). The current review will also explore the various correlates that have been linked to awareness measures. Even though a number of variables (e.g. emotional distress, memory) have been linked to TBI and to limited awareness, to the best of our knowledge, whether and in what way these correlate with or intersect the relationship between TBI and awareness has yet to be systematically combined, documented and evaluated.

2.1 Objective

In summary, the overall aim of this systematic review was to identify the various measures employed to assess intellectual awareness in adult patients following TBI as well as evaluate their properties and associated correlates. The present review thus aimed to address the following research questions:

I) Which measurement instruments/methods have been used in empirical studies investigating awareness deficits following TBI?
II) What are the characteristics, purposes and foci of the measurement instruments employed?
III) Were associated factors (e.g. age, mood, IQ, memory) investigated and do these positively correlate with the awareness measures?

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3. Method

The current systematic literature review was carried out according to the PRISMA guidelines (www.prisma-statement.org).

3.1 Search sources and strategy:

Articles were identified through a systematic computerised literature search of peer-reviewed papers using the following databases from inception to the 14th January 2018: Ovid MEDLINE, PsycINFO, Embase and PsycBITE. This was in line with search engines used in previous relevant reviews by Smeets et al (2012) and Lloyd et al (2015). Examination of both published and prospective systematic reviews investigating TBI and awareness deficits were referred to when generating search terms. For Ovid MEDLINE, PsychINFO and Embase key word searching was used for the following terms: TBI, awareness and assessment.

A list of search terms considered within the scope of TBI was generated: traumatic brain injur* or traumatic head injur* or brain injuries or brain damage or traumatic brain injuries or intracranial injur* or neurosurgery or neurosurgical lesion* or neurotrauma or acquired brain injur* or TBI or ABI.

Terms considered within the scope of awareness were generated: *awareness or anosognosia or insight or self-awareness or self-perception or self-concept or denial.

Terms focused on methods of assessing awareness included: proxy or overestimat* or underestimat* or agreement or discrepancy or perspective. These search terms were then combined with the term 'assessment'.

The key search terms and synonyms relating to each were combined using Boolean operators. Limiters and filters were used to apply the inclusion and exclusion criteria described in section 2.3.

In PsycBITE, a specialised database for brain injury research, the target areas of "insight/awareness/knowledge of condition", age group "adults", neurological group "TBI/head injury" and language "English" were selected.

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Manual searching for additional studies was also carried out by consulting reference lists of previous reviews on the topic of awareness in TBI and screening for titles that included key terms. The full search strategy for each database can be found in Appendix A. The first author (LB) completed the article selection procedure. In case of doubt, the collaborating authors were consulted on the specific article. Any lack of agreement was discussed to reach consensus regarding article inclusion.

3.2 Definitions:

In the present review, TBI and awareness measures were conceptualised as follows:

3.2.1 Definition of Traumatic Brain Injury:

Using definitions provided by the briefing paper on head injury from the National Institute for Health and Care Excellence (NICE, 2014) (https://www.nice.org.uk/guidance/qs74/documents/head-injury-briefing-paper2) Traumatic Brain Injuries were those defined as resulting from external physical trauma often due to accidents, assaults or head injury. We excluded non-traumatic injuries derived from either internal or external sources (e.g. stroke, brain tumours, infection, poisoning, hypoxia, ischemia, encephalopathy or substance abuse). Studies including congenital disorders, neurodegenerative disorders and dementias and disorders of consciousness (DOC/PDOC) and samples with mixed cause of injury were also excluded.

3.2.2 Definition of awareness measures

Instruments for which assessing awareness is the primary aim, as well as well as those adapted by design to enable a measure of awareness were included. For example, measures that included both self and proxy ratings, thus allowing a level of awareness to be identified, were sufficient. Using previous reviews as a guide (Fleming et al, 1996; Smeets et al, 2012), the relevant instruments from the selected articles were divided into three formalised methods. The first was a self-proxy rating discrepancy method. This involved comparing patient's self-report of cognitive, emotional, psychosocial, behavioural and other areas of functioning to some other standard, typically an informant's (either a significant other or clinician) report about the patient's abilities. Clinician rated was the second method. Included measures typically were clinician-lead interviews following which the professional rated the awareness of the patient using their

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clinical judgment. The third was a performance-based discrepancy method in which the level of awareness was derived from the difference between the patients' self-report about their functioning and their objective test performance. Attention was given when reviewing papers adopting performance-based methods to exclude those that focused on anticipatory awareness (e.g. predicting performance on a specific task). For all methods it was necessary that the measures yielded data producing quantifiable outcomes. Only methods and measures used to assess intellectual awareness were included. Papers focused on very specific practical tasks (e.g. driving ability) were excluded.

3.3 Eligibility criteria

To be included in the review, articles had to meet the following criteria: (1) articles described an empirical study assessing awareness of deficits after TBI; (2) TBI and awareness measures were conceptualised as described in section 2.2 above; (3) the study populations were human participants; (4) all participants had sustained a TBI and were adults (>18 years) at time of study participation; (5) studies had been published as original articles in peer-reviewed journals; (6) articles were written in English; (7) the articles had been published from inception of the relevant searched databases to 14th January 2018. Unpublished dissertations, conference proceedings, abstracts without locatable full texts, case reports, theoretical and review articles were all excluded. To contain the number of papers, only empirical studies specifically focused on awareness assessment were included. This meant that intervention studies or validation studies focused on tool development were excluded. In addition, studies focusing on acquired non-traumatic brain injury (including TBI as subgroup) and studies including patients with a mental health condition (e.g. schizophrenia) were also excluded.

3.4 Quality assessment

The information gathered from the final selection of studies was assessed for methodological quality and risk of bias. It should be recognized that no 'gold standard' tool for the quality assessment of studies currently exists (Katrak et al, 2004). The present review solely included quantitative research studies; therefore the 'Checklist for assessing the quality of quantitative studies' (Kmet, Lee & Cook, 2004) was applied. Higher scores represented a stronger methodological quality. A second rater independently evaluated seven (20%) of the total number of studies using the quality criteria to check for agreement. The checklist and rating procedure were discussed before ratings were made

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to ensure consistency in interpretation of the checklist items. Inter-rater reliability for the quality scores of these seven papers was calculated in SPSS (version 24) using Intra-Class Correlation and was found to be .97, which is considered excellent. Remaining disagreements were resolved through discussions to determine a final rating.

3.5 Data synthesis

Across the studies included there was variability in participants' age, severity of injury, time since injury and significant variability in the object of awareness (i.e. domain of functioning for which awareness was assessed) and assessment methods adopted. As a result, and in line with Lloyd et al (2015), meta-analysis was not used to synthesize the data. Findings are instead summarised in Tables 1 to 5 (full details tabulated in Appendix B) and described in subsequent sections.

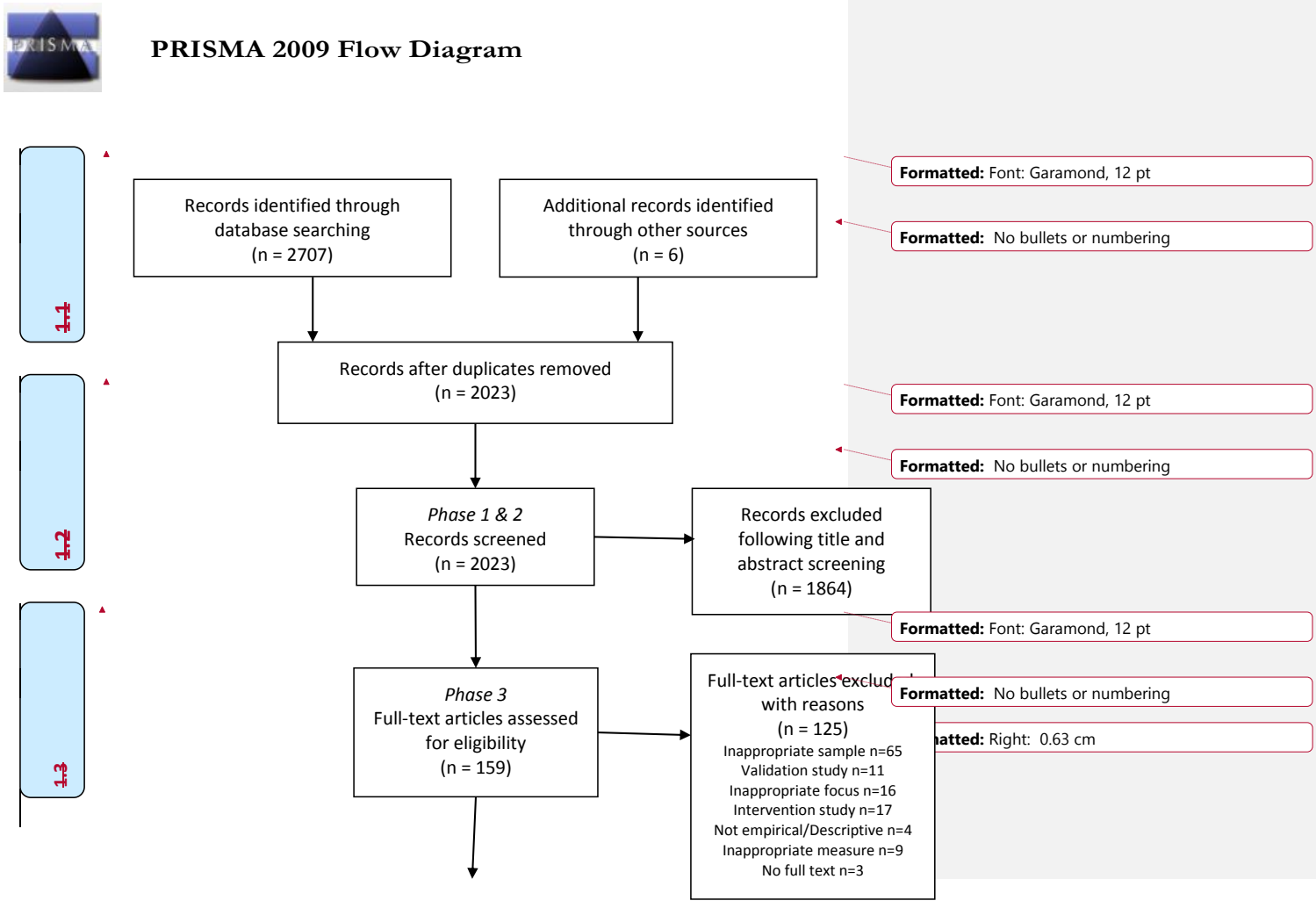

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Figure 1: Flow diagram of study selection process

4. **Results**

The review begins with a brief description of the included studies, detailing factors of particular relevance to the assessment of awareness following TBI. Appendix B includes tables summarising reviewed papers. The papers will then be discussed and critiqued in relation to the aims.

4.1 Study selection

The initial search from all four databases identified 2707 articles. Six additional studies were identified via manual searching and increased the total number of potentially eligible studies to 2713. Removal of duplicate records reduced the number of potentially relevant studies to 2023. The resulting studies were evaluated according to the inclusion criteria described in section 2.3 above. This process was completed in four phases (see Figure 1 for a pictorial summary of the study selection process). *Phase 1* involved a preliminary screening of titles to exclude studies those that had no apparent relevance to the aims of the current review (e.g. they had no reference to TBI and/or awareness). *Phase 2* involved screening the abstracts of all studies identified as potentially relevant following Phase 1.

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Phase 3 involved full text screening of the remaining studies. Studies were excluded with reference to the described eligibility criteria. *Phase 4* involved comparing summarised key information from each of the remaining studies against the eligibility criteria and resulted in 34 studies deemed eligible for review.

4.2 Rating of study quality

Overall, the methodological quality of the studies included in the review ranged from fair to good, with scores ranging from 14 to 22 (mean 19, sd 2.10) out of 22 on the 'Checklist for assessing the quality of quantitative studies' (Kmet, Lee & Cook, 2004 (see Appendix C, Table C1 & Appendix D, Table D1). Five studies were rated fair and 29 good quality. Higher quality studies involved better specification of TBI sample characteristics (e.g. injury severity; specified cause of injury) provided a clear description of the approach for assessing awareness and included statistical analyses that examined and/or controlled for potential covariates. Common limitations across studies that impacted on their quality rating included: a lack of clarity regarding time since injury, not controlling for confounds and omitting estimates of variance for main results.

4.3 Study characteristics

Demographic characteristics of the study samples

The sample sizes varied widely across studies, from 14 (Chiou et al, 2016) to 168 (Richardson et al, 2015). All included studies reported the patient groups' average age at time of study participation. One study (Kelley et al, 2014) reported the median age of sample as 35. Across the remaining 33 studies the mean age was 35.3 (SD, 12.4) years. Only 13 of the studies reported the age range of participants, which was between 18 and 72 years. When split by method of awareness assessment (see Table 1) the mean age and range remained consistent for studies using patient-proxy measures and those using multiple measures, with the majority of participant mean ages falling between 31-40 years, followed by those between 18 and 30 years. For the one study that adopted a clinician rated method, the mean age was slightly higher, with the majority of sample means falling between 40 and 50 years of age. For the two studies using a performance-based discrepancy method, mean ages were slightly lower, falling between 18-30 years. However, of the 34 studies included in our systematic review, only two specified the patients' age at injury (Anderson et al, 1989; Kelley et al 2014) confirming that the injury

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was sustained in adulthood (see section 3.5 below for further information on time since injury). Information regarding the number of male versus female participants who had sustained a TBI was reported by all studies, with the percentage of male participants ranging from 52% to 100%. One study (Niemeier et al, 2014) spilt the TBI sample by gender as this formed the focus of the analysis; however, the gender ratio was still biased towards males.

The majority of studies (n=19) recruited outpatient samples (Bivona et al, 2008, 2014; Carroll et al, 2011; Chiou et al, 2016; Ciurli et al, 2010; Dahlberg et al, 2006; Dawson et al, 2005; Donders et al, 2015; Geytenbeek et al, 2017; Goverover et al, 2014; Kelley et al, 2014; Malec et al, 2007; Pagulayan et al, 2007; Richardson et al, 2014, 2015; Roche et al, 2002; Sawchyn et al, 2005; Vanderploeg et al, 2014; Zimmerman et al, 2017). Inpatient samples were recruited in three studies (Hart et al, 2009; Niemeier et al, 2014; Medley et al, 2000). In three studies (Bogod et al, 2003; Murrey et al, 2005; Prigatano et al, 1998), TBI samples comprised individuals recruited from both inpatient and community settings. In the remaining nine studies (Anderson et al, 1989; Dockree et al, 2015; French et al, 2014; Lanham et al, 2000; Larson et al, 2009; Morton et al, 2010; O'Keeffe et al, 2007: Prigatano et al, 1996; Sherer et al, 1998) the setting was not clearly specified.

Table 1: Summary of study characteristics split by unawareness assessment method (full demographic information can be found in Appendix B, Table BI).

		Method			
	All studies	**Patient-proxy**	**Clinician rated**	**Performance-based discrepancy**	**Miscellaneous (studies using multiple measures)**
	Studies (n) Max=34	**Studies (n) Max=21**	**Studies (n) Max=1**	**Studies (n) Max=2**	**Studies (n) Max=10**
Age of TBI sample (yrs)					
Mean (SD)	35.3 (12.4) *(n=33)*	35.2 (12.2) *(n=21)*	42.9 (16.6) *(n=1)*	28.1* *(n=2)*	36.2 (11.8) *(n=9)*
Median	35 *(n=1)*				35 *(n=1)*
Range	18-72 *(n=13)*	18-72 *(n=7)*	N.S	18-56 *(n=2)*	18-70 *(n=4)*
18-30 years	11	7	0	2	2
31-40 years	18	12	0	0	6
41-50 years	5	2	1	0	2
Time since injury (months)					
Mean (SD)	37.4 (34.6) *(n=27)*	36.6 (34.8) (n=17)	7.7 (4.1) *(n=1)*	6.2 (5.3) *(n=1)*	54.1 (50.6) *(n=8)*

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Median	8.2, 9, 10.8 *(n=3)*	8.2, 10.8 (n=2)			9 *(n=1)*
Range	0.09-576 *(n=16)*	2-479 (n=9)	N.S	1-24 *(n=1)*	0.09-576 *(n=6)*
<12 months (<1 year)	10	6	1	1	2
12-36 months (1-3 years)	9	8	0	0	1
37-60 months (3-5 years)	5	3	0	0	2
61+ months (>5 years)	6	2	0	0	4
Not specified	4**	2	0	1	1
Specified age at injury	2	0	0	1	1
Included control group	8	5	0	1	2
Stated cause of injury	20	11	1	1	7
Severity classification					
Mild	1	1	0	0	0
Moderate - Severe	7	2	0	1	4
Severe	7	6	0	0	1
Full range	19	12	1	1	5
Setting					
Inpatient	3	1	0	0	2
Outpatient	19	15	1	0	3
Mixed	3	2	0	0	1
Not specified	9	3	0	2	4

*SD only reported for one of the studies **Two of these studies were longitudinal and as such reported the time points at which data was collected

4.4 Injury characteristics of TBI across studies

TBI was generally conceptualised as evidence of head trauma and altered consciousness, with length of PTA and brain scanning findings as additional aspects. All studies reported samples as comprised of individuals who experienced/survived TBI and four further described their samples as military personnel or veterans (French et al, 2014; Kelley et al, 2014; Lanham et al, 2000; Vanderploeg et al, 2007). Cause of injury was explicitly specified in 20 studies, with the most common cause being Motor vehicle accidents (MVA). All studies reported the severity of the brain injury experienced by participants by categorising severity using mild, moderate and severe classifications. The majority of studies (n=19; Bogod et al, 2005; Carroll et al, 2011; Dahlberg et al, 2006; Dawson et al, 2005; Dockree et al, 2015; French et al, 2014; Geytenbeek et al, 2017; Goverover et al, 2014; Lanham et al, 2000; Malec et al, 2007; Murrey et al, 2005; O'Keeffe et al, 2007; Pagulayan et al, 2007; Prigatano et al, 1998; Richardson et al 2014, 2015; Sawchyn et al, 2005; Sherer et al, 1998; Zimmerman et al, 2017) comprised

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participant groups with injury severity that spanned the spectrum from mild to severe. Seven studies recruited participants with severe injury alone (Bivona et al, 2008, 2014; Ciurli et al, 2010; Hart et al, 2009; Larson et al, 2009; Medley et al, 2010; Roche et al, 2005) and in seven studies participants were classed as having moderate to severe injury (Anderson et al, 1989; Chiou et al, 2016; Kelley et al, 2014; Marton et al, 2010; Niemeier et al, 2014; Prigatano et al, 1996; Vanderploeg et al, 2007). Only one study (Donders et al, 2015) focused on mild injury specifically. The same distribution of severity was seen when splitting studies by the method of unawareness assessment used, as can be seen in Table 1.

With the exception of Murrey et al (2005), all studies made reference to the method used to classify severity. A combination of the following methods were used across studies: Glasgow Coma Scale scores (GCS), duration of Post Traumatic Amnesia (PTA), duration Loss of Consciousness (LOC), Time to Follow Commands (TFC) and positive neuroimaging findings. Eleven studies (Anderson et al, 1989; Bivona et al, 2008; 2014); Dahlberg et al, 2006; Dawson et al, 2005; Dockree et al, 2015; Goverover et al, 2014; Larson et al, 2009; Prigatano et al, 1996, 1998; Sherer et al, 1998) used the GCS score alone and one study (Niemeier et al, 2014) used duration of PTA alone as an indicator of injury severity. Four studies used positive neuroimaging findings in combination with either GCS (Chiou et al, 2016; Malec et al, 2007) or PTA (Vanderploeg et al, 2007) or PTA and LOC (Lanham et al, 2000) to confirm injury severity. Of the remaining studies, nine made reference to two methods to indicate severity level (Carroll et al, 2011; Geytenbeek et al, 2017; French et al, 2014; Kelley et al, 2014 O'Keeffe et al, 2007; Pagulayan et al, 2007; Richardson et al, 2014, 2015; Roche et a, 2002) and eight studies relied on a combination of the findings from three methods (Bogod et al, 2003; Ciurli et al, 2010; Donders et al, 2015; Medley et al, 2010; Morton et al, 2010; Sawchyn et al, 2005; Zimmerman et al, 2017). See Appendix B, Table B1 for further details of injury severity and cause.

4.5 Time post injury

Twenty-seven studies reported means and standard deviations of the days, months or years since injury. Three studies reported median values (Bivona et al, 2008; Ciurli et al, 2010; Kelley et al, 2014). The mean length of time since injury across studies was 37.4 (SD 34.6) months. Sixteen studies reported the range of time since injury, which varied

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greatly from 0.09 months (3 days) to 576 months (48 years). Four studies made no reference to time since injury (Anderson et al, 1989; Geytenbeek et al, 2017; Niemeier et al, 2014; Pagulayan et al, 2007). However, two of these (Geytenbeek et al, 2017; Pagulayan et al, 2007) were longitudinal studies, so although mean data was not available relating to time post injury for each participant, they did report their follow-up timeframes as one, three and six months and one and twelve months respectively. Table 1 highlights how the mean time post injury for those studies adopting patient-proxy measures appears in line with that of the full sample. However, the mean time post injury for samples in studies using the clinician rated (Richardson et al, 2014) and performance-based discrepancy measures (Anderson et al, 1989; French et al, 2014) are shorter (both <12 months) than when using the patient-proxy measure. For the studies adopting multiple measures, mean time since injury for these samples appeared longer (54.1, SD=50.6) months.

4.6 Study design

Out of the final selection of 34 studies, 29 had a cross-sectional design and five a longitudinal design. Eight cross-sectional studies included a control group; five were comprised of neurologically healthy individuals who had never sustained a TBI (Bivona et al, 2014; Chiou et al, 2016; O'Keeffe et al, 2007; Prigatano et al, 1998; Roche et al, 2005) and one study (Malec et al, 2007) comprised individuals who had sustained an orthopaedic injury (give definition). Two studies included individuals with non-traumatic brain injuries; Anderson et al (1989) included a cardiovascular accident (CVA) and dementia sample as comparative controls and Prigatano et al (1996) included participants with no objective sign of brain impairment (e.g. individuals with a psychiatric illness, learning disability), an ABI group with left hemisphere lesions and an ABI group with right hemisphere lesions as comparative control samples (see Appendix B, Table BI for further details of the control groups).

The studies were conducted across 8 different countries with the largest contributions from the USA (15 studies) followed by the UK and Canada (5 studies each). The publication dates of the studies ranged from 1989-2017. The previous review investing awareness measures in adults with brain injury was conducted in 2012 (Smeets et al, 2012). From our search, we found 12 studies published since 2012. The majority (n=10) used patient-proxy measures (Bivona et al, 2014 (Awareness Questionnaire: AQ); Chiou et al, 2016 (AQ, Modified Fatigue Impact Scale: MFIS); Dockree et al, 2015 (Cognitive

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Failures Questionnaire: CFQ, Frontal Systems Behaviour Questionnaire: FrSBe, Patient Competency Rating Scale: PCRS); Donders et al, 2015 (Behaviour Rating Inventory of Executive Function-Adult: BRIEF-A); Geytenbeek et al, 2017 (Mayo-Portland Adaptability Inventory: MPAI-4); Goverover et al, 2014 (AQ); Kelley et al, 2014 (TBI Follow-Up Interview: TBIFI); Niemeier et al, 2014 (FrSBe, PCRS); Richardson et al, 2015 (AQ); Zimmerman et al, 2017 (PCRS); one used a clinician rated measure (Richardson et al, 2014 (Self-Awareness of Deficits Interview: SADI) and one used the performance-based discrepancy method (French et al, 2014 (Neurobehavioural Symptom Inventory: NSI vs. neurocognitive performance).

4.7 Research question I: Assessment of unawareness

Table 2 shows that across the included studies, three different assessment methods were used. These included: (i) patient-proxy discrepancy ratings; (ii) clinician rated scales; and (iii) performance-based discrepancies. Across these three methods, 23 different assessment tools were used. The most common method was patient-proxy discrepancy and 19 different measures were used. Within both clinician rating and performance-based discrepancy methods two different measures were used.

Table 2 highlights the AQ and PCRS as the most commonly used measures to assess unawareness in TBI samples, with each appearing in nine studies. Two of the studies that adopted the PCRS measure specified that they used translated versions for their study populations (Prigatano et al, 1998: Spanish; Zimmerman et al, 2017: Brazilian). The FrSBe was used by four studies and the CFQ and CIQ (Community Integration Questionnaire) used in two studies each. All of these are patient-proxy discrepancy measures. The SADI, a clinician rated measure, was also used in three studies. All remaining measures appeared once only.

Variability existed in the number of measures that studies used to assess unawareness (see Table 3 for a summary). Of the studies using one measure to assess unawareness, one administered a measure from the clinician rated method (Richardson et al, 2014 (SADI) and two studies used a performance-based discrepancy measure (Anderson et al, 1989; French et al, 2014). The remaining 21 studies used a patient-proxy discrepancy measure of which only five adopted patient-clinician discrepancy ratings. Three of these five (Carroll et al, 2011; Niemeier et al, 2014; Sherer et al, 1998) used both the patient-

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significant-other and patient-clinician versions of the same measure. The remainder used the patient-significant other ratings only. Of those studies using two measures, four of these used two measures from same method, namely two patient-proxy discrepancy measures (Chiou et al, 2016 (AQ, MFIS); Hart et al, 2009 (AQ, PCRS); Kelley et al, 2014 (CIQ, TBIFI); Niemeier et al, 2014 (PCRS, FrSBe). The remaining two studies combined a patient-proxy discrepancy measure and a clinician rating scale (Bogod et al, 2003 (Dysexecutive Questionnaire: DEX, SADI); Lanham et al, 2000 (Katz Adjustment Scale: KAS; Neurobehavioural Rating Scale: NBRS insight item). Two of the three studies that administered three measures used different patient-proxy discrepancy measures (Dahlberg et al, 2006 used the CIQ; the Craig Handicap Assessment and Reporting Technique-Short Form: CHART-SF and the Social Communication Skills Questionnaire-Adapted: SCSQ-A) and Dockree et al, 2015 used the CFQ, FrSBe, PCRS) and one study (Morton et al, 2010) combined the use of two patient-proxy discrepancy measures (DEX, SADI) with a clinician rated measure (AQ). The one study to use four measures, (O'Keeffe, et al, 2007) administered one clinician rated measure (Awareness Interview-Adapted: AI-A) and three patient-proxy rating scales (CFQ, FrSBe, PCRS).

Table 3: Number of measures included in studies

	Total	**Studies**
Studies using 1 measure	24	Anderson et al (1989**); Bivona et al (2008; 2014); Carroll et al (2011); Ciurli et al (2010); Dawson et al (2005); Donders et al (2015); French et al (2014**); Geytenbeek et al (2017); Goverover et al (2014); Larson et al (2009); Malec et al (2007); Medley et al (2010); Murrey et al (2005); Pagulayan et al (2007); Prigatano et al (1996; 1998); Richardson et al (2014*, 2015); Roche et al (2002); Sawchyn et al (2005); Sherer et al (1998); Vanderploeg et al (2007); Zimmerman et al (2017)
Studies using 2 measures	6	Bogod et al (2003); Chiou et al (2016); Hart et al (2009); Kelley et al (2014); Lanham et al (2000); Niemeier et al (2014);
Studies using 3 measures	3	Dahlberg et al (2006); Dockree et al (2015); Morton et al (2010)
Studies using 4 measures	1	O'Keeffe et al (2007)

* Studies whose single method is clinician rated ** Studies whose single method is performance-based discrepancy

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Table 2: Methods (n=3) and instruments (n=23) used to assess intellectual awareness.

Method	Instrument	Focus/Key features	Index of awareness	Times used	Study
Patient-Proxy discrepancy ratings (n=19)	AQ	Pre- and post-injury metacognitive functioning; cognitive, behavioural/affective, motor/sensory	Self vs. SO	7	Bivona et al (2008; 2014); Chiou et al (2016); Goverover et al (2014); Hart et al (2009); Morton et al (2010); Richardson et al (2015)
			Self vs. SO and self vs. clinician	2	Carroll et al (2011); Sherer et al (1998)
	PCRS	Post-injury functioning; behavioural, cognitive, emotional factors; ADLs, cognitive, interpersonal functioning, emotional regulation	Self vs. SO	8	Ciurli et al (2010); Dockree et al (2015); Hart et al (2009); O'Keeffe et al (2007); Prigatano et al (1996; 1998*); Sawchyn et al (2005); Zimmerman et al (2017*)
			Self vs. SO & self vs. clinician	1	Niemerer et al (2014)
	FrSBe	Pre- and post injury abilities; assesses apathy, disinhibition, executive function	Self vs. SO	4	Dockree et al (2015); Larson et al (2009); Niemerer et al (2014); O'Keeffe et al (2007)
	CFQ	Post-injury focus; measures propensity for everyday failures in memory, perceptions and action slips	Self vs. SO	2	Dockree et al (2015); O'Keeffe et al (2007)
	CIQ	Post-injury focus; engagement in home, social and work activities	Self vs SO	2	Dahlberg et al (2006); Kelley et al (2014)
	DEX	Three factor (cognitive, emotional, and motivational) questionnaire measuring post-TBI deficits	Self vs. clinician	1	Bogod et al (2003)
			Self vs. SO	1	Morton et al (2010)
	KAS	Post-injury; community integration subscales	Self vs. SO	1	Dawson et al (2005)
		Focused on belligerence, social irresponsibility, orientation, speech/cognitive dysfunction subscales	Self vs. SO (concordance ratings)	1	Lanham et al (2000)
	BRIEF-A	Focus on current functioning; rating of executive behaviours	Self vs. SO	1	Donders et al (2015)
	CHART-SF	Focus on current functioning: Measures societal participation and community integration; two subscales used: occupation and social integration.	Self vs SO	1	Dahlberg et al (2006)
	CAPM	Focus on current functioning: Prospective memory failure in everyday activities; Two components rated: BADL & IADL	Self vs SO	1	Roche et al (2002)
	EBIQ	Focus on current functioning: Cognitive, emotional and social difficulties following BI	Self vs. clinician	1	Medley et al (2010)
	KBCI	Pre- and post-injury functioning; assesses executive, interpersonal and emotional behaviours	Self vs SO	1	Vanderploeg et al (2007)
	MFIS	Post-injury functioning; assess physical, cognitive &	Self vs. SO	1	Chiou et al (2016)

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		psychosocial domains			
**	MPAI	Post-injury functioning; focus on total and 4 selected subscale scores: communication, emotions, Independent living skills, relationships	Self vs. SO	1	Murrey et al (2005)
	MPAI-4	Post-injury functioning; Ability subscale only	Self vs. SO	1	Geytenbeek et al (2017)
	NFI	Post-injury; NFI-Dif = constructed index of SA, combined communication, somatic, memory/attention, motor to assess impairment independent of emotional factors	Self vs SO	1	Malec et al (2007)
	SIP	Post-injury functioning; covers 12 functional domains; study used psychosocial factor, physical factor and total scores	Self vs. SO	1	Pagulayan et al (2007)
	SCSQ-A	Post-injury functioning; social communication skills	Self vs. SO	1	Dahlberg et al (2006)
	TBIFI	Post-injury; cognitive, emotional, neurological symptoms Clinician lead interview, patient/SO respond using Likert scale	Self vs, SO	1	Kelley et al (2014)
Clinician Rated (n=2)	SADI	Post injury focus; gathers qualitative and quantitative information on SA of deficits following TBI	Semi-structured interview	3	Bogod et al (2003); Morton et al (2010); Richardson et al (2014)
	NBRS insight item	Post-injury; item rating level of inaccurate insight and self-appraisal in relation to level of ability and personality change	Single item completed by clinician	1	Lanham et al (2000)
Performance-based discrepancy (n=2)	AI-A	Post-injury functioning; Awareness of current cognitive and motor impairments	Discrepancy between patient self-report on structured interview and test performance	1	Anderson et al (1989); O'Keefe et al (2007)
	NSI vs. neurocognitive test performance	Post-injury ability; 3 items included which measured self-reported cognitive complaints of attention/concentration, memory and processing speed/organisation	Compared self-rated cognitive complaints to test performance	1	French et al (2014)

AQ: Awareness Questionnaire (Sherer e al, 1998); PCRS: Patient Competency Rating Scale (Prigatano et al, 1986); FrSBe: Frontal Systems Behaviour Scale (Grace & Malloy, 2001); CFQ; Cogntive Failures Questionnaire; CIQ: Community Integration Questionnaire; DEX: Dysexecutive Questionniare; KATS: Kats Adjustment Scale; BRIEF-A: Behaviour Rating Inventory of Executive Function-Adult; CHART-SF: The Craig Handicap Assessment and Reporting Technique-Short Form; CAPM: Comprehensive Assessment of Prospective Memory; EBIQ: European Brain Injury Questionnaire; KBCI: Key Behaviours Change Inventory; MFIS: Modified Fatigue Impact Scale; MPAI/MPAI-4: Mayo-Portland Adaptability Inventory; NFI: Neurobehavioural Functioning Inventory;; SIP: Sickness Impact Profile; SCSQ-A: The Social Communication Skills Questionnaire-Adapted; TBIFI: TBI Follow-Up Interview; NBRS: Neurobehavioural Rating Scale; AI-A: Awareness Interview-Adapted; NSI: Neurobehavioural Symptom Inventory; *Prigatano et al (1998) used PCRS but translated to Spanish version; Zimmerman et al (2017) used Brazilian version of PCRS; **Counted MPAI and MPAI-4 as separate as have slightly different scoring systems

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4.8 Research question II: Properties of measures of unawareness

Only five measures (AQ, PCRS, SADI, NBRS insight item, AI-A) are specifically designed to assess unawareness. All others, through design, allowed a measure of unawareness to be derived. Table 2 provides basic information on the key features and focus of the measures of unawareness adopted in the included papers. The AQ, PCRS, DEX and EBIQ all had separate versions to allow not only patient and significant other ratings, but also patient-clinician discrepancy ratings to be obtained. Of the studies that adopt patient-proxy measures a preference appears for the patient-SO version over the patient-clinician version. Three studies (Carroll et al, 2011; Sherer et al, 1998 (AQ); Niemeier et al, 2014 (PCRS) combine and use both patient-SO and patient-clinician versions, and two studies (Bogod et al, 2003 (DEX); Medley et al, 2010 (EBIQ) solely use the patient-clinician version. Three measures allow a comparison of present and pre-morbid ratings on patient functioning, allowing changes in functioning to be highlighted. These are the AQ, FrSBe and KBCI and all are patient-proxy measures. All other assessment measures refer solely to the present self, adopting a focus on post-injury functioning.

Of the 19 patient-proxy discrepancy measures employed across studies, 18 were delivered in questionnaire format. Thirteen of these questionnaires measures were administered in full (AQ, BRIEF-A, CFQ, CIQ, DEX, EBIQ, FrSBe, KBCI, MFIS, MPAI, NFI, PCRS, SCSQ). The majority of these covered multiple domains which could be explored independently, the common areas being cognitive, emotional/affective and social, whereas two of these measures were designed to assess only one domain: the BRIEF-A assessed executive functions and the SCSQ focused on social communication skills. For the remaining five patient-proxy measures (CAPM, CHART-SF, KAS, MPAI-4, SIP), only specific subscales of the questionnaire were employed, typically those most relevant to the focus of the study. The one exception to the questionnaire method used the TBIFI, which is a clinician lead interview in which the self-reported responses of individuals with TBI and their family members are rated on a Likert scale and then compared. Questions on this interview measure are pre-defined, but cover a range of domains.

The performance-based method tended to focus on unawareness in relation to the cognitive domain specifically. French et al (2014) adopted a self-rating tool, the NSI, in

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order to compare participants' scores on this to objective performance on cognitive testing. The authors only included selected items related to targeted areas of cognition from this inventory. Anderson et al (1989) and O'Keeffe et al (2014) used the AI, which primarily includes questions targeting patients' views of their abilities across a number of cognitive skills. By comparison, for the clinician-rated method, both the SADI and the NBRS do not specify domains of functioning, thus allowing the clinician choice as to the various areas of deficit they may wish to explore. This differentiates these measures from both the other interview-based techniques above and the questionnaire-based measures.

All measures allowed participants to appraise the abilities of the individual with TBI in terms of strengths and difficulties. However, only three studies explored the implications of these deficits in everyday life. Again, each of these adopted patient-proxy discrepancy measures. Dahlberg et al (2006) used the occupation and social integration subscales of the CHART-SF to measure social participation and community integration, as well as the CIQ to assess engagement in home, social and work activities. The CIQ was also used by Kelley et al (2014). Dawson et al (2005) used the community integration subscales of the KAS.

All measures across all methods allow a certain degree of awareness to be ascertained. In the case of the clinician rated and performance-based methods the level of unawareness was derived by collating the information gained from the measure adopted (e.g. interview or inventory) to create an index score. Although the range of these indices was relatively limited (e.g. 0-3) they still provide information on the degree of unawareness as opposed to simplifying this to a dichotomous outcome (e.g. the presence or absence of awareness).

4.9 Research question III: Associated factors explored

Given that the focus of this paper is on measures of unawareness, the associated factors findings are split by measure also (see Appendix B, Table B2 for full details). 'Miscellaneous' refers to those papers that created a composite by combining different measures of awareness and then exploring associates in relation to this composite score, as opposed to in relation to one specific measure. The remaining studies that employed multiple measures to assess awareness looked at associates in relation to each individually.

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Most papers explored associated factors likely to impact levels of unawareness. Twenty-seven of the thirty-four papers included explored associated factors. The remaining seven papers that did not explore associated factors all employed patient-proxy measures. With reference to the measures themselves, this meant that associated factors were not investigated in relation to the CHART-SF, CAPM, CIQ, MPAI, SCSQ-A or SIP at all. Although one study did not explore associates in relation to the KAS, another study did, meaning that this measure still contributed to the analysis. Three papers (Donders et al, 2015: BRIEF-A; French et al, 2014: NSI vs test performance; Prigatano et al 1996: PCRS) examined associations with patient self-report scores rather than in relation to discrepancy scores, and as such were not included in this analysis. Sixteen papers investigated both cognitive and non-cognitive associates, one examined cognitive associates only and seventeen examined only non-cognitive associates. For full details the findings of each paper see Appendix B, Table B2. Results shall subsequently be presented in relation to methods of assessment and measures used to best meet the aims of the current review. Table 4 details the number of measures for which associative factors were explored as well as the number of these for which significant associations were found.

Table 4: Breakdown of number of associates explored across methods

Method **Associate type explored**	**Patient-proxy**	**Clinician rated**	**Performance-based**	**Miscellaneous**	**Total**
No. of measures	**18**	**2**	**2**	**2**	**24**
No. with associates explored	**12**	**2**	**1**	**2**	**17**
Cognitive only	0	0	1	0	1
Non-cognitive only	7	0	0	1	8
Both	5	2	0	1	8
No. of measures with sig associates	**11**	**2**	**1**	**1**	**15**
Cognitive only	0	0	1	0	1
Non-cognitive only	8	0	0	1	9
Both	3	2	0	1	5

As Table 4 highlights, patient-proxy measures (n=7; FrSBe, CIQ, EBIQ, KBCI, MPAI-4, NFI, TBIFI) were most often examined in relation to non-cognitive associates alone. All measures found some significant associations with non-cognitive factors, with the exception of the KBCI. Five of the measures (AQ, PCRS, DEX, KAS, MFIS) were investigated in relation to both cognitive and non-cognitive associates and results found

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significant associations with three measures (AQ, PCRS; DEX), but for two measures (KAS, MFIS) only the non-cognitive associate was significantly related. The two clinician rated measures were both explored in relation to both cognitive and non-cognitive associates and significant associations were found with both. Only one of the performance-based discrepancy measures was examined in relation to cognitive associates alone, and this produced significant findings. In the miscellaneous measures, significant associations with both cognitive and non-cognitive factors were seen for the composite that comprised three different patient-proxy measures (Dockree et al, 2015). However, no significant associations were found for the composite that combined three patient-proxy measures and a clinician rated interview scale (O'Keeffe et al, 2007).

The majority of associates were investigated in relation to total scores on awareness measures. However, for those measures that allowed, when associates were explored in relation to separate subscales these are specifically noted.

4.9.1 Cognitive factors found to be significantly associated with awareness measures

4.9.1.2 Executive Function

The relationship between awareness and executive function was examined in relation to thee of the awareness measurement categories (patient-proxy, clinician rated and miscellaneous measures). Across six measures (AQ, DEX, PCRS, SADI, NBRS insight item and Misc composite) perseverative responding, difficulties with cognitive flexibility, reduced fluency, reduced error monitoring and increased errors were noted. Increased unawareness as rated by the composite derived for the miscellaneous measure was found to be specifically associated with increased errors on the Modified-Six Elements Test (M-SET; subtest of the BADS: Behavioural assessment of the dysexecutive syndrome, Wilson et al, 1996). Increased errors on the Wisconsin Card Sorting Test (WCST; Arnett et al, 1994) (e.g. lower categories and higher perseverative responses and errors) were associated with increased unawareness as noted by both AQ and PCRS discrepancy scores. This remained when subscales of the AQ were considered separately, but stronger correlations were found for the cognitive subscale than the behavioural/affective and sensory/motor subscales (Bivona et al, 2008). Poor response monitoring as measured by the SOPT was associated with increased unawareness assessed with the AQ, DEX and SADI. Increased unawareness based on scores from the SADI was also associated with increased errors on the go-no-go task and Stroop test. Increased intrusions and false positives on the CVLT (California

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Verbal Learning Test, Crosson et al, 1988; memory executive factor) were associated with increased unawareness as rated in the NBRS insight item. In all cases negative associations were found, with reduced performance on a range of measures of executive function being associated with increased unawareness.

4.9.1.3 Memory

The relationship between awareness and memory ability was investigated in relation to two patient-proxy measures. Poorer performance on the Letter-Number Sequencing task was associated with increased unawareness as measured by the AQ-cognitive subscale only (Chiou et al, 2016), highlighting worse working memory performance was associated with greater cognitive unawareness. Memory performance as measured by the RAVLT (Rey Auditory Verbal Learning Test; Spreen & Strauss) was found to be negatively associated with awareness performance assessed by the PCRS; specifically poorer delayed recall was associated with increased unawareness.

4.9.1.4 Intellect

The relation between IQ performance and level of unawareness, derived from patient-proxy, clinician rated and performance-based measures, was explored. In all cases negative associations were found, with lower IQ scores being associated with increased unawareness. Lower IQ (measured by combined Vocabulary and Block Design scores) was associated with increased unawareness assessed by both DEX and SADI measures. Level of awareness as assessed by the discrepancy between AI score and test performance was also found to be negatively associated with verbal IQ (VIQ) scores, with lower VIQ scores being associated with increased unawareness.

4.9.1.5 Other

A number of other cognitive factors were explored in relation to level of awareness measured by two patient-proxy measures (AQ and PCRS). Theory of Mind ability and performance on a line orientation task was found to be negatively associated with level of unawareness on the AQ. Poorer performance on the faux-pas task (Stone et al, 1998; signifying reduced perspective taking) and lower scores on a line orientation task, were both found to be significantly related to increased unawareness.

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4.9.2 Non-cognitive factors found to significantly associate with awareness measures

4.9.2.1 Demographics (age, gender)

The relation between gender and level of unawareness was explored in relation to one patient-proxy and one clinician rated measures. In both the PCRS and the SADI men were found to show greater unawareness than women. The PCRS was found to be negatively associated with age, with younger age significantly associated with increased unawareness.

4.9.2.2 Injury characteristics (severity, chronicity)

Four measures (two patient-proxy: AQ (motor/sensory domain only), FrSBe; one clinician rated: SADI; and one miscellaneous) all found time since injury to be negatively associated with level of unawareness; less time since injury was associated with increased unawareness. Injury severity was found to be positively associated with level of unawareness (e.g. increased injury severity was associated with increased unawareness) as assessed with three patient-proxy measures (AQ, CIQ, KAS) and two clinician-rated measures (SADI, NBRS insight item). A positive association was also found between level of unawareness and frontal lobe damage, with increased unawareness associated with increased damage in the frontal regions.

4.9.2.3 Mood

Mood factors were explored in relation to five patient-proxy measures (AQ, PCRS, MFIS, MPAI-4, NFI) and one clinician rated measure (SADI). All but one measure found negative associations between mood factors (e.g. emotional distress and adjustment) and level of unawareness. Lower emotional distress scores (HADS total; Zigmond & Snaith, 1983), lower depression scores (HADS, NFI-Depression scale), lower anxiety and stress scores (DASS-21; Henry & Crawford, 2011) and lower levels of emotional adjustment (KAS-relative) were associated with increased unawareness. The one exception was found when employing the MFIS, which assessed fatigue awareness. Positive associations were found, with more symptoms of depression (measured by the BDI-II; Beck, Steer & Brown, 1996) significantly relating to increased fatigue

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unawareness (across all subscales of the MFIS). A positive association was also found between trait anxiety (measured by the STAI, Spielberger et al, 1970) and level of unawareness on the MFIS-P and MFIS-Psy subscales, indicating that high anxiety was associated with reduced fatigue awareness particularly in the physical and psychosocial domains. Three other positive associations were found with higher apathy ratings (NPI score), higher self-esteem rating (RSES) and higher depression scores in close others (HADS) being associated with increased unawareness (greater AQ discrepancy score).

4.9.2.4 Psychosocial

Three patient-proxy measures were found to be significantly associated with various measures of psychosocial functioning. The AQ was found to be positively associated with self-ratings of QoL and satisfaction with life (e.g. higher ratings associated with increased unawareness). Greater life satisfaction was also significantly associated with increased unawareness as measured by the TBIFI. The TBIFI was also found to negatively relate to work outcome, with increased unawareness being associated with poor CIQ scores. Poorer psychosocial functioning as derived from SPRS scores was also found to be associated with increased unawareness when assessed using the MPAI-4. This suggests increased unawareness to be negatively associated with psychosocial integration in terms of work and leisure, relationships and independent living skills.

4.9.2.5 Other

Level of unawareness on the EBIQ was significantly associated with outcome of the IPQ-R (Illness Perception Questionnaire-revised for TBI; Snell et al, 2010). A negative association was found with low control/ambivalent self-ratings (e.g. lower perceived control or fewer difficulties and consequences of the injury), whereas a positive association with high optimism self-ratings (e.g. high perceived personal and treatment control) was found. DRS scores were found to positively associate with level of unawareness on the AQ, with higher scores related to increased unawareness. Increased unawareness (greater difference scores on FrSBe) was also found to significantly relate to decreased Pe amplitude (an electrophysiological index of performance monitoring), highlighting a negative association.

4.9.3 Interim summary

Summarising across all methods and measures, cognitive functioning when assessed via objective test performance typically appeared to be worse when there was increased

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unawareness. The key areas of cognitive function explored included executive and memory ability as well as intellectual functioning. By comparison, greater variation was seen in non-cognitive associates, in particular mood factors and self-ratings on non-cognitive functioning, which appeared dependent on both the associate factor explored and the specificity of the awareness domain assessed.

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Table 5: Significant associates by method of awareness and measure

Method	Measures with significant associates (n=number of papers)	Positive associates More unawareness=higher/more X	Negative associates More unawareness=lower/less X
Patient-Proxy discrepancy	AQ (n=9)	Non-cognitive: DRS score; Apathy score (NPI); Increased damage in frontal regions; QoL and satisfaction with life self-ratings; Injury severity; Depression in close others (HADS); Self-esteem (RSES)	Cognitive: Performance on EF tasks: WCST, SOPT; Perspective-taking; Line orientation performance; WM (LNSeq) Non-cognitive: Emotional distress (HADS total); Depression (HADS); Time since injury
	PCRS (n=7)	Non-cognitive: Injury severity *Gender, Men showed greater unawareness than women*	Cognitive: Performance on EF tasks; WCST, semantic fluency; Memory Non-cognitive: Emotional adjustment (KAS-relative); Younger age
	FrSBe (n=2)		Non-cognitive: Pe amplitude; Time since injury
	CIQ (n=2)	Non-cognitive: Injury severity	
	DEX (n=2)		Cognitive: Performance on EF tasks: response monitoring SOPT; IQ
	KAS (n=2)	Non-cognitive: Injury severity	
	EBIQ (n=1)	Non-cognitive: High optimism ratings	Non-cognitive: Low control/ambivalent ratings
	MFIS (n=1)	Non-cognitive: Symptoms of anxiety and depression	
	MPAI-4 (n=1)		Non-cognitive: Emotional distress: Anxiety, stress; poorer psychosocial functioning (SPRS)
	NFI (n=1)		Non-cognitive: NFI-Depression scores
	TBIFI (n=1)	Non-cognitive: Life satisfaction	Non-cognitive: Work outcomes: CIQ
Total number of measures	**11**		
Clinician rated	SADI (n=3)	Non-cognitive: Increased severity *Gender: Men showed greater unawareness (less accurate goal-setting) than women*	Cognitive: Performance on EF tasks: SOPT, go-no-go, Stroop; Lower IQ Non-cognitive: Mood state: Emotional distress (combined anxiety and depression scores on HADS); Time since injury
	NBRS insight item (n=1)	Non-cognitive: Increased severity	Cognitive: Memory executive factor score (CVLT free recall intrusions and false positives)
Total number of measures	**1**		
Performance-based discrepancy	AI self-report vs. test performance (n=1)	Cognitive: Temporal disorientation scores	Cognitive: VIQ
Total number of measures	**1**		

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Miscellaneous	Composite score (n=1)	Cognitive: EF, error monitoring, M-SET scores Non-cognitive: Time since injury
Total number of measures	**1**	

Refer to Table 2 or list of abbreviations (page X) for full titles or awareness measures

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5. Discussion

Overall, the purpose of this paper was to provide a comprehensive overview of measurement instruments used to assess awareness of deficits following TBI, as well as their properties and associated factors. To the best of the authors' knowledge, our review is the first to have considered the assessment of awareness in a TBI sample specifically, with previous reviews having used samples of mixed aetiology (Smeets et al, 2012); and is the first to systematically evaluate the impact of associated factors on level of awareness.

Our systematic search identified thirty-four studies and our review highlights the diversity of instruments in the TBI field. Within these thirty-four papers, twenty-four different measurement instruments were identified, split by the three assessment methods adopted. The most commonly adopted method of assessment for TBI samples was the patient-proxy method with 19 of the measures following this approach. Within these, family members or significant others were most frequently used as proxies, with only four studies exploring patient-clinician discrepancies. This is interesting given that the existing literature often questions the accuracy of relatives' judgments about patients functioning, speculating that clinician report may be less emotionally loaded than relatives (Lanham et al, 2000; Howland et al, 2017). A further two clinician-rated measures and two performance-based discrepancy tasks were also identified.

Our review reveals that a number of factors may influence the choice of instrument (e.g. time post injury, domain of interest assessed). With reference to chronicity, it appears that particular methods are preferred dependent on the time post-injury. For patient samples assessed closer to injury, clinician rated and performance-based discrepancy methods were adopted. These may rely more on examiner judgement, and focus more on objective performance, which are typically explored earlier post-injury when the patient may be experiencing more acute difficulties with concentration and adjustment. The mean time since injury of samples completing patient-proxy measures, by comparison, was higher, suggesting that these are employed later post-injury. Patient-proxy measures are typically questionnaire based, often requiring a level of independence in completion, therefore the longer duration since injury, the more likely the success with this. Additionally, assessing later post-injury provides the patient with some experience of community living and increased opportunities to notice changes

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and challenges. With regards to the specificity of the targeted domains of awareness assessed, the patient-proxy measures showed greatest variation in the range of domains and breadth of functions assessed, marking these apart from the clinician-rated and performance-based discrepancy methods. This great variation amongst how instruments are used makes comparing across study outcomes difficult, but positively, marks a flexible use of the instruments in order to gain a wealth of information, which likely has positive clinical utility.

Additional variation across instruments was noted regarding the timings of assessment. The majority of instruments focused on current post-injury functioning. However, for two of the commonly used patient-proxy measures in this review (the AQ and the FrSBe) respondents were asked to rate both pre- and post-injury functioning to allow an index of change to be assessed, suggesting that this change index is valued following TBI. There is debate regarding whether the measures of awareness that involve pre-post-ratings may be more complex than those focused solely on current functioning (Niemeier et a, 2014), which if true may again make cross study comparison challenging and as such may warrant further attention.

An important feature of awareness is its heterogeneous presentation, which has resulted in greater reliance on measurement instruments that are able to quantify the degree of awareness impairment and are suited to both clinical and research use. This seems important, as having research based around practical and useable tools will be of most benefit when applying these clinically. The current review only included measures that obtained a quantitative output. However, qualitative tools do exist and systematically exploring the frequency of use of more qualitative assessment of awareness could form an interesting comparative future review.

Specifically, we found the AQ and the PCRS to currently be the most widely used instruments to assess awareness in TBI. Both are specifically designed to measure the degree of self-awareness in several domains. These were closely followed by the FrSBe, which by comparison was not designed specifically as an awareness measure. Our review confirms that there appears a range of instruments assessing awareness of deficits, particularly patient-proxy measures. However, awareness assessment was not the intended focus for the majority, with many instruments adapted by researcher

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design to assess patient's awareness. Adaptations typically included creating an informant version of a measure to provide a discrepancy rating. Typical reasons for this were that the measure in question was already included as part of the test battery and adapting it to allow a measure of awareness did not extend testing time or increase the demands placed on patients. However, these adaptations are not validated and although appear to have good face validity, caution is needed before judging their psychometric properties and further research would be of benefit.

The patient-proxy method appeared to show a number of strengths as a tool to assess awareness in TBI compared to clinician rated and performance-based methods, potentially highlighting the reason for its preference. To briefly summarise, it allows multiple perspectives to be gained, it appears to offer the greatest flexibility in the domain assessed, versions exist and adaptations are simple to include pre- and post-injury variants providing a reference on which to mark post-injury change, and the rating scale scoring system adopted provides a quantifiable degree of awareness. However, it should be noted that currently no criterion 'gold standard' exists and given the flexible use of the instruments employed, it appears unlikely that a single ideal means of evaluating awareness of deficits following TBI will appear in the immediate future. Given the promise of patient-proxy reports, in this absence, a sensible approach seems to be focus efforts on the development of patient-proxy methods. Further research is required to continue to establish the reliability and validity of recognised assessment instruments and to provide reliability estimates for newer, more experimental assessment tools.

The quality of the studies included in the current review was relatively high. However, a number of factors thought to be crucial determinants of awareness (e.g. severity of injury, chronicity) (Morton et al, 2010) were often omitted, impacting on our ability to make definite claims about the findings. Firstly, a number of studies did not specify the nature of the TBI and secondly, although all studies reported the age of samples at time of assessment, with the exception of two studies, the age of the sample *at time of injury* was not specified. This created ambiguity as to whether all individuals in the sample experienced TBI in adulthood. Moreover, the majority of studies did not include control groups, which raises questions regarding the reliability and interpretation of the findings.

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The studies overall provided some insight into the potential associates of awareness following TBI. It appeared that in general non-cognitive factors were explored more frequently than cognitive associates. The precise range of cognitive tests administered varied between studies making comparison across study outcomes difficult. However, summarising with reference to the skills assessed (as opposed to the specific tests used) more consistent results appeared. In terms of cognitive functions, three key areas were explored including executive and memory ability and intellectual functioning. Reduced executive skills (primarily in the area of poorer response monitoring) and weak memory ability were associated with increased unawareness. Those with lower IQ (either full scale IQ or verbal IQ) were consistently found to show increased unawareness, highlighting a negative association between IQ and level of awareness. Despite a variety of different tests being employed to assess the above cognitive functions, the findings appear to offer a relatively consistent picture suggesting that objective poor performance on cognitive tests of executive function, memory and general IQ, are associated with increased unawareness. By comparison, greater variation was seen for the non-cognitive associates. Sample demographics in terms of age and gender were explored infrequently, but results found being male and younger age to be associated with increased unawareness. Injury characteristics, for example, time since injury and severity of injury were more frequently explored. Studies consistently found that less time since injury was associated with increased unawareness as was increased injury severity. Where mood factors were explored the findings were more mixed and appeared dependent on how the mood factor was defined, the specificity of the awareness domain assessed or who was assessed (patient or proxy). Increased unawareness was associated with lower emotional distress scores when awareness was assessed using measures covering a broad range of domains. Conversely, increased unawareness was associated with higher depression scores when investigated in relation to fatigue awareness specifically. Only one study assessed caregiver depression and found increased proxy depression scores to be associated with increased unawareness. However, given how the patient-proxy method is currently the most used, future research should pay attention to the proxy group and to the factors that may influence their report (e.g. depression, caregiver burden).

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This review was designed to capture all measurement instruments published in empirical studies using relatively inclusive search criteria (see section 3.2.2). This meant that it expanded on the number of measures identified by Smeets et al (2012). However, the review may be limited by the nature of the search strategies and corresponding target words used across databases. Although every attempt was made to ensure that articles relating to the construct of intellectual awareness were included, it is possible that some articles were missed as a result of the breadth of database searches and the vast amount of literature the search yielded.

Despite our broad inclusion of instruments, we applied stricter exclusion criteria regarding the types of articles included. It could be argued that our relatively strict exclusion criteria, excluding validation and intervention studies, may have impacted the number of measures identified. However, a brief review of the methods in the excluded studies identified only one additional measure, namely the IoWA personality Index, suggesting that our criteria worked appropriately to contain the number of papers identified, but not overly limit identification of the measures employed.

There is a risk of bias in this review covering several areas. There is a language bias as only articles found in English databases were assessed and articles written in English were considered. Given that the initial search was carried out by a single author (the primary author) researcher bias may exist influencing paper inclusion. However, all named authors were consulted on the inclusion of papers, minimising this concern. Only studies published in journals were included in this review. Grey literature was excluded, as it was difficult to access further information beyond abstracts from poster presentations at conferences or brief conference proceedings. The fact that studies reporting significant results are more likely to be published than ones reporting non-significant results is well known. It is possible therefore that this review may suffer from some element of bias related to published studies.

As we have previously asserted, the current review was designed to solely capture assessment instruments used with people following TBI. This may be a reason for a number of commonly used scales appearing less frequently than may be expected (e.g. DEX and DEX-R). Conducting a similar review focused on ABI or possibly comparing the two groups may therefore be informative. This may provide a clearer picture as to

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the more sensitive measures dependent on the type of injury. Our current review did not look at the effectiveness of the instruments included (e.g. whether they successfully differentiated patients by level of awareness), which would be a logical next step.

5.1 Recommendations and future directions

The impact of awareness on engagement with, and outcome of, successful rehabilitation is repeatedly noted (Winson et al, 2017). Improving our understanding of awareness, starting with how best to assess it, therefore, is an area deserving of further attention.

Following our review, recommendations for future research include the following:

1. A more detailed examination and inclusion of participants' TBI history: In particular studies might report age at injury and specifying the cause of injury from valid and reliable sources.
2. Using a control sample. This was lacking in most previous studies and attention to this in future research may expand and strengthen available evidence.
3. Ensure established psychometric properties for the measures used: As previously mentioned, it was beyond the scope of the current review to look at the psychometric properties of the measures (particularly experimental adaptions) and the effectiveness of the assessment instruments employed. This would include reviewing the sensitivity, validity and reliability of commonly employed measures. However, both of these would be sensible areas to systematically follow up. We would recommend doing so focused on a particular sample group (e.g. TBI or ABI) in order to constrain conclusions made to the particular patient group of interest.
4. Use conjoint awareness methods to provide a balanced approach. Patient-proxy methods currently appear the preferred method of assessment, although the variation between specific instruments is large. Focusing efforts on instrument development around tools that provide multiple perspectives might be of benefit.
5. Determine the factors that impact on awareness measurement. This would involve borrowing from the dementia literature (Clare et al, 2012) and includes more systematic study of the factors effecting measurement, for example the

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quality of the patient-proxy relationship, personality traits and dispositions of the patient and significant proxy and patient self-efficacy ratings.

5.2 Conclusions

In conclusion, given the variety of different approaches and instruments used in the included studies, this review reveals that there still lacks a consensus about the preferred instrument to assess intellectual awareness of deficits after TBI specifically. There still appear major gaps in our understanding of how best to measure awareness and to date no single ideal method exists. Currently there appears a preference for employing patient-proxy measures, but our findings suggest that increased attention should be given to factors thought to influence proxy ratings, as well as those impacting patient ratings. Development of a standard for the measurement of awareness would facilitate comparability across studies, which would produce improved estimates of TBI impairment and recovery patterns. Given the far-reaching impact reduced awareness can have not only on rehabilitation, but also on both family and community integration, sound assessment is vital. As such continued input into this area is recommended.

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Appendix A

Search 4, conducted on 14.01.18

Embase (1974 to current), Ovid MEDLINE (1946 to current) PsycINFO (1806 to current). Added limits: Human, Peer Reviewed Journal, English Language, Human Age Groups Adult <18 to 64 years> Aged <65+ years>

1. traumatic brain injur*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, uui, tc, id, tm]
2. traumatic head injur*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
3. exp brain injuries/
4. exp brain damage/
5. exp traumatic brain injuries/
6. intracranial injur*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, uui, tc, id, tm]
7. neurosurgery.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, uui, tc, id, tm]
8. neurosurgical lesion*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, uui, tc, id, tm]
9. neurotrauma.mp. [mp=ti, b, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
10. acquired brain injur*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, uui, tc, id, tm]
11. TBI.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
12. ABI.mp. mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. *awareness/
15. exp anosognosia/
16. exp insight/
17. exp self-awareness/

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18. exp self-perception/
19. exp self-concept/
20. exp denial/
21. 14 or 15 or 16 or 17 or 18 or 19 or 20
22. proxy.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
23. overestimat*. mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
24. understimat*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
25. agreement.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
26. discrepancy.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
27. perspectives.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px, rx, an, ui, sy, tc, id, tm]
28. 22 or 23 or 24 or 25 or 26 or 27
29. assessment.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, fx, nm, kf, px rx, an, ui, sy, tc, id, tm]
30. 28 and 29
31. 21 or 30
32. 13 and 31

    Ovid MEDLINE 1315
    PsycINFO 951
    Embase 3083

33. limit 32 to adulthood <18+ years> [Limit not available in Embase, Ovid MEDLINE; records were retained] (4926)
34. limit 33 to English language (4709)
35. limit 34 to (adult <18 to 64 years> or aged <65+ years>) [Limit not valid in Ovid MEDLINE, PsycINFO; records were retained] (2703)
36. limit 35 to humans [Liit not valid in PsycINFO; records were retained (2657)
37. limit 36 to peer reviewed journal [Limit not valid in Embase, OvidMEDLINE; records were retained] (2652)
38. remove duplicates from 37 (**1995)**

    Ovid MEDLINE 935
    PsycINFO 112
    Embase 948

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Appendix B: Table B1: Demographic table (referenced in sample characteristics section 3.3).

Study/Design	TBI sample		Control sample		TBI age at injury	TBI Time since injury	TBI Classification		Setting
	TBI	Informant	Control	Informant			Cause	Severity	
Anderson (1989) USA Cross-sectional	N=19 (16 males 84%); Age: M=26.8, SD=N.S, 18-44 years	NT	N=32 CVA (21 males) M=57.8, SD=N.S, 28-83 years; N=49 DEM (20 males) M=71.5, SD=N.S, 44-91 years	NT	Brain damage acquired in adulthood	N.S	N.S	GCS score M=6.9, SD=3.0, 3-13 Moderate to severe	N.Spec
Bivona (2008) Italy Cross-sectional	N=37 (29 males 78%); Age: M=32.3, SD=11.6 years	First degree relatives only	NT	NT	N.S	Median interval=0.69 years (IQR: 0.45/8.52)	N.S	GCS > 8 (severe)	OP
Bivona (2014) Italy Cross-sectional	N=28 (21 males 75%); Age: M=37.2, SD=13.3, 18-63 years (split into ISA & ASA)	N=28 first degree relatives; 15 parents, 10 partners, 1 child, 2 sisters	N=28 healthy controls; Age: M=34.5, SD=9.9 years. Age, gender, years in education matched	NT	N.S	ISA: M=831, SD=772 days ASA: M=782, SD=627 days	25 (89%) sustained severe closed head injury in RTA	GCS > 8 (severe)	OP
Bogod (2003) Canada Cross-sectional	N=40 (32 males 80%) M=37.4, SD=8.37, range 22-66 years	Therapist	NT	NT	N.S	M = 132.73, SD = 103.46, 20-576 months	N.S	19 mild-mod, 21 severe (GCS or PTA/LOC score)	IP & OP
Carroll (2011) UK Cross-sectional	N=29 (21 males 72%) M=46.3, SD=12.9, 22-64 years	N=24; 12 spouses/partners, 6 parents, 3 siblings, 3 children. N=29; Clinician providing rehabilitation f-up	NT	NT	N.S	M=11.17, SD=11.4, 2.24-40 years	N.S	9 mild, 2 moderate, 18 severe (GCS or LOC)	OP
Chiou (2016) USA Cross-sectional	N=14 (10 male 71%) M=45.7, SD=12.5 years	14 significant other, relative or close friend	7 healthy control (1 male) M=41.1, SD=11.6 years, age matched	7 significant other, relative or close friend	N.S	M=73.3, SD=44.9 months	N.S	All moderate to severe (GCS <13)	OP
Ciurli (2010) Italy Cross-sectional	N=52 (44 males 85%) M=30.6, SD=11.1 years	First degree relatives only; 40 parents, 10 partners, 2 children	NT	NT	N.S	Median interval =0.9 years (IQR: 0.6/5.5)	N.S	Severe (GCS score 8); median TFC 20 days (IQR: 13/37); median PTA 60 days (IQR: 30/100)	OP
Dahlberg (2006) USA Cross-sectional	N=60 (83% male); M=39, SD=11, 20-63 years	SO; 32% parents, 27% spouses, 20% friends, 12% other (siblings/grandparents/children/carer), 10% no SO	NT	NT	N.S	M=7, SD=6, 1-21 years	Defined as injury to brain caused by external mechanical force (excludes non-traumatic e.g. stroke, hypoxic)	65% severe (GCS 3-8), 13% moderate (GCS 9-12), 8% mild (GCS 13-15), 13% unknown	OP

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Dawson (2005) Canada Cross-sectional	N=31 (61% male) M=27.97, SD=9.35 years	SO: 48.39% spouse/partner; 32.36% parent; 6.45% child; 6.45% sibling; 6.45% friend)	NT	NT	N.S	Followed prospectively M=4.3, SD=0.89 years post-injury	N.S	14 mild 9GCS 13-15) 17 moderate-severe (GCS 3-12)	OP
Dockree (2015) Ireland Cross-sectional	N=62 (49 male 79%); M=34.37, SD=11.85 years	SO: 23 parent; 18 spouse/partner; 10 siblings; 2 friends; 1 offspring; 1 cousin	NT	NT	N.S	Range 2-326 months M=37.53 months	Excluded if injury resulted from non-traumatic reason (e.g. stoke)	5 mild (13-15) 5 moderate (9-12) 37 severe (<8) 14 unknown (GCS)	N.Spec
Donders (2015) USA Cross-sectional	N=100 (52 male 52%); M=39, SD=16	SO; 48 spouse, 34 parent, 18 other	NT	NT	N.S	M=162.25, SD=93.95 days	46 MVC; 27 recreational activities; 18 falls; 9 other	Mild (GCS >12; TFC <30 mins; PTA <24 hours)	OP
French (2014) Canada Cross-sectional	N=109 (all male); M=29.3, SD=8.7, 19-56 years	NT	NT	NT	N.S	M=6.2, SD=5.3, 1-24 months	Closed TBI sustained primarily in combat; majority blast related incident	45.9% Mild (PTA<24h, LOC<15mins); 25.7% Moderate (PTA 24h-7 days, LOC<24h); 28.4% severe (PTA >7days)	N.Spec
Geytenbeek (2017) Australia Longitudinal	N=81 (67 male 83%); M=37.3, SD=13.5 years	SO: 50 spouse/partner, 26 parents, 5 other	NT	NT	N.S	F-Up 1, 3, 6 months post-injury	N.S	16 mild to moderate; 65 severe (PTA, GCS)	OP
Goverover (2014) USA Cross-sectional	N=30 (20 male 66%); M=40.3, SD=11.1, 20-54 years	Family/SO – not further specified	NT	NT	N.S	M=9.05, SD=7.33, 1-27.3 years	23 MVA, 1 all, 3 violence, 3 sport	5 Mild, 1 moderate, 20 severe, 4 undetermined (GCS)	OP
Hart (2009) USA Longitudinal	N=123 (99 male 80%): M=33.2, SD=14.6 years	SO: 56% parent, 24% spouse or cohabiting partner, 11% other family member	NT	NT	N.S	Injury to baseline: M=45.3, SD=29.4 days	59% MVC, 18% gunshot or assault with blunt weapon, 11% fall	Severe TBI with mean TFC greater than 1 week and mean PTA of 1 month, GCS	IP
Kelley (2014) USA Cross-sectional	N=62 (56 male 90%; 48 veterans,; 23-70 years (median 35)	N=62 SO: 32 parents, 12 spouses, 8 siblings, 8 close friends	NT	NT	18-62 years (median 25)	5-16 years post-injury (median 9)	Non-penetrating TBI (exclusion criteria included stroke)	Moderate to severe (PTA)	OP
Lanham (2000) USA Longitudinal	N=55 (45 male 82%): M=30.0, SD=10.3 years, veterans and active duty military personnel	SO: 20 spouse/mate, 24 parent, 8 friend, 3 other relative	NT	NT	N.S	Baseline: Ave 2 months post-injury (median 39 days, range 3-141 days)	N.S	Spanned range, but more towards moderate to severe (LOC, PTA, neuroimaging)	N.Spec
Larson (2009) USA	N=16 (12 male 75%): M=30.88, SD=12.98, 18-	SO – primary caregivers: 8 spouses/fiancée, 6 parents,	NT	NT	N.S	M=10.69, SD=7.60, 2-29 months	N.S	Severe: M=4.44, SD=1.75, 3-8 (GCS)	N.Spec

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Cross-sectional	52 years	1 grandparent, 1 aunt							
Malec (2007) USA Cross-sectional	N=93; 42 mild TBI (48% male) M=35.8, SD=20.1 years, 51 mod/severe TBI (61% male) M=35.7, SD=17.3 years	SO	N=42 orthopaedic controls (62% male)	SO	N.S	M=47.1, SD=44.5 days	N.S	42 mild, 51 moderate/severe (GCS; neuroimaging)	OP
Medley (2010) UK Cross-sectional	N=37 (31 male 84%): M=39.5, SD=12.2, 18-60 years	Clinician: professionals included ClinPscy, Assist Psyc, OTs, SLTs	NT	NT	N.S	M=21.8, SD=26.6, 2-96 months	49% RTC, 30% Assault, 21% fall	Severe (GCS < 8; PTA > 24 hours) duration LOC >6 hours	IP
Morton (2010) UK Cross-sectional	N=34 (32 male 94%): M=35.0, SD=10.2, 18-55 years	SO: 44% parents, 35% spouse/partner, 12% friends, 9% other family members	NT	NT	N.S	M=66.2, SD=60.0, 12-240 months	20 RTA, 5 Assault, 9 Fall	11 Moderate, 23 severe (GCS, LOC, PTA)	N.Spec
Murrey (2005) USA Cross-sectional	N=112 (58 males 52%); FL group M=34.1, SD=11.0 years; NFL M=34.4, SD=13.5 years	SO: spouse, parent, other relative or caregiver familiar with patient	NT	NT	N.S	At least 1 year post-injury; FL M=5.2, SD=5.4 years; NFL M=4.8, SD=6.4 years	N.S	43 (28 male) severe TBI and frontal lobe damage; 69 (30 male) mild TBI and no findings of frontal lobe damage, from confirmed neuroimaging	IP & OP
Niemeier (2014) USA Longitudinal	N=121(81 males 67%); Women M=43.67, SD=18.81 years, Men M=42.83, SD=18.76 years	SO: family member or caregiver; clinician	NT	NT	N.S	Time 1: following emergence from PTA Time 2: on discharge from IP rehabilitation	Vehicular (M: 65.8%; F: 56.9%), assault (M: 10.5%; F: 2.8%), fall (M: 15.8%; F: 26.4%), pedestrian (M: 7.8%; F: 2.8%), other (M: 0.0%; F: 11.1%)	77 severe, 44 moderate (PTA)	IP
O'Keeffe (2007) UK Cross-sectional	N=31 (27 males 87%); M=28.74, SD=8.52 years	SO, caregiver or friend	N=31 healthy controls (24 males); M=30.23, SD=14.08 years (age, sex, education matched)	SO, caregiver or friend	N.S	M=36.25, SD=22.37 months	20 RTA, 4 Assault, 5 Fall, 1 Work accident, 1 other	2 mild, 3 severe, 25 very severe, 1 N/A (PTA, GCS)	N.Spec
Pagulayan (2007) USA Longitudinal	N=120 (88% male) M=37, SD=16 years	37 Spouse, 47 parents, 12 other relative, 23 non-relative or friend, 1 other	NT	NT	N.S	1 and 12 months post-injury	N.S	73 complicated mild, 25 moderate, 10 severe, 12 missing (GCS, TFC)	OP
Prigatano (1996) USA Cross-sectional	N=31 (23 males 74%); M=25.8, SD=8.9 years	SO or relative	Neuropsychological controls (n=20); R hemi lesions n=17; Left hemi lesions n=18 (non-	SO or relative	N.S	M=1.5, SD=2.4 years	N.S	Moderate to severe (GCS)	N.Spec

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			traumatic).Matched on education, chronicity of injury						
Prigatano (1998) Spain Cross-sectional	N=30 (23 male 76%): M=29, SD=10.4, 19-60 years	Close relative: 10 spouse, 6 father, 6 mother, 2 brother, 1 other (friends)	N=28 Healthy control Age, education and gender matched	Relative: 7 spouse, 1 father, 11 mother, 3 brother, 10 other (friend)	N.S	M=24.8, SD=14.5, 5-53 months	24 MVA, 3 Pedestrian in traffic accident, 2 Fall, 1 other	Moderate-severe (GCS); 66.7% severe; 6.6% moderate, 3.3% mild, 23.3% no data	IP & OP
Richardson (2014) Australia Longitudinal	N=60 (50 males 83%): M=42.94, SD=16.66	Close others to corroborate func status and injury related changes	NT	NT	N.S	M=7.73, SD=4.11 months	39 MVA, 8 Pedestrian, 7 Cyclist, 5 Fall, 1 work related	67% severe; 22% moderate, 10.6% mild (PTA, GCS)	OP
Richardson (2015) Australia Cross-sectional	N=168 (112 male 66%); M=43.78, SD=17.15 years	N=105 SO: 37 parents, 45 spouse, 6 siblings, 12 child, 9 friend	NT	NT	N.S	M=53.56, SD=64.63 months	66.7% MVA and motorbikes, 16.1% pedestrian vs. motor vehicles, 8.3% falls, 6.5% cyclists vs. motor vehicle, 2.4% work-related	72% severe, 16.7% moderate, 11.3% mild (PTA, GCS)	OP
Roche (2005) Canada Cross-sectional	N=33 (79% males); M=29, SD=10.8 years	Close friend or relative; 14 mothers, 7 wives, 5 fathers, 4 husbands, 1 sister, 2 other	N=29 (79% males) non-brain injured controls, age, gender, education matched	Close friend or relative; 12 mothers, 10 wives, 4 husbands, 2 fathers, 1 NR	N.S	M=52, SD=36 weeks	52% MVA, 15% hit by motor vehicle, 12% fall from moving vehicle/animal, 9% in motor bike accidents, 3% falls, 3% alleged assault, 3% penetrating injury, 3% light plane accident	Severe (GCS < 8, PTA > 24 hours)	OP
Sawchyn (2005) Canada Cross-sectional	N=166 (88% males); M=39, SD=11.21 years	SO; 55% spouses, 10% parents, 10% siblings, 7% friends	NT	NT	N.S	Mild: M=687, SD=814 days; Mod M=665, SD=506 days, Severe M=745, SD=930 days	43% fall, 21% impact trauma, 23%MVA, remainder sustained crush-type injury, assault, or other trauma	83 mild, 25 moderate, 58 severe (LOC, PTA, GCS)	OP
Sherer (1998) UK Cross-sectional	1: N=64 (52 males 81%) M=28.8, SD=9.8 years 2: N=47 (36 males 76%) M=30.9, SD=12.7 years	1: SO; 14 spouses, 39 parents, 7 siblings, 2 SOs, 2 friends 1: 20 spouses, 19 parents, 4 siblings, 2 grandparents, 2 SO; Clinician	NT	NT	N.S	1: M=13.0, SD=20.8, 0.9-91.6 months 2: M=7.4, SD=12.5	1: non-penetrating TBI, motor vehicle crashes	1: 48 severe, 10 moderate, 6 mild (GCS) 2: 22 severe, 7 moderate, 7 mild (GCS)	N.Spec
Vanderploeg (2007) USA Cross-sectional	N=36 (94% male) M=38.9, SD=2.0 years	65% parents or siblings, 27% spouses or SO, 9% friends or other family members	NT	NT	N.S	M=25.5, SD=20.3, 2.4-70 months	Active military personnel. Most were injured in MVA (79%) or falls (12%)	Moderate to severe (PTA and positive neuroimaging)	OP

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Zimmerman (2017) Brazil Cross-sectional	N=65 (48 male 73%); M=36.2, SD=14.1, 18-72 years	Relatives	NT	NT	N.S	M=22.9, SD=22.7, 2-127 months	Closed TBI	26 mild, 39 moderate-severe (GCS and/or LOC or PTA)	OP

NT = Not tested; N.S = Not Stated; N.Spec = Not Specified; SO = Significant Other; RTC = Road Traffic Collision; MVA = Motor Vehicle Accident; IP = Inpatient; OP = Outpatient; CVA = Cerebrovascular accident; GCS = Glasgow Coma Scale; LOC = Loss of Consciousness; PTA = Post-Traumatic Amnesia; TFC = Time to Follow Commands;
Note: If studies included more than one time point, the baseline time point was taken as time since injury indicator.

Table B2: Full details of cognitive and non-cognitive associates explored by study (referenced in section 4.9)

Method	Measure	Associated factors explored		Analysis	Factors significantly associated with increased unawareness	Association direction	Study
		Cognitive	Non-cognitive				
Patient-Proxy discrepancy	AQ	Y	Y	Univariate	Cognitive: EF, poorer performance on WCST: number of categories completed and perseverative responses (across all subscales, but stronger for cognitive subscale)	Negative	Bivona (2008)
		Y	Y	Multivariate	Cognitive: Reduced perspective taking (poorer performance on faux-pas task). Non-cognitive: Higher DRS scores, increased damage in frontal cortical regions, higher apathy scores (NPI)	Negative Positive	Bivona (2014)
		Y	Y	Univariate	Cognitive: Poorer line orientation performance (all discrepancy subscales) and worse performance on WM (LNSeq task) on AQ-cognitive subscale only	Negative	Chiou (2016)
		Y	Y	Multivariate	Non-cognitive: More positive self-reports of QoL and satisfaction with life	Positive	Goverover (2014)
		N	Y	Multivariate	Non-cognitive: Increased injury severity (Longer TFC)	Positive	Hart (2009)
		Y	Y	Multivariate	Cognitive: Reduced executive function of response monitoring (more SOPT errors made); Reduced emotional distress; lower HADS score	Negative	Morton (2010)
		N	Y	Multivariate	Non-cognitive: Higher HADS depression scores in close others and PTA duration (cognitive, behavioural/affective domains and total) Lower HADS depression ratings in the individual with TBI cognitive, behavioural/affective domains and total), less time since injury (motor/sensory domain only)	Positive Negative	Richardson (2015)
		N	Y	Univariate	Non-cognitive: Higher self-esteem (RSES) Less Depression (HADS)	Positive Negative	Carroll (2011)
		N	Y	Univariate	Non-cognitive: Increased severity of injury (GCS)	Positive	Sherer (1998)
	PCRS	Y	Y		Cognitive: EF: Worse performance on the WCST (high perseverative errors high perseverative responses) Non-cognitive: Increased severity of injury (longer TFC)	Negative Positive	Ciurli (2010)
		N/A	N/A	N/A	N/A	N/A	Prigatano (1996)

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		N	Y	Univariate	Non-cognitive: Increased severity of injury (Longer periods of PTA)	Positive	Prigatano (1998)
		N	Y	Multivariate	Non-cognitive: Increased severity of injury (based on LOC, GCS, PTA and imaging)	Positive	Sawchyn (2005)
					Non-cognitive: Lower level of emotional adjustment (KAS-relative version)	Negative	
		Y	Y	Multivariate	Cognitive: EF: semantic fluency impairment; Memory: poorer delayed recall impairment (RAVLT); Non-cognitive: Younger age	Negative	Zimmerman (2017)
					Non-cognitive: More severe TBI (GCS)	Positive	
		N	Y	Multivariate	Gender, Men showed greater unawareness than women	-	Niemerer (2014)
	FrSBe	N	Y	Multivariate	Non-cognitive: Decreased Pe amplitude, less time since injury	Negative	Larson (2009)
		N	Y	Multivariate	N.S	-	Niemerer (2014)
	CIQ	N	N	N/A	N/A	-	Dahlberg (2006)
		N	Y	Multivariate	Non-cognitive: Greater injury severity (PTA)	Positive	Kelley (2014)
	DEX	Y	Y	Multivariate	Cognitive: IQ (Vocab/BD)	Negative	Bogod (2003)
		Y	Y	Multivariate	Cognitive: Reduced EF of response monitoring (more SOPT errors made)	Negative	Morton (2010)
	KAS	N	N	N/A	N/A	-	Dawson (2005)
		Y	Y	Univariate	Non-cognitive: Increased severity (lower MOAT score)	Positive	Lanham (2000)
	BRIEF-A	N/A	N/A	N/A	N/A	N/A	Donders (2015)
	CHART-SF	N	N	N/A	N/A	-	Dahlberg (2006)
	CAPM	N	N	N/A	N/A	-	Roche (2002)
	EBIQ	N	Y	Univariate	Non-cognitive; IPQ-R Low control/ambivalent ratings	Negative	Medley (2010)
					Non-cognitive: High optimism ratings (IPQ-R)	Positive	
	KBCI	N	Y	Multivariate	N.S	-	Vanderploeg (2007)
	MFIS	Y	Y	Univariate	Non-cognitive: More severe symptoms of anxiety (Trait anxiety, STAI; physical and psychosocial domains), and depression (BDI-II; across all subscales)	Positive	Chiou (2016)
	MPAI	N	N	N/A	N/A	-	Murrey (2005)
	MPAI-4	N	Y	Multivariate	Non-cognitive: Less emotional distress: lower anxiety, less stress (lower DASS-21 scores); poorer psychosocial functioning (SPRS)	Negative	Geytenbeek (2017)
	NFI	N	Y	Univariate	Non-cognitive: Lower NFI-Depression scores	Negative	Malec (2007)
	SIP	N	N	N/A	N/A	-	Pagulayan (2007)
	SCSQ-A	N	N	N/A	N/A	-	Dahlberg (2006)
	TBIFI	N	Y	Multivariate	Non-cognitive: Worse work outcomes (CIQ)	Negative	Kelley (2014)
					Non-cognitive: Greater Life satisfaction (QoL scale)	Positive	
Clinician Rated	SADI	Y	Y	Multivariate	Cognitive: Measures of EF; Poorer performance: more SOPT errors, go-no-go errors, Stroop errors; Lower IQ (Vocab/BD)	Negative	Bogod (2003)
					Non-cognitive: Greater severity of injury (GCS, PTA or LOC)	Positive	
		Y	Y	Multivariate	Non-cognitive: Increased severity of injury (at least two of GCS, PTA, LOC, positive neuroimaging)	Positive	Morton (2010)
					Non-cognitive: Mood state: Reduced emotional distress (combined anxiety and depression scores on HADS)	Negative	
		Y	Y	Univaritate	Non-cognitive: Time since injury	Negative	Richardson (2014)
					Gender: Men showed greater unawareness (less accurate goal-setting) than women	-	
	NBRS insight item	Y	Y	Univariate	Cognitive: Reduced memory executive factor score	Negative	Lanham (2000)
					Non-cognitive: Increased severity (lower MOAT score)	Positive	
Performance-based discrepancy	AI self-report vs. test performance	Y	N	Univariate	Cognitive: Lower VIQ scores	Negative	Anderson (1989)
					Cognitive: Higher temporal disorientation scores (Benton Orientation Questionnaire)	Positive	

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	NSI vs. test performance	N/A	N/A	N/A	N/A	N/A	French (2014)
Miscellaneous	Composite score CFQ, FrSBe, PCRS	Y	Y	Univariate	Cognitive: EF: Reduced error monitoring, Poorer M-SET scores Non-cognitive: Reduced time since injury	Negative	Dockree (2015)
	Composite score AI-A, PCRS, FrSBE, CFQ	N	Y	Univariate	N.S	-	O'Keeffe (2007)

Appendix C: Table C1: Quality ratings outcome (referenced in section 4.2)

Paper	**Items of the 'Checklist for assessing the quality of quantitative studies' (Kmet, Lee & Cook, 2004)**												
	Q1	**Q2**	**Q3**	**Q4**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**	**Q13**	**Q14**	**Total**	**Rating**
Anderson (1989) USA	1	1	2	1	1	1	1	2	2	2	2	16	Fair
Bivona (2008) Italy	2	1	2	2	2	1	2	2	1	2	2	19	Good
Bivona (2014) Italy	2	2	2	1	2	1	2	2	2	2	2	20	Good
Bogod (2003) Canada	2	2	2	2	1	2	2	1	1	2	2	19	Good
Carroll (2011) UK	1	2	2	2	2	1	1	2	1	2	2	18	Good
Chiou (2016) USA	2	2	2	2	2	1	2	2	2	2	2	21	Good
Ciurli (2010) Italy	2	2	2	2	2	2	2	1	2	2	2	21	Good
Dahlberg (2006) USA	1	2	2	2	2	2	2	1	0	2	2	18	Good

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Dawson (2005) Canada	2	2	2	1	2	1	2	2	2	2	2	20	Good
Dockree (2015) Ireland	2	2	2	2	2	2	2	2	2	2	2	22	Good
Donders (2015) USA	2	2	2	2	2	2	2	2	2	2	2	22	Good
French (2014) Canada	2	2	2	2	2	2	1	2	1	2	2	20	Good
Geytenbeek (2017) Australia	1	2	2	1	2	2	2	0	2	2	2	18	Good
Goverover (2014) USA	2	2	2	2	2	1	2	2	2	2	2	21	Good
Hart (2009) USA	2	2	1	2	2	2	2	1	2	2	2	20	Good
Kelley (2014) USA	2	2	2	2	1	2	2	2	1	2	2	20	Good
Lanham (2000) USA	1	2	2	1	2	2	1	0	2	1	2	16	Fair
Larson (2009) USA	2	2	2	1	2	1	2	2	2	2	2	20	Good
Malec (2007) USA	1	1	1	1	1	2	2	0	1	2	2	14	Fair
Medley (2010) UK	2	2	2	2	1	2	2	0	0	2	2	17	Good
Morton (2010) UK	2	2	2	2	2	1	1	1	2	2	2	19	Good
Murrey (2005) USA	2	2	2	2	2	2	2	0	0	2	2	18	Good
Niemeier (2014) USA	2	2	2	2	2	2	2	2	2	2	2	22	Good
O'Keeffe (2007) UK	2	2	2	2	2	1	1	0	2	2	2	18	Good
Pagulayan (2007) USA	2	2	2	1	2	2	2	2	1	2	2	20	Good
Prigatano (1996) USA	2	2	2	1	1	1	2	0	0	2	2	15	Fair
Prigatano (1998) Spain	2	2	2	2	2	1	2	2	2	2	2	21	Good
Richardson (2014) Australia	2	1	2	2	2	1	2	2	2	2	2	20	Good
Richardson (2015) Australia	2	2	2	2	2	2	2	2	2	2	2	22	Good
Roche (2005) Canada	2	2	2	2	2	2	2	1	0	2	2	19	Good
Sawchyn (2005) Canada	2	2	2	2	2	2	1	0	2	2	2	19	Good
Sherer (1998) UK	1	2	2	2	1	2	2	1	1	2	2	16	Fair
Vanderploeg (2007) USA	2	2	2	2	2	2	2	0	2	2	2	20	Good
Zimmerman (2017) Brazil	2	2	2	2	2	2	2	2	2	2	2	22	Good

Note: scores 1 – 8 = poor quality; scores 9 – 16 = fair quality; scores 17 – 22 = good quality. Questions 5, 6 and 7 were excluded as these relate to intervention studies and were therefore deemed inappropriate for the current review.

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Appendix D: Table D1: **Checklist for assessing the quality of quantitative studies**

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Criteria		YES (2)	PARTIAL (1)	NO (0)	N/A
1	Question / objective sufficiently described?				
2	Study design evident and appropriate?				
3	Method of subject/comparison group selection *or* source of information/input variables described and appropriate?				
4	Subject (and comparison group, if applicable) characteristics sufficiently described?				
5	If interventional and random allocation was possible, was it described?				
6	If interventional and blinding of investigators was possible, was it reported?				
7	If interventional and blinding of subjects was possible, was it reported?				
8	Outcome and (if applicable) exposure measure(s) well defined and robust to measurement / misclassification bias? Means of assessment reported?				
9	Sample size appropriate?				
10	Analytic methods described/justified and appropriate?				
11	Some estimate of variance is reported for the main results?				
12	Controlled for confounding?				
13	Results reported in sufficient detail?				
14	Conclusions supported by the results?				

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Empirical Research Project

The Self and Self-Knowledge after Frontal Lobe Neurosurgical lesions

Supervised by Professor Robin Morris and Dr Jessica Fish,
Discussants: Dr Daniel Mograbi and Professor Keyoumars Ashkan

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The Self and Self-Knowledge after Frontal Lobe Neurosurgical lesions

1. Abstract

Background: Evidence suggests that damage to the frontal lobes can be associated with changes in cognitive and behavioural functioning and reduced awareness that such changes have occurred (Mah et al, 2004; Simpson et al, 2015). However, the neurocognitive mechanisms underpinning reduced awareness remain to be fully understood.

Aim: In the current project, the Cognitive Awareness Model (Morris & Mograbi, 2013) was used as a framework to understand knowledge of the self in people with acquired frontal lesions. Fifteen individuals with frontal lobe lesions and their nominated informants were compared with fifteen healthy matched control-informant dyads on a number of questionnaires designed to assess awareness of difficulties, as well as on novel experimental tasks exploring individuals' perception of atypical behaviour.

Results: Individuals with frontal lobe lesions showed adequate awareness of their post-surgery changes, which was substantiated by their informant report. Compared to the control group, the patient group was found to acknowledge more difficulties in current functioning. Analyses exploring the congruence between participant and informant ratings of current abilities showed some trends suggestive of within group differences according to self-perception of abilities (e.g. over- or under-reporting of difficulties). Performance on the novel experimental task revealed that compared to the control group patients with frontal lobe lesions tended to over-interpret and therefore misperceive neutral situations as potentially atypical. The psychosocial impact of this finding is discussed. Within the frontal lobe lesion group, the lesion laterality subgroups had comparable performance on all awareness measures and experimental tasks.

Conclusions: These results demonstrate the effectiveness of adapting measures to incorporate pre-injury perceptions and highlight the importance of obtaining multiple viewpoints when examining an individual's level of awareness. The clinical utility of the novel tools adopted and the potential benefits of these findings in supporting the rehabilitation process are noted and discussed.

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2. Introduction

Damage to the frontal systems of the brain is often associated with behaviour change in which multiple functional domains may be affected (David et al, 2012). Broadly speaking, the symptoms of frontal lobe disorder fall into three main categories: cognitive, emotional and behavioural – often referred to as a dysexecutive syndrome. Such deficits may be observed behaviourally or measured using neuropsychological assessment but there are reports of patients with frontal lobe lesions performing relatively normally on cognitive testing yet experiencing quite debilitating changes in social and emotional behaviour (Shallice & Burgess, 1991; Burgess et al, 2006). Apparent changes in personality and social behaviour have been consistently found following damage to the frontal lobes (Adolphs, 2001; Stuss et al, 2001) and are noted by caregivers to be the factors most strongly associated with poor quality of life (Sterckx et al, 2013). As such, the social impact of frontal lobe damage has particular significance.

However, the report of behaviour experienced or exhibited can at times vary between patients and proxy (informant: caregiver or clinician) report. A general pattern emerges in which patients judge their functioning to be better than the judgement of proxies. This is often taken as evidence for a lack of awareness in the patient, shown in turn to affect multiple facets of cognition and behaviour.

Within the field of clinical psychology particular importance is given to the language used to describe and capture clinical phenomenon. Awareness is a difficult term to conceptualise and is often deemed synonymous with insight. Despite these terms often appearing interchangeably in the literature, argument exists for a distinction to be made between the two. Awareness is posited to refer to one's appraisal of functional impairment, whereas insight appears more in the psychiatric literature and is said to relate to symptoms or disorders of mental health (Markova & Berrios, 2011). For the current project, the term awareness was employed throughout.

People may exhibit lack of awareness in relation to specific cognitive deficits, social functioning, judgments of behavioural efficacy, activities of daily living (ADLs) or general life circumstances (Trigg et al, 2012; Clare et al, 2012a). This unawareness of deficit is not only frequently reported following frontal lobe damage but has been

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demonstrated in a number of different neurological conditions (Clare et al, 2012a; Morris & Mograbi, 2013). Its effects can be extremely debilitating, with unawareness predicting worse prognosis (Ofrei et al, 2007), less motivation for and compliance with treatment (David et al, 2012) and greater exposure to dangerous behaviours (Starkstein et al, 2007). In addition, unawareness has been noted to be associated with greater distress in relatives or caregivers (Turro-Garriga, 2013).

A range of cognitive and non-cognitive factors have been associated with the extent of awareness following brain injury. Common cognitive factors include executive and memory ability and intellectual functioning (Zimmerman et al, 2017), whereas non-cognitive associates include time since injury, injury severity and mood factors (Richardson et al, 2015). Often allied to awareness, an important concept is that of emotional distress, with anxiety and depression frequently being shown to impact post-injury awareness (Chiou et al, 2016; Geytenbeek et al, 2017; Morton et al, 2010). However, despite a growing literature the nature of these relationships remain unclear.

Lack of awareness is often attributed to frontal dysfunction and has been explored quite extensively in affected populations (Philippi, Feinstein et al, 2012; Shany-Ur et al, 2014). Evidence suggests that different anatomical regions of the frontal lobe and connecting pathways may mediate self-awareness impairments (Damasio, 1999; 2010). However, the underlying neurocognitive mechanisms explaining awareness deficits are still poorly understood.

Numerous theoretical accounts of unawareness have been proposed that endeavour to explain the different processes underlying impaired self-awareness. Some explanations have emphasised the involvement of domain specific processes, suggesting that a lack of awareness is due to reduced perception of sensory input (e.g. diminished consciousness), a failure of executive control mechanisms (e.g. poor monitoring of current functioning; Cosentino et al, 2007) or impairments in aspects of memory function (Mograbi et al, 2009). Other influential models link impaired self-awareness to comparator mechanisms, which suggest a disconnection between recently registered self-related information and previous self-knowledge (Schacter, 1990; Agnew & Morris, 1998). Recent models additionally point out the role of motivational and emotional factors on awareness (Rosen, 2011). A number of explanations of awareness are

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condition-specific, often focused on dementia samples. For this sample, frameworks for understanding awareness have proposed declining cognitive abilities as impacting on awareness (Clare 2004). In individuals with brain injury the degenerative element is likely to be more static and therefore these accounts may not best apply. The Cognitive Awareness Model (CAM; Morris & Mograbi, 2013) was adopted for the current study as it purports to account for unawareness following a range of conditions, including focal brain damage. It also allows different levels of awareness to be explored allowing investigation of the potential complexity of this phenomenon.

The Cognitive Awareness Model (CAM; Morris & Hannesdottir, 2004; Morris & Mograbi, 2013) provides a theoretical framework in which to formulate possible explanations of unawareness. It has been asserted that unawareness can be explained by a failure in ability to update personal (self-trait) knowledge (Klein et al, 2002). In the CAM model, the formation of self-knowledge is thought to form throughout development through consolidating experiences of personal efficacy, resulting in a stored Personal Database (PDB), a specialised storage of information about current function. The essential features of the CAM model are that incoming knowledge concerning task or activity performance is monitored by comparator mechanisms that contrast this information to that stored in a Personal Database (PDB). One of the main predictions of the CAM is that evaluation of current performance relies on the intact recollection of recent memories about personal abilities (self-traits). It is then argued that a lack of, or reduced awareness can be explained by an absence in recollection of recent memories leading to a failure to recalibrate information stored in the PDB (Hannesdottir & Morris, 2007). This results in patients reverting to their strongest sense of self, which due to an inability to update self-knowledge is the more powerfully embedded sense of self that was stored prior to the frontal lesion. A small amount of experimental work exists that supports this theory (Klein et al, 2003; Rankin et al, 2005), in which patients' current behavioural ratings are compared to informant ratings for past and current traits. It is possible to extend investigation to include patient ratings of their own past behaviour, which can then be benchmarked by informant rating, who will corroborate past behaviour. As such, a more systematic investigation of the model's ideas is warranted.

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A further postulation of the CAM model is that there are two potential routes to self-understanding, that is, a functional distinction exists between self-related semantic memory versus general semantic memory. This is based on ideas posited by Klein et al (2002) who report evidence that trait self-knowledge is functionally distinct from semantic world knowledge. More recently neuroimaging findings have supported proposed distinctions differentiating personal semantic memories (those related to personal experiences) from declarative memory (memory for unique events) and semantic memory (memory for general facts) (Renoult et al, 2016). It is suggested that it may be the special self-memory that is dysfunctional in patients who lack awareness, but that general semantic memory is intact. This idea is based on literature that explores the relationship between awareness and perspective taking or learning about self in the surrogate form (see Bertrand et al, 2016 for a concise review).

It has been documented that in some disorders unaware patients may be able to acknowledge deficits in others (Clare et al, 2012b) or in themselves when exposed to evidence from a third person perspective (Fotopoulou et al, 2009). The notion of a surrogate self is a clinically observed phenomenon in both patients with dementia and those with schizophrenia. These patients have been documented to be able to identify abnormal behaviours in themselves once it has been pointed out to them by a third person, despite not spontaneously reporting these deficits in themselves. These ideas allow us to hypothesise that if patients have an intact general semantic memory they will be able to identify that others rate them to behave in a certain way and this is despite the fact that they might not own or freely report this behaviour themselves. However, to date a paucity of work has explored this idea of a 'surrogate self'. Furthermore, to the best of the current author's knowledge, the idea of the surrogate has not been looked at in conjunction with general levels of awareness (self-reported awareness) in the same sample. Additionally, it has also been suggested that it may be the case that patients who lack perspective-taking abilities are less able to benefit from general semantic knowledge when evaluating their own abilities (Ruby et al, 2008). However, it appears that no studies to date have directly examined and tested mediation effects of participants' ability to take another's perspective. It is currently unclear how this may affect patients' ability to evaluate their own abilities when given evidence from a third person perspective.

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Finally, in exploring people with prefrontal lesions' ability to acknowledge and detect altered behaviour in themselves, either freely (self-report) or when exposed to evidence from a third person perspective (surrogate-self), it is relevant to determine whether they can detect and make accurate judgment of atypical behaviour more generally. This allows further exploration of the existence of different networks involved in self/other appraisal thought to impact self-understanding, as posited by the CAM model. To the best of the current author's knowledge, this control has not systematically been applied in previous investigations into patient self-awareness.

2.1 Rationale and aims of the study

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The main objective of the current project aimed to systematically investigate the understanding of self-ability and self-behaviour in people with acquired frontal lobe lesions (FLL group) using the CAM model as a guiding framework. The study had three aims:

1) To investigate whether people with FLLs estimate their current abilities and behaviour using pre-injury self-representations, rather than representations that have been updated to incorporate post-injury changes. This involved systematically looking at past and current appraisals of behaviour by both people with prefrontal lesions and informants through the use of various questionnaire measures.
2) To explore whether people with FLLs develop a 'surrogate' understanding of the changes they have experienced in the domains of cognition and behaviour. This involved adapting questionnaire measures so people with frontal lesions were required to rate their own behaviours from the perspective of the informant.
3) To compare self-knowledge to generic knowledge through the use of vignettes to establish a third person perspective on atypical behaviour. In order for this exploratory measure to be comparable with previous investigations in this project, vignettes were based on the executive constructs assessed via the questionnaires given.

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2.2 Research questions and hypotheses

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Research question 1: Do the self-ratings of people with surgical frontal lesions regarding their cognitive ability and behaviour before and after their injury differ from the ratings of informants?

- H1: Focused on the FLL group only; it was predicted that they would show reduced awareness of their difficulties. We hypothesised that there would be a significant difference between the post-injury ratings of informants and people with prefrontal lesions, with informants rating FLL patients as more impaired. Proportionally smaller differences were predicted between the pre-injury ratings of FLL patients and informants.
- H2 compared the FLL groups' level of awareness to that of a healthy control sample. It was predicted that the patients with FLL would show reduced awareness of current abilities with higher self-informant discrepancy scores based on post-injury ratings compared to healthy control dyads.

Research question 2: Are participants with surgical frontal lesions able to acknowledge changes in themselves when these are viewed from third-person (informant) perspective? This was an exploratory investigation testing the relationships between current self and surrogate ratings versus current informant and surrogate ratings. If the frontal lobe groups' surrogate ratings correlate with their self-ratings, this suggests that they lack awareness into how others actually see them, instead believing that others perceive them as they see themselves. If there is a discrepancy between surrogate and current self-rating, this suggests that the frontal lobe group can acknowledge that others note a behavioural change in them, but this is not something they personally experience. Alternatively, if surrogate ratings correlate with informant-ratings, this suggests that participants are fully aware of how they are perceived by others. If there is a discrepancy between surrogate and informant-ratings, this suggests unawareness as to how others view them.

Research question 3: Can people with frontal lobe damage detect behavioural changes in others? This too was exploratory and it was hypothesised (H3) that people with prefrontal lesions would be able to correctly identify problem behaviours described in presented vignettes, suggesting that general semantic memory remains intact. However,

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it is possible, in line with findings from Clare et al (2012) that this will be to a lesser extent than healthy controls.

3. Method

3.1 Participants

Two groups of participants were included in this study. The first group comprised 15 adults with acquired frontal lobe lesions (following surgical resection of brain tumours), recruited from the joint neuro-oncology clinic at King's College Hospital, London. All individuals in the FLL group lived independently in the community. Five of the FLL group were retired, five were currently working, three had not returned to work following their treatment and two had taken early or medical retirement from work since their surgery. The second group comprised 15 neurologically healthy controls that acted as a comparison for the clinical group. In the control group nine were currently working and six were retired. Each participant was able to express choices and both verbal and written consent was obtained prior to participation (see Appendix 1 for copy of patient and informant consent forms).

3.2 Matching of participant groups

As detailed in Table 1, the FLL and control groups were specifically matched for chronological age, gender ratio, years in education and pre-morbid IQ. Although controls were not matched 1:1 to patients, periodic analysis of patient group characteristics allowed us to target the recruitment of controls so that samples would be comparable on sociodemographic variables such as age, gender and education. This was in line with the procedure adopted by Hart et al (2017).

All participants were also asked to nominate a significant other with whom they had regular and meaningful contact. Importantly for the FLL group only, patients were required to identify a significant other who knew them both before tumour symptoms

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were apparent and subsequent to tumour resection, to allow them to rate both pre-and post-injury functional abilities. All informants were over the age of 18 years and the relationship between participants and informants are detailed in Table 1.

Table 1: Participant demographics and sample characteristics

	FLL group (n=15)			Control group (n=15)			Statistics		
	M	SD	Range	M	SD	Range	*t*	*p*	*d*
Gender ratio	4 Male: 11 Female			4 Male: 11 Female					
Age (Years)	54.85	12.03	31.0 - 71.9	52.32	13.78	29.1 – 73.4	.54	.596	0.20
Years of education	12.60	2.67	10 - 16	13.27	1.87	11 - 16	-.79	.435	0.29
TOPF (premorbid IQ)	97.07	10.07	82 - 117	100.33	9.83	83 - 119	-.89	.376	0.33
Months since lesion resection	42.07	37.46	6 - 135	-	-	-	-	-	-
Informant (n)									
Partner/Spouse	9			11					
Parent	2			1					
Sibling	1			0					
Adult Child	2			3					
Other	1			0					

3.3 Eligibility criteria

All participants were required to be over 18 years of age at time of testing and those participants with FLLs had undergone surgery after the age of 18 years. It was ensured that all FLL participants were at least six months post-surgery to reduce acute post-operative effects on cognitive functioning. All FLL participants received a recent 1.5 Tesla Magnetic Resonance Imaging (MRI) scan following tumour resection and before participation to establish neurosurgical lesion. The neurological histories and neuroimaging reports indicated damage predominantly to the frontal lobes. Lesion data are summarised in Table 2. The test procedures all involved verbal instructions in

English, and as a consequence, participants were required to be fluent in English. In addition it was ensured that both groups had full-scale IQ >70, as measured using the abbreviated two subtest version of the Wechsler Abbreviated Scale of Intelligence (WASI-II; Wechsler, 2011). Study exclusion criteria included the following: the presence of additional neurological conditions, language impairment, uncorrected hearing or vision, a severe psychiatric disorder (e.g. schizophrenia, bipolar, personality disorder), a primary diagnosis of substance abuse or history of autistic disorders or attention deficit hyperactivity disorder (ADHD) or those currently suffering from a depressive disorder.

Table 2: Frontal lobe lesion group characteristics and lesion aetiology

Participant	Gender	Lesion location	Frontal region	Tumour classification
1	F	L	Fronto-parietal	Oligodendroglioma Grade II
2	F	R	Fronto-parietal parafalcine	Meningioma Grade II
3	F	R	Frontal SOL	Oligodendroglioma Grade III
4	M	R	Sphenoid wing, Medial	Meningioma Grade II
5	F	R	Frontal parasagittal	Meningioma Grade II
6	F	L	Fronto-temporal	Meningioma Grade I
7	M	R	Multi-focal frontal	Glioblastoma Grade IV
8	F	B	Bifrontal olfactory groove	Meningioma Grade I
9	M	L	Frontal SOL	Meningioma Simpson Grade II
10	M	R	Middle frontal gyrus	Oligodendroglioma Grade II
11	F	L	Posterior frontal parafalcine	Meningioma Grade II
12	F	L	Middle frontal gyrus	Malignant neoplasm, PNET
13	F	L	Frontal parafalcine	Meningioma Grade III
14	F	L	Frontal SOL	Oligodendroglioma Grade III
15	F	R	Fronto-temporal-insular SOL	Astrocytoma Grade III

SOL = space occupying lesion

3.4 Recruitment

Over a seven-month period (from September 2017 to March 2018), all active cases attending the neuro-oncology service at King's College Hospital were reviewed to prospectively recruit patients who met study criteria. Approximately 300 patients were screened during MDT case review meetings in order to identify those who had undergone tumour resection of the frontal lobe. The medical records of potentially

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eligible cases (approximately n=60) were then reviewed to confirm lesion location and aetiology, date of surgery and any medical history of relevance to the study's inclusion criteria. Following this process 49 patients were deemed eligible. Of these 49 patients, 30 were successfully contacted by phone and invited to take part. Twenty-six of those contacted expressed an interest in participating and were sent a letter and information sheet detailing the project (see Appendices 2 and 3). Willing participants were then contacted two weeks later in order to consent or decline to participate. Ultimately, 15 of the 26 willing candidates were successfully enrolled. Failed recruitment occurred for a number of reasons; in seven cases it was due to an inability to re-establish successful telephone contact to arrange an appointment time; two patients cancelled planned appointments due to current health concerns, and two declined to participate. Healthy control participants were recruited through advertisements across the University and local community or identified through the researcher's social network. Each control participant was recruited on the basis of matching the gender, age and years in education of a FLL participant. Hence, a combination of convenience and purposive sampling methods were used.

3.5 Measures

3.5.1 Background neuropsychology measures

The following established neuropsychological tests, which measure pre-morbid IQ, general intellectual functioning, verbal memory and executive function were used: The Test of Pre-morbid IQ: Test of Premorbid Functioning – UK version (TOPF-UK) (Wechsler, 2011) was used to estimate premorbid ability; The two subtest version of the Wechsler Abbreviated Scale of Intelligence (WASI-II; Wechsler, 2011) was administered to calculate a full scale IQ on the basis of the Vocabulary and Matrix Reasoning subtests; The Logical Memory subtest from the WMS-IV (Wechsler, 2009) was used as a measure of auditory-verbal memory with both immediate and delayed recall trials; A test of mental flexibility known to be sensitive to the effects of frontal lobe damage was administered, namely the Brixton Spatial Anticipation Test (Burgess & Shallice, 1997) and the PHQ-9 (Spitzer, Kroenke & Williams, 1999) and GAD-7 (Spitzer, Kroenke, Williams & Lowe, 2006) were completed to assess current ratings of depression and anxiety respectively.

3.5.2 Questionnaires

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Two questionnaire measures aimed to assess changes (e.g. behavioural, cognitive, emotional, personality) often associated with frontal lobe damage were administered. Questionnaires included were specifically designed to measure and are noted to be sensitive to frontal behavioural change. Each questionnaire had four versions that followed the following format: Self rating of pre-injury functioning by the participant; Self rating of current post-injury functioning by the participant; Informant rating of pre-injury functioning of the participant; Informant rating of current post-injury functioning of the participant. Here, pre-injury refers to before symptoms of tumour diagnosis were apparent and post-injury refers to after tumour resection. In order to assess this some established measures already exist. The questionnaire measures used included:

The Frontal Systems Behaviour Scale (FrSBe; Grace & Malloy, 2001). This scale provides a brief, reliable and valid measure of three frontal systems behavioural syndromes: apathy, disinhibition and executive dysfunction. It quantifies behavioural change over time by including both baseline (retrospective) and current assessments of behaviour. It includes a total score as well as scores on three subscales that correspond to the three frontal systems behavioural syndromes (Apathy, Disinhibition and Executive Dysfunction). The FrSBe already has ratings prior to and after injury/illness and includes both self- and informant rating version for both aspects. The FrSBe has been demonstrated to be sensitive to behaviour change following focal frontal lesions and has acceptable psychometric properties (Grace & Malloy, 2001).

The Dysexecutive Questionnaire-Revised (DEX-R; Simblett, Ring & Bateman, 2016). This is a rating scale designed to sample everyday problems commonly associated with frontal systems dysfunction. It can be used as a measure of awareness by calculating the discrepancy score between self- and informant responses. It is designed to measure four areas of change: emotional or personality changes, motivational changes, behavioural changes and cognitive changes and comprises four subscales (Activating-Regulating functions, Behavioural-Emotional Self-Regulating functions, Executive Cognition functions, Meta-Cognitive functions). The DEX-R has two forms, Self and Informant, which contain the same items but phrased as appropriate and focus on current functioning. Further adaption was made for this study to create a pre-injury variant for both self and informant versions, in order to create experimental procedures. There are

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currently no normative data available for the DEX-R. However, research into the psychometric properties of the DEX-R is being undertaken (Simblett, Ring & Bateman, 2017).

3.5.2.1 Scoring methods for the two questionnaire measures

The DEX-R was scored using a 5-point rating scale regarding the frequency of a range of behaviours: 0=never, 1=occasionally, 2=sometimes, 3=fairly often, 4=very often. The FrSBe was scored similarly, also adopting a 5-point scale: 1=Almost never, 2=Seldom, 3=Sometimes, 4=Frequently, 5=Almost always. For both measures, individual item ratings are summed together and a higher total score indicates greater impairment.

The discrepancy score method is considered a sensitive measurement of deficit awareness following brain injury (Hart et al, 2003) and was therefore also adopted in the current study. Adapted discrepancy scores were calculated as used by Clare et al (2011) and in subsequent studies (Geytenbeek et al, 2017), whereby the difference between the two ratings (patient total score minus informant total score) was divided by the mean of the two ratings. This is proposed to prevent scaling effects (Geytenbeek et al, 2017). Discrepancy scores focused on current, post-lesion resection functioning only, with larger scores indicating more severe deficits of awareness. Negative scores indicate a consistent underestimation of deficit, whereas positive scores suggest an overestimation of impairment by the patient.

3.5.3 Surrogate self-understanding of behavioural changes

A novel questionnaire-based technique was adopted, focused on whether the participant with frontal lesion experiences a significant other person telling them they have particular symptoms that they disavow. To measure this the FrSBe and DEX-R underwent a further wording adaption and participants were asked to rate the forms as if they were the informant in relation to current behaviour only. An example of the wording is as follows: My partner/relative/friend thinks that I have difficulty expressing emotion. Participants were asked to rate how frequently they felt this occurs using the particular measure's rating scale and scoring method, described above. This aimed to assess participants' understanding of whether informants report behaviours of a type that is abnormal that they themselves do not think they engage in or view as abnormal.

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A copy of these novel questionnaires can be found in Appendix 4).

3.5.4 Third person understanding of abnormal behaviour

A series of vignettes were created that outline scenarios that describe subtler behavioural disturbance. These were used to test understanding of abnormal behaviour in general. The use of vignettes followed a methodology adopted by Clare et al, (2012b). The vignettes themselves used a similar methodology to the Faux Pas Test (Stone, Baron-Cohen & Knight, 1998), in which the person rates the protagonist in the story for their appropriateness in terms of comments. Vignettes were informed by the FrSBe measure in order to contain examples to a larger range of behaviours likely mediated by frontal lobe constructs. In all, nine vignettes were used, relating to apathy, disinhibition and executive functioning, with three items for each, with a further nine control vignettes in which no abnormal behaviour was featured. Participants were required to rate vignettes using a 5-point scale to highlight the extent to which they felt a character in the story did something they shouldn't have done, or did something awkward (see Appendix 4 for task example). If atypical behaviour was attributed to an incorrect character in the story, that score was discarded. Ratings were summed to produce an overall total score. The higher the rating given the more extreme they perceived the behaviour. Given this was a novel experimental measure, pilot testing was conducted prior to main data collection on a neurologically healthy sample to ensure the most valid and reliable vignettes were adopted for study use (see Appendix 5 for pilot results).

3.5.5 Third person perspective in understanding other people's thinking

The two experimental tasks above required the participant to acknowledge deficits in others or in themselves when exposed to evidence from a third-person perspective. This requires the ability to take the perspective of another. The ability to infer other people's mental states, thoughts and feelings, referred to as theory of mind (ToM), is a key aspect of social cognition. A ToM task, namely the Faux Pas task by Stone, Baron-Cohen & Knight (1998) was employed to test the hypothesis that disturbances in awareness seen following frontal lobe damage may be mediated by impairment in this domain. This enabled us to determine whether surrogate understanding of symptoms is affected by ToM ability.

3.6 Procedure

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Participants were seen for one testing session, which lasted for approximately 2-3 hours with appropriate breaks given, and during which participants were administered the neuropsychological test battery, awareness questionnaires and vignette tasks. Written informed consent was obtained from all participants prior to data collection, with capacity to consent determined by the primary researcher (current author). All tasks were administered in a fixed order. Informants, for both the FLL patients and controls, were simply required to complete two questionnaire measures. If the informant was present at the testing session, he/she was given the questionnaires to complete while waiting. If the informant did not accompany the participant to the testing session, a blank copy of the informant versions and a stamped addressed envelope were posted to the designated informant, with the expectation that they mail the completed questionnaires back to the primary researcher (current author). The FLL patient group and their significant-others completed pre- and post-injury versions of the awareness questionnaires. Controls and their informants provided only current ratings. All participants were offered a small honorarium (£20 for participants and £5 for informants) for their participation.

3.7 Ethics

The study was approved by both the local research governance NeuroRAG committee and the London - Central Research Ethics Committee (REC reference: 17/LO/0531; see Appendices 6, 7 & 8 for approval letters).

3.8 Power

A power calculation for the primary analysis of main effect of group (frontal versus informant: paired data) on awareness (rated using the FrSBe measure) was conducted using G*Power (Faul, Erdfelder, Lang & Buchner, 2007). It was guided by the effect size of d=0.5, reported by Simpson et al (2015), who recruited primary brain tumour patients and family informants. A sample size calculation based on a one-tailed hypothesis, power of 0.80 and alpha of .05 predicted a sample size of 23 participants per group was necessary. Given the planned use of correlational analysis, power for this type of analysis was also considered. This too was conducted using G*Power and was guided by the effect size of d=0.5, reported by Simpson et al (2015). A sample size calculation based on a one-tailed hypothesis, power of 0.80 and alpha of .05, predicted a sample size of 21 participants per group was necessary. This is consistent with sample

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sizes from previous relevant studies, including Rankin et al (2005) and previous DClinPsy studies, which have recruited 19-20 participants from the same clinic over the same duration. Although the final number of participants recruited is consistent with samples sizes gained in previous relevant studies, (Rankin et al, 2005; Chiou et al, 2016), given that it falls slightly below the predicted necessary number, and as power is reduced accordingly, analyses should be considered exploratory.

3.9 Statistical analysis

T-tests were used to compare participants with FLLs and controls with respect to demographic characteristics and background neuropsychological measures. Repeated-measures ANOVAs were run to compare within group differences with regards to appraisals of behaviour between raters (self and informant) and time points (pre- and post-illness). Mixed-ANOVAs were run to compare explore between groups differences regarding appraisals of behaviour, focused on the two participant groups (FLL and control) and rater (self and informant). Intra-class correlational analyses were adopted as a measure of reliability, reflecting both degree of correlation and agreement between measurements. They also account for non-linear relationships and small sample sizes. All statistical tests were performed two-tailed and alpha was set at .05 throughout, as these analyses were considered exploratory. SPSS 24.0 was used to perform all descriptive and inferential statistics in this study, apart from effect sizes for t-tests and ANOVAs, which SPSS 24.0 cannot generate and so were calculated by hand using the formulas proposed by Field (2013; pages 341 and 531 respectively).

4. Results

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4.1 Background neuropsychological measures

Participants were tested on a range of neuropsychological measures reported to impact awareness following brain injury, with findings presented in Table 3. There were no significant differences between the groups on Vocabulary and Matrix Reasoning performance, FSIQ, nor on tests of verbal memory recall (immediate and delayed). Significant differences were found between groups on the Brixton (a test of executive functioning), with the control group outperforming the FLL group. Anxiety and depression ratings were also found to significantly differ between the groups, with the FLL group reporting more symptoms than the control group.

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Table 3: Group differences on background neuropsychological measures

	FLL group (n=15)			Control group (n=15)			Statistics		
Variable	**M**	**SD**	**Range**	**M**	**SD**	**Range**	***t***	***p***	***d***
Vocabulary (SS)	8.80	2.57	5 -14	10.33	2.64	7 - 18	-1.61	.118	0.59
Matrix Reasoning (SS)	9.73	3.04	5 -15	11.20	2.43	7 - 15	-1.46	.155	0.53
FSIQ-2	95.53	13.17	74 - 124	104.13	12.02	85 - 129	-1.87	.072	0.68
LM Immediate verbal recall (SS)	8.27	3.08	2 - 13	9.00	3.16	2 - 14	-.64	.525	0.23
LM Delayed verbal recall (SS)	7.93	2.96	1 - 12	9.87	3.14	2 - 13	-1.74	.094	0.64
Brixton (SS) (mv = 2)	5.08	2.63	1 - 10	6.60	.99	5 - 8	-2.09	.047*	0.75
Fauk Pas test (mv = 3)	18.50	1.38	16 - 20	19.20	.86	17 - 20	-1.61	.119	
Anxiety	5.60	4.55	0 - 19	1.73	2.02	0 - 7	3.01	.005*	1.09
Depression	6.07	4.23	0 - 18	3.07	2.71	0 - 9	2.31	.028*	

mv = missing values; Anxiety measured using GAD-7; Depression measured using PHQ-9; Vocabulary and Matrix Reasoning measured using WASI-II; Verbal recall measured using WMS-IV; FSIQ-2: Full Scale IQ-2 subtest estimate.

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4.2 Research question 1

4.2.1 Assessment of degree of awareness (DEX-R and FrSBE)

Initial analysis for hypothesis 1 focused on the FLL group only because it required pre-illness and post-surgery comparison and did not therefore apply to the control group. All subsequent analyses focused on current functioning only, allowing comparison between the FLL group and controls.

4.2.2 Hypothesis 1

Hypothesis 1 predicted that the FLL group would show reduced awareness on both the DEX-R and FrSBe measures, with a difference evident between patient and informant

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ratings post-surgery and no difference between patient and informant ratings pre-illness. It was expected that the informants would rate the FLL patients worse post-surgery compared to pre-illness, whereas there would be proportionally smaller change between patients pre-illness and post-surgery self-ratings.

The data were approximately normally distributed and there were no obvious outliers allowing data to be analysed by means of two repeated measures 2x2 ANOVAs (one for the DEX-R (n=14)[2] measure and another for the FrSBE (n=15) measure), with Time (pre- versus post-surgery) and Rater (self versus informant) as the two within-subjects factors. As is shown in Table 5, for both the DEX-R and FrSBe measures, the analysis yielded a significant main effect of Time (DEX-R: $F(1, 13) = 41.87$, $p < .001$, partial $\eta^2 = .763$, $r = .76$; FrSBe: $F(1, 14) = 27.88$, $p < .001$, partial $\eta^2 = .666$, $r = .67$) with mean scores (presented in Table 4) suggesting that both patients and their informants rated an increase in difficulties for the patient following lesion resection compared to their prior functioning (Figure 1 displays this visually). Across both measures, there was no significant main effect of Rater (DEX-R: $F(1, 13) = .018$, $p = .895$, partial $\eta^2 = .001$, $r = .01$; FrSBe: $F(1, 14) = .031$, $p = .863$, partial $\eta^2 = .002$, $r = .01$) nor was there an interaction between factors (DEX-R: $F(1, 13) = .490$, $p = .496$, partial $\eta^2 = .036$, $r = .04$; FrSBe: $F(1, 14) = .438$, $p = .519$, partial $\eta^2 = .030$, $r = .03$). The analysis was repeated splitting the measures into their relevant subscales to explore if either rater more or less readily identified change in any specific area of difficulty. Results are again presented in Tables 4 and 5. In all cases, the results were comparable to the total score findings; a significant main effect of Time was found across all individual subscales ($p < .01$), whereas Rater and interaction factors were all non-significant (all Fs equal to or less than 1).

[2] For one patient the informant version of the DEX-R was not returned and their data was excluded from these analyses.

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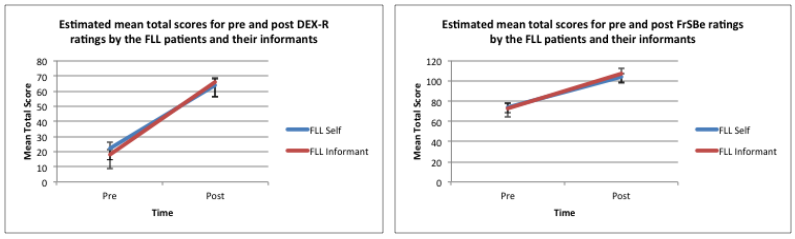

Figure 1: Graphs to show the estimated mean total scores (and Std. Error) for pre and post ratings by the FLL patients and their informants for both awareness measures

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4.2.3 Additional analysis

A number of tests were administered that assess factors reported to impact an individual's level of awareness. These findings are presented in table 3 and highlight that the FLL group appeared to show significantly higher anxiety and depression ratings (measured using the GAD-7 and PHQ-9 respectively) than the control group. With reference to the GAD-7 and PHQ-9 scoring cut-offs, we considered a score of 10 and under to be within normal limits, as this spanned the mild to moderate range and was reflected in the control sample. Anything above this could therefore be classed as outside normal limits and represent an elevated score. Although none of the participants reported having received a formal diagnosis of anxiety or depression, one participant scored above our imposed cut-off (with a depression score of 18 and an anxiety score of 19). As stated in the literature, an increased level of apparent awareness is often noted to be positively associated with increased emotional distress. To ensure that this outlier was not skewing the results, the case was removed and the above analysis was repeated. Consistent with previous findings, a significant main effect of Time was found across both measures ($p < .001$), whereas Rater and interaction factors all remained non-significant (all Fs equal to or less than 1). This suggests that the group difference (in part driven by this elevated score) was not unduly influencing outcomes and therefore the case was included in all subsequent analysis.

Table 4: Descriptive statistics for pre and post ratings by the FLL patients and their informants

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Measure	Time	Rater	Mean	SD	N
DEX-R	Pre	Self	22.14	16.29	14
		Informant	18.07	12.04	14
	Post	Self	63.50	27.97	14

Measure	Time	Rater	Mean	SD	N
FrSBe	Pre	Self	73.87	14.96	15
		Informant	72.80	18.97	15
	Post	Self	103.67	22.09	15

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		Informant	65.79	35.49	14			Informant	107.33	33.72	15
A-R	Pre	Self	3.57	3.44	14	Apathy	Pre	Self	20.87	4.70	15
		Informant	2.57	2.44	14			Informant	20.67	6.59	15
	Post	Self	12.64	7.37	14		Post	Self	33.93	7.94	15
		Informant	13.43	7.78	14			Informant	33.33	10.23	15
B-E	Pre	Self	6.50	3.92	14	Disin	Pre	Self	24.93	6.10	15
		Informant	5.07	3.27	14			Informant	22.53	6.47	15
	Post	Self	13.64	6.42	14		Post	Self	31.53	8.45	15
		Informant	14.57	8.24	14			Informant	30.33	10.58	15
E-C	Pre	Self	4.93	5.87	14	Ex Dys	Pre	Self	28.67	7.23	15
		Informant	4.29	4.57	14			Informant	28.93	9.52	15
	Post	Self	20.50	10.28	14		Post	Self	38.20	9.56	15
		Informant	21.07	11.29	14			Informant	43.87	15.24	15
M-C	Pre	Self	6.57	5.05	14						
		Informant	5.64	4.52	14						
	Post	Self	15.29	7.33	14						
		Informant	14.36	9.53	14						

Note: A-R = Activating Regulating functions; B-E = Behavioural-Emotional Self-Regulating functions; E-C = Executive-Cognition functions; M-C = Meta-Cognitive functions; Disin = Disinhibition; Ex Dys = Executive Dysfunction

Table 5: 2x2 ANOVA summary table exploring time and rater effects on DEX-R and FrSBE total and subscale scores

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Measure	Source	df	MS	F	*p*	Effect size
DEX-R	Time (T)	1	27768.018	41.87	<.001*	.763
	Rater (R)	1	11.161	.018	.895	.001
	T x R interaction	1	565.786	.490	.496	.036
	Error	13	1155.170			
A-R	Time (T)	1	1390.018	38.80	<.001*	.749
	Rater (R)	1	.161	.005	.943	.000
	T x R interaction	1	11.161	.523	.483	.039
	Error	13	21.353			
B-E	Time (T)	1	969.446	28.66	<.001*	.688
	Rater (R)	1	.875	.020	.891	.002
	T x R interaction	1	77.786	1.318	.272	.092
	Error	13	59.016			
E-C	Time (T)	1	3664.446	43.894	<.001*	.772
	Rater (R)	1	.018	.000	.986	.000
	T x R interaction	1	20.643	.125	.730	.009
	Error	13	165.720			
M-C	Time (T)	1	1063.143	25.913	<.001*	.666
	Rater (R)	1	12.071	.202	.661	.015

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	T x R interaction	1	.000	.000	1.000	.000
	Error	13	38.615			
FrSBe	Time (T)	1	15520.417	27.877	<.001*	.666
	Rater (R)	1	25.350	.031	.863	.002
	T x R interaction	1	336.067	.438	.519	.030
	Error	14	767.067			
Apathy	Time (T)	1	2483.267	40.651	<.001*	.744
	Rater (R)	1	2.400	.028	.870	.002
	T x R interaction	1	2.400	.019	.891	.001
	Error	14	123.686			
Disin	Time (T)	1	777.600	16.712	<.01*	.544
	Rater (R)	1	48.600	.433	.521	.030
	T x R interaction	1	21.600	.290	.599	.020
	Error	14	74.457			
Ex Dys	Time (T)	1	2244.817	17.98	<.001*	.562
	Rater (R)	1	132.017	.869	.367	.058
	T x R interaction	1	437.400	1.723	.210	.110
	Error	14	253.829			

Note: MS = Mean squares; Effect size = partial η^2; A-R = Activating Regulating functions; B-E = Behavioural-Emotional Self-Regulating functions; E-C = Executive-Cognition functions; M-C = Meta-Cognitive functions; Disin = Disinhibition; Ex Dys = Executive Dysfunction

4.2.4 Interim summary

The results above demonstrate that this group of FLL patients in fact showed adequate awareness of their difficulties, with no difference being seen between raters' (self or informant) appraisal of the patients' functioning. Time (pre- and post-surgery) was found to be significant, suggesting that both parties noticed and were able to identify changes following surgery, with both reporting an increase in difficulties overall. These findings, therefore, do not support our first hypothesis (H1).

4.2.5 Hypothesis 2

Hypothesis 2 explored whether the FLL groups' level of awareness differed to that of a healthy control sample.

Our previous findings highlight that the FLL group appears to acknowledge a change in their functioning that is similar to that noted by their informants, implying little discrepancy between self and informant ratings. However, they do not inform us how the FLL patient-informant dyads compare to the healthy control dyads. Hypothesis 2, focused on current post-surgery functioning only, and allowed this comparison. It

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predicted that compared to the control sample the FLL group would show reduced awareness, with higher discrepancy scores found compared to control dyads. Consistent with previous existing literature, this was tested by comparing discrepancy scores between the two groups. As shown in Table 6, independent samples t-tests found no significant differences ($p>.05$) between the two groups on the discrepancy between self-reported and informant-reported scores for total or by subscale for either measure. These findings inform that the FLL patient-informant discrepancies are comparable to those found in healthy control-dyads.

However, despite no difference being found between the groups, examination of the mean difference scores suggests that the direction of the discrepancy score varied between groups on certain subscales. It was observed that for the DEX-R measure for both patient and control groups, the total mean discrepancy scores were positive. This suggests that there was a consistent tendency for FLL patients to slightly over-report difficulties compared to their informants, and that this slight over-reporting was also observed within the healthy control group. This was also the case for all subscales, with the exception of the Activating-Regulating functions subscale, on which FLL patients consistently rated themselves as less impaired than their informant, resulting in a negative discrepancy score. For the FrSBe measure, the total mean discrepancy score was negative for the FLL group, suggesting patients slightly underreported their difficulties compared to their informants, whereas the opposite was found for the control group. For the majority of subscales in both groups the discrepancy scores were positive with participants (FLL patients and controls) slightly over-reporting difficulties compared to their informants. There were two exceptions: on the executive-dysfunction subscale in the FLL group, patients rated themselves as less impaired compared to their informants and on the apathy subscale in the control sample, participants rated themselves as less impaired compared to their informants.

Table 6: Between group differences on post-surgery discrepancy scores

Measure	**Score** Adapted discrepancy = self - informant/mean	**FLL group**			**Control group**			**Statistics**		
		M	**SD**	**Range**	**M**	**SD**	**Range**	***t***	***p***	***d***
DEX-R	Adapted Discrepancy total	.01	.74	-1.13 - 1.12	.14	.64	-.87 – 1.39	-.48	.636	0.19

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Subscales	A-R functions adapted discrepancy	-.15	.87	-2.00 – 1.30	.08	.69	-.86 – 1.33	-.81	.424	0.29
	B-E functions adapted discrepancy	.02	.83	-1.45 – 1.43	.07	.67	-.93 – 1.79	-.19	.854	0.07
	E-C adapted discrepancy	.01	.74	-1.25 – 1.27	.23	.87	-1.00 – 1.73	-.74	.464	0.27
	M-C functions adapted discrepancy	.16	.92	-1.60 – 1.62	.15	.86	-1.33 – 1.69	.04	.966	0.01
FrSBe	Adapted Discrepancy	-.01	.38	-.75 - .58	.07	.26	-.39 - .59	-.64	.530	0.25
Subscales	Apathy adapted discrepancy	.04	.38	-.56 - .74	-.04	.29	-.42 - .60	.61	.548	0.24
	Disinhibition adapted discrepancy	.05	.41	-.48 - .95	.23	.29	-.30 - .75	-1.29	.210	0.51
	Executive Dysfunction adapted discrepancy	-.06	.40	-1.12 - .47	.02	.29	-.48 - .56	-.66	.515	0.23

4.2.6 Further exploratory analyses

Contrary to a priori predictions, the findings from HI and H2 inform us that FLL patient self-ratings appear in line with informant ratings, suggesting adequate awareness of abilities, and that these self-informant discrepancies do not significantly differ from those of a healthy control sample, suggesting a level of awareness that is comparable to controls. However, they do not allow a sense of whether patient ratings are elevated compared to a healthy comparison group. If the previous hypotheses had been supported, and patients had shown a lack of awareness it would have been reasonable to expect that the FLL group would have lower overall scores, rating themselves to engage in frontal behaviours as frequently or even less frequently that the controls. However, given the current findings we can suppose that there will be a difference between the groups in the rated frequency of the frontal behaviours engaged in, with the FLL group reporting that they more frequently exhibit problem behaviours (which would be evidenced by higher mean scores on rating measures).

To allow us to explore how the FLL group appraised their current abilities compared to healthy controls a mixed 2x2 ANOVA was conducted with group (FLL or control) as the between-subjects factor and rater (self or informant) as the within-subjects factor[3]. This test was adopted as it also allowed the inclusion of covariates. Results are presented in Tables 7 and 8. Significant between group differences were found for total and all subscale scores on both measures ($p<.01$), with mean scores suggesting that the FLL group reported engaging in more frontal behaviours than the control group. In

[3] The assumption of homogeneity of variances was violated (Levene's test $p<.05$) for all DEX-R and FrSBe scores, so data were log transformed. Transforming the data had no impact on the outcome of the analyses compared to using raw scores. As a result the data presented used the original raw scores. Assumption of homogeneity of regression slopes was tenable ($p>.05$).

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keeping with previous findings, there was no significant main effect of rater nor was there an interaction between factors.

A series of 2x2 mixed ANCOVAs were then conducted to examine the impact of three covariates (namely anxiety, depression and Brixton scores), as these were shown to differ between groups. As is shown in Table 8, inspecting the covariates alone, no relationship was found between the Brixton and participant ratings ($p>.05$) across measures or subscales. A significant relationship between participant ratings and depression was seen across both measures and all subscales with the one exception of the Executive-Cognition subscale of the DEX-R. A slightly more variable pattern was found for anxiety scores, with anxiety showing no relationship with participants' ratings on the Executive-Cognition subscale of the DEX-R, the FrSBe total, or apathy and executive dysfunction subscale scores, but appearing to relate to all remaining subscales.

As presented in Table 8, overall, the inclusion of covariates did not change the pattern of results with significant group differences remaining and all other main effects and interactions yielding non-significant results across both total and the majority of subscale scores. There were however two exceptions: the covariates, anxiety and depression, had a significant relationship with participants ratings on the Meta-Cognitive subscale of the DEX-R (anxiety: $F(1, 26) = 11.33$, $p = <.01$, partial $\eta^2 = .304$, $r = .30$; depression: $F(1, 26) = 8.36$, $p = <.01$, partial $\eta^2 = .243$, $r = .24$). However, the effect of group on participant ratings of M-C functioning became non-significant after controlling for the effects of anxiety ($F(1, 26) = 2.16$, $p = .154$, partial $\eta^2 = .077$, $r = .08$) and depression ($F(1, 26) = 3.94$, $p = .058$, partial $\eta^2 = .132$, $r = .13$). The same pattern was seen for the disinhibition subscale of the FrSBe. Both anxiety and depression were found to significantly relate to participants ratings on this subscale (anxiety: $F(1, 27) = 10.45$, $p = <.01$, partial $\eta^2 = .279$, $r = .28$; depression: $F(1, 27) = 10.06$, $p = <.01$, partial $\eta^2 = .271$, $r = .27$), however, the group difference failed to reach significance after controlling for the effects of these covariates (anxiety: $F(1, 27) = 1.81$, $p = .190$, partial $\eta^2 = .65$, $r = .06$ and depression: $F(1, 27) = 3.30$, $p = .080$, partial $\eta^2 = .109$, $r = .11$).

These findings suggest that overall FLL groups tend to rate themselves as more functionally impaired on a range of executive and frontal behaviours than a healthy control group. For the most part this group difference remains even when controlling

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for covariates such as levels of emotional distress (e.g. anxiety and depression scores) which were known to differ between the groups. These covariates were, however, found to impact participant ratings on two subscales, namely the Meta-Cognitive subscale of the DEX-R and the Disnihbition subscale of the FrSBe.

Table 7: Mixed 2x2 ANOVA summary table (focused on current functioning only)

Measure	Group	Rater	Mean	SD	N	Measure	Group	Rater	Mean	SD	N
DEX-R	FLL	Self	63.50	27.97	14	**FrSBe**	FLL	Self	103.67	22.09	15
		Informant	65.79	35.49	14			Informant	107.33	33.72	15
	Control	Self	32.47	15.62	15		Control	Self	82.13	17.99	15
		Informant	29.73	32.71	15			Informant	76.60	17.08	15
A-R	FLL	Self	12.64	7.37	14	Apathy	FLL	Self	33.93	7.94	15
		Informant	13.43	7.78	14			Informant	33.33	10.93	15
	Control	Self	5.47	2.36	15		Control	Self	23.87	6.21	15
		Informant	5.73	3.45	15			Informant	24.47	4.82	15
B-E	FLL	Self	13.64	6.42	14	Disin	FLL	Self	31.53	8.45	15
		Informant	14.57	8.24	14			Informant	30.33	10.58	15
	Control	Self	7.40	4.47	15		Control	Self	27.13	5.55	15
		Informant	6.87	4.12	15			Informant	21.87	6.49	15
E-C	FLL	Self	20.50	10.28	14	Ex Dys	FLL	Self	38.20	9.56	15
		Informant	21.07	11.29	14			Informant	43.87	15.24	15
	Control	Self	9.73	5.22	15		Control	Self	31.13	8.43	15
		Informant	8.13	5.79	15			Informant	30.07	6.62	15
M-C	FLL	Self	15.29	7.33	14						
		Informant	14.36	9.53	14						
	Control	Self	9.13	4.12	15						
		Informant	8.13	5.46	15						

Note: A-R = Activating Regulating functions; B-E = Behavioural-Emotional Self-Regulating functions; E-C = Executive-Cognition functions; M-C = Meta-Cognitive functions

Table 8: Mixed 2x2 ANOVA/ANCOVA summary table (for current functioning only)

ANOVA							ANCOVA	
Measure	**Source**	**df**	**MS**	**F**	***p***	**Effect size**	**Covariate *p***	**Adj. Group *p***
DEX-R	Group (G)	1	8147.444	20.21	<.001*	.428	Anx: <.05*	<.05*

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	Rater (R)	1	1.451	.002	.969	.000	Dep: <.05*	<.05*
	G x R interaction	1	182.416	.199	.659	.007	Brixton .844	<.01*
	Error	27	403.141					
A-R	Group (G)	1	2514.858	127.794	<.001*	.430	Anx: <.05*	<.01*
	Rater (R)	1	8.020	.160	.692	.006	Dep: <.05*	<.05*
	G x R interaction	1	1.951	.039	.845	.001	Brixton .848	<.01*
	Error	27	19.679					
B-E	Group (G)	1	352.177	16.761	<.001*	.383	Anx: <.05*	<.05*
	Rater (R)	1	.566	.019	.891	.001	Dep: <.05*	<.01*
	G x R interaction	1	7.738	.261	.614	.010	Brixton .886	<.01*
	Error	27	21.012					
E-C	Group (G)	1	1017.261	20.906	<.001*	.436	Anx: .456	<.01*
	Rater (R)	1	7.661	.083	.776	.003	Dep: .245	<.01*
	G x R interaction	1	34.144	.368	.549	.013	Brixton .433	<.01*
	Error	27	48.659					
M-C	Group (G)	1	277.291	9.108	<.01*	.252	Anx: <.01*	.154
	Rater (R)	1	26.933	.377	.545	.014	Dep: <.01*	.058
	G x R interaction	1	.037	.001	.982	.000	Brixton .780	<.01*
	Error	27	30.446					
FrSBe	Group (G)	1	5122.133	15.584	<.001*	.358	Anx: .071	<.05*
	Rater (R)	1	26.133	.028	.868	.001	Dep: <.01*	<.01*
	G x R interaction	1	634.800	.686	.415	.025	Brixton .947	<.01*
	Error	28	328.687					
Apathy	Group (G)	1	672.133	19.371	<.001*	.409	Anx: .226	<.01*
	Rater (R)	1	.000	.000	1.000	.000	Dep: <.05*	<.01*
	G x R interaction	1	10.800	.102	.751	.004	Brixton .845	<.01*
	Error	28	34.699					
Disin	Group (G)	1	310.408	8.572	<.01*	.234	Anx: <.01*	.190
	Rater (R)	1	313.633	2.813	.105	.091	Dep: <.01*	.080
	G x R interaction	1	124.033	1.113	.301	.038	Brixton .845	<.01*
	Error	28	36.212					
Exec Dys	Group (G)	1	816.408	12.544	<.001*	.309	Anx: .306	<.05*
	Rater (R)	1	158.700	.891	.353	.031	Dep: <.05*	<.05*
	G x R interaction	1	340.033	1.909	.178	.064	Brixton .805	<.01*
	Error	28	65.083					

Note: MS = Mean squares; Effect size = partial η^2; Adj. Group p = p-value after controlling for covariate

4.3 Research question 2

Are participants with prefrontal lesions able to acknowledge changes in themselves when these are viewed from a third-person (informant) perspective?

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Intra-class correlations (ICCs) were run to explore the associations and agreement between current self-ratings and surrogate ratings versus current informant ratings and surrogate ratings. ICCs are presented in Table 9. Both the DEX-R and the FrSBe achieved values in the range generally accepted to indicate moderate (0.50 – 0.75) to good (>0.75) reliability, or in this case agreement, between self and surrogate ratings (Koo & Li, 2016). By comparison the agreement between informant ratings and surrogate ratings for both measures failed to reach significance. Inspection of the coefficients in Table 9 reveals moderate to strong agreement (0.73 to 0.89) between self and surrogate ratings, suggesting that participants believe their informants' perception of them is strongly aligned with their own experience. In contrast, the agreement between informant and surrogate ratings was consistently lower (0.19 to 0.29). These findings suggest that participants (both FLL patients and controls) do not appear to fully understand how their informants perceive them. Instead, they seem to think that informants view them similarly to how they view themselves.

Table 9: ICCs explored the notion of surrogate awareness

		DEX-R surrogate	FrSBe surrogate
FLL	Self	0.91**	0.91**
	Informant	0.43	0.32
Control	Self	0.84**	0.94**
	Informant	0.45	0.41

**p<.001

Given previous findings suggesting a lack of discrepancy between self and informant ratings, it is somewhat surprising to find significant agreement between surrogate and self-ratings only. Although no significant difference in mean discrepancy scores was found, it was noted that the direction of the discrepancy scores within samples varied and mean analyses might have masked the impact of any differences in individual ratings. ICCs for the self and informant ratings on both measures confirmed weaker agreement between individual ratings (DEX-R: FLL: 0.44; Control: 0.48; FrSBe: FLL:

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0.32; Control: 0.27). An 'unsigned' analysis was run on the self-informant discrepancy scores in order to examine whether patients were less 'accurate' overall than the controls. Independent t-tests on these unsigned discrepancy scores revealed no significant differences between groups on either the DEX-R ($t(27) = .47$, $p=.642$, $d=0.17$) or FrSBe ($t(28) = 1.77$, $p=.087$, $d=0.70$) measure. However, the FrSBe measure score yielded a large effect size, suggesting that a difference between the groups is detectable and with a slightly larger sample it may have reached significance.

To explore whether this variation at the individual level impacted surrogate ratings, the ICC analysis was re-run, crudely[4] grouping samples on the basis of the direction of their discrepancy scores. Using the DEX-R measure, six FLL patients and six controls were noted to have negative discrepancy scores suggesting that these participant's under-reported atypical behaviours compared to informants. The remaining eight FLL participants[5] and nine control participants in each group had positive discrepancy scores and therefore were deemed to over-report atypical behaviours compared to informants. For the FrSBe measure, eight FLL patients and five controls had negative discrepancy scores (under-reporting atypical behaviours) meaning seven FLL patients and ten controls over-reported atypical behaviours compared to informants (positive discrepancy scores). Table 10 displays the ICCs split by subgroup.

Table 10: ICCs between self and surrogate and informant and surrogate by subgroup

Subgroup	Rater	n	DEX-R	*p*	n	FrSBe	*p*
FLL under-reporters	Self	6	0.78*	<.05	8	0.84*	<.01
	Informant	6	0.33	.070	8	0.27	.136
FLL over-reporters	Self	9	0.87*	<.01	7	0.83*	<.01
	Informant	8	0.48	.052	7	0.39*	<.05
Control under-reporters	Self	6	0.71*	<.05	5	0.82*	<.01
	Informant	6	0.69*	<.05	5	0.66*	<.05
Control over-reporters	Self	9	0.74*	<.01	10	0.90**	<.001
	Informant	9	0.09	.391	10	0.24	.151

n=sample size

[4] Due to the small sample size, this did not take into account the size of the discrepancy. Therefore, it was a crude sample split simply looking at the difference between over and under reporting atypical behaviours in comparison to informants.

[5] One informant failed to return DEX-R questionnaire, therefore discrepancy could not be obtained and case was excluded from analyses.

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The findings in Table 10 show that all self and surrogate ratings across both measures continued to achieve moderate to good agreement. Interestingly, these analyses also revealed significant agreement between informant and surrogate ratings for certain subgroups. For the FLL participants who under-report atypical behaviours compared to informants, the findings suggest that they believe informants reports to be congruent with their own only (good agreement between self and surrogate ratings; informant-surrogate agreement was non-significant). Conversely, there appeared poor, but significant, agreement between informant and surrogate ratings on the FrSBe in those patients that over-report atypical behaviours compared to informants. This implies that this subgroup of FLL patients have a more accurate or reliable understanding of how their informants perceive them. The agreement between informant and surrogate ratings on the DEX-R for this same subgroup was also poor, but it failed to reach significance (p=.052). However, for the control sample, the opposite pattern was seen; moderate agreement between informant and surrogate ratings appeared in those participants that under-report atypical behaviours compared to informants. For this subgroup of control participants it seems that they believe that their informants perception of them is aligned with their own experiences (good agreement between self and surrogate) and that this appears congruent with actual informant report (moderate agreement between informant and surrogate). For the control participants who over-report atypical behaviours compared to informants, the findings suggest that they believe informants reports to be congruent with their own only.

From the above analyses it appears that initial ICC analyses on the full samples suggested that neither FLL nor control participants were reliable in assessing how their informants perceived them, with poor (non-significant) agreements found between informant and surrogate ratings). Instead, they seemed to report that informants' views are more congruent with their own self-report. However, further exploration by subgroups suggests a possible difference in the attribution of surrogate ratings between participants who under-report versus those who over-report. However, it is possible that the small sample sizes of the subgroups impacted outcomes due to being underpowered, which should be taken into account when interpreting this exploratory analysis.

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4.4 Research question 3

Can people with frontal damage detect atypical behaviour in others compared to controls?

Table 11: Mean scores and test statistics comparing FLL and control ratings on novel experimental vignette task

	FLL group (n=15)			Control group (n=15)			Statistics		
Variable	**M**	**SD**	**Range**	**M**	**SD**	**Range**	***t***	***p***	***d***
Total (A+Dis+EDys)	9.48	1.69	6.3 – 11.9	10.61	1.43	7.9 – 13.3	-1.97	.059	0.72
A: Apathy items	2.96	.87	1.3 – 4.6	3.14	.62	2.0 – 4.3	-.65	.519	0.24
Dis: Disinhibition items	3.93	.66	3.0 – 5.0	4.26	.49	3.0 – 5.0	-1.56	.129	0.57
EDys: Executive Dysfunction items	2.59	1.02	1.0 – 4.0	3.21	.85	1.6 – 4.3	-1.79	.084	0.66
Control items	1.26	.15	1.1 – 1.5	1.07	.08	1.0 – 1.2	4.36	.001*	1.58

Given the novel and exploratory nature of this research question, no directional predictions were made. As is presented in table 11, a series of independent t-tests found no significant between-group differences for the total score (combined executive subscales) or for the three executive subscales individually (apathy, disinhibition, executive dysfunction). Mean scores inform that the FLL patients are less sensitive at perceiving atypical behaviour compared to the control sample and a trend for differences between the groups was detected for the total score (p=.059) with an effect size above 0.70. This suggests that the between group difference is notable, and that with a slightly larger sample this would have likely reached significance. Looking at the subscales individually, this difference appears to be driven by difference between the groups on the EF subscale. The EF scale also showed a trend for difference with mean scores suggesting that the FLL group are not as sensitive to perceiving executive behavioural difficulties as controls. Although this does not reach significance (p=.084, d=0.66), the medium effect size marks the difference in mean scores between the groups as note worthy. However, a significant between-groups difference was found for the neutral control items (t(28)=4.36, p<.001, d=1.58), with mean scores suggesting that the FLL group rated these neutral vignette items higher than healthy control subjects, suggesting that they perceive neutral situations as more atypical. These findings suggest that patient with FLLs appear to misjudge and over-interpret neutral situations.

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4.5 Supplementary analyses

Supplementary analyses were conducted to investigate the effects of laterality within the frontal lobe group on performance on the background neuropsychological battery, on level of awareness (self-informant discrepancy and surrogate) as assessed by both DEX-R and FrSBe measures and vignette task performance. The method used by Rowe et al., (2001) was adopted, where individuals who had an operation in a specific location were compared to the rest of the sample who did not have an operation in this region. For laterality analyses, unilateral left (n = 7) were compared with unilateral right hemisphere lesions (n = 7) (this excluded the one patient with a bilateral lesion). The groups significantly differed on verbal memory task performance, on which patients with left hemisphere lesions performed worse than those with right hemisphere lesions and on depression scores, for which patients with right hemisphere lesions reported increased depression compared to patients with left hemisphere lesions. However, although it did not reach significance, the effect size suggested a trend for difference between subgroups based on time since lesion, with the right hemisphere group having less time since surgery, which likely impacts results. No significant effects of laterality were found on level of awareness or on vignette task performance (see Appendix 9 for tables of demographic data for the subgroups). Using subgroup analyses, the resulting sample sizes are too small to account for mediator effects, but with a larger sample, further exploring the effects of laterality and of lesion location would likely be informative.

5. Discussion

In this study we explored the understanding of self-ability and behaviour in people with acquired frontal lobe lesions (FLL group). A number of hypotheses were made and tested using the CAM model as a guiding framework.

The present investigation yielded five main findings:

1. Patients with FLL show adequate awareness of their abilities and acknowledge post-surgery changes in their behaviours similarly to their nominated informant.
2. Discrepancy scores of the FLL patients and their informants do not differ from those of the healthy control group.

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3. Individuals with FLL lesions were rated (by self and nominated informants) as being less competent than controls (engaging in more frequent 'frontal behaviours').
4. The level of awareness participants have into how others perceive them may be dependent on their own self-perceptions (i.e. whether they under or over-report self-difficulties compared to informants).
5. When appraising the atypical behaviour of others, patients with frontal lesions appear to misjudge and over-interpret neutral situations and conversely show a tendency to be less sensitive to perceiving behavioural difficulties in others.

In order to more accurately test the CAM model's assertion, that unawareness can be explained by a failure in ability to update personal (self-trait) knowledge, measures were required to assess both pre- and post-injury ratings in order to obtain an estimate of change. The standardised FrSBe measure met these requirements. However, for the DEX-R measure, novel adaptions were required and implemented in the current study to allow this. The FLL group reported significantly higher post-surgery difficulties as reflected in the overall scores of the FrSBe and the DEX-R relative to pre-illness scores. This finding replicates other research studies with similar populations (Gregg et al, 2014; Legenfelder et al, 2015). Our findings suggest that this specific patient group, patients with frontal lesions, show adequate awareness with both patients with frontal lesions and informants who know them well acknowledging and reporting behavioural changes following surgery. It appears, therefore, that contrary to the CAM model's predictions, FLL patients are in fact able to update their self-representation to reflect current abilities. Although our findings did not support our hypothesis, the results do highlight the sensitivity of the measures used in identifying change following surgery. This is particularly informative for the DEX-R measure, implying that the novel adaption and inclusion of the pre-injury questions (to elicit a comparative change score) adopted in this project was successful.

The above analyses confirmed that FLL patients as a group were able to update their sense of self with self-ratings appearing comparable to their nominated informants. However, it did not provide information as to how this patient group compared to a healthy control sample. Findings from these discrepancy analyses confirmed patients' appraisal of their current functioning to be in line with informant viewpoint and that

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these discrepancies were comparable to those found in a demographically similar sample of healthy controls. However, variability was found among the discrepancy ratings with some participants underestimating their difficulties compared to informants and others overestimating their difficulties. This was true for both the patient and control group but more marked for the patient group. The typical pattern for the healthy control group was to overestimating their difficulties compared to their nominated informants, whereas for the patient group it was more equally split between over- and under-estimators. Despite the lack of discrepancy, there also appeared a lack of agreement between participant and informant ratings. This finding that participant and informants may not precisely map on to each other, reassuringly, is not novel (Ediebah, Reijneveld et al, 2017) and a number of reasons have been asserted to explain this incongruency. A failure to distinguish between different types of proxy has been implicated (Olino & Klein, 2015), as it has been argued that the depth and breadth of shared information is likely to vary dramatically dependent on this, which may make impact the comparative observations required in assessment of awareness. This point shall be returned to later in the discussion. Despite the variation in the number of over and under-reporters between the groups, that fact that these measures appeared to capture variability in executive behaviour, with over and under-reporting apparent across both groups, highlights that both over and underreporting of abilities may not be just the result of brain injury. Pre-injury ratings therefore seem crucial for placing post-injury behaviours in context, marking the inclusion of the pre-illness ratings in the current project (a design specification to more systematically investigate the CAM models ideas) as warranted and important for future research.

Despite finding no group differences when comparing discrepancy scores suggesting patients' appraisal of their abilities to be in line with their nominated informant, a significant difference was found between the FLL and control group on the frequency of 'frontal behaviours' engaged in. This is in keeping with previous studies with similar samples that have found patients and their informants to report increased difficulties compared to non-brain injured control samples (Grace, Stout & Malloy, 1999; Chiou et al, 2016). Patients and informants yielded significantly higher mean scores than control and informants implying that the patients are engaging in more problem behaviours than the control sample. Together, these findings suggest that patients are engaging in more atypical behaviours compared to healthy controls, but importantly and contrary to

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predictions, they are aware of and acknowledge these difficulties. Limited evidence exists comparing behavioural ratings and responses from individuals with frontal lobe lesions to typical control groups and as such this study marks a positive addition to the literature.

As established, the current patient group did not demonstrate discrepant scores from their nominated informants, nor did discrepancies significantly differ from the healthy control sample. This finding could be related to the sample tested. The current patient sample was recruited from an outpatient neuro-oncology clinic on the basis that they had frontal lobe lesions, rather than due to any reported behavioural or cognitive difficulties following their tumour resection. Studies that found awareness deficits using these measures (Bogod et al, 2003; Niemerer et al, 2014) have included samples recruited from hospital and rehabilitation settings where these difficulties may be more prominent. However, the prevalence of behavioural problems varies greatly across studies with behavioural problems being reported in 13% (in small studies) to 34% (in large studies) (Zwinkels, Dirven et al, 2015). Additionally, previous studies that have found reduced awareness using these measures typically include samples comprised of survivors of TBI (Morton et al, 2010; Hart et al, 2017). These samples are often associated with larger lesions and more likely diffuse damage. Prigatano (2010) posits that diffuse bilateral brain aetiology is more likely to produce awareness deficits than unilateral lesions, as such the severity of the injury in our studied patient group may not be large enough to impact awareness. Our supplementary analysis that compared level of awareness between patients with left hemisphere lesions to those with right hemisphere lesions found no difference. Only one patient had bilateral lesion therefore a comparison between unilateral and bilateral lesions was not possible. This could be considered in future research.

Our second research question explored another assertion of the CAM model: that a distinction exists between self-related semantic memory and general semantic memory. Here, we essentially aimed to investigate the notion of a surrogate self with the prediction that even if patients with FLLs appear to show reduced awareness, failing to self-report deficits in themselves, will they be able to identify that others rate them in a certain way. Although our initial hypothesis was unsupported and suggested that the FLL sample have adequate awareness, failing to allow our a priori avenue of

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investigation, we could still investigate how participants perceived nominated informants to perceive them.

Findings revealed that neither FLL nor control participants were reliable in assessing how their informants perceived them, with poor (non-significant) agreements found between informant and surrogate ratings. Instead, they seemed to report that their informants' views were more congruent with their own self-report, with moderate to strong agreements found between self and surrogate ratings. It is possible that this is an artefact of the testing procedure. Although the self and surrogate questionnaires were not administered in the same testing block (separated by a testing break), all testing happened over one session and this may have caused difficulties in switching perspectives (from self-perspective ('I act without thinking') to surrogate ('My partner thinks that I act without thinking'). The fact that no group (FLL versus control) difference was found on a task that provides a measure of perspective-taking (faux-pas task) suggesting that neither group had difficulty with this skill, should minimise these concerns. However, future analyses may wish to more stringently assess perspective-taking ability and investigate its mediation effect. Further exploration by subgroups suggested a possible difference in the attribution of surrogate ratings between participants who under-report versus those who over-report. It is possible that the small sample sizes of the subgroups impacted outcomes due to being underpowered, which should be taken into account when interpreting this exploratory analysis and repeating the analyses with a larger sample size is recommended. However, this variability between over and under-reporters in both the patient and control samples and the impact this can potentially have on an individuals view of how they are perceived by others supports the need to obtain multiple perspectives when assessing awareness. Furthermore, even if repeated with a larger sample, it is difficult to know how much weight to put on the findings as the variation in positive and negative bias between patients' self-report and informant rating seen in the current study (and indeed noted in the literature; Silva, Moser et al, 2016) likely reflects many factors that may influence differences in both participant and proxy responses. These include the construct being measured, characteristics of the proxy, characteristics of the participants and the participants-proxy relationship (Olino & Klein, 2015). This suggests that future research may benefit from applying more stringent controls to the participant informant dyads recruited. Despite the limitations mentioned, whereas previous studies have failed to look at the idea of the surrogate self and self-reported awareness in the same sample,

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the current study remedied this and explored the extent to which participants felt others perceptions of them were in line with their own experiences. Again, marking this investigation as a positive contribution to the literature.

The final research question provided a novel control task and explored whether patients with FLL were able to accurately detect atypical behaviour in general. This was felt to potentially act as an important precursor to assessing awareness, as we hypothesised that information about the way behaviour is perceived would likely impact on self-appraisal of behaviour in terms of what individuals deemed acceptable behaviour. Between group comparison highlighted that the FLL patient group appeared less sensitive than the control group at identifying atypical behaviours. Trends were noted, supported by substantial effect sizes, suggesting that significant between group differences would have been found with a slightly larger sample. The key finding from this investigation was that FLL patients were found to potentially misperceive and misjudge neutral situations as involving atypical behaviour. This is a striking finding; although a trend was found suggesting less sensitivity to atypical behaviour, patients with FLLs clearly show increased oversensitivity to neutral situations. This may have implications for social integration. It is reported that individuals who experienced a TBI often misjudge social situations (McDonald, Togher & Code, 2013) and these misattributions may to born out of diminished communication or interpersonal skills. Our findings offer evidence that even with the online social element removed (i.e. when rating written vignettes as opposed to in vivo interactions with others) patients with FLLs appear to perceive neutral scenarios as atypical. Gaining a better understanding of this appears important as difficulties can have a significant effect on psychosocial outcomes. For example problems in this area could create obstacles in maintaining relationships, which may result in reduced opportunities for employment and lead to the individual becoming socially isolated. Compared to controls, patients also appeared weaker at identifying executive difficulties (e.g. planning, monitoring etc.). Given this was a newly developed experimental task, the substantial effects sizes suggest that our findings are detecting a real area of difficulty for this patient group and further investigation certainly seems valuable.

5.1 Limitations

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This study is not without limitation and should be noted when interpreting the results. Although our sample size was in keeping with previous investigations (Larson et al, 2009; Chiou et al, 2016) and relatively large considering the specific patient group recruited, it is still possible that a larger sample may uncover more behavioural variability within this sample, as well as allow further exploration of factors suspected to impact the outcome (e.g. mood variables). It would further provide the opportunity to conduct appropriate subgroup analyses (detailed in section 4.5). As research has highlighted frontal circuits and regions as potentially key in awareness, our targeted population appeared apt to test our theories, given the location of their post-surgical lesions. Although it can be helpful to limit the focus of research to a specific patient group, especially given the heterogeneity in clinical presentation following different types of injury, doing so does mean that the findings may not be generalisable to the wider population. Due to the relatively stringent eligibility criteria, the applicability to individuals with psychiatric histories or those with more diffuse injuries is unknown. Additionally, the level of education of included sample was not particularly diverse and therefore the generalisability of the findings within this study is limited by the homogeneity of the samples that were tested. Furthermore, there was variability within the patient sample in terms of the amount of post-surgery treatment that individuals had or indeed were receiving. This may indeed have impacted on both self and informant ratings in terms of how 'well' patients were perceived to be recovering. It is conceivable, therefore, that these results would not generalise if these group variations were taken into account – or at least applying these findings to patients beyond the parameters of the current study requires acknowledgement of its limited applicability.

Another caveat for interpreting these results is the fact that the psychometric properties of the FrSBe instrument have not been as thoroughly studied in healthy samples as they have in those with neurological impairment. Therefore, caution should be applied when interpreting the between samples comparison made. However, as we did not employ the standard T-scores for the FrSBe measure, instead using raw score data to allow us to compare our novel adaption (surrogate version) to the pre- and post versions, this may not be such a heavy criticism.

Although a limitation more generally when using these self-proxy measurement instruments, it may still have impacted the current study. It is not possible to validate

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reports from patients or informants to inform whether informant or indeed patient reports are more veridical. Further research is necessary to establish the best way of validating the measurement of pre-injury status in this sample. As we were asking participants to rate themselves pre- any symptoms of the tumour, it is possible that this was difficult to pinpoint temporally and that participants may have rated pre-surgery (which we can presume likely involved some symptoms) as opposed to pre-illness (pre-symptoms). With the patients themselves difficulties with this are less likely as the questionnaires were completed with the researcher and reminders were given when required focusing patients appropriately. However, nominated informants of the FLL group, in the majority of cases, completed their questionnaires remotely and therefore their understanding of the temporal element of the task instructions cannot be confirmed. Additionally, the ratings of pre-illness functioning were completed retrospectively. Therefore, it post-surgery factors may have distorted ratings of pre-illness functioning. However, of note is that self and informant ratings of pre-illness functioning were comparable, which suggests that the retrospective rating was in fact an effective and reliable approach in this sample at least.

5.2 Future directions

Reflecting on the results and limitations presented above, there appear a number of avenues for future consideration emerging from this research. Replicating our results with a slightly larger size in order to further corroborate our substantial effects sizes, increase power and improve our ability to draw meaningful and generalisable conclusions is deemed valuable. Increasing the sample would also allow the patient group to be split by lesion location (unilateral, left or right or bilateral) in order to explore the impact of specific neuroanatomical lesion site. This would allow exploration into the impact of more diffuse versus more focal lesions, adding to this field of exploration (Ham, Bonnelle et al, 2014; Stuss, 1991). It would also potentially allow a sample spilt between over and under-reporters in order to further explore the impact these self-perceptions have on patients opinions of how others perceive them (surrogate ratings). Although the relationship between participant and informant was relatively well matched between the FLL and control groups, it has been noted that the way an individual is perceived can depend on patient-proxy relationship. It may be insightful to further control for that in future studies as it may impact on the amount of time the two individuals spend together and in turn the range of situations in which

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they observe each other and interact. Furthermore, assessing personality factors and sample characteristics that may bias perception and motivation, e.g. mood and self-efficacy ratings may offer more information on the factors mediating ratings and awareness of atypical behaviours. Finally, repeating the study with a TBI sample, for which behavioural challenges are more typically reported, may provide interesting insights and we could predict that a TBI sample may indeed show less awareness.

5.3 Clinical implications

Understanding the emotional, behavioural and psychosocial changes that may follow neurosurgery is important for the clinical management of these patients. The current study aimed to expand out understanding of the level of awareness within a group of patients who have frontal lobe lesions following tumour resection. A key finding of this study is that patients with FLLs seem relatively aware of behavioural changes in themselves. However, this does not mean that they are ready or willing to accept these changes and therefore the struggle with rehabilitation is still how to manage this altered sense of self that people experience (Bamm, Rosenbaum et al, 2015). Not feeling like they are the person they once were (altered sense of self, marked by updating sense of self) implies that a potential helpful focus of rehabilitation should be to support patients to understand and accept the 'current them' and what this entails for their recovery journeys and future (Baker, Rickard et al, 2015). Exploring these issues including measures of sense of control and self-efficacy, particularly over a rehabilitation journey, may help explore this further and be a lucrative avenue to pursue in future studies. In addition, a potential strength of research into awareness more generally is the inclusion of the views and opinions of family members. Both patients and their significant-others experience extraordinary stress during both diagnosis and treatment (Ownsworth, Goadby & Chambers, 2015) yet the views and experiences of next of kin are sparsely reported in the literature. Our inclusion of investigation into the surrogate in the current study, offered a novel angle on the potentially differing views of patients and family members. Understanding more the experiences of both patients and their significant-others to direct appropriate information and support may support the recovery process for both parties.

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5.4 Conclusion

Taken together, the results appear to suggest that FLL patients have adequate awareness into their post-surgery changes and that they acknowledge more difficulties than controls, which is substantiated by their informant report. This is likely to be mediated in part by mood, but would need further exploration. One of the difficulties that this patients group exhibits is over-interpreting and therefore misperceiving neutral situations as potentially atypical. This may have implications particularly for social functioning and would be an interesting area for future exploration in order to direct rehabilitation input. Ultimately, results of this study support the need to gain information from multiple raters when examining an individual's level of awareness. Self-ratings are particularly important and valuable to include in the assessment of functioning, even if there are concerns about the validity of these reports due to reduced awareness, as this may allow a shared understanding between all parties about the others experiences.

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7. Appendices

Appendix 1: FLL group consent forms
Appendix 2: Letter to FLL group from neurosurgeon
Appendix 3: FLL group participant information sheets
Appendix 4: Novel surrogate version of DEX-R and FrSBe measures
Appendix 5: Vignette task – Final vignette stories
Appendix 6: Novel vignette task development and pilot testing
Appendix 7: NeuroRAG Letter of ethical approval
Appendix 8: REC Letter of ethical approval
Appendix 9: HRA Letter of ethical approval
Appendix 10: Additional analyses of subgroups (based on laterality of lesion)

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Appendix 1: FLL group consent forms

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London SE5 9RS

Tel: 020 3299 9000
Fax: 020 3299 3445
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KING'S College LONDON

Consent Form for Patient

Title of Project: The Self and Self-Knowledge following Prefrontal Neurosurgical lesion.

This project has been approved by the London-Central Research Ethics Committee. Project Number: 17/LO/0531.

Participant ID:

Please initial box

1. I confirm that I have read and understand the information sheet dated 8/5/17 Version 5.0 for the above study, I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that the relevant sections of my medical notes and data collected during the study may be looked at by individuals from the Institute of Psychiatry, King's College London, where it is relevant to my taking part in this research. I give permission for these individuals ☐

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to have access to my records.

4. I understand that any MRI or CT scans of my brain I have had will be looked by individuals from the Institute of Psychiatry, King's College London, as is relevant to the research. I give permission for these individuals to have access to these.

5. I am happy for an informant (friend or relative) to complete questionnaires about their experiences of my behaviour, personality and mood.

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

_____ _____ _____

Name of patient Date Signature

_____ _____
_____

Name of researcher Date Signature

1 copy for participant, 1 copy for researcher, 1 copy for medical notes

King's College Hospital NHS
NHS Foundation Trust

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KING'S College LONDON

Consent Form for Informant

Title of Project: The Self and Self-Knowledge following Prefrontal Neurosurgical lesion. This project has been approved by the London-Central Research Ethics Committee. Project Number: 17/LO/0531.

Participant ID:

Please initial box

1. I confirm that I have read and understand the information sheet dated 8/5/2017 Version 5.0 for the above study, I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.

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

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_____ _____
_____

Name of informant Date Signature

_____ _____
_____

Name of researcher Date Signature

1 copy for participant, 1 copy for researcher

Appendix 2: Letter to FLL group from Neurosurgeon

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NHS Foundation Trust

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Letter from Neurosurgeon
This study has been approved by the London Central Research Ethics Committee (project number: 17/LO/0531)

Dear

Study: The Self and Self-Knowledge after Prefrontal Neurosurgical lesions

You are invited to take part in a research study looking into different perspectives on personal and mental functioning in people with disorders of the frontal lobes of the brain. Enclosed is an information sheet providing details of the study, which we invite you to read.

1) The researcher on the project, Laura Brown, will contact you via telephone to provide more information about the study, approximately two weeks after receiving this letter.

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2) At this appointment, Laura Brown will go through the information sheet with you and you will have the opportunity to ask any questions about the study.
3) If you are interested in taking part, a mutual time and date will be arranged where you can meet with Laura Brown in person to discuss the study further.
4) If you agree to take part, you will be asked to sign a consent form and complete the tasks at the same appointment to avoid you having to come back to the Clinic another day.

Your help with this research is very much appreciated.

Yours sincerely,
Professor Keyoumars Ashkan
Consultant Neurosurgeon

Appendix 3: FLL group participant information sheets

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KING'S College LONDON

Participant Information Sheet
The Self and Self-Knowledge after Prefrontal Neurosurgical lesions (Project Number: 17/LO/0531).

We would like to invite you to take part in our research study. This study has been reviewed and given favourable opinion by the London-Central Research Ethics Committee. It is an educational project and contributes to the College's role in conducting research, and teaching research methods. It is co-sponsored by both King's College Hospital and King's College London.

Before you decide whether you would like to take part, we would like you to understand why the research is being done and what it would involve for you. The researcher will go through the information sheet with you and answer any questions you have. We suggest this should take around 10 minutes and this can be done on the telephone if you prefer.

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Please read this information sheet carefully and discuss it will friends and relatives if you like. Please ask if there is anything not clear or if you would like more information.

Why have I been invited to take part?
You have been invited to take part as you have undergone resection of a tumour in the frontal lobes, and you have attended the Neuro-oncology clinic at Kings College Hospital. An informant (friend of relative of yours) will also be invited to complete a questionnaire if you give consent for us to contact them.

What is the purpose of the study?
Some patients who have damage to areas of the frontal lobes of the brain can experience changes in their behavior and the way they think and feel, which can impact on various aspects of everyday life. Successfully identifying the changes that may occur is still relatively difficult. As such there is a real need to develop measures that accurately assess different perspectives on personal and mental functioning.

The present study will explore different perspectives on personal and mental functioning using a number of questionnaire measures, and by doing various tasks. It is hoped that this will further our understanding of some of the changes and difficulties that someone with frontal lobe damage may experience, and inform how we can develop better assessment measures, which may, in turn, better inform treatment.

Do I have to take part?
It is up to you to decide whether to take part in the study. You will have two weeks to decide. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What will happen to me if I take part?
The study requires one visit to complete various questionnaire measures as well as a number of pen and paper tasks. If you decide to take part, you will be asked to complete a set of questionnaires about your current mood, the way you respond in certain situations and your personality. These questionnaires have often been used with patients with neurological conditions. If the results from the mood questionnaires indicate the presence of clinically significant symptoms of depression, we would discuss these with you and, with your consent, inform your care team and direct you towards appropriate healthcare resources of support.

Involvement in the project requires that you give consent for an informant (a relative or person that knows you well) to be approached. Your named informant will also be asked to complete two questionnaires about different aspects of your mood and personality, if you consent to this. These two questionnaires are the same as the questionnaires you will be asked to complete, only they are worded from their perspective. The researcher will show you copies of these questionnaires and you can make an informed decision as to whether you can both take part. Following their consent and questionnaire completion, this will conclude their involvement in the study.

You will be a given a set of tasks that are to do with more general abilities and memory as well as the questionnaires and two short story-based tasks. It is anticipated that the visit will take no longer than 3 hours, this includes two 15 minute breaks and the possibility of additional breaks. There are no risks involved, but you may find the visits and doing the tasks a little tiring. However, you may take breaks when you wish. Individuals taking part can withdraw from helping with the research at any time, including during the visits.

The visit can take place at King's College London University or arrangements can be made to visit you at your home if you would prefer.

Expenses and payments
We will be happy to cover travel expenses for attending the testing sessions. We will also offer you £20 for participating in this study.

What are the possible benefits of taking part?
There is no direct benefit of the study for you. However, the information we get from this study will help us develop better tasks for assessing the problems a person may face following damage to the brain. You may also find that you enjoy some of the tasks.

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What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researcher (Dr Laura Brown) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office can be obtained by asking your study doctor, GP, telephoning your local hospital or looking on the NHS choices website.
http://www.nhs.uk/pages/home.aspx

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have ground for a legal action for compensation against King's College Hospital, NHS Trust, but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any adverse events you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this.

Every care will be taken in the course of this study. However in the unlikely event that you are harmed by taking part, compensation may be available.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. If you consent to take part in this study, the records obtained while you are in this study will remain strictly confidential at all times by use of a coding system. This means that your records will be given a trial code with personally identifiable data removed. All paper forms will be stored in a locked cupboard. Personal contact details will be stored for up to 3 years and study data for 20 years.

What will happen to the results of the study?
The study will be published in academic and professional journals, and will be talked about at conferences. It will also be published as a doctoral thesis. The results should inform the development of new ways of measuring and understanding personal and mental functioning in patients with neurological or neurosurgical conditions.

Further information and contact details
If you have any further questions, please do not hesitate to contact me:
Dr Laura Brown
Clinical Psychologist in training
Institute of Psychiatry
Department of Psychology, Psychology and Neurosciences
PO box 78
ASB, 4 Windsor Walk
Denmark Hill
London
SE5 8AF
Tel: 07393728785
Email: laura.1.brown@kcl.ac.uk

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Participant Information Sheet
The Self and Self-Knowledge after Prefrontal Neurosurgical lesions (Project Number: 17/LO/0531).

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Before you decide whether you would like to take part, we would like you to understand why the research is being done and what it would involve for you. The researcher will go through the information sheet with you and answer any questions you have. We suggest this should take around 10 minutes and this can be done on the telephone if you prefer.

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Please read this information sheet carefully and discuss it will friends and relatives if you like. Please ask if there is anything not clear, or if you would like more information.

Why have I been invited to take part?
You have been invited to take part as you are a relative or friend of a person who has undergone resection of tumour in the frontal lobes, and has attended the Neuro-oncology clinic at the hospital. This person has decided to take part and has given consent that it is okay for us to contact you.

What is the purpose of the study?
Some patients who have damage to areas of the frontal lobes of the brain can experience changes in their behavior and the way they think and feel, which can impact on various aspects of everyday life. Successfully identifying the changes that may occur is still relatively difficult. As such there is a real need to develop measures that accurately assess different perspectives on personal and mental functioning.

The present study will explore different perspectives on personal and mental functioning using a number of questionnaire measures, and by doing various tasks. It is hoped that this will further our understanding of some of the changes and difficulties that someone with frontal lobe damage may experience, and inform how we can develop better assessment measures, which may, in turn, better inform treatment.

Do I have to take part?
It is up to you to decide whether to take part in the study. We will describe the study and go through this information sheet. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time, without giving a reason.

What will happen to me if I take part?
The study requires you to complete two questionnaires.

If you decide to take part, you will be asked to complete a set of questionnaires regarding your friend or relative, which assess different aspects of behaviour and personality. Your friend or relative will also be asked to complete questionnaires. These questionnaires can be posted to you or completed online and you can complete them in your own time at home. This concludes your involvement in the study.

Expenses and payments
We will offer you £5.00 for participating in this study.

What are the possible benefits of taking part?
There is no direct benefit of the study for you. However, the information we get from this study will help us develop better tasks for assessing the problems a person may face following damage to the brain.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak to the researcher (Dr Laura Brown) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office can be obtained by asking your study doctor, GP, telephoning your local hospital or looking on the NHS choices website.
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In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have ground for a legal action for compensation against King's College Hospital, NHS Trust, but you may have to pay your legal costs.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any adverse events you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this.

Every care will be taken in the course of this study. However in the unlikely event that you are harmed by taking part, compensation may be available.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence.

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If you consent to take part in this study, the records obtained while you are in this study will remain strictly confidential at all times by use of a coding system. This means that your records will be given a trial code with personally identifiable data removed. All paper forms will be stored in a locked cupboard. Personal contact details will be stored for up to 3 years and study data for 20 years.

What will happen to the results of the study?
The study will be published in academic and professional journals, and will be talked about at conferences. It will also be published as a doctoral thesis. The results should inform the development of new ways of measuring personal and mental functioning in patients with neurological or neurosurgical conditions.

Further information and contact details
If you have any further questions, please do not hesitate to contact me:
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Appendix 4: Novel surrogate version of DEX-R and FrSBe measures

DEX-R surrogate version

Instructions

Brain tumours can affect people in lots of different ways and this can sometimes be hard to notice. For this form we would like you to let us know how your partner/relative/friend would rate you at the moment on the items below.

Please rate on the five-point scale what your partner/relative/friend might put concerning you now.

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DEX-R (surrogate-rating)

0 – never 1 – occasionally 2 – sometimes 3 – fairly often 4 – very often

1	My partner/relative/friend thinks that I act without thinking, doing the first thing that comes to mind	0	1	2	3	4
2	My partner/relative/friend thinks that I find it hard to remember to do things I want to do	0	1	2	3	4
3	My partner/relative/friend thinks that I am lethargic or unenthusiastic about things	0	1	2	3	4
4	My partner/relative/friend thinks that I find it difficult to start something	0	1	2	3	4
5	My partner/relative/friend thinks that I have difficulty planning for the future	0	1	2	3	4
6	My partner/relative/friend thinks that I do or say embarrassing things when I am in the company of others	0	1	2	3	4
7	My partner/relative/friend thinks that I have difficulties deciding what I want to do	0	1	2	3	4
8	My partner/relative/friend thinks that I tell people openly when I disagree with them	0	1	2	3	4
9	My partner/relative/friend thinks that I struggle to find the words I want to say	0	1	2	3	4
10	My partner/relative/friend thinks that I seem to lose my temper easily	0	1	2	3	4

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11	My partner/relative/friend thinks that I find it hard to stop repeating saying or doing things once I've started	0	1	2	3	4
12	My partner/relative/friend thinks that I find it difficult to notice if I make a mistake or do something wrong	0	1	2	3	4
13	My partner/relative/friend thinks that I have difficulty thinking ahead	0	1	2	3	4
14	My partner/relative/friend thinks that I get concerned when I have worrying thoughts	0	1	2	3	4
15	My partner/relative/friend thinks that I am unconcerned about how I should behave in certain situations	0	1	2	3	4
16	My partner/relative/friend thinks that I have difficulty showing emotion	0	1	2	3	4
17	My partner/relative/friend thinks that I find it difficult to keep several pieces of information in mind at once	0	1	2	3	4
18	My partner/relative/friend thinks that I get overexcited about things and can get a bit 'over the top' at these times	0	1	2	3	4
19	My partner/relative/friend thinks that I have difficulty realising the extent of my problems and am unrealistic about the future	0	1	2	3	4
20	My partner/relative/friend thinks that I tend to be very restless and cant sit still for any length of time	0	1	2	3	4
21	My partner/relative/friend thinks that I get events mixed up with each other and get confused about the correct order of events	0	1	2	3	4

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22	My partner/relative/friend thinks that I worry persistently, no matter how I try to stop	0	1	2	3	4
23	My partner/relative/friend thinks that I really want to do something one minute, but couldn't care less about it the next	0	1	2	3	4
24	My partner/relative/friend thinks that I seem to get uncontrollable urges to hit something or someone	0	1	2	3	4
25	My partner/relative/friend thinks that I seem to find it hard to complete tasks or activities without structure or direction	0	1	2	3	4
26	My partner/relative/friend thinks that I seem to find it difficult to stop myself from doing something even if I know I shouldn't	0	1	2	3	4
27	My partner/relative/friend thinks that I talk about events or details that never actually happened, but I believe did happen	0	1	2	3	4
28	My partner/relative/friend thinks that I seem to laugh or cry uncontrollably	0	1	2	3	4
29	My partner/relative/friend thinks that I find it difficult to keep my mind on something and am easily distracted	0	1	2	3	4
30	My partner/relative/friend thinks that I seem to find that doing or saying things is effortful	0	1	2	3	4
31	My partner/relative/friend thinks that I have problems trusting my memory	0	1	2	3	4
32	My partner/relative/friend thinks that I will say one thing, but will do something different	0	1	2	3	4
33	My partner/relative/friend thinks that I have difficulty expressing emotion	0	1	2	3	4

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34	My partner/relative/friend thinks that I have problems understanding what other people mean unless they keep things simple and straightforward	0	1	2	3	4
35	My partner/relative/friend thinks that I am unaware of, or unconcerned about how others feel about my behaviour	0	1	2	3	4
36	My partner/relative/friend thinks that I find it difficult to do or concentrate on two things at once	0	1	2	3	4
37	My partner/relative/friend thinks that I have trouble making decisions	0	1	2	3	4

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FrSBe surrogate version

Instructions

Brain tumours can affect people in lots of different ways and this can sometimes be hard to notice. Below you will see a list of phrases that can be used to describe a person's behaviour. Please read each phrase carefully.

For this form we want you to let us know how your partner/relative/friend would rate you at the moment on the items below.

Please rate on the five-point scale what your partner/relative/friend might put concerning you now.

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FrSBE (surrogate-rating)

1 – Almost never **2 – Seldom** **3 – Sometimes** **4 – Frequently** **5 – Almost always**

1	My partner/relative/friends thinks that I speak only when spoken to	1	2	3	4	5
2	My partner/relative/friend thinks that I am easily angered or irritated; I have emotional outbursts without good reason	1	2	3	4	5
3	My partner/relative/friend thinks that I repeat certain actions or get stuck on certain ideas	1	2	3	4	5
4	My partner/relative/friend thinks that I do things impulsively	1	2	3	4	5
5	My partner/relative/friend thinks that I mix up a sequence, get confused doing several things in a row	1	2	3	4	5
6	My partner/relative/friend thinks that I laugh or cry too easily	1	2	3	4	5
7	My partner/relative/friend thinks that I make the same mistakes over and over, do not learn from past experience	1	2	3	4	5
8	My partner/relative/friend thinks that I have difficulty starting an activity, lack initiative, motivation	1	2	3	4	5
9	My partner/relative/friend thinks that I make inappropriate sexual comments and advances, am too flirtatious	1	2	3	4	5
10	My partner/relative/friend thinks that I do or say embarrassing things	1	2	3	4	5
11	My partner/relative/friend thinks that I neglect my personal hygiene	1	2	3	4	5
12	My partner/relative/friend thinks that I can't sit still, am hyperactive	1	2	3	4	5

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13	My partner/relative/friend thinks that I am unaware of my problems or when I make mistakes	1	2	3	4	5
14	My partner/relative/friend thinks that I sit around doing nothing	1	2	3	4	5
15	My partner/relative/friend thinks that I am disorganised	1	2	3	4	5
16	My partner/relative/friend thinks that I lose control of my urine or bowels and it doesn't seem to both me	1	2	3	4	5
17	My partner/relative/friend thinks that I cannot do two things at once (for example talk and prepare a meal)	1	2	3	4	5
18	My partner/relative/friend thinks that I talk out of turn, interrupt others in conversations	1	2	3	4	5
19	My partner/relative/friend thinks that I show poor judgment, poor problem solver	1	2	3	4	5
20	My partner/relative/friend thinks that I make up fantastic stories when unable to remember something	1	2	3	4	5
21	My partner/relative/friend thinks that I have lost interest in things that used to be fun or important to me	1	2	3	4	5
22	My partner/relative/friend thinks that I may say one thing then do another thing	1	2	3	4	5
23	My partner/relative/friend thinks that I start things but fail to finish them, "peter out"	1	2	3	4	5
24	My partner/relative/friend thinks that I show little emotion, am unconcerned and unresponsive	1	2	3	4	5
25	My partner/relative/friend thinks that I forget to do things but then remember when prompted or when it is too late	1	2	3	4	5
26	My partner/relative/friend thinks that I am inflexible, unable to change routines	1	2	3	4	5
27	My partner/relative/friend thinks that I get in trouble with the law or authorities	1	2	3	4	5

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28	My partner/relative/friend thinks that I do risky things just for the heck of it	1	2	3	4	5
29	My partner/relative/friend thinks that I am slow moving, lack energy, inactive	1	2	3	4	5
30	My partner/relative/friend thinks that I am overly silly, have a childish sense of humour	1	2	3	4	5
31	My partner/relative/friend thinks that I complain that food has no taste or smell	1	2	3	4	5
32	My partner/relative/friend thinks that I swear	1	2	3	4	5
	Read each of the following items carefully before responding					
33	My partner/relative/friend thinks that I apologise for misbehaviour (for example apologise for swearing)	1	2	3	4	5
34	My partner/relative/friend thinks that I pay attention, concentrate even when there are distractions	1	2	3	4	5
35	My partner/relative/friend thinks that I think things through before acting (for example consider finance before spending money)	1	2	3	4	5
36	My partner/relative/friend thinks that I use strategies to remember important things (for example, write notes to myself)	1	2	3	4	5
37	My partner/relative/friend thinks that I am able to plan ahead	1	2	3	4	5
38	My partner/relative/friend thinks that I am interested in sex	1	2	3	4	5
39	My partner/relative/friend thinks that I care about my appearance (daily grooming)	1	2	3	4	5
40	My partner/relative/friend thinks that I benefit from feedback, accept constructive criticism from others	1	2	3	4	5
41	My partner/relative/friend thinks that I get involved with activities spontaneously (such as hobbies)	1	2	3	4	5

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42	My partner/relative/friend thinks that I do things without being requested to do so	1	2	3	4	5
43	My partner/relative/friend thinks that I am sensitive to the needs of other people	1	2	3	4	5
44	My partner/relative/friend thinks that I get along well with others	1	2	3	4	5
45	My partner/relative/friend thinks that I act appropriately for my age	1	2	3	4	5
46	My partner/relative/friend thinks that I can start conversations easily	1	2	3	4	5

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Appendix 5: Vignette task - Final vignette stories (n = 18)

	Story vignette	Questions	Subscale
Grade 6	**Story 1** It was Kelly and Ben's wedding day. The church was decorated with lots of flowers. The vicar asked Ben's mum what she thought of the church and the service. She said the day was lovely and all the decorations looked beautiful. All the guests were saying how relaxed and happy the couple looked. Everyone was looking forward to the reception, as Kelly and Ben were known to throw a good party!	Story 1 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think the vicar felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. What was the church decorated with? Why was everyone looking forward to the reception?	Control

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Grade 6	**Story 2** Mr Smith had a new next-door neighbour called Mrs Wilde. Mr Smith went to introduce himself to Mrs Wilde and to welcome her to the neighbourhood. After introducing themselves Mr Smith told Mrs Wilde that her perfume was too strong and her lipstick did not suit her. He then asked her how she liked the area and if she had been to the new café that had opened down the road. Before leaving, he invited her to knock on his door anytime she needed anything.	Story 2 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think Mrs Wilde felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Did Mr Smith and Mrs Wilde know each other well? Did Mrs Wilde visit Mr Smith?	Disinhibiton Verbal disinhibition

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Grade 4	**Story 3** Joe promised to help his wife clean the car and paint the shed. As they started washing the car the phone rang. Joe went inside to answer the phone. Ten minutes later his wife went to find him, as he hadn't come back outside to help her. She found him in the sitting room watching a TV show. Joe thought that his wife looked cross. She asked him to come back outside and continue helping her.	Story 3 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think his wife felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. What was Joe doing when the phone rang? Where does his wife find him?	Executive Function Attention, distraction

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Grade 6	**Story 4** James was planning a trip to America. He had booked six months off work and wanted to visit most of the East coast. His friend Oliver was joining him. Oliver was quite relaxed about the trip, but James wanted everything booked and sorted before they went. He made a plan of all the places they would visit and the order in which they would visit them. When Oliver saw the plan he told James that it looked great and that it was sensible to have it.	Story 4 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think James felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Who made the travel plan? Where were they planning to travel?	Control

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Grade 6	**Story 5** Jenny returned from holiday and was checking her emails when she saw that she had a message reminding her that the final payment on her car was due the next day. She immediately called the garage and apologised for not paying the last instalment yet. She explained that it was because she had been on holiday, but that she could pay it today. He told her not to panic as the due date was tomorrow. He said she could pay over the phone now if she liked to put her mind at ease.	Story 5 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think the landlord felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Why did Jenny receive a reminder letter? Why hadn't she paid the last instalment yet?	Control

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Grade 7	**Story 6** John's wife let him know that all the family was coming over that evening to discuss plans for Christmas. She said she was looking forward to John helping with the arrangements since they were going to his favourite holiday destination. When the family arrived everyone went into the living room. They turned off the TV and began to talk about their plans. Everyone was very excited. John did not say anything during the discussion and after ten minutes he turned the TV back on and began watching a quiz show. John's son had baked a cake, which he shared with everyone.	Story 6 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think his family felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. What was the family discussing? In what room did the discussion take place?	Apathy Lack of interest

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Grade 6	**Story 7** Shaun went to the supermarket. He wanted to make a curry from scratch. He wandered around all the aisles looking for some spices for the sauce. He finally came across a member of staff and he asked her where he might find them. The member of staff was unsure. She asked Shaun to wait while she checked with her manager. She returned two minutes later with her manager who apologised, and told him that they didn't stock spices; however, he thought that the corner shop at the end of the road does. Shaun thanked them and headed to the other shop.	Story 7 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think Shaun felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Why did Shaun go to the shop? Where could Shaun possibly get what he needs?	Control

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Grade 5	**Story 8** Mrs Williams lives in the same town as her son. They have lived there all their lives and know the area well. She walks to her son's house every week to have Sunday lunch together. There are three routes to get to her son's house that each take around ten minutes to walk. However, Mrs Williams always takes the same path, walking over the bridge. One week on her journey she found the bridge was closed for repairs, so she turned around and headed home. Her son called her when lunch was ready to be served to find out if she was nearly there. She told him that the bridge was closed, so she had come home.	Story 8 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think her son felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Who does Mrs Williams visit every week? How many routes are there to her son's house?	Executive Function Planning, problem-solving, flexibility

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Grade 6	**Story 9** Ellen had been feeling unwell for about a week. Her partner had been telling her to visit the GP. Today, she woke up feeling even worse so rang the doctors to book an appointment for that day. The receptionist told her that the doctor couldn't see her until tomorrow and asked her if that was OK. Ellen said it was fine and noted down the time of the appointment. She then rang her partner, who agreed to drive her to the doctor for her appointment tomorrow.	Story 9 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think the Ellen felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Did Ellen get a doctors appointment? Was it on the day she wanted?	Control

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Grade 7	**Story 10** Sarah and John moved in together about six months ago. Sarah was very tidy whereas John didn't seem to mind the house being a mess. Both had very busy jobs. This meant that they still hadn't finished unpacking all their boxes from moving in. Sarah's parents were visiting next week and she really wanted the house to be tidy. John knew that this was important to Sarah so he suggested that they spend the weekend unpacking and tidying the house together.	Story 10 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think Sarah felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Who was visiting? How long ago did Sarah and John move in together?	Control

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Grade 6	**Story 11** Jim and his wife, Katy, have been married 30 years. They have a happy marriage and share lots of the same interests. They both particularly love their pet dog, Milo, who they have had for four years. On a routine visit to the vet Katy received some sad news about Milo's health. She went home and tried to keep busy, but she was very upset and couldn't concentrate on anything. As soon as Jim got home from work she told him the news about Milo. He replied "Oh right. That's sad. Is dinner nearly ready?" Jim then went into the living room to watch the TV. Katy began looking for the takeaway menus, as she didn't feel like cooking.	Story 11 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think Katie felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Who was Milo? How long had they had Milo?	Apathy Diminished emotional response, (emotionally flattened)

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Grade 7	**Story 12** James was expecting the nurse to visit him at home today to check he had enough medication. When the nurse arrived James answered the door wearing only his underpants. He quickly invited the nurse in. The nurse was very nice. Although James was worried about the nurse's visit, he quickly felt at ease. The nurse told him that his treatment was progressing well.	Story 12 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think the nurse felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. What was James wearing when he answered the door? Who visited James?	Disinhibition Social inappropriateness

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Grade 6	**Story 13** Sally walked to the local library to collect a book that she had requested. She was eight months pregnant and the walk made her very tired. When she got to the library she went to the Help Desk and asked if they had her book. The librarian said she would just find out where it had been put and go and collect it for her. She suggested that Sally wait in the seating area, as it may take a few minutes to find the book. The library was very busy and there were no seats available. A young lady, who was very friendly, noticed Sally as she entered the seating area, and politely offered her seat.	Story 13 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think the young lady felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Why did Sally go to the library? Why did the librarian suggest that Sally wait in the seating area?	Control

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Grade 5	**Story 14** Pete and his wife were looking forward to their weekly trip out with his sister and her partner. They had confirmed the trip the night before and the plan was for his sister to pick them up at 10a.m. the following morning. The phone rang about quarter to ten. It was his sister. She told him she had a flat tyre, but she would sort it as quickly as she could and would only be about an hour late. Pete began swearing loudly at his sister, he told her not to come over and then hung up.	Story 14 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think his sister felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Who was Pete going out with? Why was his sister going to be late?	Disinhibition Explosiveness

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Grade 5	**Story 15** Mrs Roberts lives alone. Over the last couple of years she has begun to struggle to carry her shopping bags back from the supermarket on the bus. Her neighbour, Mike, was going shopping by car and popped in to ask if she would like to come along and get her shopping. She said no, as she was waiting for a visitor but thanked him for the offer. Mrs Roberts is very close to her neighbours and she likes to bake for them. They all look out for her and someone pops in to visit her each day.	Story 15 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think Mike felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Why did Mike pop in to see Mrs Roberts? Who does Mrs Roberts live with?	Control

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Grade 7	**Story 16** Sophie moved into her brother's house, as she could no longer afford the rent payments on her own flat and had spent all of her savings. Her brother called and told her that he had furnished and decorated the room especially for her in the style she liked. The day before she moved in, Sophie bought several pieces of expensive new furniture for her new room. Sophie had lived in London for the past 5 years. Her brother lives in the countryside and she was excited to explore the local parks and woods.	Story 16 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think her brother felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. How long did Sophie live in London? Why did Sophie move into her brother's house?	Executive Function Self-monitoring, modifying behaviours

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Grade 6	**Story 17** Jenny spent the day at home. It was her turn to cook for her family. She wanted to make vegetable lasagne, as it is her favourite dish. She kept reminding herself to start cooking soon and going over the recipe in her mind. She did this all day. When the family got home for dinner, Jenny hadn't started cooking. She told the children to start their homework upstairs. Jenny's husband told her about his day. They also discussed next week's cooking rota.	Story 17 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think the family felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. What is Jenny's favourite dish? What do Jenny and her husband discuss?	Apathy Diminished overt behaviour, diminished productivity, effort or initiative

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Grade 7	**Story 18** The county athletics club was holding trials for athletes to compete for places on the masters' team, for people over 35 years of age. Samantha and Gill, who have been friends for years, were competing in the sprint races. On the day of the trials Samantha won all her heats. Gill was happy for Samantha but disappointed in her own performance. After all the races, she congratulated Samantha on her performance and on likely making the team. Samantha thanked her and told her she had run really well too.	Story 18 Questions To what extent did someone in the story do something they perhaps shouldn't have done or did something awkward? 1. Not at all 2. A little bit but it was acceptable 3. It was clear they should not have done it but it might not have caused a problem 4. It was inappropriate and would have been noticed 5. Definitely and very awkward If yes, ask: Who did something they shouldn't or something awkward? Why shouldn't he/she have done it or why was it awkward? Why do you think he / she did it? How do you think Samantha felt? Control questions (simple facts about the story – comprehension) – ask even if give option 1 above. Why was Gill disappointed? What were they competing for?	Control

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Appendix 6 – Novel vignette task development and pilot testing

A novel vignette task was designed to answer ***Research question 3***: Can people with frontal damage detect behavioural changes in others?

Aim: to assess Third Person Understanding of Abnormal Behaviour
A series of vignettes will be created that outline scenarios that describe subtler behavioural disturbance following the questionnaire constructs, to be used to test understanding of abnormal behaviour in general.

Methodology/Task Design:
Vignettes were informed by the FrSBe measure in order to contain examples to a larger range of behaviours likely mediated by frontal lobe constructs. Vignettes specifically related to the three subscales of the FrSBe and their content was directed by the definitions given for the three subscales:

- **Apathy**: Item content for the apathy scales include: 'problems with initiation, psychomotor retardation, spontaneity, drive, persistence, lost energy and interest, lack of concern about self-care and/or blunted affective expression.
- **Disinhibition**: these items assess problems with inhibitory control of action and emotions, including impulsivity, hyperactivity, social inappropriateness, emotional liability, explosiveness and irritability.
- **Executive dysfunction**: problem areas addressed here include sustained attention, working memory, organisation, planning, future orientation, sequencing, problem solving, insight, mental flexibility, self-monitoring, and on-going behaviour and/or the ability to benefit from feedback or modify behaviour following errors.

For further content for the vignettes, example activities of daily living were referenced from Buck et al's, (2006) Bristol Activities of Daily Living Scale, to try and direct a range of scenarios across the subscales. ADLs mentioned on this scale include: Eating, Food preparation, Dressing, Hygiene, Mobility, Orientation – time/space, Communication, telephone, housework gardening, shopping, finances, games hobbies, transport.

Readability Range
Each vignette was run through a free online 'readability checker'. This provides a 'Readability score' obtained from: http://www.thewriter.com/what-we-think/readability-checker/. All vignettes obtained scores between the following levels: **Grade 5** = comic book; **Grade 6** = Happy Potter; **Grade 7** = same level as 'the writer's website'; **Grade 8** = level of Obama's speeches; **Grade 9** = BBC news website level. This allowed us to ensure that the stories were pitched at an appropriate reading level for the general population. Table 1 below takes an average of the grades obtained per subscale and shows how the subscales were relatively well matched.

Table 1: Average readability ages per subscale

EF	Disnihibition	Apathy	Control
Ave Grade: 5.3	Ave Grade: 6.0	Ave Grade: 6.3	Ave Grade: 6.1
10-11 years	11-12 years	11-12 years	11-12 years

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Task Administration and instructions
This followed the administration of the faux-pas task. Two versions, a participant and a researcher version, were created. The participant version displayed the vignette stories only, whereas the researcher version also included questions about each vignette.

The participant version was placed in front of the participant. The researcher then said, "I'm going to be reading you some brief stories and asking you some questions about it. You have a copy of the story in from of you so you can read along and go back to it".

The vignettes were then read aloud and followed up with a series of questions. The first question required participants to respond using a 5-point rating scale and rate the level of atypical or inappropriate behaviour. This was included to provide more information with regards to the degree of difficulty participants exhibit, as opposed to previous tasks with binary responses, which only allow a sense of whether or not behaviour was detected.

E.g. Rating scale for Question 1: To what extent did someone in the story do something they perhaps shouldn't have done or do something awkward?

1. Not at all

2. A little bit but it was acceptable

3. They should not have done it but it might not have caused a problem

4. It was inappropriate and would have been noticed

5. Definitely and very awkward

If participants gave number 1 as their response on the rating scale questions ('not at all' for anything awkward having occurred in the story), the researcher skipped to the control questions for that story. It was ensure that the control questions were asked whatever the rating response to the first questions. If participants rate the story between 2-5, all follow-up questions were asked, including the control questions for that story.

Scoring:
The higher the rating, the more awkward the behaviour is deemed. If a participant assigns awkward behaviour to an incorrect character in the vignette, that item was deemed incorrect and excluded from final scoring.

Sensitivity
Across subscales sensitivity was checked through pilot testing. Results found a healthy range of responses (with neither floor nor ceiling effects for any subscale). This, encouragingly, mirrored the expected subjectivity of this type of task. This is more fully detailed in the sections below detailing the pilot testing results.

Pilot testing
A pilot of the vignette task was run given it is a novel experimental task. Initially 5 neuro-typical adults consented to pilot the full task. This group consisted of three females and two males, aged 21-57 years.

Findings from this were promising and indicated that the control stories were mostly being rated as 1 (not at all (awkward). All other stories for each subscale were rated (2-

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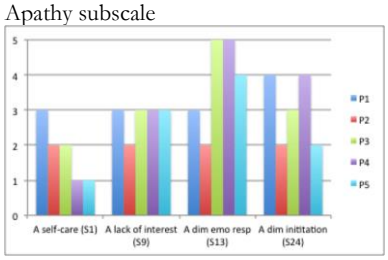
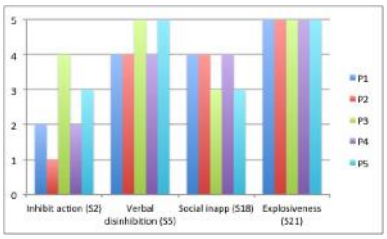
5) on the rating scale indicating that something awkward happened. The responses are graphed (see Figure 1 below) and from these a discrepancy is noted in the strength of the rating given with disinhibition items scoring more highly than both apathy and executive function. EF was particularly lower by comparison.

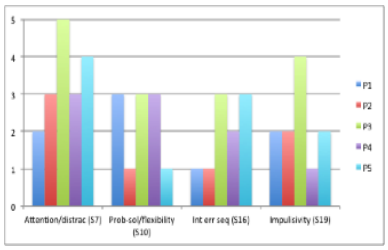
Apathy subscale



Disinhibition subscale



Executive function subscale



Control items

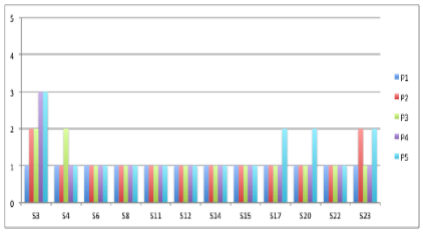


Figure 1: Results from initial stage pilot testing of vignette task by subscale

In an attempt to make the three subscales more equal in ratings, specific items for which the lowest rating were given, were amended in order to make the awkward act more salient and to achieve a higher rating. Control items that scored over '1' were also amended.

The original 5 pilot participants kindly consented to re-read the amended items and rate them. For all items a higher rating was given following these amendments to experimental items and control items all scored '1' (see Figure 2 below).

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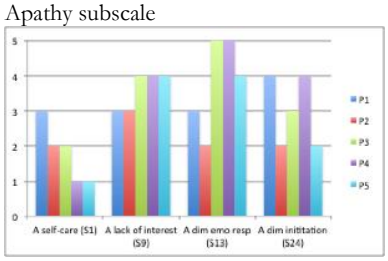
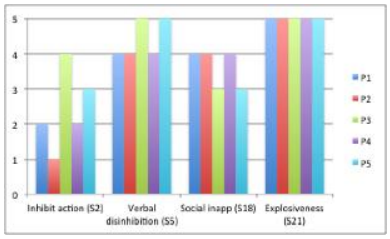
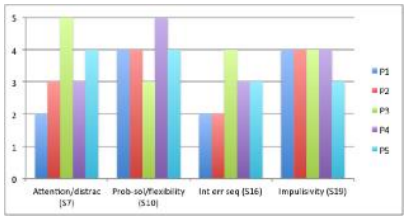
Apathy subscale



Disinihibition subscale



Executive function subscale



Control items

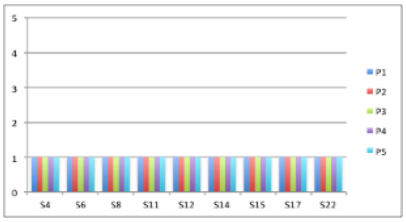
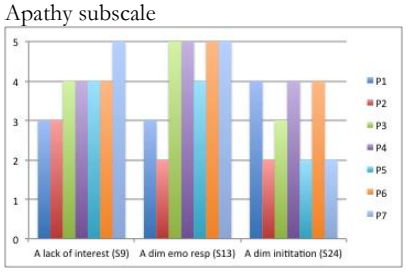


Figure 2: Results from full revised pilot task by subscale

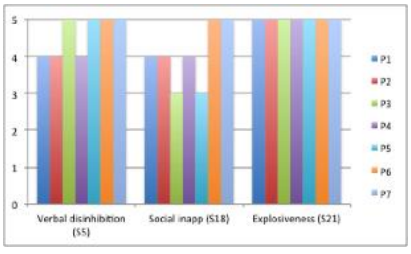
The items from each subscale with the lowest rating was dropped which left three remaining items for each subscale, and 9 control items were chosen (the nine that most consistently scored 1).

The scores from these 18 items were pulled out from the initial 5 pilot participants and in addition 2 novel pilot participants (one male, one female, aged 30 and 33 respectively) consented to complete this revised full version of 18 items. Results from this are below and show that the ratings across the subscale are better matched than previously (see Figure 3 below).

Apathy subscale



Disinhibition subscale



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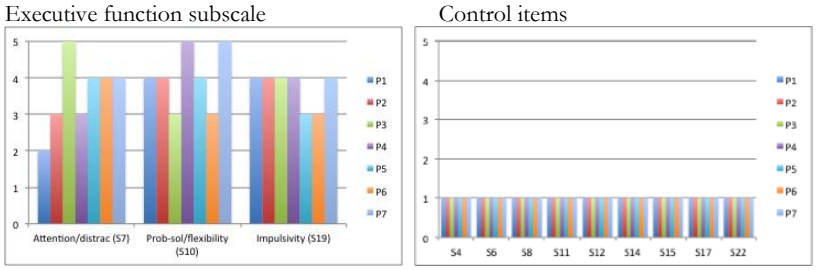

Figure 3: Results from shortened revised task by subscale (18 stories)

This process resulted in 18 vignettes stories: 9 experimental and 9 control to be used in the full project. These are detailed in the Appendix B (Final vignette stories N-18).

Pseudo-randomisation

For this finalised task, vignettes were pseudo-randomised with the following constraint: No more than two examples from a particular category (namely: EF, Disinhibition, Apathy or control) appeared consecutively. Attempts were made to ensure approximately equal proportion of control stories in each half of the task (5/4 split between first and second half).

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Appendix 7: NeuroRAG Letter of ethical approval

King's College Hospital NHS
NHS Foundation Trust

NeuroRAG approval

Dear Dr Laura Brown, Date: 12/12/2016

Thank you for completing the feasibility review and presenting the study "The Self and Self-knowledge after Prefrontal Neurosurgical lesions" in the Neurosciences Research and Advisory Group meeting on 06/12/2016.

"The Self and Self-knowledge after Prefrontal Neurosurgical lesions" was approved on 06/12/2016 by the committee.

The action points requested by the RAG committee are to:

- Submit this study for adoption onto the NIHR portfolio.
- Ensure you have up to date GCP training prior to starting the study.

With this clinical approval you can now move onto the next stage of the process, which is to contact the King's College Hospital Research and Innovation department/King's Health Partners Clinical Trials Office to assist with the HRA process and local confirmation and capacity.

The committee would like to extend their congratulations and the best of luck with your study.

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Kind regards

Prof K Ray-Chaudhuri Prof. K. Ashkan

Chair Vice Chair

Appendix 8: REC Letter of ethical approval

NHS
Health Research Authority

London - Central Research Ethics Committee
3rd Floor, Barlow House
4 Minshull Street Manchester M1 3DZ
Telephone: 0207 1048 007

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

17 May 2017

Dr Laura Brown
Trainee Clinical Psychologist
Institute of Psychiatry, Psychology and Neuroscience
3rd Floor ASB building, 4 Windsor Walk
Denmark Hill
London
SE5 8BB

Dear Dr Brown

Study title: **The Self and Self-Knowledge after Prefrontal Neurosurgical lesions**
REC reference: **17/LO/0531**
IRAS project ID: **217694**

Thank you for your documents of 8 May 2017 , responding to the Committee's request for further information on the above research and submitting revised documentation. The further information has been considered on behalf of the Committee by the Chair and Sophie Forsyth.

We plan to publish your research summary wording for the above study on the HRA website, together

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with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

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, subject to the conditions specified below.

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 NHS permission for research is available in the Integrated Research Application System, 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 publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

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. 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

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management

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permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Confirmation of any other Regulatory Approvals (e.g. NIGB) and all correspondence [RAG feasibility approval presented for review and approved]	Version 2	17 January 2017
Confirmation of any other Regulatory Approvals (e.g. NIGB) and all correspondence [Confirmation letter of RAG approval]	Version 1	12 December 2016
Copies of advertisement materials for research participants [Advertisement for control participant recruitment]	Version 1	09 January 2017
Copies of advertisement materials for research participants [Circular email for healthy control recruitment]	Version 1	09 January 2017
Covering letter on headed paper [Cover letter]	Version 1	17 February 2017
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [KCL insurances evidence]	Version 1	17 February 2017
IRAS Application Form [IRAS_Form_08032017]	Version 1	08 March 2017
IRAS Checklist XML [Checklist_08032017]	Version 1	08 March 2017
Letter from funder [Funding confirmation letter]	Version 1	24 January 2017
Letter from sponsor [Sponsor confirmation letter]	Version 1	14 February 2017
Letters of invitation to participant [Participant invitation letter from Neurosurgeon]	Version 1	09 January 2017
Non-validated questionnaire [Patient DEX-R self-rating]	Version 1	17 February 2017
Non-validated questionnaire [Patient DEX-R informant rating]	Version 1	17 February 2017
Non-validated questionnaire [Patient DEX-R surrogate version]	Version 1	17 February 2017
Non-validated questionnaire [Patient FrSBe Self rating]	Version 1	17 February 2017
Non-validated questionnaire [Patient FrSBe informant rating]	Version 1	17 February 2017
Non-validated questionnaire [Patient FrSBe surrogate rating]	Version 1	17 February 2017
Non-validated questionnaire [Control DEX-R self-rating]	Version 1	17 February 2017
Non-validated questionnaire [Control DEX-R informant rating]	Version 1	17 February 2017
Non-validated questionnaire [Control DEX-R surrogate rating]	Version 1	17 February 2017
Non-validated questionnaire [Control FrSBe self-rating]	Version 1	17 February 2017
Non-validated questionnaire [Control FrSBe informant rating]	Version 1	17 February 2017
Non-validated questionnaire [Control FrSBe surrogate rating]	Version 1	17 February 2017
Other [Brief description of all measures]	Version 1	17 February 2017
Other [Schedule of assessments]	Version 1	09 January 2017
Other [Reply slip – consent to contact]	Version 1	26 March 2017
Participant consent form [Patient consent form]	Version 2	17 January 2017
Participant consent form [Healthy control consent form]	Version 2	17 January 2017
Participant consent form [Informant consent from (for both patient and control)]	Version 2	17 January 2017
Participant consent form	3	25 April 2017
Participant information sheet (PIS) [Patient]	5	08 May 2017
Participant information sheet (PIS) [Patient informant]	5	08 May 2017
Participant information sheet (PIS) [Healthy control]	5	08 May 2017
Participant information sheet (PIS) [Healthy control informant]	5	08 May 2017
Referee's report or other scientific critique report [Course review and approval]	Version 1	24 October 2016
Research protocol or project proposal [KCH KCL research protocol]	Version 2	17 January 2017
Response to Request for Further Information		
Summary CV for Chief Investigator (CI) [Summary CV]	Version 1	09 January 2017
Summary CV for student [Summary CV]	Version 1	09 January 2017
Summary CV for supervisor (student research) [Supervisor 1 CV]	Version 1	21 February 2017
Summary CV for supervisor (student research) [Supervisor 2	Version 1	22 February 2017

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CV]		
Summary, synopsis or diagram (flowchart) of protocol in non-technical language [Gantt chart of timeline of project]	Version 1	09 January 2017
Validated questionnaire [GAD-7 (Anxiety Questionnaire)]	Version 1	17 February 2017
Validated questionnaire [PHQ-9 (Depression Questionnaire)]	Version 1	17 February 2017

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.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received 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/

HRA Training

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

17/LO/0531 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely
pp
Dr Andrew Hilson Chair

Email:NRESCommittee.London-Central@nhs.net
Enclosures: "After ethical review – guidance for researchers"

Copy to: Mr Keith Brennan, King's College London
King's College Hospital NHS Foundation Trust

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Appendix 9: HRA Letter of ethical approval

Health Research Authority

Email: hra.approval@nhs.net

Dr Laura Brown Trainee
Clinical Psychologist Institute of Psychiatry,
Psychology and Neuroscience
3rd Floor ASB building, 4 Windsor Walk
Denmark Hill
SE5 8BB

17 May 2017

Dear Dr Brown

Letter of HRA APPROVAL

Study title: The Self and Self-Knowledge after Prefrontal Neurosurgical lesions
IRAS project ID: 217694
REC reference: 17/LO/0531
Sponsor: KCL

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England
The sponsor should now provide a copy of this letter to all participating NHS organisations in England. *Appendix B* provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular

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the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices
The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval The document *"After Ethical Review – guidance for sponsors and investigators",* issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures. In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website. **Scope** HRA Approval provides an approval for research involving patients or staff in NHS organisations in England. If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/. If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

User Feedback
The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received 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/.

HRA Training
We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **217694**. Please quote this on all correspondence.

Yours sincerely

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Alex Thorpe Senior Assessor

Email: hra.approval@nhs.net

Copy to: *Mr Keith Brennan, King's College London, Sponsor's Representative*

Appendix 10: Additional analyses of subgroups (based on laterality of lesion)

Table 12: Participant demographics and sample characteristics

	Right hemi (n=7)			Left hemi (n=7)			Statistics		
	M	SD	Range	M	SD	Range	*t*	*p*	*d*
Gender ratio	3 Male: 4 Female			1 Male: 6 Female					
Age (Years)	52.93	11.53	31.0 – 67.0	54.94	13.16	41.1 – 71.9	.30	.766	0.16
Years of education	12.14	2.67	10 - 16	13.43	2.70	10 - 16	.89	.388	0.48
TOPF (premorbid IQ)	98.00	12.78	82 - 117	97.00	8.15	90 - 114	-.175	.864	0.09
Months since lesion resection	24.43	10.13	6 - 40	62.71	47.30	7 - 135	2.09	.058	1.12

Table 13: Group differences on background neuropsychological measures

	Right hemi (n=7)			Left hemi (n=7)			Statistics		
Variable	**M**	**SD**	**Range**	**M**	**SD**	**Range**	***t***	***p***	***d***
Vocabulary (SS)	9.14	2.97	6 - 14	8.29	2.43	5 - 12	-.591	.565	0.31
Matrix Reasoning (SS)	10.00	3.87	5 -15	9.43	2.51	6 - 14	-.328	.749	0.17
FSIQ	97.29	15.95	74 - 124	93.43	11.87	77 - 109	-.513	.617	0.27
LM Immediate verbal recall (SS)	9.71	2.36	7 - 12	6.14	2.27	2 - 9	-2.88	<.05*	1.54
LM Delayed verbal recall (SS)	9.57	1.62	7 -12	5.86	2.85	1 - 9	-2.99	<.05*	1.60
Brixton (SS) (mv = 2)	5.29	1.98	2 - 8	5.60	3.21	1 - 10	.211	.837	0.12
Faux-pas test (mv = 3)	18.80	1.30	17 - 20	18.67	1.21	17 - 20	-.18	.864	0.10
Anxiety	8.14	5.37	2 -19	3.43	2.29	0 - 6	-2.14	.054	1.14

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Depression	8.71	4.23	6 - 18	4.00	2.83	0 - 9	-2.45	<.05*	1.31

mv = missing values; Anxiety measured using GAD-7; Depression measured using PHQ-9; Vocabulary and Matrix Reasoning measured using WASI-II; Verbal recall measured using WMS-IV; FSIQ: Full Scale IQ.

Table 14: Descriptive statistics for pre and post ratings (on DEX-R and FrSBe) by Right and Left hemisphere lesion patients and their informants

Right hemisphere						Left Hemisphere					
Measure	**Time**	**Rater**	**Mean**	**SD**	**N**	**Measure**	**Time**	**Rater**	**Mean**	**SD**	**N**
DEX-R	Pre	Self	22.17	19.89	6	**DEX-R**	Pre	Self	24.29	14.20	7
		Informant	18.17	9.97	6			Informant	15.86	13.72	7
	Post	Self	71.50	32.86	6		Post	Self	59.71	25.24	7
		Informant	76.33	33.52	6			Informant	51.43	34.79	7
FrSBe	Pre	Self	73.29	17.30	7	**FrSBe**	Pre	Self	75.43	14.55	7
		Informant	69.43	14.11	7			Informant	74.86	24.69	7
	Post	Self	107.43	28.03	7		Post	Self	99.86	17.87	7
		Informant	115.07	34.86	7			Informant	94.29	31.41	7

Table 15: 2x2 ANOVA summary table exploring time and rater effects on DEX-R and FrSBE total for left and right hemisphere lesion subgroups

Measure	**Source**	**df**	**MS**	**F**	***p***	**Effect size**
DEX-R	Time (T)	1	25734.894	37.86	<.001*	.775
	Rater (R)	1	203.704	.39	.544	.034
	T x R x L interaction	1	244.002	.19	.669	.017
	Error	15	1262.699			
FrSBe	Time (T)	1	123547.161	25.48	<.001*	.680
	Rater (R)	1	2.161	.002	.962	.000
	T x R x L interaction	1	1045.786	1.329	.271	.100
	Error	12	786.925			

Note: L = Laterality; MS = Mean squares; Effect size = partial η^2

Table 16: Between group differences on post-surgery discrepancy scores

Measure	**Score**	**Right hemi**			**Left hemi**			**Statistics**		
	Adapted discrepancy = self - informant/mean									
		M	**SD**	**Range**	**M**	**SD**	**Range**	***t***	***p***	***d***
DEX-R	Adapted Discrepancy total	-.12	.62	-1.13 - .60	.25	.81	-.93 – 1.12	.93	.375	0.51
FrSBe	Adapted Discrepancy	-.07	.39	-.75 - .39	.09	.39	-39 - .58	.74	.476	0.41

Table 17: ICCs explored the notion of surrogate awareness

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		DEX-R surrogate	FrSBe surrogate
Right	Self	0.93**	0.93**
	Informant	0.28	0.20
Left	Self	0.96**	0.89**
	Informant	0.58	0.46

**p<.001

Table 18: Mean scores and test statistics comparing FLL and control ratings on novel experimental vignette task

		Right hemi (n=7)		**Left hemi (n=7)**			**Statistics**		
Variable	**M**	**SD**	**Range**	**M**	**SD**	**Range**	***t***	***p***	***d***
Total (A+Dis+EDys)	9.04	2.11	6.3 – 11.9	9.96	1.30	7.9 – 11.6	.97	.349	0.52
A: Apathy items	2.83	1.04	4.0 – 2.83	3.14	.78	2.3 – 4.6	.639	.535	0.34
Dis: Disinhibition items	3.73	.64	3.0 – 4.6	4.03	.68	3.0 – 5.0	.849	.413	0.45
EDys: Executive Dysfunction items	2.49	1.24	1.0 – 4.0	2.79	.89	1.0 – 3.6	.521	.612	0.28
Control items	1.21	.11	1.1 – 1.4	1.33	.16	1.1 – 1.5	1.57	.143	0.87

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