An exploration of PTSD symptoms and psychosocial adjustment following awake and asleep craniotomy.

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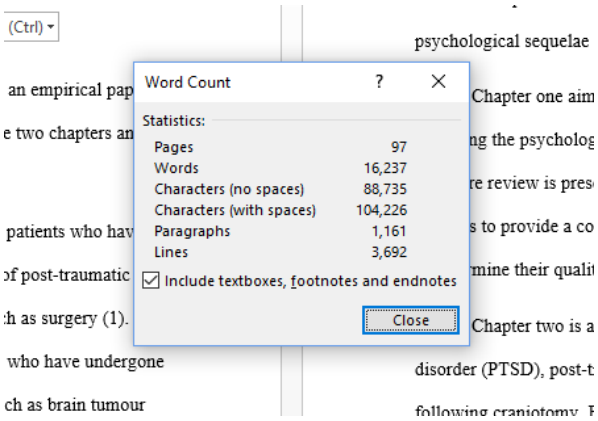

Introductory Chapter; Thesis

Overview

This thesis consists of two main chapters, a literature review and an empirical paper. An overview of the topic area, along with specific details regarding these two chapters and how they relate, is provided within this introductory chapter.

There is increasing research into the psychological outcomes for patients who have undergone medical treatments, with emerging evidence of the presence of post-traumatic stress disorder and symptomatology following medical interventions such as surgery (1). The focus of this thesis is to explore the psychological outcomes for patients who have undergone a craniotomy, which is a neurosurgical technique used for procedures such as brain tumour removal.

Typically, a craniotomy is conducted with the patient unconscious, under general anaesthesia, however, in some cases an 'awake craniotomy' is used, during which the patient is conscious during part or all of the procedure. This technique allows the surgical team to complete intraoperative neuropsychological monitoring, via asking the patient to complete tasks such as picture naming, and brain mapping which allows for the location of functional areas. This technique is useful in cases where tumours are located within or near to eloquent areas of the brain, e.g. language or motor areas, as the awake technique allows the neurosurgeon to identify how much of the tumour can be removed whilst preserving these functions.

Research consistently demonstrates that a craniotomy under general anaesthesia ('asleep') and awake craniotomy are safe and effective procedures for the removal of brain tumours. However, to date, there is limited available literature regarding the psychological

outcomes of patients undergoing these procedures, despite research suggesting negative psychological sequelae following other surgical procedures.

Chapter one aims to provide the reader with an overview of the current literature base regarding the psychological experience of undergoing an awake craniotomy. A systematic literature review is presented which critically examines fourteen papers and synthesises findings to provide a coherent summary of research findings. Papers were critically appraised to determine their quality.

Chapter two is an empirical paper exploring the levels of post-traumatic stress disorder (PTSD), post-traumatic stress symptom severity and psychosocial outcomes following craniotomy. Furthermore, this paper explores whether there is a difference between the two surgery groups (awake and asleep craniotomy) in terms of PTSD and psychosocial functioning. Utilising a quantitative methodology and statistical analysis, this paper presents novel findings which are discussed in the context of clinical implications and future research.

What is the psychological experience of awake craniotomy patients? An integrative systematic review of the literature. [1]

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[1] To be submitted to: *British Journal of Neurosurgery*. Author guidelines can be found in Appendix A.

Abstract

Awake craniotomy is well-established as a safe and effective procedure for the removal of brain tumours within eloquent areas of the brain. However, little is known about the psychological impact of this procedure, despite literature highlighting negative psychological sequelae for patients following other forms of awake surgery. The aim of this systematic review is to identify and critically synthesise the current literature on patient's experiences of undergoing an awake craniotomy. A comprehensive database search was performed, using MEDLINE and PsychINFO with the search terms; 'awake craniotomy' OR 'awake surgery' AND 'experienc*'OR 'acceptance' OR 'tolerance' OR 'patient'. This search identified 327 articles; from this, 14 articles were accepted for inclusion within the review. The review adopts an integrative approach, including studies with quantitative and qualitative designs. The findings of the included studies were considered with particular emphasis on the psychological experiences of the participants. Whilst most studies reported the procedure to be acceptable and tolerable to patients, some participants reported to have experienced fear and anxiety prior to, and during the procedure. Post-operatively, one study reported the prevalence of post-traumatic stress symptomatology; however the literature regarding long term psychological consequences of this procedure is limited. The findings of the included studies are critically considered in the context of methodological weaknesses. Clinical implications and areas for future research are explored.

Key words: Awake craniotomy, brain tumour, patient experience, psychological outcomes, systematic review.

Introduction

Within the UK, it is estimated that more than 9000 people are diagnosed with a primary brain tumour each year (1). For many of these people, a craniotomy to remove the tumour will be deemed the most appropriate method of treatment. Typically, this is carried out with the patient under general anaesthesia, however, in cases where the brain tumour is located within or near to eloquent areas of the brain (i.e. language or motor cortex), an awake craniotomy is often indicated (2). An awake craniotomy allows for intraoperative localisation of function via the use of neuropsychological monitoring (e.g. language testing) and cortical mapping (2). This enables the surgeon to identify which areas are safe to remove, thereby reducing the risk of damage and related disability (3). The evolution of the awake craniotomy procedure has resulted in the removal of tumours which previously would have been deemed too 'high risk' to operate on, and therefore has enhanced the quality of life and life expectancy for many patients. There is extensive literature demonstrating the awake craniotomy method to be a safe and effective procedure, associated with reduced hospital stay, shortened length of surgery and fewer post-operative deficits (3, 4).

There are two methods by which awake craniotomy can be carried out. The asleep-awake-asleep technique involves the patient being deeply sedated during the craniotomy, and then returned to consciousness to allow for intraoperative mapping and neuropsychological monitoring. Following this, the patient is sedated once again for the closure of the skull. However, due to the use of anaesthesia there are risks associated with this technique, including respiratory complications, hemodynamic dysregulation, nausea and vomiting (5, 6). To minimise these risks the awake-awake protocol has been developed. With this method the patient retains consciousness throughout the entire procedure, thereby reducing the risk of complications (2).

Whilst awake craniotomy is proven to be an effective method of brain tumour excision (3, 7), comparatively little is known about the psychological impact of undergoing this procedure. This is despite literature suggesting that within an oncology population, those with brain tumours rank amongst the highest in terms of psychological distress (8) with depression and anxiety frequently observed (9, 10). Consequently, quality of life within this population is also found to be reduced (11). Thus, the literature suggests that many brain tumour patients may be experiencing psychological distress at the point of presentation for surgery.

General surgery is associated with pre-operative stress and anxiety (12-14) and it is reasonable to suggest that the potential complications related to brain surgery (e.g. disability, language dysfunction) may further heighten this distress. Studies with patients who have been conscious during their surgery, including during a caesarean or hip replacement, report intra-operative anxiety linked to environmental factors, such as noise (e.g. sound of drilling), low room temperature and darkness (15-17). The long-term impact of this intra-operative distress is unknown, however, for patients who experience 'anaesthetic awareness' that is, unexpectedly gaining consciousness whilst under general anaesthesia, symptoms of post-traumatic stress disorder (PTSD) have been observed (18-20). Although patients undergoing an awake craniotomy are informed and have given prior consent to being woken during the procedure, it is possible that similar patterns of psychological distress may emerge.

From the literature it can be surmised that brain tumour patients may be experiencing psychological distress, related to their diagnosis, both in the lead up to and at the point of presentation for surgery. Furthermore, it is established that consciousness whilst undergoing a surgical procedure can be anxiety provoking both pre-operatively and intra-operatively.

In consideration of the above, it is of interest to explore the available literature of the experiences of those undergoing awake craniotomy. A previous review was completed in this area presenting a summary of current findings, however there was limited critique of study quality or exploration of implications of study findings (21).

The present review aims to identify, synthesise and critically review the current literature regarding patient's experiences of undergoing an awake craniotomy with a particular interest in the psychological impact of this procedure. This review takes an integrative approach, incorporating findings from both qualitative and quantitative studies, to ensure a comprehensive review of the psychological experiences of awake craniotomy patients.

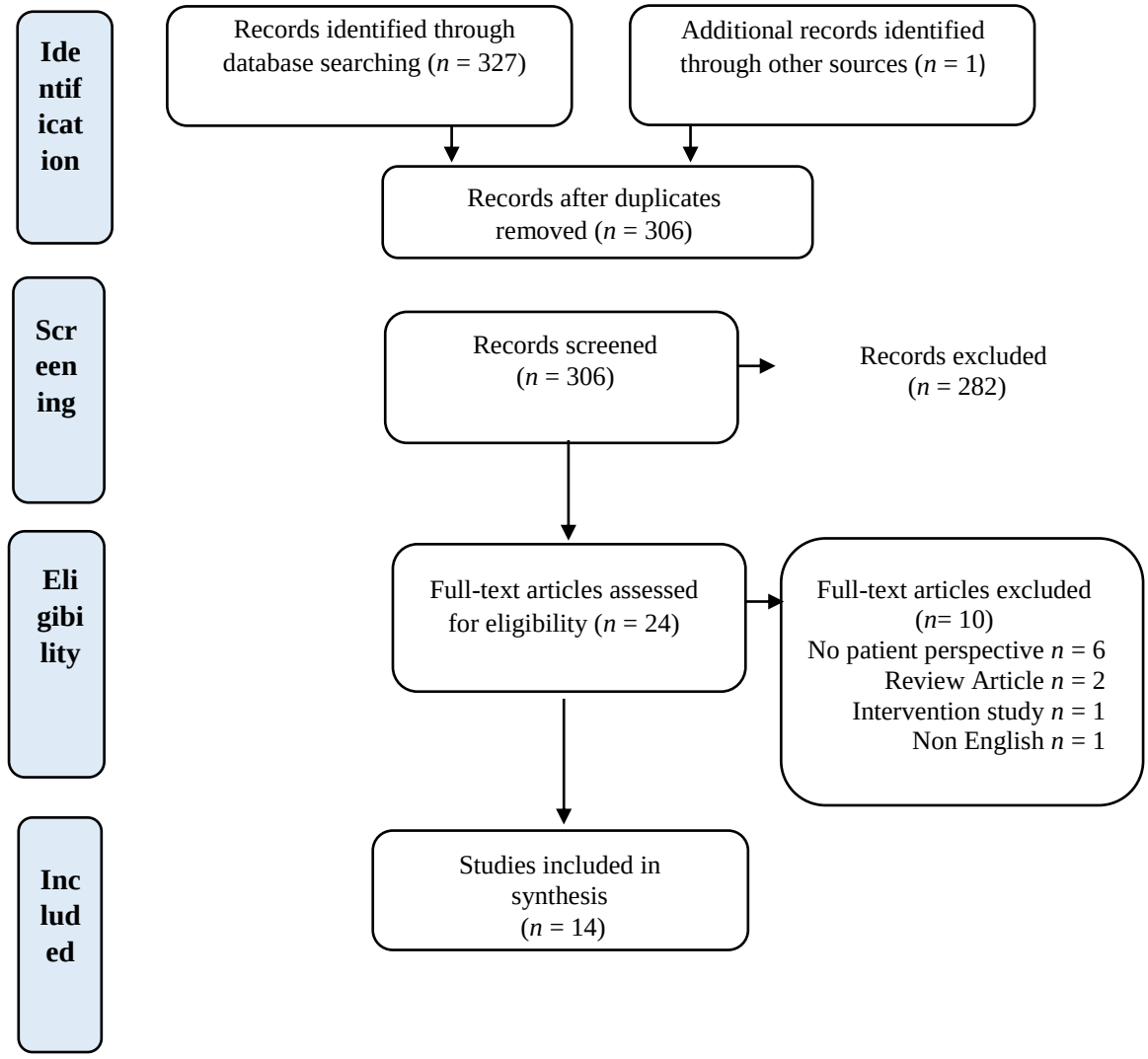
Method

Search Strategy

A literature search was conducted, without restriction by publication date or other filters, using MEDLINE and PsychINFO on the 20th October 2015. The search terms were as follows: (awake craniotomy OR awake surgery) AND (experienc* OR acceptance OR tolerance OR patient). This initial database search identified 327 articles, 301 from MEDLINE and 26 from PsychINFO; the removal of duplicates resulted in 306 articles. The literature search was managed using bibliographic citation management software (EndNote X7). Titles were screened initially, from which 23 papers progressed to stage two of screening which involved a full text read. To ensure all relevant studies were identified, reference lists of all manuscripts chosen for full-text review were manually searched and authors were contacted to identify additional or unpublished research. From this process one further paper was identified, following eligibility screening this paper was then included in the review. Following full text read, a further 10 papers were excluded resulting in a total of 14 papers to be included in the review. Reasons for exclusion included; the paper not

focusing on the patient experience (*n* = 6), paper being a review (*n* = 2), intervention study involving a change in the standard awake craniotomy procedure (*n* = 1) and paper not being available in English (*n* = 1).

Figure 1.PRISMA flowchart illustrating the process of the search which concluded with 14 papers.



Inclusion and Exclusion Criteria

To be accepted into the review, studies had to include an adult (aged >18) sample of participants who had undergone an awake craniotomy for the removal of a tumour or to treat another condition, e.g. epilepsy. Studies using either type of anaesthetic protocol (i.e. awake-awake and asleep-awake-asleep) were accepted and no restrictions were placed on the time

since surgery at the point of study participation. Review papers or intervention studies which changed some element of the procedure were not included. Studies were carried out in a range of countries, however, papers had to be published in English for inclusion; this lead to the exclusion of one paper. No exclusions were made on the basis of publication date. Studies presenting quantitative and qualitative data were included to allow for a comprehensive understanding of the patient experience. Whilst quality assessment was completed, papers were not excluded on this basis (see Appendix B). The details of all included studies can be found in Table I.

Quality Assessment

All 14 included papers were reviewed by the author using validated measures of quality assessment. Two separate tools were used, the Critical Skills Appraisal Programme tool for qualitative studies (22) and the Centre of Evidence Based Management tool for assessing the quality of surveys (23) as these were deemed the most appropriate means of appraising the studies. Quality analysis was completed by the author (RD), (see Appendix B).

Data Extraction

The studies for review included qualitative and quantitative data with some studies utilising a mixed methods design. Data extraction for all papers included (1) study design (2) methods (3) dates and country (4) sample size (5) surgical technique (6) time since surgery and (7) summary of findings (see Table I).

Table 1. Data extracted from included studies.

Study	Study design and data type (quantitative, qualitative, mixed)	Methods	Dates, Country	*N* patients	Surgical technique	Time since surgery at participation	Summary of findings
Bajunaid & Ajlan, 2015 (24)	Cross-sectional survey	Questionnaire	Canada	9	Awake-awake	Post discharge - not stated	Focus on experience of procedure. Psychological distress not explored, however 1/3 reported pain.
Beez et al., 2013 (25)	Cross-sectional Quantitative	Visual analogue scales (VAS) measuring intraoperative pain and anxiety. Post-operative questionnaire.	2010-2011 France, UK, Italy & Germany	105	Asleep-awake-asleep (*n* = 97), asleep-awake (*n* = 8)	VAS completed intra-operatively; questionnaire completed prior to discharge	VAS: majority experienced mild pain during procedure, anxiety between 2-3cm. Questionnaire: 50.6% reported moderate fear, 11.4% severe fear. Pain moderate for 63.3% and severe for 5.1%.
Danks, Rogers, Aglio, Gugino, & Black, 1998 (26)	Cross-sectional Mixed data	Structured interview, Brief profile of mood states (POMS) Psychiatric Interview	1995 USA	21	Awake-awake	Structured interview 2-3 days post procedure Psychiatric interview – 1 month post-operative. POMS completed pre and post operatively.	15/21 reported complete satisfaction. Pain – 5 reported moderate – severe pain. POMS – 1 patient had declined mood post-operatively, 10 had improved. Existing psychiatric disorder not correlated with difficulties during procedure. No evidence of PTSD or psychiatric disorder as a consequence of surgery.
Fletcher, das Nair, Macniven, Basu & Byrne, 2012 (27)	Cross-sectional qualitative design	Semi structured interview	UK	7	Not stated	Between 5months – 42 months	Themes included use of self-preservation strategies prior and during procedure. Importance of relationship with neurosurgeon. Participants reported positive experience of surgery.

Study	Study design and data type (quantitative, qualitative, mixed)	Methods	Dates, Country	*N* patients	Surgical technique	Time since surgery at participation	Summary of findings
Goebel, Nabvi, Schubert, & Mehdorn, 2010 (28)	Cross-sectional mixed data	Survey and interview. HADS pre and post-operative. SCID post-operative	2007-2008 Germany	25	Awake-awake	5±2 days post op	76% highly satisfied with procedure; some dissatisfied due to pain/discomfort, seizure, anxiety and exhaustion. No difference between pre and post-operative HADS scores.
Howie, Bambrough, Karabatsou, & Fox, 2015 (27)	Cross-sectional qualitative design	Semi-structured interview	UK	6	Asleep-awake-asleep	6-16 weeks	Themes; control and responsibility, dissociation and fear. Surgery as threat to sense of self.
Khu et al, 2010 (29)	Qualitative	Semi structured interviews with thematic analysis.	Canada	27 (awake craniotomy *n* =19, craniotomy under general anaesthesia *n* = 8)	Awake-awake	Pre-operative interview and post-operative 1-2 weeks following procedure	Patients had a positive experience of awake craniotomy; high satisfaction with outpatient craniotomy, trust in surgeon importance, patients more concerned about disease than procedure.
Manchella et al., 2011 (30)	Qualitative	Semi-structured interviews with thematic analysis.	Australia	26	Asleep-awake-asleep	Pre op (1 days before) x2 postop time points (3days, 6weeks)	Patients generally tolerated procedure however 8% reported more than slight intra-operative pain; 15% more than slight intra-operative fear.
Manninen, Balki, Lukitto, & Bernstein, 2006 (31)	Survey design Quantitative	Structured interview	Canada	50	Awake-awake	x3 post-operative time points (1hour, 4hours and 24hours post-surgery)	93% completely satisfied at each time point.

Study	Study design and data type (quantitative, qualitative, mixed)	Methods	Dates, Country	*N* patients	Surgical technique	Time since surgery at participation	Summary of findings
Milian et al., 2013 (32)	Cross-sectional survey design Quantitative	Developed measure to assess for PTSD symptoms. SF-36 (HRQOL). Pulse rate and blood pressure measured to report on anxiety.	2010-2011 Germany	16	Awake-awake	Range 1-284 weeks, mean = 96 weeks	No participants met the criteria for PTSD; 2 experienced 'strong anxiety' during surgery and presented PTSD symptoms. Distressing recollections negatively affect HRQOL.
Palese, Skrap, Fachin, Visioli, & Zannini, 2008 (33)	Qualitative	Structured interview; phenomenographic approach	Italy	21	Awake-awake	x2 time points, day before surgery and day after surgery	Emergent themes: pre-operatively focus on self-preservation and working out the intra-operative role. Intra-operatively focus was on controlling the situation. Post-operatively focus on reassuring selves and others.
Wahab, Grundy, & Weidmann, 2011 (34)	Cross-sectional survey design; qualitative and quantitative data collected	Questionnaire – patient satisfaction (open and closed questions)	2006-2010 UK	45	Awake-awake	Post discharge	87% felt at easy during surgery; 80% felt supported post discharge; 24% experienced some discomfort during surgery.
Whittle, Midgley, Georges, Pringle, & Taylor, 2005 (35)	Cross-sectional survey design; qualitative and quantitative data collected	10 item questionnaire open and closed questions	UK	15	Asleep-awake-asleep	Prior to discharge (approx. 4-5 days post-surgery	Overall well tolerated; responses indicated intra-operative discomfort in 20%, fear in 15% and anxiety in 29%.

Study	Study design and data type (quantitative, qualitative, mixed)	Methods	Dates, Country	*N* patients	Surgical technique	Time since surgery at participation	Summary of findings
Wrede et al., 2011 (36)	Cross-sectional survey design Quantitative	PPP33- Patient evaluation in the perioperative phase 33 item questionnaire	Germany	87. Awake craniotomy (*n* = 46), craniotomy under general anaesthesia (*n* = 41)	Awake-awake	2-4 days post operatively	Awake patients showed better overall acceptance of surgery than controls. Significantly better scores on pain and physical disorders. Fear was higher amongst controls.

Results

Fourteen studies were included in the review, (24-37). All were published between 1998 and 2015. The studies included a total of 460 participants, of which 411 had undergone an awake craniotomy (controls *n*= 49). Sample size ranged from 6-105 participants with a mean of 33 total participants; two of the studies used a control sample (29, 36). Of the 14 studies included within the review, six collected only quantitative data using both standardised measures and closed question surveys (30-32, 34-36), four were classed as qualitative, using semi-structured interview designs (27, 29, 33, 37) and four used a mixed methods design collecting both quantitative and qualitative data (24-26, 28). The majority of the quantitative studies were considered to be survey designs, exploring patient's experiences of surgery through the use of questionnaires or structured interviews. Two of the included studies utilised a control group of patients who underwent craniotomy under general anaesthesia (29, 36). The awake-awake protocol was utilised in 64% (*n* = 9) of the studies (24, 26, 28, 29, 31-34, 36-38), 21% (*n* =3) used the awake-asleep-awake method (30, 35); two studies did not state the anaesthetic protocol used (27, 37). Time since surgery at the point of participation in the studies varied widely from one hour post-surgery (31) to five years after the operation (32).

Quality Assessment

The quality assessment process scored papers in domains relating to design, analysis and clinical application of findings. Due to the heterogeneity of the included papers it is necessary to exert caution when comparing quality scores. The qualitative papers were all deemed to be of good quality however the remaining papers, which were considered to be most appropriately grouped as 'survey' designs were of mixed quality (see Appendix B).

Studies considered to be of lower quality tended to lack clarity regarding aims and provided insufficient statistical analysis of data which limited conclusions.

Pre-operative Experiences

Seven studies provide insight into the psychological experiences of patients prior to the procedure. Five of these studies collected data prior to the surgery (26, 28-30, 33) with the remaining asking patients retrospectively about this time (27, 37). Two of the studies (26, 28) administered standardised psychometric measures of mood prior to the procedure. Goebel's and colleagues (28) administered the Hospital Anxiety and Depression Scale (HADS) (39) which revealed that 44% of patients reported anxiety prior to the procedure, along with 28% reporting of depression. However, there was limited further exploration of the pre-operative experience and thus it is unclear whether the reported levels of anxiety were related to procedure, or other factors, such as their health or life stressors. The Profile of Mood States (POMS) (40) was administered pre and post-operatively by Danks et al.(26), with no significant change reported between the two scores[2]. The potential outcomes associated with complications during brain surgery are life changing and the impact of this was highlighted by structured interviews completed by Manchella et al. (30). In their study, pre-operative concerns themed around the risk of disability and death. For some the prospect of being awake during surgery seemed less distressing when considered in the context of having a brain tumour. For these patients it seemed that any concerns they may have had about the procedure were negated by their hope that the surgery would relieve them of their tumour. A similar response was elicited from Khu et al. (29) in their interviews one week prior to surgery. At this point, participants described their surprise at the idea of having the procedure awake, however they generally reported feeling prepared for surgery. Participants

[2] POMS data were not presented within the research article.

in this study identified their concerns to be focused on treating the cancer, rather than about the procedure per se.

Semi-structured interviews completed the day before surgery by Palese et al. (33), highlighted differences in patient concerns about potential outcomes of the surgery such as disability, whilst others felt more optimistic and involved in the process. When asked to think about the procedure, many participants felt afraid and tried to avoid thinking about the intra-operative phase. For some, their active role in the procedure prompted fears that they would not be able to do as they were asked. The theme of the patients role within the procedure was also discussed by participants during semi-structured interviews completed by Howie et al. (37). In their study, participants retrospectively discussed the pre-operative period, reflecting on the importance of sufficient information about the procedure to give them a sense of control. However, for some there was recognition that this information could be "too much", with some participants reporting they did not want to think about the procedure, suggesting that some individuals coped through avoidance. Similarly, when retrospectively asking participants about their feelings and preparations prior to the procedure, Fletcher et al. (27) also identified avoidance and the use of distraction as coping mechanisms. In addition, they explored the process of deciding to have an awake craniotomy and identified that many placed the responsibility onto the neurosurgeon, thereby avoiding facing the implications of the decision themselves.

Whilst the pre-operative period was also explored by Wahab and colleagues (34), their questions focused on the format of the pre-operative consultation and did not explore patient thoughts or feelings about the upcoming procedure.

The findings synthesised here suggest that many patients understandably experience anxiety and worry prior to their procedure.

Intra-operative Experiences

Thirteen of the studies included within this review explore some element of the patient's intra-operative experience (24-31, 33-37). Twelve studies retrospectively ask patients about the intra-operative experience, in one case up to 16 weeks following the procedure (37), and thus may be subject to recall bias. One study utilised visual analogue scales to gather pain and anxiety levels during the procedure itself (25). The focus of these 13 studies is primarily whether patients were able to tolerate the operation in terms of pain, discomfort and psychological distress.

Psychological distress.

Twelve of the studies explore the thoughts and feelings experienced by patients during the procedure (25-31, 34-37). This was elicited either through asking patients specifically about feelings of fear or anxiety during the surgery, or was emergent from discussion within qualitative studies.

Beez and colleagues (25) reported that VAS scores revealed a mean anxiety level of 2.4cm (scale range 0-10cm) which was not considered to indicate significant anxiety. However, the authors reported to have utilised a high cut off score to increase specificity, leading to a reduced sensitivity (36.9%) and thus there is an increased risk of Type II error, i.e. the level of anxiety may be an underestimation. The post-operative questionnaire indicated that 50.6% (n = 40) of participants experienced 'moderate' fear and 11.4% (n = 9) experienced 'severe' fear during the procedure determined by an endorsement of the response "I was very frightened" when asked about intra-operative fear. The range of participant's VAS scores were not reported, this would have been of interest for comparison with post-operative questionnaire responses.

Whilst the Beez et al. (25) study was considered to be of low quality, their findings were supported by higher quality papers. Intra-operative anxiety was also explored post-operatively by Goebel's et al., (28), with 17% of patients reporting to have experienced some anxiety during their procedure. Similarly, in the study by Danks et al. (26) one third of participants (n = 7) reported intra-operative anxiety when asked via questionnaire post-operatively; two participants rated this to be 'severe'. Responses to an open-ended question about difficulties with the procedure revealed that six patients reported the noise of the drill to be a problem and one patient reported to have felt claustrophobic. Another patient remembered feeling worried following the experience of a brief seizure, and another reported feeling "terrified" when their speech was disrupted by brain mapping. Furthermore the study reports one participant presenting with "marked emotional lability" during the procedure, however there is no further explanation of this. 'Fear' also emerged from semi-structured interviews completed by Howie et al. (37) and was described as the overarching theme from their analysis. Their analysis proposed that participants adopted dissociation as a method of coping with the "unspeakable fear" they experienced during surgery. Similar to the participant within the Danks study (26), one respondent reported feelings of fear when they found themselves unable to speak during the procedure. More than 'slight fear' during the procedure was also reported by 15% of participants in the Manchella et al. (30) study and Wahab et al. (34) reported that 7% (n = 3) of participants did not feel at ease during the procedure, however reasons for this were not explored. Consistent with this, 15% of participants reported fear and 29% reported anxiety within Whittle et al.'s study (35). During interviews, some participants in Palese et al.'s study recalled feeling anxious in anticipation of their first 'task' during the procedure (33).

In contrast, participants in Fletcher et al.'s study reported the intra-operative experience to have been positive, and it seemed that participants in this study adopted self-

perseveration strategies, and benefited from a good relationship with their neurosurgeon to help them cope during the procedure (27). In addition, whilst some of Palese et al.'s participants reported anxiety, others reported that they found the tasks offered a sense of control (33). Furthermore, no distress was reported by participants during semi-structured interviews completed by Khu et al. (29); in contrast, participants reported the experience to have been positive. All three of these papers were all considered to be of high quality. Whilst Wrede et al. (36) explored intra-operative fear via the use of a standardised measure (PPP33), their reporting of this grouped pain, discomfort and anxiety into one variable and thus it is not possible to determine reported anxiety.

Pain.

Research indicates a link between the experience of post-surgical pain and the development of negative psychological sequelae (41). The experience of intra-operative pain or discomfort was explored by several of the studies (24-26, 28, 30, 31, 34, 35), this was primarily retrospective, however, one study utilised visual analogue scales (VAS) to measure intra-operative pain (25).

The VAS scales suggested intra-operative pain was mild and well controlled, however, the post-operative questionnaire of this sample indicated that moderate pain was reported by 63.3% of participants (25). Post-operatively, 43% (n = 9) of participants within Danks et al.'s study reported to have experienced pain, 29% rated this either 'moderate' or 'severe'; similarly 28% of participants in Goebel et al.'s study reported intra-operative pain.

Across all of the studies exploring intra-operative pain, the numbers of participants reporting pain ranged from 8% in the Manchella et al. (30) study, to 76% within the Manninen et al. (31) study. This difference could be related to the surgical protocol used. Manchella et al. utilised asleep-awake-asleep whilst Manninen et al. utilised the awake-

awake technique, thus participants within the latter study were conscious during the opening and closing of the skull. Furthermore, the studies vary in terms of the language used e.g. ‘pain’ or ‘discomfort’, and the response options offered to participants (e.g. rating pain in terms of ‘mild’, ‘moderate’, ‘severe’ or simply asking whether pain was experienced). Thus responses are based on subjective interpretations of the terminology used which may account for some difference in findings.

Recall of surgery.

A number of the studies explored participant’s recall of the surgical events (24-26, 28, 30, 31, 33-35) with all studies reporting that some participants had incomplete recall. Two studies reported that up to a third of participants reported having no recollection of the procedure (24, 30), in contrast, two other studies reported low levels of no recollection, between 4-8% (28, 34). The majority of participants reported partial recollection or no recollection of surgical events in three of the studies (25, 26, 31). Despite this seemingly high level of impaired memory of the procedure, none of the studies explore reasons or present hypotheses for this.

Post-operative Psychosocial Outcomes

Three of the studies explored psychosocial outcomes following the procedure (26, 28, 32). This included the use of psychometrics measuring mood (HADS and POMS) along with measures of post-traumatic stress and health-related quality of life (26, 28, 32). Danks et al. (26) reported no significant difference between pre and post-operative POMS scores. Furthermore, they completed psychiatric interviews one month post operation and reported no indications of adverse psychological sequelae (26). The post-operative HADS revealed a slight increase in both depression and anxiety, however, this increase was not statistically significant. It is noteworthy that these findings were based on a relatively small sample (*n* =

25). This finding is interesting as it would be reasonable to imagine patients may have felt more anxiety prior to the procedure and that this would have reduced post-operatively. These findings offer insights in the psychosocial functioning of patients following awake craniotomy, however, the lack of a control group limits the extent to which these findings can be attributed to the nature of being awake. Interesting insights into the psychological consequences of awake craniotomy are provided by Milian et al. (32). They report two cases of symptomatology resembling PTSD, along with a high prevalence of key post-traumatic symptoms, such as distressing recollections (44%), avoidance of surgery related stimuli (18.8%) and symptoms of increased arousal (62.5%). However, in addition to a small sample size this study recruited people up to four years post-surgery. Research suggests that PTSD will recover within the first 12 months for around half of those who develop it, regardless of treatment (42) and thus it may be that a higher number of Milian's participants had experienced PTSD but that this had remitted by the point of recruitment. Only one other study explored post-traumatic stress and reported that one participant experienced surgery related intrusions (28).

Methodological Limitations

When considering findings of the reviewed studies it is necessary to understand their methodological drawbacks; this was an area not considered by a previous review in this field (43). The quality analysis of the studies highlighted that whilst the qualitative studies were deemed to be of good quality, the quantitative studies were mixed with three of the studies identified as having significant drawbacks (24, 25, 35)

A number of the studies were completed by the neurosurgical department within which the patients had their operation, on some occasions data collection was completed by a member of the neurosurgical team (24) and thus the possibility of response bias needs to be

considered. Given the life changing nature of the procedure and the emphasis which individuals place on their relationship with the neurosurgeon (27, 29) it is possible that participants may have felt obliged to report positively about the procedure (44).

Furthermore, only two of the studies utilised a control group of participants who had undergone their operation with general anaesthesia (29, 36). As such, the conclusions which can be drawn from the current literature are limited in the extent to which they inform our understanding of the psychological aspects of awake craniotomy when compared with craniotomy under general anaesthesia.

Sample size is also a methodological constraint for a number of the studies (25, 32, 35, 37) however, it is acknowledged that this may be reflective of the available sample pool, with awake craniotomies a fairly infrequent procedure. Despite this, it is still noteworthy to consider the basis on which conclusions have been drawn and exert caution where small samples are reported.

A number of the studies were limited by their design and use of non-standardised measures. These studies utilised questionnaires with a mixture of open and closed questions (24, 25, 28, 34, 35). Furthermore, some of these studies collected qualitative information via interviews but there was no clarity of the theoretical framework utilised to analyse this data. Whilst useful, these studies tend to lack depth by using closed questions.

The timing of participation is also worth consideration with many participants engaging with the study soon after their operation and at times whilst still in hospital (see Table 1); one study interviewed participants one hour after their procedure (31). In this early recovery phase it is arguable that patients would not have had sufficient time to reflect on their experience. Similarly, two of the studies recruited participants years after their procedures (27, 32) at which point participants memory of the operation may be less reliable

possibly leading to a recall bias, or a natural remittance of psychological distress may have occurred (45).

Discussion

The studies included in this review provide interesting insights into the psychological experiences of patients who undergo awake craniotomy. As outlined initially, this review is focused on our current understanding of the psychological aspects of this procedure and as such this review does not provide an overview of all of the findings of each of these studies per se. As highlighted, the studies within this area typically focus on the patient's intra-operative experience and this review has identified a comparative paucity in the literature base regarding patient's psychological outcomes following this procedure. Furthermore, the literature available is of mixed methodological quality.

Overall, the available literature presents awake craniotomy as an acceptable and tolerable procedure for patients, however, as identified within this review, psychological distress can present at the pre, intra and post-operative stages. It is apparent from the included studies that a number of patients report to experience anxiety and fear prior to, and during, their procedure (25-31, 33-35, 37). Furthermore, a number of patients reported pain during the procedure which is itself considered distressing. Whilst the prevalence of psychological distress reported appears to be within the minority of patients, the impact of methodological issues such as small sample sizes, potential bias and the use of non-validated measures should be taken into account as these factors may contribute to an underrepresentation of true incidence. Furthermore, there is currently little known about the long term consequences of this psychological distress with only one study exploring post-operative psychological outcomes (32). The pilot study completed by Milian and colleagues (32) suggests that in some cases, symptoms of post-traumatic stress can develop following an awake craniotomy. Whilst only two of Milian's sample presented with probable PTSD, a high proportion

presented with PTSD symptomatology. It is not clear from the data whether any of these participants could be considered as experiencing subthreshold PTSD in accordance with proposed criterion (46-48). A key predictor of the development of PTSD is the peri-traumatic emotional response at the time of the trauma (49). Negative emotional responses, such as those involving fear or anxiety, are predictive of PTSD. In light of the current literature reviewed, which highlights that many patients feel anxious or fearful during their procedure, this area is certainly warrants further exploration. Furthermore, the rate of reported impaired memory for the surgery is of interest. Nine studies explore participant recall of the surgery with all reporting that some participants experience incomplete or no recall of the procedure (24-26, 28, 30, 31, 33-35). Despite this there is no discussion within these studies of possible explanations for this variation in memory. This is an important finding in the context of understanding the psychological impact of awake craniotomy. In terms of PTSD, incomplete memory of the traumatic event is considered an avoidance symptom and is theorised to be associated with peri-traumatic dissociation, a strong predictor of PTSD development (49). Furthermore, research suggests the risk of peri-traumatic dissociation is increased when an individual is expecting the threat in contrast to when the event is unexpected (50).

Clinical Implications

The work of Milian and colleagues (32) has identified the potential for the development of negative psychological sequelae following an awake craniotomy. Specifically, their research highlighted PTSD symptomatology following surgery. Co-morbidity is common with PTSD and subthreshold PTSD with anxiety, depression, reduced quality of life and increased suicidal ideation often reported (42, 48, 51). Furthermore, given the nature of PTSD symptoms such as avoidance, there is the possibility that these symptoms could negatively impact upon patient's physical health if avoidance symptoms lead to a failure to attend medical appointments (52).

Future Research

The literature presented within this review highlights a need for further exploration of the psychological impact of undergoing an awake craniotomy in light of findings of intra-operative anxiety, distress and discomfort. As highlighted by this review, the current evidence base is small and the available literature is of mixed methodological quality which limits the extent to which conclusions can be drawn. Thus, further research is warranted aimed specifically at assessing the extent of the psychological impact of awake craniotomy for patients. A more stringent methodological approach is required, utilising validated measures of psychological functioning and within a specific post-operative time period and with a control group for comparison. Through further research the psychological impact of this procedure can be better understood which will inform appropriate service provision for patients at all stages of their journey. Initial research into this area has emerged with researchers reporting benefits of using music as a therapeutic aid to reduce anxiety before, during and after the procedure (53). Furthermore, a small case study reported the benefits of family support within the operating room for patients who are particularly distressed about the procedure (54).

Limitations

Whilst efforts were made to contact all authors of the studies included within this review, responses were not received from all and thus there is the potential of existing unpublished literature which may have added to this discussion.

Conclusions

In conclusion, the present review has identified that the literature regarding the psychological experience of undergoing an awake craniotomy is sparse. Of the available literature, methodological limitations reduce the extent to which conclusions can be drawn

and generalised to this population group. Despite a number of the studies reporting generally positive feedback from participants about the procedure, the prevalence of psychological distress prior to, during and following the procedure is consistently identified, albeit within a relative minority. The current literature base is particularly lacking with regards to the long term psychological outcomes for these patients and thus this is an area warranting further research.

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An exploration of PTSD symptoms and psychosocial adjustment following awake and asleep craniotomy.[3]

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[3] To be submitted to: *British Journal of Neurosurgery*, for author guidance see Appendix A.

Abstract

Introduction. Craniotomy is an effective neurosurgical technique for brain tumour excision, and can be conducted with the patient awake, or 'asleep' under general anaesthesia. However, little is known about the psychological outcomes for patients following both methods of this procedure. This study aimed to provide a preliminary exploration of the level of post-traumatic stress symptoms, and psychosocial outcomes following awake and asleep craniotomy.

Materials and methods. *N* = 44 patients who were between 3-12 months post craniotomy, (awake *n* = 16, asleep *n* = 28), completed five standardised measures: Posttraumatic Stress Diagnostic Scale (PDS), Patient Health Questionnaire (PHQ-9), Generalised Anxiety Disorder (GAD-9), Short Form 36 (SF-36) and the Multidimensional Scale of Perceived Social Support (MSPSS).

Results. 20% (*n* = 9) of the total sample met the diagnostic criteria for PTSD according to DSM-IV (1). However, mean post-traumatic stress symptom severity was mild for the total sample. For the whole sample, post-traumatic stress symptom severity was significantly correlated with poorer outcomes on measures of depression, anxiety and quality of life. Descriptive data presented a higher prevalence of PTSD diagnosis amongst the asleep group (25%) compared with the awake group (13%).

Conclusions. The findings reveal a high level of PTSD (20%) following craniotomy, along with mild depression, mild-moderate anxiety and reduced health-related quality of life (HRQOL). The study is the first to administer standardised measures of psychosocial outcomes within a defined post-surgery period and to compare these outcomes between awake and asleep craniotomy patients. Findings of this study should be interpreted with caution due to the small sample size which limited data analysis. Implications of these

preliminary findings are discussed with reference to the current literature base and areas for future research.

Key words: Craniotomy, awake craniotomy, post-traumatic stress, psychosocial outcomes, health-related quality of life.

Introduction

A craniotomy is a well-established neurosurgical technique for brain tumour removal. This procedure is most often carried out whilst the patient is 'asleep' under general anaesthesia, however, there is growing use of an 'awake craniotomy' in which the patient is conscious for part, or all, of the procedure (2). The benefit of this method is that it allows for the removal of tumours within eloquent areas of the brain (i.e. language or motor cortex) (3, 4). During awake craniotomy patients are conscious for intra-operative neuropsychological monitoring and brain mapping which permits tumour removal with a significantly reduced risk of damage to eloquent areas of brain functioning (2).

Although considerable literature demonstrates the clinical effectiveness of both awake and asleep craniotomy (3, 4) little is known about the psychological impact upon patients who have undergone these procedures. This is despite the knowledge that psychological distress is common within the brain tumour population (5, 6) and furthermore, stress and anxiety are frequently reported prior to general surgery (7). In addition, there is growing research reporting presentations of post-traumatic stress disorder (PTSD) following surgical procedures including cardiac surgery (8), lung resection (9) and caesarean. The development of PTSD following 'anaesthetic awareness', a phenomena whereby patients unexpectedly gain consciousness during general anaesthesia, has also been reported (10).

Currently the literature exploring the psychological impact of undergoing craniotomy predominantly focuses on the experiences of patients undergoing awake craniotomy. Of the awake craniotomy literature, the findings are mixed, with some studies concluding the procedure to be acceptable to patients (11, 12), whilst others report the presence of psychological distress (13). Furthermore, research regarding the intra-operative experience of undergoing awake craniotomy finds that patients report feeling anxiety, pain and fear (13-16). This is of interest as negative peri-traumatic emotional responses, e.g. feeling fearful or

anxious during the event, have been found to predict the development of PTSD (17, 18). To date, one paper has explored the prevalence of PTSD symptomatology following awake craniotomy. In their pilot study, Milian and colleagues (19) reported two cases (12.5%) of symptomatology resembling PTSD. Additionally, they reported a high level of distressing recollections related to the surgery (44%), increased arousal (62.5%) and avoidance of stimuli associated with the surgery (18.8%). Whilst these initial findings are interesting, design weaknesses including the use of a non-standardised measure of PTSD, a small sample size (*n* = 16) and the wide variation in time since surgery (1-284 weeks) limit the conclusions of this study. Furthermore, there is currently no literature exploring PTSD symptomatology within a population who underwent craniotomy under general anaesthesia, and thus it is not possible to fully understand the context of Milian's findings, i.e. whether these presentations are related to unique aspects of the awake procedure.

PTSD is categorised as an anxiety disorder within the Diagnostic and Statistics Manual of Mental Disorders – 4th edition (DSM-IV) and can develop following exposure to an event involving actual or threatened death or serious injury which is accompanied by feelings of intense fear, helplessness or horror (1). The DSM-IV also specifically recognises diagnosis of a life threatening illness as a potential trigger of PTSD (1). The risks associated with brain surgery are considered to meet this criteria and thus patients who are undergoing a craniotomy are proposed to be exposed to this threat. Furthermore, research suggests that acute stress disorder, which is predictive of PTSD development (20), is common amongst patients who have recently completed neurosurgery for brain tumour removal (21). PTSD and subthreshold PTSD, where a patient presents with post-traumatic stress symptoms but does not meet diagnostic criteria, are associated with negative psychological sequelae including depression, anxiety and reduced quality of life (22, 23). Additionally, within a medical

context PTSD may be associated with poorer reports of health (8) and a reluctance to engage with health care providers (24).

The aims of this study were to explore the levels of post-traumatic stress presentations and psychosocial outcomes (depression, anxiety and health-related quality of life) following awake and asleep craniotomy. Furthermore, the study was interested to identify whether the mode of craniotomy i.e. awake or asleep, was associated with differences in post-traumatic stress and psychosocial outcomes. This is the first time psychological outcomes following awake and asleep craniotomy have been explored via the use of reliable and validated psychometric measures, and within a standardised time period post-surgery. Thus, this study adds insight into the psychosocial experiences of the brain tumour population, a group whom are typically under researched (25).

Hypotheses:

(i) For the whole sample, there will be evidence of PTSD diagnosis, psychological distress and poor health-related quality of life (HRQOL) for the period 3-12 months post-surgery.

(ii) PTSD diagnosis and post-traumatic stress symptom severity will be different between the awake and asleep surgery groups.

(iii) Psychosocial outcomes (i.e., depression, anxiety and HRQOL) will be different between the awake and asleep surgery groups.

(iv) For the whole sample, there will be associations between PTSD symptom severity, depression, anxiety and HRQOL for the period 3-12 months post-surgery.

Materials and Methods

Participants

Participants were recruited from a North West National Health Service (NHS) Neurosurgery centre. To be eligible for inclusion in the study participants had to be aged over 18, English speaking to complete standardised measures and between 3-12 months post craniotomy for the removal of a brain tumour. This time period was set to capture 'chronic' PTSD presentations (>3 months) as identified by DSM-IV (1) and limited to 12 months as untreated PTSD may naturally remit over time (26). Participants were identified by the Neurosurgery department. The awake participants included had all undergone their procedure via the asleep-awake-asleep technique, whereby the patient is initially unconscious at the start of the procedure and is then 'woken up' to complete intra-operative testing; the patient is then returned to unconsciousness for closure of the skull. The final sample consisted of 44 (n = 16 awake, n = 28 asleep) participants from 100 who were invited (44% response rate). The sample were 59% female (n = 26) and 41% male (n = 18), age ranged between 19 to 80 years (M = 49.09, SD = 12.95).

Study Design and Procedure

The study design was approved by the University Research Review Committee, Local Research Ethics Committee and the Research and Development department within the Trust (see Appendices C- F). Participants were contacted via post with information detailing the study (see Appendix G). Written informed consent was obtained from all participants (see Appendix H) following which they were contacted by the primary researcher. To enhance the accessibility of the study within a small population, three modes of data collection were offered including; via telephone, face to face interview, or via an online survey platform. Participation took approximately 25 minutes following which participants were debriefed. As an incentive, participants had the opportunity to win high street shopping vouchers. At the end of the study all participants were sent a short report detailing study findings (see Appendix I).

Measures

Participants completed five standardised measures. Four of these measures explored the dependent variables of PTSD and psychosocial adjustment which utilised measures of mood and HRQOL. A measure of social support was also administered. Measures can be found in Appendices J-N.

Posttraumatic Stress Diagnostic Scale (PDS).

The PDS (27) measures symptom severity and can be used for diagnosis of PTSD in accordance with DSM-IV (1) criteria. Participants were asked to respond in terms of the surgical event and items on the measure were worded specifically to ask about the surgery. The measure has strong test-retest reliability with a correlation coefficient of .83. Symptom severity scores range from 0-51 with four rating classifications. Scores of 1-10 are interpreted as mild, 11-20 as moderate, 21-35 as moderate to severe and 36-51 as severe post-traumatic stress symptoms.

Patient Health Questionnaire (PHQ-9).

The PHQ-9 (28), is a nine item scale of depression with strong internal reliability (α=.89), test re-test reliability (r =.84), and strong content and construct validity. Scores range from 0 to 27 with interpretations of 5-9 as mild, 10-14 as moderate, 15-19 as moderately severe and 20-27 as severe depression.

Generalised Anxiety Disorder (GAD-7).

The GAD-7 (29) is a seven item scale of anxiety with strong internal reliability (α= .92), test re-test reliability (r =.83), and good criterion, construct, factorial and procedural validity. Scores range from 0 to 21 with 0-5 interpreted as mild, 6-10 as moderate, 11-15 as moderately severe, and 15-21 as severe anxiety.

Short Form -36.

The SF-36 (30) is a 36 item questionnaire exploring HRQOL. Items correspond to eight dimensions; physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and general mental health. The SF-36 has good internal consistency with the eight scales ranging from α =.73 to α =.92 and good test re-test reliability (*r* =.72 to *r* =.87). Two component scores are derived corresponding to physical health (PCS) and mental health (MCS). Scores are expressed on a percentile ranging from 0-100 with higher scores indicative of better functioning; a score of 50 is considered 'average'.

Multidimensional Scale of Perceived Social Support (MSPSS).

The MSPSS (31) is a 12 item scale measuring perceived social support. The measure has good internal reliability, (α=.88) and test re-test reliability (*r* =.85) (17, 18). Scores range from 1-7, with higher scores associated with greater perceived social support.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0. Where appropriate, extreme outliers were removed from variable data sets when computing means and standard deviations. In cases where distributions exceeded a criteria of +1 or -1 skewness and kurtosis, log transformations were utilised to attempt to normalise these distributions to meet parametric assumptions and conduct bivariate analysis. Descriptive statistics were calculated to provide sample demographics and present data regarding mean scores across psychometric measures along with levels of PTSD diagnoses. Correlational analyses were performed to assess the level of association between variables.

Power.

The final sample size of 44 (*n* = 16 awake, *n* = 28 asleep) was below the target of 56 (i.e., 28 awake and 28 asleep participants) which had been calculated as sufficient to perform

regression analysis assuming a medium effect size, alpha of 0.05 and power of 0.8. The study was therefore underpowered limiting the planned statistical analysis, further details regarding changes to analysis are provided in Appendix O.

Results

Patient Characteristics

Table I presents demographic data regarding the sample as a whole and by group. Independent samples t-tests were conducted to compare age, time since surgery and time in hospital between surgery groups. Chi-square analysis was utilised to compare gender between surgery groups. There was a significant difference in time since surgery between awake craniotomy (M= 174.76, SD= 74.94) and asleep craniotomy (M= 250.56, SD= 115.33), $t(42) = -2.35$, $p = .023$. A significant difference was also observed with time in hospital between awake (M= 6.40, SD= 3.42) and asleep craniotomy (M= 13.25, SD= 11.29), $t(41) = -2.82$, $p = .028$. Age did not significantly differ between awake and asleep craniotomy. A Chi-square test for independence (with Yates Continuity Correction) indicated no significant association between gender and surgery type.

Table I. Demographic data for the total sample and by surgery group.

Variable	Total *N* = 44		Awake *N* = 16		Asleep *N* = 28	
Age – M (*SD*)	49.09	(12.95)	46.69	(9.51)	50.46	(14.54)
Gender						
Male *N* (%)	18	(41%)	9	(56%)	9	(32%)
Female *N* (%)	26	(59%)	7	(44%)	19	(68%)
Days in hospital M (*SD*)[4]	10.86	(9.84)	6.40*	(3.42)	13.25*	(11.29)
Days since surgery M (*SD*)	223.00	(108.03)	174.76*	74.94	250.56*	(115.33)

Note: M = mean, SD = standard deviation. * = difference between groups significant at the 0.05 level

[4] Note: *N*= 43, outlier removed.

Post-traumatic Stress Presentations

Table II. Summary descriptive statistics for the Posttraumatic Stress Diagnostic Scale (PDS) presented by total sample and surgery group.

Variable	Total *N* = 44		Awake *N* = 16		Asleep *N* = 28	
PTSD DSM IV diagnosis	9/44	(20%)	2/16	(13%)	7/28	(25%)
Subthreshold PTSD[5]	4/44	(9%)	2/16	(13%)	2/28	(7%)
PTSD sub-scale responses						
Re-experiencing N (%)	16/44	(36%)	4/16	(25%)	12/28	(43%)
Avoidance N (%)	31/44	(70%)	10/16	(63%)	21/28	(75%)
Arousal N (%)	37/44	(84%)	13/16	(81%)	24/28	(86%)
PDS Severity M (*SD*)	8. 66	(7.51)	8.06	(7.78)	9.00	(7.48)
Trauma history *N* (%)	17/44	(38%)	5/16	(27%)	12/28	(43%)

Note: PTSD sub-scale responses = total *N* within group endorsing ≥1 symptom within each symptom cluster and percentage of group. PDS Severity = Post-traumatic stress symptom severity score. Trauma history = total *N* of participants reporting a history of trauma prior to surgery.

Table II presents the results from the PDS in terms of PTSD diagnosis and post-traumatic stress symptom severity score for the total sample and for each surgery group. The frequency of 1 or more symptoms reported within each cluster (i.e. re-experiencing, arousal and avoidance) are also presented. Total numbers reporting a prior history of trauma are also provided as this variable is predictive of PTSD development (17). The findings indicate that a high proportion of the sample met PTSD diagnostic criteria (20%), with the majority of this

[5] In accordance with criteria suggested by Blanchard et al.

total comprising of participants within the asleep group. A Chi-square test for independence (with Yates Continuity Correction) indicated no significant association between PTSD diagnosis and surgery type. Furthermore, an independent samples t-test revealed that mean post-traumatic stress symptom severity did not significantly differ between surgery groups $t(42) = -.39$ $p = .70$. In addition, 9% of the sample met the criteria for subthreshold PTSD as outlined by Blanchard et al. (32). The mean post-traumatic stress symptom severity score across the whole sample fell within the 'mild' category, in accordance with the cut-off score (≤10) provided by the PDS (27). Over one third of the sample (n = 17) reported a prior traumatic event, and five participants reported that this trauma was still affecting them at the time of presentation for surgery. In terms of symptom clusters, arousal symptoms were the most commonly reported across the total sample and by group, followed by avoidance and re-experiencing symptoms. In total, 86% (n = 38) of the sample endorsed one or more symptom of post-traumatic stress.

Psychosocial Outcomes

Table III. Means and SD for key outcome variables in the study.

Outcome Measure	Total *N*=44		Awake *N*=16		Asleep *N*=28	
PHQ-9 M (*SD*)	8.18	(7.02)	7.13	(6.80)	9.00	(7.48)
GAD-7	5.43	(5.04)	5.88	(5.98)	5.18	(4.52)
SF – 36 PCS	41.79	(10.18)	47.69	(7.92)	38.42	(9.90)
SF- 36 MCS	36.74	(9.44)	37.37	(10.41)	36.39	(9.02)
MSPSS	5.63	(1.53)	6.18	(1.12)	5.32	(SD=1.65)

Note: PHQ-9 = Patient health questionnaire 9, GAD-7= Generalized anxiety disorder 7, SF-36 PCD= Short Form – 36 physical component score, SF-36 MCS= Short-Form -36 mental component score, MSPSS= Multi-dimensional scale of perceived social support.

Table III presents means and standard deviations for measures of depression (PHQ-9), anxiety (GAD-7), HRQOL (SF-36 PCS, SF-36 MCS) and social support (MSPSS). The PHQ-9 score for the whole sample, and each surgery group, suggests ‘mild’ depression. The GAD-7 score is at the upper end of the ‘mild’ anxiety category for the whole sample and for the asleep group; for the awake group the score is interpreted as ‘moderate’ anxiety. With regards to HRQOL, the mean percentile scores for the total sample indicates slightly lower quality of life related to mental health (SF- 36 MCS = 37.21) compared with physical health (SF-36 PCS = 41.88). In terms of social support, mean scores for the total sample, in addition to means from each group are indicative of high social support. Independent samples t-tests

were conducted to compare depression, anxiety, HRQOL and social support between surgery groups; no significant differences between surgery groups were found for these variables.

The correlation matrices presented in Table IV indicates that for this population, post-traumatic stress symptoms are significantly correlated with increased levels of depression (r =.784, p <0.05), anxiety (r =.750, p < 0.05), and reduced HRQOL on both physical (r = -.370, p < 0.01) and mental (r = -.651, p < 0.01) components. Furthermore, PDS scores were significantly positively correlated with time since surgery (r =. 333, p < 0.05) such that as time since surgery increased, PDS symptom severity also increased.

Table IV. Correlation coefficients demonstrating relationships between variables for the total sample.

Variable	PDS Severity	PHQ-9	GAD-7	SF-36 PCS	SD-36 MCS	MSPSS	Trauma history	Time since surgery	Time in hospital
PDS Severity	1	.784**	.750**	-.370*	-.651**	-.183	.030	.333*	.117
PHQ-9		1	.706**	-.587**	-.622**	-.177	.275	.293	.067
GAD-7			1	-.243	-.698**	-.170	.128	.190	.150
SF-36 PCS				1	.050	.244	-.243	-.155	-.187
SF-36 MCS					1	.240	-0.98	-.148	.011
MSPSS						1	.067	.018	.005
Trauma history							1	.117	-.171
Time since surgery								1	.188
Time in hospital									1

Note: * = significant at the 0.05 level. ** = significant at the 0.01 level.

PDS Severity = post-traumatic stress symptom severity, PHQ-9 = Patient health questionnaire 9, GAD-7= Generalized anxiety disorder 7, SF-36 PCS = Short form 36 Physical Component Score, SF-36 MCS= Short Form 36 Mental Component Score, MSPSS= Multi-dimensional scale of perceived social support, Trauma history = *N* reporting trauma history, Time since surgery= M days since surgery at recruitment, Time in hospital= M days in hospital post-surgery.

Discussion

The aims of this study were to explore the general level of PTSD, post-traumatic stress symptoms, psychological distress and social adjustment in the period 3-12 months following awake and asleep craniotomy. Secondly, the study aimed to ascertain whether type of craniotomy (i.e. awake or asleep) was associated with differences in these psychosocial outcomes. Whilst previous literature with an awake craniotomy population indicated the presence of intra-operative psychological distress (13) and post-operative post-traumatic stress symptomatology (19), the lack of literature regarding psychological experiences and outcomes for those who had their surgery under general anaesthesia limited the context within which these findings could be understood.

The findings from a total sample of 44 participants, suggest support for hypothesis (i) in highlighting the presence of PTSD, psychological distress and poor social adjustment for the whole sample following craniotomy. Twenty percent of the total sample met diagnostic criteria for PTSD according to DSM-IV (12). In terms of hypothesis (ii), a difference between the groups was observed with levels of PTSD, with 25% of the asleep group meeting diagnostic criteria, compared to 13% of the awake group. However, post-traumatic stress symptom severity was ‘mild’ across the total sample and between surgery groups. With regards to hypothesis (iii), no difference was observed between groups on measures of depression; a slight difference between groups was observed in terms of anxiety. The awake group reported better physically related HRQOL compared to the asleep group. When exploring hypotheses (ii) and (iii) the lack of statistical power limited the ability to identify statistically significant differences between the groups and the role of surgery type in influencing psychological outcomes. Hypothesis (iv) was supported with data analysis indicating significant correlations between post-traumatic stress symptom severity and scores on measures of depression, anxiety, and HRQOL. This finding is consistent with previous

literature highlighting the negative psychological presentations associated with post-traumatic stress, and demonstrates this relationship within a neurosurgical population. Bivariate analysis also identified a significant correlation between time since surgery and post-traumatic stress symptom severity.

Whilst the literature base highlights that undergoing surgery can be a traumatic experience, the higher levels of PTSD within the asleep group are interesting. Although this pattern may be related to the longer time since surgery which this group typically had, rather than their surgery type per se, the notion of PTSD being higher following an experience for which the individual was under general anaesthesia, rather than conscious, is unexpected. When considering predictors of PTSD development, the peri-traumatic emotional response, i.e. the feelings experienced during the trauma, is evidenced as a significant predictor with effect sizes ranging from r =.15 to r =.55 (18, 20) and the high prevalence of intra-operative fear and anxiety previously reported by those who had undergone awake craniotomy would therefore suggest that this group were vulnerable to PTSD development (13, 16). Although, as the intra-operative experience was not explored with the awake sample the level of their peri-traumatic distress is speculative. Furthermore, given the lack of literature regarding the psychological experiences of those undergoing asleep craniotomy, the emotional state of this group during the events surrounding the surgery is also unknown. The phenomena of PTSD development following an event where consciousness is variable is acknowledged, with previous literature reporting trauma presentations following a traumatic brain injury (33), periods within intensive care (34), and most relevant here, following other surgical interventions where general anaesthesia was used (9, 35).

Literature regarding PTSD after critical illness suggests that PTSD development is associated with feelings of helplessness at the time of the trauma (24). Whilst speculative, it is possible that the difference in PTSD diagnosis observed between the two surgery groups

within this study may be related to an enhanced sense of control felt by the awake group which may have protected against feelings of helplessness. Whilst the awake participants in this study were not asked about intra-operative experiences, research from Palese et al. reported that patients found their intra-operative role (i.e. engaging in tasks) helpful in providing a sense of control (36). Furthermore, a small study of people who had experienced life-threatening events but had not developed trauma symptoms, suggested that the use of problem solving techniques during the event helped individuals to maintain a sense of control and this seemed to protect against feelings of helplessness (37).

Understanding the development of PTSD and symptomatology within the asleep participants is limited as qualitative data regarding their experiences, particularly the nature of re-experiencing symptoms, were not captured during data collection. It is unlikely that 'anaesthetic awareness', whereby patients unexpectedly gain consciousness during surgery, accounts for this presentation given the low occurrence of this phenomena (38). Similarly, it is unclear whether all of the awake participants within this sample had a full recollection of the procedure, with previous research reporting that up to one third of participants had no recall (11, 39). However, further research is necessary to explore levels of symptomatology between the two groups before speculating on the nature of these differences.

Furthermore, prior history of trauma is a significant risk factor for PTSD development (18) and reported levels of this were higher in the asleep group which may account for some of the difference in PTSD compared to the awake group. However, literature suggests that this variable is associated with a small effect size (r = .17) thus it is unlikely that this fully accounts for the difference between the groups. The initial study design included a regression analysis to explore the role of surgery type, prior history of trauma, time since surgery, time spent in hospital and social support as predictors of post-traumatic stress symptom severity; unfortunately, the lack of statistical power limited this analysis.

Subthreshold PTSD was also explored as research suggests that post-traumatic stress symptomatology is more common than diagnostic levels of PTSD following medical illness and treatment (8); furthermore sub-threshold PTSD is associated with negative co-morbidity such as depression, anxiety and reduced HRQOL. When considering both PTSD diagnosis and subthreshold PTSD, a quarter of the awake group could be considered to be experiencing clinically relevant trauma reactions, compared to 32% of the asleep group, suggesting that the groups may not differ considerably in the development of post-traumatic stress.

Symptom severity suggested PTSD presentations were mild, however the correlations with depression, anxiety and HRQOL highlight the extent of the psychological burden associated with post-traumatic stress within this sample. As previous literature did not explore symptom severity (19) this finding provides the first insight into the clinical severity of presentations within this population.

This study is the first within the field to explore PTSD and psychosocial outcomes following awake and asleep craniotomy via the use of standardised psychometric measures and within a stipulated post-surgery time period (3-12 months). Thus, the study builds on previous literature reporting negative post-operative psychological sequelae within an awake craniotomy population (19) by allowing for a comparison with asleep craniotomy. Furthermore, by recruiting participants within a specific post-surgery time period, the levels of chronic PTSD could be explored (1) and there is a reduced possibility of natural remittance of symptoms as research suggests this is more common after one year post trauma (40).

Limitations

Limitations of the present study are acknowledged. The desired sample size to detect a medium effect size was not reached, thus the study was underpowered, with the associated risk of type II errors, i.e. failing to observe an effect that is present. Whilst the findings

provide new insights into the outcomes for this neurosurgical population, and a preliminary exploration of differences between the two methods of craniotomy, it may have been beneficial to recruit a non-clinical control group to provide a comparator against which to compare the effect of surgery overall. Additionally, it would have been interesting to ask participants about their recall of the procedure for comparison between groups and to provide context to the findings. Furthermore, the cross-sectional design of the study restricts the interpretation of psychological outcomes as attributable to surgery.

Future Research

Whilst the results of this study are preliminary, the implication that one in five patients may experience PTSD following craniotomy warrants further exploration. If these findings are supported in future research, then studies to explore the predictors of PTSD development within this neurosurgical population and the differences between these two surgical groups are required. Once predictors of PTSD development are understood, studies could explore preventative interventions to reduce the rate of occurrence and inform service delivery.

Conclusions

This study explores the level of PTSD and psychosocial outcomes during a defined period (3-12 months) post awake and asleep craniotomy via the use of reliable and validated standardised measures. Despite an underpowered study, the preliminary findings suggest that post-traumatic stress is evident in the 3-12 months following craniotomy. Furthermore, surgery type appears associated with a substantial, but not statistically significant, difference in levels of PTSD diagnosis, with the asleep group presenting nearly twice the levels of diagnosable PTSD compared to the awake group. Additionally, the data highlights that post-traumatic stress symptom severity is correlated with depression, anxiety and reduced HRQOL. Further research is warranted to explore whether these findings are representative

of the population and to investigate whether surgery type has a significant effect upon psychological outcomes. Through this, the clinical implications of these findings upon service delivery can be considered.

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Appendix A

Appendix A: British Journal of Neurosurgery Author Guidelines

British Journal of Neurosurgery
Instructions for Authors

The ***British Journal of Neurosurgery*** welcomes original contributions from all parts of the world that present significant and important new findings. Papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere, that they are subject to editorial revision and that the Editor-in-Chief is responsible for the order of publication.

Manuscript Preparation
All manuscripts should be written in English and typed in double spacing (including references and figure legends). Spelling should be in English not American style, e.g. tumour and haemorrhage as opposed to tumor and hemorrhage. When referring to scales such as the Glasgow Outcome Scale, outcome should be referred to in words and not numbers in order to avoid ambiguity.

All submissions should be made online at the ***British Journal of Neurosurgery's*** ScholarOne Manuscripts site.

Manuscripts should be accompanied by a cover letter signed by the corresponding author, which should be scanned and uploaded as an attached file. The cover letter should include the statement "*No work resembling the enclosed article has been published or is being submitted for publication elsewhere. We certify that we have each made a substantial contribution so as to qualify for authorship as detailed at the end of the manuscript. We have disclosed all financial support for our work and other potential conflicts of interest*".

Authors must declare and submit copies of any manuscripts in preparation or submitted elsewhere that are closely related to the manuscript to be considered. Potential financial interests and funding sources must be disclosed to the Editor-in-Chief in a covering letter and will be acknowledged at publication. Any attempts at dual publication will be referred back to the head of the author's host institution for appropriate action.

Editorial correspondence will be by e-mail to the person given as corresponding author. This should be someone whose address is likely to remain permanent until the time of possible publication and for at least a year thereafter. Preferably, the corresponding author should be the most senior author - that is a person whose address is not likely to change.

Authors, Contributors and Guarantors
The ***British Journal of Neurosurgery*** does not believe that authorship should be artificially constrained by numbers but authors must be able to identify how they have made substantial contributions to the conception, design and conduct (including recruitment and counselling of patients) of the study, data collection and interpretation to the writing of the paper (including revising it critically for important intellectual content) and final appraisal for publication. In the new world of research governance, all authors will be held publicly responsible for the content of the paper but one author should be nominated as the guarantor. At the end of the paper authors should briefly outline their individual contributions and any conflicts of interest

should be declared. (Rennie D, Flanagin A, Yank V, The contributions of authors JAMA, July 5,2000; 284(1):89-91 and www.icmje.org).

Patient Consent
All papers that include identifiable patients will require consent from the patient (or assent from the family if the patient has died) to publish any information that might alone or in combination identify a patient, whether living or dead, adult or child. Case reports that include such data will not even be sent out for review until appropriate consent is provided by the authors. Download the Consent Form, obtain consent, and upload scanned copy with the submission as an attached supplementary file and not within the manuscript.

Randomised Controlled Trials
Reports of randomised controlled trials should conform to the revised Consort Statement (www.consort-statement.org) The ***British Journal of Neurosurgery*** would be prepared to review any neurosurgical trials, whether with a positive or negative outcome, which have not been published except as an abstract under the Medical Editors Trial Amnesty arrangement. (Br J Neurosurg 1998;12:183-184)

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The ***British Journal of Neurosurgery*** welcomes submissions in the following categories:
Original Articles
The recommended maximum length of an original article is up to 4500 words. This should be in the form of a title page including author and institution details. The first page of the text should be a structured abstract of not more than 300 words followed by a maximum of 5 key words. The text in original articles should be presented under the headings: Introduction, Material(s) and Methods, Results, Discussion, Conclusion(s), Declaration of Interest, Acknowledgements and up to 40 references.

Please see below for more information of Declaration of Interest and Acknowledgement sections.

Short Reports and Case Reports
Case reports will be published in the Short Reports section of each issue and should be restricted to 1000 words, be headed by an abstract of no more than 50 words followed by Clinical Details and Discussion. A maximum of two images/tables and three most relevant references should be included. When preparing a case report, authors should consider the following criteria (Sarnat HB, Lee RG, The case report: clutter or contribution to medical literature. Can J Neurol Sci.1988;15:1-2):

1. Does the case offer insight into the aetiology or pathogenesis of the disease?
2. Does the case provide positive (or negative) evidence of a new or improved treatment that might benefit (or harm) patients?
3. Does the case describe an unrecognised association of two or more diseases that is more than random coincidence?
4. Does the case describe a new disease not previously recognized, or confirm previous case reports of this disease?

Review Articles and Invited Articles
The Journal welcomes unsolicited and solicited reviews. These should cover areas of current interest and should be well researched. They should be to a maximum of 6000 words and should include an abstract of 300 words, 5 key words and up to 40 relevant references.

Acknowledgments and Declaration of Interest sections
Acknowledgments and Declaration of interest sections are different, and each has a specific purpose. The Acknowledgments section details special thanks, personal assistance, and dedications. Contributions from individuals who do not qualify for authorship should also be acknowledged here. Declarations of interest, however, refer to statements of financial support and/or statements of potential conflict of interest. Within this section also belongs disclosure of scientific writing assistance (use of an agency or agency/ freelance writer), grant support and numbers, and statements of employment, if applicable.

Acknowledgments section
Any acknowledgments authors wish to make should be included in a separate headed section at the end of the manuscript preceding any appendices, and before the references section. Please do not incorporate acknowledgments into notes or biographical notes.

Declaration of Interest section
All declarations of interest must be outlined under the subheading “Declaration of interest”. If authors have no declarations of interest to report, this must be explicitly stated. The suggested, but not mandatory, wording in such an instance is: The authors report no declarations of interest. When submitting a paper via ScholarOne Manuscripts, the “Declaration of interest” field is compulsory (authors must either state the disclosures or report that there are none). If this section is left empty authors will not be able to progress with the submission.

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References
References should be denoted in the text by superscript numbers and listed at the end of the paper in the order in which they appear. Quote the titles of journals as abbreviated in Index Medicus. References should be cited according to the Uniform requirements for manuscripts submitted to biomedical journals (4th edition, 1993) the Vancouver rules, as follows:
Article in a journal

Gleave JRW, Macfarlane R. Cauda equina syndrome: what is the relationship between timing of surgery and outcome? *Br J Neurosurg* 2002;16:325-328
List all authors but if the number exceeds six give first three followed by *et al.*
Monograph
Jennett B, The vegetative state. Cambridge: CUP 2002
Book chapter
Gjerris F, Borgesen SE, Pathophysiology of cerebrospinal fluid circulation. in Crockard A, Hayward R, Hoff JT, Neurosurgery - The scientific basis of clinical practice. Blackwell Science, 2000:147-168

Tables and Illustrations
Type each table double-spaced on a separate sheet. Number the tables consecutively (roman numerals) and supply a brief title for each. Indicate in the margin of the manuscript the approximate position for each table and figure.

Figures
Figures should be the submitted the size the authors would wish them to be printed (single column figure no more than 80mm wide and double 160mm wide). Cost for print reproduction of colour illustrations must be borne by the authors. All files must be 300 dpi or higher. Please note that it is in the author's interest to provide the highest quality figure format possible.
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Appendix B

Appendix B: Quality Assessment of included studies

Quality Assessment: Qualitative Studies. Tool: Critical Appraisal Skills Programme; Qualitative Studies. (Yes= 1, No=0)

	Fletcher et al., 2012	Howie et al., 2015	Khu et al., 2010	Palese et al., 2008	Manchella et al., * interview with open and closed questions
Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes	Yes
Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes	Yes
Was the recruitment strategy appropriate to the aims of the research?	Yes	Yes – however small sample size	Yes	Yes	Yes
Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes	Yes	Yes
Has the relationship between researcher and participants been adequately considered?	No	No	No	No	No
Have ethical issues been taken into consideration?	Yes	Yes	Yes	Yes	No
Was the data analysis significantly rigorous?	Yes	Yes	Yes	Yes	Yes
Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes
How valuable is the research?	Adds to understanding of the importance of doctor-patient relationship (1)	Informs understanding of patient experience of the procedure however generalisability limited by sample size (1)	Provides useful recommendations for clinical practice (1)	Findings are informative to clinical practice with explicit recommendations (1)	Informative regarding patient experience supporting use of awake craniotomy technique. (1)
Total (max= 10)	9	10	9	9	8

Quality Assessment: Survey studies - CEMBa Centre Evidence Based Management – Critical Appraisal of a Survey (CT= Can't tell)

	Bajunaid & Ajlan, 2015	Beez et al., 2013	Danks, Rogers, Aglio, Gugino, & Black, 1998	Goebel, Nabvi, Schubert, & Mehdorn, 2010	Manninen, Balki, Lukitto, & Bernstein, 2006	Milian et al., 2013	Wahab, Grundy, & Weidmann, 2011	Whittle, Midgley, Georges, Pringle, & Taylor, 2005	Wrede et al., 2011
Did the study address a clearly focused question / issue?	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Is the research method (study design) appropriate for answering the research question?	CT	CT	Yes	Yes	Yes	Yes	Yes	CT	Yes
Is the method of selection of the participants clearly described?	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No
Could the way the sample was obtained introduce (selection) bias?	No	CT	No	No	CT	No	CT	CT	CT
Was the sample of subjects representative with regard to the population to which the findings will be referred?	No	Yes	Yes	Yes	Yes	Yes	CT	Yes	Yes
Was the sample size based on pre-study considerations of statistical power?	N/A (no statistical analysis)	CT	CT	No	CT	CT	CT	CT	CT
Was a satisfactory response rate achieved?	Yes	CT	Yes	CT	CT	Yes 50%	Yes- 75%	CT – doesn't state number contacted.	CT

Are the measurements (questionnaires) likely to be valid and reliable?	CT	CT	Yes	CT	CT	(2 measures, 1 x CT, 1 Y)	CT	CT	Yes
Was the statistical significance assessed?	No	For VAS scores, not question naire	CT	Yes	Yes	Yes	No	No	Yes
Are confidence intervals given for the main results?	N/A	No	No	No	No	Yes	No	No	Yes
Could there be confounding factors that haven't been accounted for?	Can't tell	N/A	Yes	CT	CT	No	CT	CT	No
Can the results be applied clinically?	No – small sample	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Total (max = 12)	2	3	8	6	5	9	4	3	7

Appendix C

Appendix C: DClinPsy Research Review Committee Approval

D.Clin.Psychology Programme
Division of Clinical Psychology
Whelan Building, Quadrangle
Brownlow Hill
LIVERPOOL
L69 3GB

Tel: 0151 794 5530/5534/5877
Fax: 0151 794 5537
www.liv.ac.uk/dclinpsychol

Rachel Aitchison
Trainee Clinical Psychologist
Doctorate of Clinical Psychology Programme
University of Liverpool
L69 3GB

27/10/2014

Dear *Rachel*,

RE: An exploration of PTSD and psychological adjustment following awake and asleep craniotomy

Thank you for our response to the reviewers' comments of your research proposal submitted to the Chair of the D.Clin.Psychol. Research Review Committee (*dated 27/10/2014*).

I can now confirm that your amended proposal (*dated 27/10/2014*) meet the requirements of the committee and have been approved by the Committee Chair.

Please take this Chairs Action decision as ***final*** approval from the committee.

You may now progress to the next stages of your research.

I wish you well with your research project.

Dr Peter Taylor
Vice-Chair D.Clin.Psychol. Research Review Committee

Appendix D

Appendix D: University Sponsorship Approval

LIVERPOOL HEALTH PARTNERS

Dr Pierce O'Carroll
Doctorate of Clinical Psychology,
Whelan Building,
University of Liverpool,
Brownlow Hill
Liverpool,
L69 3GB

Mr Alex Astor
Head of Liverpool Joint Research Office

University of Liverpool
Research Support Office
2nd Floor Block D Waterhouse Building
3 Brownlow Street
Liverpool

2. Inform the Research Support Office as soon as possible of any SAE's;

3. Approval must be gained from the Research Support Office for any amendments to, or changes of status in the study **prior to** submission to REC and any other regulatory authorities;

4. It is a requirement that Annual Progress Reports are sent to the NHS Research Ethics Committee (REC) following Favourable Ethical Approval. You must provide copies of any reports submitted to REC and other regulatory authorities to the Research Support Office;

5. Maintain the study master file;

6. Make available for review any study documentation when requested by the sponsors and regulatory authorities;

7. Upon the completion of the study it is a requirement to submit and an End of Study Declaration and End of Study Report to REC. You must provide copies of this to the Research Support Office;

The University also requires you to comply with the following:

1. University professional indemnity and clinical trials insurances will apply to the study as appropriate. This is on the assumption that no part of the clinical trial will take place outside of the UK. If you wish to conduct any part of the study in a site outside the UK or you wish to sub-contract any part of the study to a third party specific approvals and consideration of appropriate indemnity would be required;

If you have any queries regarding the sponsorship of the study or the above conditions please do not hesitate to contact the Joint Research Office governance team on 0151 794 8373 (email sponsor@liv.ac.uk).

Yours sincerely

Mr Alex Astor
Head of Liverpool Joint Research Office

Cc

Appendix E

Appendix E: NHS Ethics Committee Approval

study.

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

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System 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 approvals 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. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

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

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

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. 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 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*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Marsh]		01 August 2015
Interview schedules or topic guides for participants	1	14 January 2015
Letter from sponsor [Liverpool Health Partners]		04 December 2014

Letters of invitation to participant [Participant reminder letter Version 1 17.2.15]	2	17 February 2015
Participant consent form [Consent Form Version 1]	2	17 February 2015
Participant information sheet (PIS) [Participant Information Sheet]	2	17 February 2015
REC Application Form [REC_Form_28012015]	3.5	27 January 2015
Referee's report or other scientific critique report [University of Liverpool]	1	27 October 2014
Research protocol or project proposal	1	14 January 2015
Summary CV for Chief Investigator (CI) [Dr Pierce O'Carroll]		12 December 2014
Summary CV for student [Dr Rachel Aitchison]		
Summary CV for supervisor (student research) [Dr Perry Moore]		
Validated questionnaire [Patient Health Questionnaire 9]		
Validated questionnaire [Posttraumatic Stress Diagnostic Scale Parts 1 and 2]		
Validated questionnaire [Posttraumatic Stress Diagnostic Scale Parts 3 and 4]		
Validated questionnaire [Generalised Anixety Disorder 7 Item]		
Validated questionnaire [Multidemensional Scale of Perceived Social Support]		
Validated questionnaire [SF-36 Health Survey]		

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/

15/NW/0127	Please quote this number on all correspondence

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

Yours sincerely

Dr Lisa Booth
Chair

Email:nrescommittee.northwest-lancaster@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Mr Alex Astor*
Mr Dave Watling, The Walton Centre NHS Foundation Trust

Appendix F

Appendix F: Research and Development Department Approval

Non-CTIMP Permission

The Walton Centre NHS
NHS Foundation Trust

Excellence in Neuroscience

Dr P. Moore
The Walton Centre NHS Foundation Trust
Lower Lane
Fazakerley
Liverpool
L9 7LJ

Date: 31st March 2015

Dear Dr Moore,

Study Title: An exploration of PTSD and psychosocial adjustment following awake and asleep craniotomy study.

REC Reference: 15/NW/0127 R&D Reference: RG148-15 IRAS/CSP ID: 164063

Thank you for providing all of the documentation for the above study.

I am pleased to inform you that the above study has been given full R&D permission and you may begin this at the Walton Centre NHS Foundation Trust. This has been granted for the duration of the REC approval for your study.

Permission is granted on the understanding that the study is conducted in accordance with the Research Governance Framework, Trust policies and procedures, and all applicable legislation including, but not limited to, the Data Protection Act, the Health and Safety at Work Act, Human Tissue Act. As Principal Investigator you retain overall responsibility for compliance with these requirements by all members of the research team. The recruitment target is 56 patients for this study.

You must ensure that you read and understand the enclosed conditions of approval

Should you have any queries, or feel that we can be of assistance, please do not hesitate to contact a member of the R&D office on 0151 529 5446.

I would like to take this opportunity to wish you well with your research

Yours Sincerely,

DAVID GRIFFITHS R+D manager.

Dr M. Steiger
Director of Research, Development & Innovation

Appendix G

Appendix G: Participant Information Sheet

The Walton Centre NHS
NHS Foundation Trust
Excellence in Neuroscience

Participant Information Sheet

UNIVERSITY OF LIVERPOOL

Title of Project: An exploration of psychosocial adjustment following awake and asleep craniotomy.

You are being invited to take part in a research study because you have undergone brain surgery (craniotomy) with **[Surgeon's name]** at the Walton Centre. The study consists of completing questionnaires which will look at your experiences following the surgery. Before you decide to take part it is important that you understand why the research is being done and what it will involve.

What is the purpose of this study?

We are looking at the psychological outcomes (i.e. how we think and feel) following a craniotomy operation. Some people are 'woken up' during their craniotomies whilst other people have this operation under general anaesthesia; we are interested in the experiences of people following both types of surgery. During the study we will ask you specific questions about your experiences at the time of your surgery along with questions about how your mood has been recently. We will also ask questions about your day-to-day living and contact with family and friends.

Do I have to take part?

No, it is your choice. 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 if I consent to take part?

You will be contacted by the researcher who will discuss with you how you would like to take part, either over the telephone, face to face (at the Walton Centre) or via the internet (email address required). If you would like to attend a face to face appointment we may be able to reimburse reasonable travel expenses. An appointment will then be scheduled for you to complete the study. The study will take approximately 20 minutes to complete.

Why is this research useful?

There is currently very little research that helps to inform our understanding of the psychological effects of undergoing this type of surgery. Developing our understanding will help us plan services to meet the needs of our patients.

What will happen if I don't want to carry on?

You are free to withdraw at any time from the study without giving a reason and without it affecting your future care. If you chose to withdraw from the study any identifiable data will be destroyed and all non-identifiable data will be retained in the study.

Complaints

If you have a concern about any aspect of this study, you should contact the researchers on the details below and they will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do so in accordance with the NHS complaints procedure by contacting Research Officer Rebecca McDonald on 01515298006. So please keep this part of the information sheet for future reference.

What are the possible disadvantages and risks of taking part?

It is possible that you may find it upsetting to think about your current day-to-day circumstances, your inner thoughts and feelings. Should you wish to stop the study you can do so at any time. Should you wish to skip a question on a questionnaire this is also fine. If you feel you need to talk to someone further about any issues that have been then we can provide you details of how to access this (see contact details below).

What are the benefits of taking part?

By participating in this research and offering your own experiences, you will be helping us to understand how best to support people following this procedure.

As a **thank you** participants will be entered into a prize draw with the chance to win one of five Love2shop vouchers (three £25, one £50 and one £100) which can be used in a variety of high street stores!

Will my taking part be kept confidential?

All information you provide will be treated and stored confidentially. The only circumstances where we would be obliged to pass on information to other appropriate persons would be when there were concerns about yours or another's safety. In this situation, you would be made aware of what information would be passed on and to whom.

The consent form containing personal information will be locked in a secure place, and only the research team will have access to it. Any data and written results will be anonymised in accordance with the Data Protection Act 1998.

What will happen to the results of the study?

The data will be collected and anonymised so that your results cannot be identified, and analysed to write up for peer reviewed journals and for presentation at international conferences. The findings will also be written up in a newsletter and available to all patients.

Finding out more before deciding

If you would like more information on taking part in research in general please contact Patient Advice and Liaison Services (PALS) in the Customer Care Team:

Customer Care Team,
The Walton Centre NHS Foundation Trust,
Lower Lane,
Fazakerley,
Liverpool
L9 7LJ
0151 529 5530 or 0151 529 6100

Customer.CareTeam@thewaltoncentre.nhs.uk

If you would like to discuss this study further or if there are any questions you would like to ask, please contact the lead Clinical Neuropsychologist Dr Perry Moore at:

The Walton Centre NHS Foundation Trust,
Jubilee House,
Longmoor Lane,
Fazakerley
L9 7LJ
Telephone: 0151 529 5693

Thank you for taking the time to read this information sheet. Should you not wish to be contacted again about this study you may return the below slip in the prepaid envelope provided.

Appendix H

Appendix H: Participant Consent Form

Consent Form

Title of Project: An exploration psychosocial adjustment following awake and asleep craniotomy.

Name of Researcher: Rachel Aitchison (Trainee Clinical Psychologist)

Please initial the boxes

1. I confirm that I have read and understand the information sheet 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 relevant data collected during the study, may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to this data.	
4. I agree that if I disclose information regarding my safety and the safety of vulnerable others then this information will have to be disclosed to the relevant authorities.	
5. I agree to take part in the above study. My preference for participating is via telephone, face to face interview or online (email address required) (You may tick more than one option but will only be required to complete the questionnaires once).	

Please provide the following personal contact details where you would be happy for us to contact you directly.

Telephone number _____ Email address _____

Your Name	Signature	Date
_____	_____	_____
Researcher	Signature	Date
_____	_____	_____

Appendix I

Appendix I: Draft participant summary report- To be distributed upon completion of data collection.

Psychosocial adjustment following awake and asleep craniotomy; Study outcomes report for participants.

What was the study about?

A craniotomy is most often carried out whilst the person is under general anaesthesia; however sometimes when clinically indicated, this procedure is carried out with the person awake for part of the operation. There is currently very little literature looking at the psychological outcomes (i.e. how we think and feel) following both types of craniotomy. As we are keen to learn more about the ways we can effectively support our patients, we set out to explore the psychological outcomes for our patients following this neurosurgical procedure.

What did we do?

Approval was received from the local NHS Research and Ethics committee to carry out the study. As part of this study we invited people who had undergone a craniotomy at our hospital to take part in this research by completing a number of questionnaires. We started recruitment in 2015 and successfully recruited (TBC) people into the study.

During the study we asked participants questions relating to their experiences following the surgery along with questions about how their mood. We also asked you questions about day-to-day living and contact with family and friends.

What did we find?

The findings of this study indicated that the majority of participants had experienced low mood or anxiety following their craniotomy and some participants had experienced mild distress related to the surgery. However, it was positive to note that

the majority of participants who completed the study felt they were supported by those around them.

What next?

Now that we have completed this study we are hoping to publish the findings within a scientific journal. This will mean that a report about the study and its findings will be available to other clinicians and medical professionals working within a neurosurgical setting. By sharing these findings we hope to encourage further research within this area to build on our understanding and help us to shape our service provision. In particular, we hope to see larger scale projects which recruit a bigger sample in order to explore whether the findings we observed from this study are representative of the population group as a whole.

Accessing support

The study findings highlighted that some participants experienced psychological distress following their surgery such as low mood and anxiety. Undergoing a craniotomy is a significant life event and it is understandable that many people may experience changes in mood following this. However, if you feel you are experiencing distress, and would like advice or support, then this can be found via contacting your GP or through mental health charities, such as Mind. Mind can be contacted on **0300 123 3393** or info@mind.org.uk

We would like to take this opportunity once again to thank you for your involvement within this study. If you have any questions about this study you can contact (insert contact details).

Appendix O

Appendix O: Changes to Analysis

The proposed analysis strategy was to run four separate hierarchical multiple regressions with the five independent variables (PDS, PHQ-9, GAD-7, SF-36 physical and SF-36 mental) and the dependent variable of surgery type. A power analysis using G*power assuming a medium effect size, alpha of 0.05 and power of 0.8 reported a total sample of 56 (28 awake, 28 asleep) would be required. Unfortunately the final sample of 44, (16 awake, 28 asleep) failed to reached the target and thus the data were underpowered for regression analyses. As a consequence, the data were explored via univariate and bivariate analysis. Data collection continues post submission with a view to completing the proposed analytic strategy for publication.