The Efficacy of a Seizure Assessment Risk Tool in Predicting Occurrence of Tonic-Clonic Seizures

And Clinical Research Portfolio

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First and foremost I would like to thank Professor Jon Evans for all of his patience and guidance over the last couple of years. You have taught me so much that will stay with me for the rest of my career. Further huge thanks go to James Anderson for all your hard work and effort in setting up this research and also imparting your knowledge and humour along the way. I am truly thankful to you both.

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Additional Information

This is an additional note to inform the examiner that this Major Research Project (The Efficacy of a Seizure Assessment Risk Tool in Predicting Occurrence of Tonic-Clonic Seizures) is the second project proposed and planned by the student.

The initial research project which was accepted was entitled "Accelerated Forgetting in Temporal Lobe Epilepsy" and intended to look at the incidence of accelerated forgetting in patients with temporal lobe epilepsy who were undergoing EEG monitoring. The intention was to see if inter-ictal activity was correlated with accelerated forgetting of information, with a strong focus on anterograde autobiographical memories. This project received ethics approval through IRAS.

Unfortunately due to unforeseen technical issues within the EEG monitoring department, our projected participant sample was unable to be admitted and therefore we were unable to recruit.

As a result, this current project was proposed and carried out within a constricted timescale. All documents relating to the previous project are available on request.

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CHAPTER 1: SYSTEMATIC LITERATURE REVIEW

THE IMPACT OF TEMPORAL LOBE EPILEPSY ON AUTOBIOGRAPHICAL MEMORY: A SYSTEMATIC REVIEW OF THE LITERATURE

Prepared in accordance with guidelines for submission to the Journal of Epilepsy and Behaviour (see Appendix 1.1).

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Abstract

Background: Research has suggested that Temporal Lobe Epilepsy (TLE) has a negative impact on the ability to retrieve autobiographical memories. There are differing theories regarding the involvement of the medial temporal lobes and the hippocampus in the encoding, consolidation, and subsequent retrieval of autobiographical memories. The literature addresses differences in type of information which may be more difficult to retrieve, and the possible impact of lateralisation of TLE, with mixed results.

Aims: This review aims to answer the following questions through systematic review and methodology screening of the current research: Does temporal lobe epilepsy have a negative impact on autobiographical memory? What role does hippocampal atrophy play? Does this negative impact extend to both episodic and semantic memories? Does TLE impact the consolidation process of autobiographical memory? What role does epilepsy lateralisation have to play? Are there any other relevant areas highlighted by the research?

Methods: 16 studies were selected through a systematic search of online databases and further manual searches using eligibility criteria. A Quality Criteria Appraisal Questionnaire was developed and the selected articles were rated accordingly and results were synthesised.

Results: There is a consensus within the literature that TLE does have a negative impact on autobiographical memory. Few studies investigated hippocampal atrophy directly, however those that did noted a correlation between hippocampal abnormalities and deficits in autobiographical memory in TLE populations. The majority of studies found deficits in autobiographic episodic information, however only a very small sample found similar deficits for semantic information. The studies which considered anterograde memory and the impact of TLE on the consolidation process suggest that TLE disrupts the consolidation of memories, leading to accelerated forgetting of autobiographical information in TLE populations. There is also indication that seizure activity can impact

memories consolidated prior to epilepsy onset, however these results are mixed. There are also mixed results regarding the impact of epilepsy lateralisation, however the majority of the studies conclude that both right and left TLE have a detrimental impact on autobiographical memory retrieval. Finally, there appear to be other factors which may also contribute to autobiographical memory deficits, including seizure frequency and polypharmacy.

Conclusion: Improvements could be made to standardise the research methodology in regards to studying TLE and memory deficits. This could include consideration of the impact of abnormal hippocampal structures through more stringent assessment in recruitment stages and ensuring standardisation of the tests of autobiographical memory. The review also highlighted the lack of neuroimaging studies. The review also considers the possible clinical implications of our understanding of autobiographical memory deficits and how these may be addressed.

Keywords: Temporal Lobe Epilepsy, Autobiographical Memory, Hippocampus, Lateralization, Consolidation

1. Introduction

Epilepsy is a common neurological disorder thought to affect around 50 million people worldwide, making it one of the world's most prevalent neurological conditions [1]. People with epilepsy often report cognitive difficulties. There is no consistent profile of cognitive impairment that fits all epilepsy sufferers, however, as epileptic activity is more commonly found within the fronto-temporal networks, the most common impairments tend to be memory, attention and processing speed [2] . Temporal Lobe Epilepsy (TLE) is a specific form of epilepsy originating from the temporal lobes. Features of a TLE seizure can include aura, motionless stare, oral or manual automatisms, and distonic posturing.

Temporal lobe structures are involved in the encoding and storage of memories within the neocortex [3]. The medial temporal lobe system houses structures such as the hippocampus, parahippocampal cortex, fornix and mammillary bodies, which are believed to contribute to the process of memory consolidation, in which memories move from a form of temporary representation to being more permanently established[4]. Given the impact that epileptic seizures can have on neural anatomy, it is reasonable to expect that epileptic activity within the medial temporal regions will disrupt the memory consolidation process, and possibly also impact on the retrieval of previously stored memories, something that is particularly relevant to debates concerning the specific role of medial temporal structures in memory consolidation.

1.1 Theories of Memory Consolidation and Retrieval

There are two main competing theories of medial temporal, and specifically hippocampal, involvement, in memory consolidation. The Standard Consolidation Model (SCM) [5] suggests that the role of the hippocampus is to encode all aspects of memory, including semantic and episodic information, and consolidate this in the wider neocortex. The length of this consolidation process can vary. This model theorises that consolidation is dependent on the hippocampus, however once these memories have been consolidated, the hippocampus is redundant in terms of their retrieval.

The Multiple Trace Theory (MTT) [6] suggests that the hippocampus has a life-long role in accessing episodic memories, and is always necessary to achieve the level of

autonoetic consciousness associated with rich autobiographical memories [7]. The MTT suggests that the hippocampus lays down multiple cortical traces and relationships within the cortex. These links can subsequently be strengthened by further activations or by extra hippocampal memory processes. These could be via other connections within the hippocampal cortex, such as mammiliary bodies, fornix or parahippocampal tissues or through cortical co-activation. MTT posits that semantic knowledge exists consolidated within the cortex and can be accessed without requiring full functioning of the hippocampus. However it also states that the full memory engram including episodic and perceptual details is retained in the hippocampus and so this structure is necessary for all of the components of specific episodic memories to be retrieved and re-experienced. There is still debate on exactly what the hippocampal region's involvement in the recall of autobiographical memories is in relation to these theories [8].

Many studies considering the impact of damage to the medial temporal structures have looked at deficits within the Temporal Lobe Epilepsy (TLE) population, due to the physical damage which can occur to the temporal and hippocampal regions as the result of prolonged seizure activity. As mentioned previously, individuals with TLE often report memory difficulties. In terms of this research in relation to the two possible theories of memory retrieval, if the SCM was correct, we would expect people with TLE to display a temporal gradient in recall, whereby more recent memories are more poorly recalled than distant memories due to earlier memories having been consolidated in the neocortex while more recent memories would not be properly consolidated due to hippocampal damage. However, if the MTT is correct, we would expect a flat gradient in autonoetic recall due to the requirement of the hippocampus for fully integrated autobiographical memories.

Several studies have shown that individuals with TLE report autobiographical memory (AM) deficits [9]. Some of these studies have indicated that the nature of these AM difficulties tends to show more of a difficulty with episodic retrieval and a lack of perceptual richness to the individual's memory with a general retention of the semantic facts of the event [10]. These findings are consistent with MTT. However, some studies

also suggest that personal semantic information is also impacted which may counteract the MTT hypothesis [11].

The impact of TLE on the consolidation of new autobiographic memories has a relatively small evidence base. Studies have begun incorporating anterograde measures of autobiographic episodic information to further inform our understanding of the medial temporal involvement in this process [8][12], however this is still a relatively new area of research. One particular form of deficit that is apparent in some individuals with TLE is the phenomenon of accelerated forgetting [13]. Individuals with TLE perform to an equivalent level as their non-epileptic counterparts on immediate recall and standardised test delays of 30 minutes, but over longer time periods (days/weeks) their performance considerably declines disproportionately to healthy controls [14][15][16]. The majority of the research has focused on standard tests of visual and verbal memory, however more recently research has begun to focus on the occurrence of accelerated forgetting within the domain of AM [9]. AM deficits may increase the burden and the frustration of an individual's experience of epilepsy, and so this is an important area for researchers to consider. An interesting development in the field has been the move towards developing real life tasks to measure the impact of TLE on anterograde AM [12].

One aim of this review is to examine research investigating retrograde and anterograde AM, looking at the characteristics of any impairment and determining whether results are more consistent with SCM or MTT.

1.2 The Effects of Lateralisation

Another question which has arisen within the literature on memory and TLE is the impact of lateralisation of epilepsy, and if this alters the modality, or the extent of memory deficits. Markowitsch [17] proposed that the left hemisphere was responsible for holding semantic information and the right hemisphere for episodic information. Based on this theory we would expect that individuals with TLE originating from the left temporal lobe (LTLE) would show impairments in semantic memory, and those with right originating

TLE (RTLE) would show episodic memory deficits. However, the literature addressing this area shows mixed results. In terms of autobiographical memory, there has been evidence that both LTLE and RTLE show similar deficits in perceptual richness of their episodic memories [11]. However, some studies show that LTLE have deficits in their autobiographical episodic recall while RTLE seem relatively unimpaired [12]. Other studies have shown that, while both LTLE and RTLE show deficits in episodic recall, the RTLE individuals show a significantly greater impairment than their LTLE counterparts [18]. At present there does not seem to be a unified understanding of the impact, if any, of TLE lateralisation.

As the research in this area expands and diversifies, it would be helpful at this stage to review the current literature, taking into account methodological quality, with a view to clarifying some of the discrepancies and informing future directions.

1.3 Objectives of Review

This review aims to identify and evaluate the literature relating to autobiographical memory difficulties in individuals with temporal lobe epilepsy. Considering the main themes of the literature so far, we wish to address the following questions:

- Does temporal lobe epilepsy have a negative impact on autobiographical memory?
- What role does hippocampal atrophy play?
- Does this negative impact extend to both episodic and semantic memories?
- Does TLE impact the consolidation process of autobiographical memory and are results more consistent with SCM or MTT?
- What role does epilepsy lateralisation have to play?
- Are there any other relevant areas highlighted by the research?

2. Method

2.1 Identification of Papers

2.1.1 Electronic Databases

An initial search was conducted with the assistance of a research librarian to identify common and alternative terms for use in the systematic search and also to identify which databases were most relevant. Some databases, including EMBASE and CINHAL were excluded from the systematic search following the initial trial searches, as these were deemed to not contain papers relevant to our search. The following electronic databases were searched using the terms and search strategy outlined below: PsychINFO, Psychology and Behavioural Sciences Collection, Medline, and PsychArticles.

2.1.2 Search Strategy

An initial search was carried out using the following primary terms:

- Autobiographical Memory
- Temporal Lobe Epilepsy

A detailed search was then conducted using the following terms:

- Autobiograph* OR autobiographical memory
- Epilep* OR Epileptic Seizures OR experimental epilepsy
- Temporal lobe OR temporal lobe epilepsy

"*" represents the unlimited truncation command, which will identify all words which begin with a common prefix.

Following this search, the results within each database were combined with AND.

The results of the searches were combined within Refworks, and duplicates were removed. The remaining articles were then subject to the inclusion and exclusion criteria as described below.

Hand searching of full journals was not employed as searching of electronic databases was deemed adequate in identifying all relevant papers. A hand search of the reference lists of all relevant articles was also conducted to identify any papers that had not been included in the database search. These were subsequently examined on the basis of title, abstract, or full text as appropriate. No additional papers were identified through this method.

2.2 Inclusion and Exclusion of Articles

The following inclusion and exclusion criteria were used to select the studies for this review:

2.2.1 Inclusion Criteria

The following inclusion criteria were applied during the literature search:

- Papers published in peer-reviewed international journal
- Papers published in English
- Population with a diagnosis of TLE
- Specific Measurement of AM

2.2.2 Exclusion Criteria

The following exclusion criteria were applied during the literature search:

- Case studies
- Animal research

- Non- clinical research papers (such as letters, comments and discussion papers)
- Unpublished dissertations
- Research using participants under 18 years of age
- Studies published in a foreign language whose translation was not freely accessible
- Research using populations with an intellectual disability
- Book chapters
- Review papers

Journal articles were initially excluded on the basis of their titles, then their abstracts by screening these for relevance to the review topic. Studies deemed to comply with the review topic were then obtained in full and examined in respect of the above criteria. A total of 16 studies were selected for inclusion within this review. This process is outline in Figure 1.

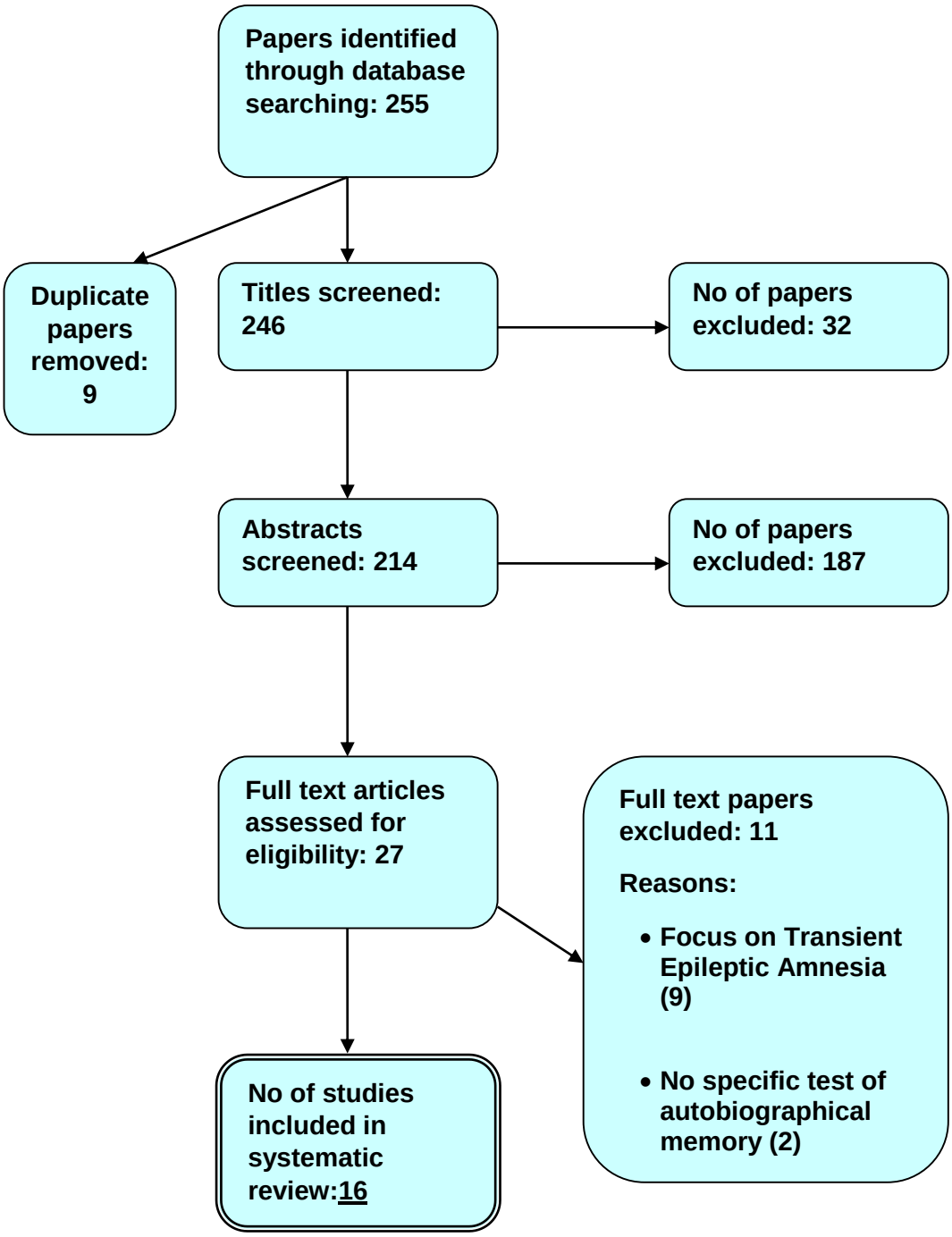

Figure 1. Flow diagram of papers screened

2.3 Quality Criteria Appraisal Questionnaire

A checklist for this review was developed in order to address the quality and appropriateness of the selected studies. The criteria were drawn from aspects of the Scottish Intercollegiate Guidelines Network (SIGN) [19] checklist for case-controlled studies, and the CONSORT Guidelines [20]. Aspects were taken from these quality assessment tools as they are highly regarded, evidence based recommendations which provide clear guidelines for how research should be structured, and set a gold standard for appraisal of research literature. These were modified where relevant to our chosen area of review. Additional questions were produced based on the relevant methodological issues that arise in studies specifically focusing on TLE as informed by previous research. The maximum achievable Quality Rating score was 11. The questions asked of each paper were as follows:

Methodology

1. The study outlines an appropriate and clearly focused question (yes=1; no=0)

2. Was the methodology clearly defined? Could you repeat the study on reading the paper? Was there a methods and procedure section? (yes=1; no=0)

3. Has the test of Autobiographical Memory demonstrated validity or reliability? (yes=1; no/not reported=0)

Participants

4. Was a diagnosis of TLE obtained prior to participation in the study and is the diagnostic process clearly documented? (yes = 1; no=0)

5. Was a seizure history obtained for each participant, including age of onset and seizure frequency? (yes=1; no=0)

6. If a control group was used, were they matched to the experimental group with respect to age and educational level? (yes=1; no=0)

7. Are there clear exclusion criteria and do they include other neurological disorders? (yes=1; no=0)

8. Is the presence and extent of hippocampal sclerosis obtained for each participant? (yes=1; no=0)

Analysis

9. Is the analysis appropriate to the design and the assessments used, and the type of data generated? (yes=1; no=0)

10. Did the paper address trial limitations, potential sources of bias, imprecision, and, if relevant, multiplicity of analyses? (yes=1; no=0)

11. Were the conclusions drawn appropriate for the interpretation of the results generated? (yes=1; no=0)

2.4 Inter-rater Reliability

All 16 papers were rated by the lead author. In addition, a random sample of six papers was selected and rated by two Trainee Clinical Psychologists, rating three papers each. There was 96% agreement, with just seven discrepancies across these six studies. Five of these were misunderstandings by the external raters of what constituted hippocampal "sclerosis", and it was agreed that the identification of a hippocampal lesion was sufficient to gain a mark in the checklist. The remaining two discrepancies concerned the exclusion criteria. The external raters noted that in two of the articles [21][22] the exclusion criterion, namely other neurological disorders, was only outlined for the control participants. Due to this, it was decided that these papers should lose a mark for this question.

2.5 Data Collection and Synthesis

After initial screening of the literature, the following list was compiled to guide data extraction and synthesis of the included papers:

- Participant group and attributes (number, diagnosis, lateralisation)
- Test of Autobiographical Memory used
- Main findings relating to autobiographical memory in the context of TLE

- Main findings in regards to the aims of our study (epilepsy lateralisation, impact of hippocampal atrophy, episodic vs semantic memories)

Data were extracted from each paper manually by the individual researcher and entered into a summary table along with their quality rating score.

3. Results

Table 1 contains a summary of each paper included in this review. It describes the participant populations, the tests of AM used, and a summary of the main findings. Effect sizes are included where possible. The final column contains the Quality Rating Score obtained for each paper, and entries are ranked according to their quality score. Please see Appendix 1.2 for full quality scoring for each paper.

Table 1: Summary of the study characteristics plus the scores received on the Quality Criteria Checklist

Study	Participants	Autobiographical Measures	Main Findings	Quality Score
Addis et al. (2007) ***Canada***	Patient Group n=11; LTLE (5 male, 6 female) Control Group n=14 (6 male, 8 female; healthy adults with no neurological or psychiatric diagnosis)	**Retrograde** Autobiographical Interview (AI) fMRI paradigm – retrieving specific autobiographical memories in response to personalised cues	***AI data*** -LTLE group showed a mild deficit for retrograde episodic memory retrieval approaching significance (Effect Size: d=0.378; medium effect) -LTLE group retrieved significantly fewer episodic details in their autobiographical memories (Effect Size: d=0.53; large effect) -no group difference for semantic retrieval ***fMRI data*** - lower activation of AM network in LTLE group, particularly in hippocampus - reduced signal strength in left hippocampus of LTLE group - increased signal strength for extra-hippocampal nodes in LTLE group suggesting compensatory mechanisms.	11

Lah et al. **(2006)** ***Australia***	Patient Group n=29 TLE (12 male, 17 female; surgical candidates) RTLE n=14; LTLE n=15 Control Group n=15 (6 male, 9 female; no information regarding recruitment)	**Retrograde** Autobiographical Fluency Test (AFT)	- Both LTLE and RTLE recalled fewer semantic autobiographical memories compared to controls. - Only RTLE group recalled significantly fewer episodic autobiographical memories compared to controls. LTLE group performed below controls but this difference failed to meet significance (p=0.07) -patients receiving polypharmacy showed significantly poorer autobiographic episodic recall than those on monopharmacy (Effect Size: d=1.2; large effect).	11
Múnera et al. **(2014)** ***Argentina***	Patient Group n=20 TLE (12 male, 8 female; surgical candidates) LTLE n=10; RTLE n=10 Control group n=20 (12 male, 8 female; no information regarding recruitment)	**Retrograde** Autobiographical Interview (adapted) -3 stages: free recall, general probe and specific probe (semi-structured interview to obtain further details)	- TLE significantly lower recall for episodic details compared to controls but only after specific probe condition -RTLE recalled significantly fewer episodic memories after specific probe compared to controls -LTLE retrieved higher amounts of semantic details compared to control during recall however this difference disappeared after specific probe condition. No overall differences between TLE group and control group for semantic recall -both TLE groups had poorer performance compared to controls for each life period, but only statistically significant for adolescence after specific probe.	11

			(Unable to calculate Effect Sizes)	
Voltzenlogel et al. **(2006)** ***France & Germany***	Patient group n= 38 (12 male, 26 female; surgical candidates) LTLE n=19; RTLE n=19 Control group n=35 (13 male, 22 female; healthy matched controls)	**Retrograde** Autobiographical Memory Interview (AMI) Modified Crovitz Test	-both RTLE and LTLE recalled significantly fewer autobiographic incidents on the AMI. -RTLE group performed significantly better than LTLE on AMI episodic section. -There was no difference between controls and TLE patients on recall of personal semantic information -Both RTLE and LTLE recalled fewer autobiographic episodes using the Modified Crovitz Test than controls. RTLE recalled significantly more than LTLE. (Unable to calculate any Effect Sizes)	10
Voltzenlogel et al. **(2014)** ***France***	Patient group n=71 (28 male, 43 female; pts with refractory epilepsy) High seizure frequency (seizures weekly) n=31 Low seizure frequency (seizures monthly) n=40 Control group n=35 (13 male, 22 female; healthy matched	**Retrograde** Autobiographical Memory Interview -semantic section Modified Crovitz Test	-no difference between TLE participants and controls for recall of personal semantic information -both LTLE and RTLE groups were significantly impaired on recall of personal events information -high seizure frequency group significantly more impaired on recall of personal events than low seizure frequency group (Unable to calculate Effect Sizes)	10

	controls)			
Herfurth et al. **(2010)** ***Germany***	Patient group n=54 (30 male, 24 female; no recruitment information) TLE n=47; ETE n=7 Control group n=38 (17 male, 21 female; no recruitment information)	**Retrograde** Autobiographical Memory Interview (AMI) Rating of emotional valence and intensity of memories	-patients with LTLE were significantly impaired in recall of childhood episodic specific memories compared to RTLE (Effect Size: d=1.46; large effect) and early childhood episodic memories (Effect Size: d=1.3; large effect size). -LTLE trended towards impairment for perceptual richness of childhood episodic memories however this did not reach significance (Effect Size: d=1.1; large effect). -both RTLE and LTLE were significantly impaired for episodic richness and specificity compared with controls -patients with ETE only differed from controls by trend -patients with LTLE recalled significantly less personal semantic information compared to controls, although less pronounced than for episodic. This was most pronounced for childhood memories (Effect Size: d=0.98; large effect). -TLE group rated their memories as less emotionally positive and intensive – emotionally neutral (Effect Size: d=0.56; large effect)	9.5

Ricci et al. **(2015)** ***Australia***	Patient Group n=32 (no information regarding gender, recruited from Epilepsy Service in hospital) TLE n=21 (with and without hippocampal lesions: TLE+ n=12; TLE- n=9) Extra-temporal epilepsy (ETE) n=11 Control Group n=29 No information regarding gender distribution or recruitment)	**Anterograde** Autobiographical experience recall and recognition task	-patients with TLE plus hippocampal lesions showed poorer recall of autobiographic information at delays of 30 mins and 24hrs compared to controls and ETE (Effect Size: η^2=0.29; large effect) - hippocampal lesions most significant factor for memory decay in first 24hrs (Effect Size: η^2=0.49; large effect) - patients with ETE showed poorer recognition than controls (Effect Size: R^2=0.31; large effect)	9
Narayanan et al. **(2012)** ***Scotland***	Patient Group n=15 TLE (7 male, 8 female; recruited through epilepsy clinics in hospitals) LTLE n=9; RTLE n=6 Control group n=17 (3 male, 14 female;	**Anterograde** Autobiographical Event Test (AET) -staged event tested for recall	-LTLE were significantly poorer than controls on recall of the autobiographical memory task at a delay of 4 weeks (Effect Size: d=1.16; large effect). No significant difference was found for RTLE. -patients with a unilateral abnormal left hippocampus showed significantly poorer performance than controls on the AET recall task at 4 week delay (Effect Size: d=1.54; large effect) -patients who experienced generalised seizures	9

	relatives and volunteers)		after the initial assessment showed higher decay of autobiographical memory. This was not significant (p=0.065) however the effect size was large (d=1.54). -no correlation was found between hippocampal volume and performance on AM task.	
St-Laurent et al. **(2011)** ***Canada***	Patient group n=25 (8 male, 17 female; recruited through Toronto epilepsy programme) LTLE n= 14; RTLE n=11 Control Group n=20 (9 male, 11 female; recruited through staff and community advertising)	**Retrograde** Autobiographical Interview (adapted)	-both RTLE and LTLE reported significantly fewer episodic details of autobiographical events compared to controls. They also reported fewer temporally specific and temporally indefinite actions and events (Unable to calculate Effect Size). -LTLE patients had significantly lower scores of temporal coherence of their autobiographical memories compared to controls. This was not true for RTLE patients (unable to calculate Effect Size)	9
Tramoni et al. **(2011)** ***France***	Patient group n=5 TLE (4 male, 1 female; recruited through memory clinic) Control group n=5 (1 male, 4 female;	**Retrograde** 2 semi structured interviews prompting recollection of past personal episodes, using verbal and visual cues **Anterograde**	***Retrograde*** - found TLE patients displayed a U shaped pattern of forgetting for autobiographic episodic material, with early and recent memories being preserved, but poorer recall and recognition for memories in the last 5-10 years.	9

	spouses of patients)	Memorising a chain of events through a staged event (recall and recognition at one hour and six weeks)	***Anterograde*** TLE group retrieval of episodic memory task was significantly poorer at 6 week delay for both recall and recognition compared to controls (Unable to calculate Effect Sizes)	
St-Laurent et al. **(2009)** ***Canada***	Patient group n=25 (8 male, 13 female; recruited through Toronto epilepsy programme) LTLE n= 14; RTLE n=11 Control Group n=19 (6 male, 8 female; recruited through staff and community advertising)	**Retrograde** Autobiographical Interview (adapted)	-both LTLE and RTLE recalled significantly fewer internal details (details pertaining specifically to that event) than controls for both event specific memories (Effect Size: d=1.19; large effect) and generic memories (Effect Size: d=1.21; large effect)	8
Viskontas et al. **(2000)** ***Canada***	Patient group n=25 (surgical candidates and post-surgical patients; no information regarding gender distribution) RTLE n=11; LTLE	**Retrograde** Autobiographical Memory Inventory (AMI)	-both RTLE and LTLE performed significantly poorer on episodic recall of autobiographic memories. -no significant difference on semantic memory (Unable to calculate Effect Sizes)	8

	n=14 Control group n= 22 (Healthy matched controls; no gender distribution information)			
Park et al. **(2011)** ***Canada***	Patient group n=25 (8 male, 17 female; recruited through Toronto epilepsy programme) LTLE n=14; RTLE n=11 Control group n=21 (10 male, 11 female; recruited through staff and community advertising)	**Retrograde** Autobiographical Interview (adapted)	-TLE patients were less likely to use the Historical Present (HP) when recalling autobiographical memories -TLE patients recall fewer details and temporal specificity within episodic memories (Unable to calculate Effect Sizes)	8
Protzner et al. **(2013)** ***Canada***	Patient Group n=23 TLE (10 male, 13 female, recruited through Toronto epilepsy programme) LTLE n=10; RTLE n=13	**Retrograde** fMRI paradigm – Participants instructed to retrieve autobiographical memories silently in response to a cued event title	-BOLD signal variability in the medial temporal lobes, including the hippocampal regions, was shown to be positively correlated with autobiographical memory performance (unable to calculate Effect Size) -this was not true for signal amplitude	8

	No control group			
St-Laurent et al. **(2014)** ***Canada***	Patient group n= 31 (13 male, 18 female, recruited through Toronto epilepsy programme) LTLE n= 14; RTLE n=17 Control group n=15 (3 male, 12 female; recruited through staff and community advertising)	**Retrograde** Participants recalled cued autobiographical memories alongside laboratory shown film clips and narratives. They also rated their memories for story content and vividness	-TLE patients perceived themselves to have retrieved fewer memories than controls -TLE patients recalled significantly fewer perceptual details within their autobiographic episodic memories than controls -TLE patients recalled significantly fewer perceptual details than story details -no differences found between RTLE and LTLE (Unable to calculate Effect Sizes)	8
Metternich et al. **(2013)** ***England***	Patient group n=12 (2 male, 9 female; recruited in hospital and research facilities) LTLE n= 7; RTLE n= 4 Control group n= 15 (4 male, 11 female; no information regarding recruitment)	**Retrograde** Cued recall questionnaire on a 'Flashbulb Memory' event (Death of Princess Diana) and a control event (Hong Kong's reunion with China) questioning details of the event and emotional impact ratings. Questionnaire administered twice and consistency of answers was measured	-LTLE had significantly lower overall consistency scores than controls (Effect Size: d=1.5; large effect) -there was no significant difference for RTLE on overall consistency (Effect Size: d=0.38; medium effect). -both LTLE and RTLE had significantly lower consistency scores for canonical items (e.g. time of day, presence of others) compared to controls (Effect Size: d=1.1; large effect; d=1.46; large effect, respectively).	7

Key

AET: Autobiographical Event Test (Narayanan et al. 2012)

AFT: Autobiographical Fluency Test (Dritschel et al. 1992)

AI: Autobiographical Interview (Levine et al. 2002)

AM: Autobiographical Memory

AMI: Autobiographical Memory Interview (Kopelman et al. 1989)

ETE: Extratemporal Epilepsy

TLE: Temporal Lobe Epilepsy

TLE+: Temporal Lobe Epilepsy plus hippocampal lesions

TLE-: Temporal Lobe Epilepsy without hippocampal lesions

LTLE: Left Temporal Lobe Epilepsy

RTLE: Right Temporal Lobe Epilepsy

3.1 Quality of Methodology Checklist

Three papers achieved the highest score of 11 [23][24][25]. The lowest mark achieved on the tool was seven [21]. Seven studies [8][10][11][12][21][26][27] lost marks on Question 3 which asked if the test of AM demonstrated validity or reliability. Eight studies [9][10][12][21][22][27][29][30] lost marks on Question 5 which looked at the reporting of seizure history. Six studies [8][9][11][21][22][30] lost marks on Question 7 which addressed the exclusion criteria outlined in the studies, while two studies [21][28] lost marks on Question 8 which looked at the reporting of hippocampal abnormalities. Finally, eight studies [9][10][18][22][26][27][29][30] lost marks on Question 10 which looked at whether the study addressed its limitations.

3.2 Synthesis of the Papers

This section considers the information gathered from the included studies in light of our previous objectives.

Sixteen studies recruited a total of 451 TLE participants and 330 controls. The median value of the mean ages of the TLE participants was 39.16, and of the control subjects was 37.8. Two of the studies did not provide information regarding gender distribution. Gender distribution of the TLE participant population within the 14 studies which did report this was 42% male (n=159) and 58% female (n=220). Within the control participants gender distribution was 39% male (n=103) and 61% female (n=161).

3.2.1 Impact of TLE on AM

All studies indicate that TLE does have a negative impact on AM, with patient groups retrieving less AM information than their control counterparts.

3.2.2 Hippocampal Atrophy

All of the studies reported on whether or not participants had hippocampal atrophy. However, only five papers [8] [12][23][26][27] examined the relationship between hippocampal abnormalities and AM performance.

Tramoni et al. [26] reported that all patients involved in the study displayed some degree of mild hippocampal dysfunction in their neuroimaging proposing that this may contribute to the observed memory deficits. Two studies [8][12] both reported a correlation between the presence of hippocampal damage and poorer performance on AM tasks. Narayanan et al. [12] found a significant decay in autobiographical memory with TLE patients who also had a left abnormal hippocampus. No such relationship was found for those with a right abnormal hippocampus. They reported no correlation between hippocampal volume and accelerated forgetting of autobiographical memories. Ricci et al. [8] suggested that the most important factor in the decay of autobiographic information within the first 24 hours was the presence of a hippocampal lesion. However, their study also found no significant interaction with these lesions and memory decay over longer periods of time.

Two studies [23][27] used neuroimaging techniques to look at the AM network, which typically incorporates the medial temporal lobes and hippocampal regions. Addis et al. [23] noted that there was lower activation of these areas in participants with LTLE, with particular reductions in the hippocampus. They also noted a reduced strength in signal of the left hippocampus and an increase in signal strength in connections to extra-hippocampal nodes. They suggested this may indicate a compensatory mechanism but also highlights that the left hippocampus is an important structure in the AM network. Protzner et al. [27] looked more specifically at the variation and intensity of signal output in these areas during testing and showed that higher rates of variability, but not signal amplitude, was positively correlated with performance on tests of AM.

It appears that the consensus within the small number of studies is that hippocampal abnormalities contribute to deficits in AM. Although each study addressed a variation on

hippocampal involvement, each identified the presence of both hippocampal abnormality and a decreased ability in episodic recall. There is still uncertainty in regards to lateralisation of hippocampal atrophy. There is also evidence of possible compensatory strategies within extra hippocampal structure. This may be evidence for MTT with the activation of those structures indicating the multiple connections made in memory consolidation that continue to be activated through the hippocampus in subsequent retrieval.

3.2.3 Episodic vs Semantic memory deficits

There was variability in regards to the differential impact on semantic and episodic autobiographical memories. The majority of studies investigated both episodic and semantic autobiographical recall. 14 papers reported episodic memory retrieval deficits in TLE patients, however only two studies found additional deficits in autobiographical semantic memory retrieval [11][24].

Four papers [9][23][26][28] found evidence of a general impact on episodic AM but not on semantic AM. Other studies reported on more specific aspects of the episodic deficits. St-Laurent et al. [29] looked at the detail of episodic memories and found that TLE patients recalled fewer specific details. St-Laurent et al. [10] reported TLE patients recalling fewer perceptual details in both story recall and autobiographic episodic memories, again discussing the idea that individuals with TLE lose a sense of perceptual richness to their memories. This was also true for the condition of recalling perceptually enriched video clips.

Park et al. [22] discussed the idea of the use of the Historical Present (HP) being an indication of an individual reliving a memory. HP is defined as a present tense form in both oral and written communication, which refers to a past event. Their study found that TLE patients used the HP significantly less than controls during episodic recall. They also recalled less perceptual detail in their narratives indicating that the experiential reliving of these memories was less for TLE patients.

Metternich et al. [21] looked at the impact of TLE on Flashbulb Memories. They reported that TLE patients had significantly less consistency in their recollection of the event. The control group showed a significant correlation between the emotional impact of the event at the time and the subsequent ability to consistently recall the event, however there was no such correlation for the TLE group. This may tie into previous studies which suggest that perceptual richness and the experience of reliving autobiographical memories is diluted in TLE patients which could therefore diminish this correlation.

Lah et al. [24] found a significant reduction of semantic autobiographical information in RTLE participants. However, while LTLE patients showed some reduction in the amount of semantic information recalled, this did not meet significance. Herfurth et al. [11] also reported that patients with LTLE showed deficits in both autobiographical episodic and semantic recall. However, the authors acknowledge that the deficit is much more pronounced for episodic information. Interestingly, Munera et al. [25] found that LTLE participants retrieved higher amounts of semantic details in comparison to the control group, however this discrepancy disappeared after participants were given a semi-structured interview to probe for further details. The authors suggest this may be the result of a compensatory cognitive strategy. It is unclear why this result may have occurred, however it is important to keep in mind that adaptations, including probe conditions and a change of language and culturally relevant questions, were made to the standardised Autobiographical Interview which may have an impact on results.

It seems that there is a general consensus that TLE has a negative impact on episodic AM recall. Many of the studies report specific deficits in the recall of perceptual detail and experiential reliving of memories in TLE patients, as well as reports of memories having less of an emotional weighting to them. In contrast a very small percentage of the papers reported semantic AM deficits, and even these were acknowledged to be to less of an extent as their episodic counterparts. It is possible that these occurrences of semantic memory loss may be indicative of an overall amnestic picture for these participants where epileptic activity is disrupting all aspects of memory and initial consolidation and there is a general decline in function.

3.2.4 Does TLE impact the consolidation process?

Two studies specifically investigated the impact of TLE on Anterograde Amnesia [8][12], and three studies considered the impact of epilepsy on long term consolidated memories [9][24][26]. Ricci et al. [8] concluded that the presence of hippocampal lesions had a significant impact on the consolidation process of autobiographical memories. Their study also inferred that seizure activity was associated with accelerated rates of forgetting over longer periods of time (days). They concluded that the consolidation and subsequent retention of autobiographical memories is dependent on different mechanisms at different stages of the consolidation process.

Narayanan et al. [12] investigated accelerated forgetting for anterograde AM at 30 minutes and 4 week delays. There was no difference between the epilepsy population and controls on the recall or recognition of an autobiographical event at 30 minutes delay, however there was a significant difference at a delay of 4 weeks. They reported that only those patients with LTLE showed significant levels of AM decay, with large effect sizes, while no such effect was found for those with RTLE.

Tramoni et al. [26] looked at AM in individuals with adult onset epilepsy. They reported a U-shaped pattern of forgetting showing good memory recall for episodic information in participants' childhood and early adulthood, and in the few weeks prior to testing, but higher decay of these memories for most of their adult life. These findings suggest that the onset of their epilepsy may have disrupted the long term consolidation of new autobiographical memories.

Lah et al. [24] and Viskontas et al. [9] found that there was a generalised deterioration in all retrograde autobiographical memories with participants struggling to recall early episodic memories, regardless of whether epilepsy onset was before or after these episodes, indicating that previously consolidated memories were impacted by TLE activity.

There is a consensus across the two studies [8][12] which investigated anterograde autobiographical episodic memory that TLE patients show accelerated forgetting for this information. Narayanan et al. suggest that this only applies to LTLE while Ricci et al. did not control for lateralisation of epilepsy. The studies looking at the impact on memories consolidated prior to epilepsy onset indicate that patients with TLE appeared to have their autobiographical episodic memories disrupted, regardless of the timescale of these. This indicates that seizure activity interfered with already stored memories suggesting that medial temporal disruption caused by TLE does result in memory deficits. This was so for both RTLE and LTLE.

3.2.5 Lateralisation

There was variability between the studies in regards to the impact of laterality of TLE on AM deficits. Thirteen studies specifically examined lateralisation, two studies did not specifically measure laterality [8][26],and one study [23] only used individuals with LTLE in their patient sample.

Nine studies reported some degree of AM deficit in both LTLE and RTLE patients [9][10][11][18][22][25][28][29][30]. Five of these studies additionally found no significant differences between LTLE and RTLE patients groups [9][10][22][28][30]. However, four of these studies reported differences between left and right lateralisation depending on what aspects of AM were being measured and how. Both Voltzenlogel et al. [18] and Herfurth et al. [11] noted that RTLE participants recalled significantly more episodic autobiographical memories than those with LTLE. However Herfurth et al. [11] noted that this was only true for childhood memories in their study. St Laurent et al. [29] reported variations in regards to the temporal coherence of their recounted memories, suggesting that only the LTLE group showed significantly poorer recall coherence in relation to controls. Munera et al. [25] reported that both right and left TLE showed poorer overall performance compared to controls, but this only reached significance for the recall of adolescent memories. They also noted that the RTLE group showed a significant deficit for episodic memory retrieval on aspects of the Autobiographical Interview, however this was only highlighted after participants were probed for further details of their memories using a semi-structured interview. The authors suggested that it may be that the probe condition

triggered both controls and LTLE participants to access further information, however for RTLE patients this fronto-temporal executive route of retrieval was not an accessible compensation strategy, perhaps due to a disruption to a specific pathway.

Three studies found unilateral deficits [12][21][24]. Lah et al. [24] found that RTLE patients recalled significantly less episodic autobiographical information than controls, however LTLE patients, although trending towards recalling less information, did not meet significance. It should be noted that there is a notable discrepancy between the average number of seizures experienced by each patient group in the year prior to testing (LTLE mean=80.3; RTLE mean=170.8). However, the authors do note this and report that, due to the degree of variability between patients, this difference did not reach significance. Two studies found deficits only in LTLE participants [12][21]. Of note, Narayanan et al.'s study [12] used an innovative paradigm to look at the encoding and consolidation of anterograde autobiographical memories, and so differs from the other studies in this respect. It should also be noted that Metternich et al.'s [21] study obtained the lowest score on our methodology checklist. The study lost marks as their test of AM had not demonstrated validity or reliability, there was no reported seizure history for participants, there was no clear exclusion criteria of other neurological disorders, and there was no report of the presence or extent of hippocampal abnormalities in participants. They also used a different paradigm to our other studies by looking at "Flashbulb Memories" which focus on the recall of hearing about famous events, which may account for some difference.

Protzner et al. [27], assuming AM deficit, investigated lateralisation in BOLD activation patterns during autobiographical recall and found no differences in activation variability between LTLE and RTLE. The only difference noted was that of dominant hippocampal voxels, with these being lateralised to the site of epilepsy origin (left hippocampal activation dominance in LTLE, right hippocampal activation in RTLE).

It seems that, while the majority of papers report that both RTLE and LTLE patients displayed AM deficits, differences in lateralisation were highlighted when looking at more explicit aspects of these memories or using more specific paradigms.

3.2.6 The impact of additional variables

Five studies looked at the impact of other clinical variables on autobiographical recall [8][12][18][24][28]. Voltzenlogel et al. [18] found no correlation for seizure frequency, age at onset, years of ongoing seizures, or presence of etiologic factors. However Voltzenlogel et al. [28] found that patients with a higher seizure frequency (weekly) performed worse on tests of autobiographical episodic recall than those with lower seizure frequency (monthly). Narayanan et al. [12] found that individuals who experienced generalised seizures after the initial presentation of autobiographical information showed a trend towards a higher level of decay of this information.

Ricci et al. [8] suggested that multiple aspects of epilepsy may play into the disruption in the consolidation process for autobiographical memories, including right hemisphere involvement, increased duration of epilepsy, seizure activity, epileptiform discharges, and symptoms of depression. However, regression analysis indicated that none of these aspects were in themselves a significant factor for accelerated forgetting. Lah et al. [24] examined the number of AEDs being taken and found a significant negative correlation with polypharmacy and autobiographic event recall.

It seems that there are other factors associated with epilepsy which may have an impact on AM which are important to consider in analysis.

4. Discussion, Future Directions and Clinical Implications

4.1 Discussion

This review aimed to address a number of questions, including: whether TLE has a negative impact on autobiographical memory; what the role of hippocampus might be; whether both episodic and semantic memory are affected; and whether lateralisation of epilepsy affects AM. In addition the question of whether the effect of TLE is consistent with the standard consolidation model, or multiple trace theories of consolidation was examined.

Screening the research methodology has shown a relatively high standard of research design, however there are some issues which have been highlighted. Eight of the studies included in this review did not report a detailed seizure history of participants, and seven of them did not specify exclusion criteria in relation to other neurological disorders. These are important aspect of the participant sample to know as this information will allow the researcher to consider the impact on consolidation processes and also determine that all disordered process are due to epileptic activity. Many studies did not use fully validated measures of AM. The use of adapted measures which have not been robustly tested for validity or reliability means that we must interpret many results with caution. Future direction in AM testing is discussed in a later section.

A synthesis of the current literature on TLE and AM has shed some light on our initial objectives. It seems reasonable to conclude that TLE does have a negative impact on AM. Few studies have specifically examined the impact of hippocampal atrophy, however the ones that have shown a consensus that the presence of abnormalities within the hippocampal regions correlate to AM deficits. The inclusion of the consideration of hippocampal structures in future research would be beneficial to build on our understanding of the extent to which these abnormalities are causal.

4.1.1 Episodic vs Semantic

There is a consensus that episodic autobiographical memories suffer far greater impairment than their semantic counterparts. This seems true of both RTLE and LTLE. If we consider these findings in relation to the two main theories surrounding the encoding, consolidation and subsequent retrieval of autobiographical information, namely Multiple Trace Theory (MTT; Nadal et al.[6]) and the Standard Consolidation Theory (SCM; Squire et al.[3]) it seems that there is far greater evidence in support of MTT to help us understand the neurological underpinnings of these processes. Episodic memories, and more specifically the perceptually rich details and the feeling of re-experiencing events, is impaired with relative retention of semantic details. This indicates that the semantic knowledge is stored safely in the cortex and relatively undisrupted by TLE activity, which is in agreement with Nadal et al.'s theory of memory storage. However the connections that build up autobiographical episodic memory with its rich emotional and experiential content are amalgamated and accessed by the hippocampal structures, indicating that these have a life-long role in the recall of personal events. In terms of the temporal gradient, most studies suggest this impact is present across the temporal gradient extending back many years, again supportive of the MTT hypothesis. This is supported further by neuroanatomy studies reviewing memory storage mechanisms [32].

4.1.2 Consolidation

There is a limited number of studies which directly address the consolidation process using anterograde methodologies, however this research suggests that TLE does have a negative impact on the encoding and consolidation of new autobiographical memories. Both studies that looked at anterograde memory showed clear accelerated forgetting of newly presented autobiographical information. A few studies also reported that TLE seemed to impact episodic memories that would have been consolidated prior to epilepsy onset. This again adds support for MTT indicating that hippocampal regions are a life-long requirement for accessing episodic information. This is an area that would benefit from further research using innovative techniques for presenting new event information. Such new techniques are beginning to be utilised in current research looking at the incidence of Accelerated Long-term Forgetting (ALF) in epilepsy populations (Blake et al, 2000; Ricci et al. 2015), with a focus more on prospective memory. Hopefully our

synthesis will help guide future research with a stronger focus on novel prospective AM tests.

4.1.3 Lateralisation

In regards to the role of lateralisation, there are mixed results which may be a result of the different methodologies used between the studies, including different specific tests of AM. Most studies suggest that both RTLE and LTLE impact autobiographical episodic retrieval [9][10][11][18][22][25][28][29][36]. However there were some discrepancies highlighted when looking at more specific elements of these memories. Herfurth et al. noted that RTLE participants could recall more childhood memories than their LTLE counterparts, while St Laurent et al. noted differences in temporal coherence in LTLE compared to controls but not in RTLE. It was clear that the studies investigating lateralisation focused on different smaller aspects of memory which makes it more challenging to synthesise and compare their results. Perhaps this suggests that research should now investigate the intricacies of the different aspects of AM, including perceptual details and emotional content, and the possible neurological underpinnings of this complex network, with the knowledge that both hemispheres play a part in the network, but with possible lateralised specific functions. It also highlights the need for valid and reliable tests of AM, as many of the measures used in the studies could be interpreted in multiple ways, particularly with the adaptations many of the researchers made.

4.1.4 SCM vs MTT

In terms of support of the current theoretical debate it seems that the majority of the literature supports the MTT hypothesis. Most of the studies indicate a specific deficit in episodic autobiographical information with relative preservation of the semantic autobiographical facts. This suggests that these aspects of memory are accessed differently, with the richer engram being accessed through complex networks which aid experiential remembering (Nadal et al. [6]. The neuroimaging studies also support the MTT hypothesis that the hippocampus has a life long role in AM recall, indicating activation of a complex AM network involving the hippocampal structures during retrieval. This is also in line with additional neuroimaging studies which note the activation of the hippocampus in episodic recall regardless of the acquisition timescale

[32]. However, most studies did not specifically comment on the temporal gradient of forgetting within the recall tests of AM, instead reporting an overall deficit of episodic recall. Future research would benefit from including specific analysis on the temporal gradient to further inform our understanding of AM consolidation, storage and subsequent recall.

4.2 Future Directions

Our review of the methodology indicates that future research would benefit from including specific demographic information, including seizure history, frequency and age of onset, as some of the studies have shown that these additional factors may influence consolidation and subsequent recall of memories. It is important to know participants' seizure history to ensure we can accurately measure the impact of epileptic activity on events experienced before and after epilepsy onset. The studies reviewed here also point towards the detrimental impact of seizure frequency and the experience of generalised seizures. We would suggest that future researchers gather data on these aspects of epilepsy and consider them as possible confounding factors.

Previous studies [17] have suggested that the right hemisphere is more important in the accurate retrieval of autobiographic memories. However, the majority of the more recent studies reviewed have failed to show a significant effect of side of epilepsy origin in autobiographic event recall. What was clear from the studies reviewed is that there is a distinct lack of functional neuroimaging studies exploring AM. This is an area that may benefit from further exploration in the future utilising fMRI paradigms. Also in regards to neuroimaging data, there is a general consensus that the hippocampal network does form an important part of AM structures. Future research into the neurological underpinnings would benefit from incorporating hippocampal information into their analysis as this was often collected but rarely used.

It may also help to keep in mind how participants are recruited to future studies. Many studies recruited specifically from memory clinics and many participants were also

surgical candidates. While these patients make an important contribution to research, we must ensure that we are not looking at skewed samples of people with memory complaints and misjudging the prominence of these deficits within the TLE population. At this time there is no literature available on the possible recruitment bias which may exist in epilepsy research. This may be another area of interest for future projects.

There is a possible limitation in our Quality checklist in regards to multiple areas of research being considered within one point on the checklist. For example, considering whether a test of Autobiographical Memory has demonstrated both validity and reliability becomes a more complex issue when many of the studies have adapted already standardised AM tests. It may have been more helpful to separate this point and consider these elements of the test as two individual aspects. This may also apply to the questions surrounding trial limitations, sources of bias, imprecision and multiplicity of analysis. Future quality checklists in this area may benefit from separating these points to look at more specific elements of methodology in this area.

4.3 Tests of Autobiographical Memory

It is important to note that, in many of the studies included in this review, cultural differences may be a confounding factor in relation to discrepancies in results. Many of the studies adapted tasks into different languages and the reliability of the translated versions was often not established.

In recent years, there has been advancement in the investigative measures of AM. As well as the use of standardised measures, such as the Autobiographical Memory Interview, Autobiographical Interview, Autobiographical Fluency Test, and the Modified Crovitz Test, there has been a development of studies looking at more ecologically valid ways of measuring this area using real life scenarios and events within testing procedures. St-Laurent et al. [10] developed a new technique to measure the complexities of episodic memory in the laboratory setting by showing participants perceptually enriched video clips. They observed similar patterns of differences displayed by the TLE group in recounting perceptual details of these clips to recalling autobiographic memories.

Narayanan et al. [12] also utilised a new way of investigating anterograde AM by staging an event in the testing session and having participants recall specific details about this after a delay.

The benefit of the advancement in this area is that researchers are able to examine AM functions and deficits in the anterograde domain which provides a richer understanding of the AM consolidation process. However, as yet these staged events tasks are difficult to standardise and cannot be compared across studies. It may be helpful for more standardised measures to be researched and put in place to aid future studies using these methods.

4.4 Clinical Implications

It seems that the research can confidently suggest that AM is impacted by TLE, and the majority of this research indicates that this deficit can occur regardless of laterality. Clinical implications for this may include educating individuals who are recently diagnosed with epilepsy in regards to the memory deficits that they may encounter and helping to normalise their experience. The few neuroimaging studies indicate that the neural pathways do not seem to build a compensatory network for autobiographical deficits. Therefore, it will be important for individuals to become practiced in the use of external strategies to help them retain their personal memories. Cognitive rehabilitation research could consider how best to work with individuals experiencing these deficits. Modern technology may take an active role in these rehabilitation strategies. It will be important to build upon resources such as the SenseCam [36] and employ the use of various recording methods which help to strengthen episodic autobiographical memories and help this clinical population to retain their experiences.

The discrepancy between loss of episodic memories but retention of semantic memories also leads to consideration of appropriate memory measures when assessing individuals with TLE. The preservation of personal semantic knowledge indicates that the individuals do not display a typical amnestic profile, however their true memory difficulties may be missed on typical screening measures. Additional considerations must be made by

clinicians assessing cognitive deficits in TLE patients. It may be helpful to develop a standardised screening questionnaire to assess the extent of autobiographical episodic memory loss.

4.5 Conclusion

Research is developing a greater understanding of the impact of Temporal Lobe Epilepsy on Autobiographical Memory. It seems that the Multiple Trace Theory may be a valuable way of understanding the neurological underpinnings of complex episodic memory consolidation and recall. However, there are still some mixed results and further complexities that are not understood in the realm of Autobiographical Memory. Hopefully this review will serve to guide future directions of research into the area and help to inform clinical practice.

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CHAPTER 2: MAJOR RESEARCH PROJECT

THE EFFICACY OF A SEIZURE ASSESSMENT RISK TOOL IN PREDICTING OCCURRENCE OF TONIC-CLONIC SEIZURES

Prepared in accordance with guidelines for submission to Epilepsia (see Appendix 2.1).

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Plain English Summary

Background: People with epilepsy are more likely to be seriously injured or die suddenly compared to the rest of the population. One of the reasons for this is patients experiencing a generalised seizure, in which the electrical activity moves over the whole of the brain. When this happens the person becomes unconscious and the control of their breathing and heart can be disrupted. This can be very dangerous, and in some cases leads to serious injury or death if the person is not helped quickly by medical staff. At this time there are no specific guidelines for medical staff to help them to assess the risk of a person with epilepsy experiencing a generalised seizure when they are admitted to hospital. The William Quarrier's Scottish Epilepsy Centre (SEC) developed a screening questionnaire to help measure how likely it is that a patient will experience a generalised seizure when they are admitted to their specialist centre. This questionnaire was called the Seizure Assessment Risk Score (SARS) and was given to all new patients admitted to the Centre. Data were also collected on how many generalised seizures were experienced by these patients.

Aim: This study aimed to see if the SARS was an effective tool at predicting if a patient would have a generalised seizure during their stay at the Scottish Epilepsy Centre.

Method: We collected SARS scores and seizure activity information from 37 people admitted to the SEC. This data was then explored to determine if the SARS tool was able to predict if a patient would have a generalised seizure.

Results: We found that the SARS tool was not good at predicting if a patient would have a generalised seizure.

Conclusion: This study highlights that the SARS tool needs to be developed further in order to be able to screen patients for their risk of experiencing a generalised seizure. We suggest ways in which the tool could be developed. However the study also highlights that it is difficult to screen people with epilepsy being admitted to a specialist centre as many patients are at high risk. It is still unclear if we can predict if a person will have a generalised seizure.

Abstract

Background: Previous research has identified that the occurrence of a Global Tonic Clonic Seizure (GTCS) is a high risk factor for serious injury or death within the epilepsy population. Fast intervention during a GTCS accompanied by EEG suppression is needed to reduce the risk of serious injury or death. Research has suggested that intervention should optimally occur within 50 seconds of EEG suppression commencing. Identifying patients who are at greatest risk of GTCS could enable targeted monitoring of patients and facilitate quicker intervention. However, at this time there are no specific guidelines for risk assessment in regards to risk of GTCS. The William Quarrier's Scottish Epilepsy Centre (SEC) developed a Seizure Assessment Risk Score (SARS) tool for use in Video Telemetry (VT) epilepsy units based on risk factors highlighted by previous research. The SARS was implemented with all new admissions to the SEC and data was collected on seizure activity through routine clinical practice.

Aim: The aim of this study was to investigate the efficacy of the SARS tool at predicting the occurrence of GTCS activity in patients admitted to the SEC.

Methods: Seizure activity data and daily SARS scores were collected from 37 patients admitted to the SEC over an 8 month period. The data were then explored to determine if there was a predictive relationship between higher SARS scores and GTCS occurrence.

Results: Data from 37 patients indicated that there was no significant relationship between higher scores on the SARS and the incidence of GTCS. The current SARS tool does not appear to adequately differentiate between those patients who do experience a GTCS during their admission to the VT unit and those who do not.

Conclusion: The study highlights that the SARS tool requires further development to ensure that patients are adequately assessed for risk of experiencing a GTCS. While the majority of the sample was rated 'high risk' according to the SARS tool, the incidence of GTCS was in fact relatively low. The study also discusses the difficulties surrounding risk assessing an already specialised and clinically risky population.

Keywords: Epilepsy, Generalised Seizure, Video Telemetry, Risk Assessment

Introduction

Epilepsy is thought to affect around 50 million people worldwide [1] making it one of the most common neurological conditions. Around 30% of people with epilepsy are unresponsive to treatment [1].Sudden Unexpected Death in Epilepsy (SUDEP) is one of the leading causes of death in individuals with refractory epilepsy and is of great concern to the epilepsy population and those involved in their clinical care[2]. There is growing evidence that specific risk factors can be identified to help predict an individual's level of risk of serious injury or death as a result of their epilepsy. A previous study [3] has conducted an investigation into the factors which may be associated with SUDEP and discovered that most of the individuals who met criteria for SUDEP had experienced an increase in seizure frequency and/or intensity within 6 months of their death. Shankar and colleagues conducted a literature review looking at risk factors associated with SUDEP[6]. They found evidence that there were agreed risk factors that should be considered when evaluating the risk of death or serious injury to an epileptic patient. These included having uncontrolled generalised tonic-clonic seizures (GTCS), not taking anti-epileptic drugs (AEDs) as prescribed, having tonic-clonic seizures that are not controlled by AEDs, having sudden and frequent changes to AEDs, being a young adult (in particular male), having sleep seizures, having seizures when alone, and drinking large amounts of alcohol.

A retrospective audit of patients undergoing EEG video telemetry (VT) was performed by Semmelroch and colleagues [4]. They found that 10.2% of patients experienced at least one GTCS, and of these, 27% showed peri-ictal EEG suppression. They also discovered that if an individual experienced more than one GTCS they demonstrated more incidences of EEG suppression alongside other seizures. A link was previously identified between prolonged (duration longer than 50 seconds) post-ictal EEG suppression and individuals with refractory epilepsy who are more at risk of SUDEP[5]. This highlights the need for close monitoring and fast intervention from nursing staff to ensure that EEG suppression is not sustained for longer periods (>50s).

A small number of studies have investigated the risk and safety issues within VT units across the United Kingdom. Research has looked at the incidence of adverse events, such

as physical injury or respiratory difficulties that occurred during seizure activity in 27 different VT units over the period of one month[7]. This study found that these adverse events occurred in 12% (n=33) of seizure incidences. However, they found that staff did not attend the patient in 44% (n=120) of cases.

A risk awareness checklist was developed and piloted for individuals with epilepsy and a learning disability[8]. Qualitative analysis of nursing staff who piloted the checklist reported that staff confirmed the need for a risk checklist and that they found this beneficial for reducing patients' risk of injury. This checklist was developed for individuals with a learning disability living in the community and was directed at the staff supporting them.

The British Society for Clinical Neurophysiology published safety guidelines for EEG VT admissions, which outlined staffing levels and monitoring procedures[9]. However there are currently no explicit guidelines for risk assessment in regards to risk of incidence of GTCSs or SUDEP. This is therefore an important area of study.

Given the high risk nature of the patients admitted to VT Units due to their complex epilepsy presentations and the nature of treatment and exploratory procedures that are undertaken, the William Quarrier's Scottish Epilepsy Centre (SEC) developed a new checklist based on the findings of previous research [9] and adapted for inpatients. It was developed by the Clinical Psychologist working in the centre after consultation with nursing and medical staff. There have been no previous audits of the usefulness or outcomes of the tool to date.

The tool was designed to calculate the risk of an inpatient experiencing a GTCS and to be completed daily with each patient. The reason for daily monitoring is that there are aspects of routine care, such as reducing medications or sleep depriving, which can change on a daily basis and which may increase the risk of the patient subsequently experiencing a GTCS. There may also be information gained that changes the level of risk, such as a new diagnosis or indeed the experience of a GTCS during the inpatient stay. This checklist is known as the Seizure Assessment Risk Score (SARS) tool (see Appendix 2.3).

This study examined the effectiveness of the SARS tool to determine if the tool is an accurate predictor of patients' risk of experiencing a GTCS. We hypothesised that increased scores on the SARS tool would be associated with higher incidence of GTCS activity in inpatients within a specialist epilepsy VT unit.

Method

Procedure

The Seizure Assessment Risk Score (SARS)

The SARS is completed for each patient every night by one of the nursing staff in the SEC clinical team. The total score (out of 27) on the SARS form indicates the level of risk thought to be relevant for the individual, and subsequently determines the level of observation a patient should be under for the following 24 hours. The forms are stored in the patients' medical notes and the same form is updated on each assessment. Seizure activity is recorded by nursing staff separately on a dedicated sheet held in the medical notes. The location, presentation and duration of each seizure is recorded.

The tool provides scores on a number of areas deemed to increase a person's risk of experiencing a GTCS. Each question has an allocated risk score (in brackets).

- History of possible Generalised Tonic Clonic Seizure (GTCS) (2)
- Confirmed experience of a Generalised Tonic Clonic Seizure (GTCS) in the past 3 months while on optimal medical treatment (3)
- Nocturnal Seizures (1)
- Outstanding diagnostic uncertainty (1)
- Reduced Anti-Epileptic Drugs (AED) but on therapeutic dose (3)
- Reduced AED sub therapeutic level (4)
- AED withdrawn (no AED) (5)
- Non-Compliance with AED (1)
- Sleep deprivation (3)
- Breathing/Cardiac Issues (1)

- Any Other Risk (0-3) *e.g. falls, psychosis, wandering*

Total scores are calculated and categorised as follows:
0-4: Low risk; normal monitoring
5+: High risk; highest level of monitoring

The SARS tool was implemented in the SEC in September 2014.

Data Collection

Daily SARS scores were obtained prospectively as part of routine clinical practice. All data were then collated on site at the SEC by the researcher. All data from the SARS scoring sheets were transferred from the clinical notes in an anonymous form into a spreadsheet, along with the matched daily data concerning seizure activity which was obtained from the nursing notes and the summary neurology reports. Other information gathered from the clinical notes included gender, age, diagnosis, other health conditions, learning disability diagnosis and presence of brain injury. This was then coded and transferred to SPSS for analysis.

Participants

All consecutive admissions to the Scottish Epilepsy Centre during the period of September 2014 and April 2015 (n=43) were included in the screening stage of our study. The clinical notes documented during their admission, subsequent discharge reports, and medical files of all 43 participants were reviewed. Of these, six were deemed unsuitable for inclusion due to the individual receiving a diagnosis of Non Epileptic Attacks with no suspected epileptic activity. SARS data was subsequently collected for the remaining 37 participants. All individuals were between the ages of 17 and 81 years old.

Seven of our 37 participants (18.92%) experienced a GTCS during their admittance to the SEC. In terms of days, a GTCS occurred on 2.2% of the total of 768 days considered,

taking each participant's length of admission separately. Analyses compared those with GTCS (N=7) with those without (N=30).

GTCS Group

The GTCS group consisted of 7 participants (4 female, 3 male) ranging from 17 to 37 years of age (mean: 29.57; SD: 6.83).

NoGTCS Group

The No GTCS group consisted of 30 participants (16 female, 14 male) ranging from 21 to 81 years of age (mean 39.23; SD: 13.06).

Participants' scores on all elements of the SARS tool for each day of their admittance were collected alongside the associated record of seizure activity for each individual, including the number and type of event for each day. Demographic information, including epilepsy diagnosis, learning disability diagnosis, diagnosis and history of other health conditions, and presence of a brain injury, was also collected.

Analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS, Version 22). Due to the small sample size within the GTCS group, non-parametric analysis was used to investigate whether higher scores on the SARS predicted the occurrence of generalised seizures. Average scores were initially used to explore the patterns within the data. For each patient who did not experience a GTCS during their admission, the average scores for each element of their SARS record, including their total scores, were calculated over the duration of their stay. For individuals who did experience a generalised seizure (n=7), their average scores were calculated on the days up until the day prior to their first seizure. This controlled for the fact that SARS total scores may increase if the individual experienced a generalised seizure during their stay due to the tool measuring the history of experiencing a GTCS.

We then conducted exploratory post-hoc analysis, looking specifically at each participant within the GTCS group to determine if there were factors specific to this population which indicated higher levels of risk of experiencing a GTCS. This is intended to aid in any subsequent development of the SARS tool and further inform clinical practice.

Ethics

This project was reviewed by the scientific advisor of the West of Scotland NHS Research ethics committee and deemed not to require formal ethics approval. It was also reviewed through the Scottish Epilepsy Centre Clinical Research Governance procedure and approved.

Results

During data collection it was noticed that there were 46 errors in the SARS documentation across 5 separate participants. All errors related to Question 1 of the tool and highlighted a common mistake of staff scoring patients for Question 2 in relation to experiencing a GTCS within the last three months, however not scoring them for Question 1 for a history of possible GTCS. These errors were corrected by the researcher, and the correct score for Question 1 and the amended total scores for each entry were included in the data set.

Participant Sample

Table 1 summarises the demographic characteristics of the study population.

Sample	Age	Gender	Diagnosis	Learning Disability	Other heath conditions	Brain Injury
All participants	17-81 x̄:37.41 SD: 12.65	M: 17 F: 20	E: 22 E+NES: 14 Unknown:1	LD:13 NoLD: 24	Present:20 Not Present: 17	Present:3 Not Present:34
GTCS	17-37 x̄: 29.57 SD: 6.83	M: 3 F: 4	E:4 E+NES:3 Unknown:0	LD:1 NoLD: 6	Present:1 Not Present:6	Present:1 Not Present:6
NoGTCS	21-81 x̄: 39.23 SD: 13.06	M: 14 F: 16	E:18 E+NES:11 Unknown:1	LD: 12 NoLD: 18	Present:16 Not Present:14	Present:2 Not Present:28

Table 1: Participant Demographics, including age, gender, epilepsy diagnosis where confirmed (Epilepsy (E); Non Epileptic Syndrome (NES)), Presence of a Learning Disability (LD), presence of other health conditions (e.g. cancer, neuropathy, depression), and presence of brain injury, of the whole sample, and then split into sub groups (GTCS and NoGTCS).

SARS data and seizure activity logs were recorded for all 37 participants. The mean SARS scores were calculated for each participant for the duration of their stay. This included their total SARS scores and also the mean score for each individual question on the SARS tool (see Appendix 2.4 for summary).

Descriptive Statistics

Figure 1 and Table 2 provide a descriptive summary of the mean SARS scores for both *NoGTCS* and *GTCS* groups. There were no significant differences between the groups in terms of age (p=0.45) or gender (p=1.00).

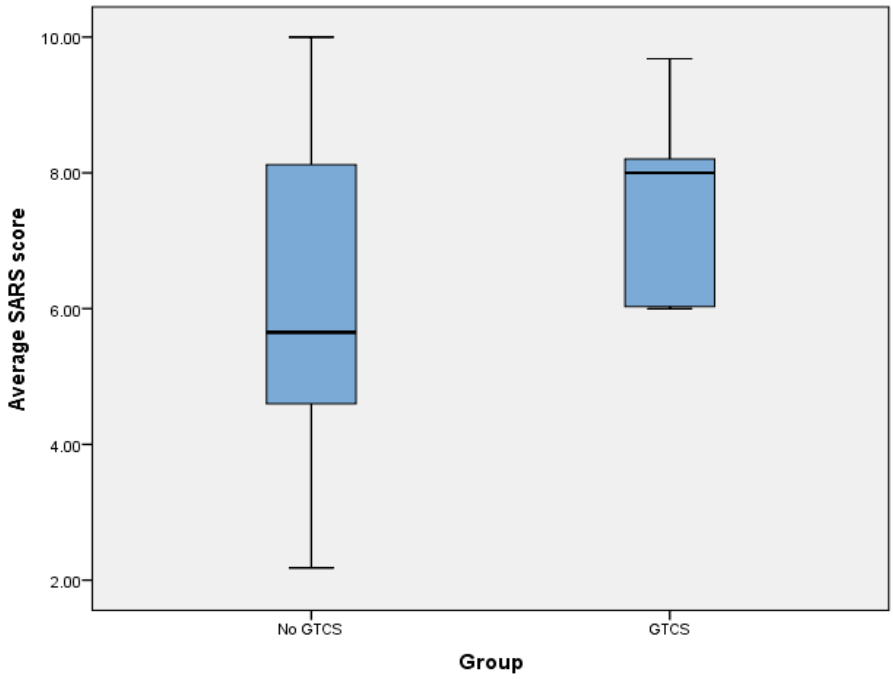


Figure 1. Boxplot showing the Median and Quartiles for each group's mean SARS scores

Group	Mean	Median	Mode	Standard Deviation
No GTCS (n=30)	6.08	5.65	4	2.022
GTCS (n=7)	7.45	8	6	1.451

Table 2. Mean, median, mode, Standard Deviation values for Mean Total SARS scores split by group.

Due to the small sample size of the GTCS group (n=7) non-parametric tests have been used.

We first looked at the relationship between total SARS score category (0-4: low; 5+: high) and the occurrence of a GTCS. Table 3 presents the contingency table of SARS category scores and how many of these preceded a GTCS the following day.

	GTCS	NoGTCS
Low SARS	0	147
High SARS	17	602

Table 3 Contingency table summarising the number of total SARS scores which fell into each risk category (Low: 0-4; High: 5+) and if they corresponded to the incidence of a GTCS the following day.

A Chi-square did not reveal a significant effect ($p=0.55$, $\varphi=0.042$, small effect size).

A Mann-Whitney-U test was conducted to determine if there was any difference between groups in total SARS score. The total SARS score between *GTCS* and *NoGTCS* groups was not significantly different ($U=63$, $p=0.109$). Effect size calculations suggested a small-medium effect size ($r=0.27$).

Table 4 shows the mean, median, standard deviation and range for each question within the SARS for both groups.

		Q1	Q2	Q3	Q4	Q5	Q6
Mean	**No GTCS** **GTCS**	1.64 1.7143	0.72 1.52	0.85 0.71	0.55 0.7	0.9 1.04	0.23 0.2
Median	**No GTCS** **GTCS**	2 2	0 1.64	1 1	0.72 1	0.42 1	0 0
St. Dev.	**No GTCS** **GTCS**	0.74 0.76	1.28 1.5	0.34 0.49	0.46 0.48	1.07 1.07	0.64 0.55
Range	**No GTCS** **GTCS**	2 2	3 3	1 1	1 1	3 2.47	3 1.45

		Q7	Q8	Q9	Q10	Q11
Mean	**No GTCS** **GTCS**	0.27 0	0.003 0.04	0 0	0.22 0.29	0.66 1.22
Median	**No GTCS** **GTCS**	0 0	0 0	0.25 0	0 0	0.95 1
St. Dev.	**No GTCS** **GTCS**	0.78 0	0.015 0.1	1 0	0.41 0.49	0.67 1.14
Range	**No GTCS** **GTCS**	3 0	0.08 0.27		1 1	2 3

Table 4. Mean, Median, Standard Deviation and Range for each SARS question split by group

Table 4 indicates that the group who did experience a GTCS during their admission had higher median scores on questions 2, 4, 5, and 11 of their SARS tool. Mann Whitney analysis was conducted on each of the individual questions of the SARS to compare the difference between groups. None of these comparisons were significant (see Table 5).

Question	Mann Whitney U	P value	Effect Size (r)
1	100.5	.865	0.04
2	76	.276	0.22
3	98	.805	0.057
4	84	.435	0.14
5	100	.865	0.033
6	97	.776	0.07
7	91	.608	0.166
8	93	.662	0.2
9	98	.805	0.11
10	98.5	.805	0.05
11	74	.243	0.2

Table 5. Summary of Mann Whitney U scores, p-values and Effect Sizes for mean SARS scores for individual questions compared between groups. (Effect Size r: 0.1=small effect; 0.3=medium effect; 0.5=large effect).

Table 5 shows that questions 2, 4, 5, and 11 whose medians highlighted a possible difference between groups were not significant and had small effect sizes (r).

Sensitivity and Specificity

Receiver Operating Characteristic (ROC) curve analysis allows us to consider the levels of sensitivity and specificity of a new assessment tool. For the SARS tool sensitivity is defined as the probability that a high SARS score would indicate the likelihood that the individual will have a GTCS. Specificity is the probability that when the SARS score is low the individual will not have a GTCS. The area under the ROC curve (AUC) is a measure of how well the tool can distinguish between the two groups. Figure 2 shows the

ROC curve of mean SARS scores against the occurrence of a GTCS during admission to the SEC.

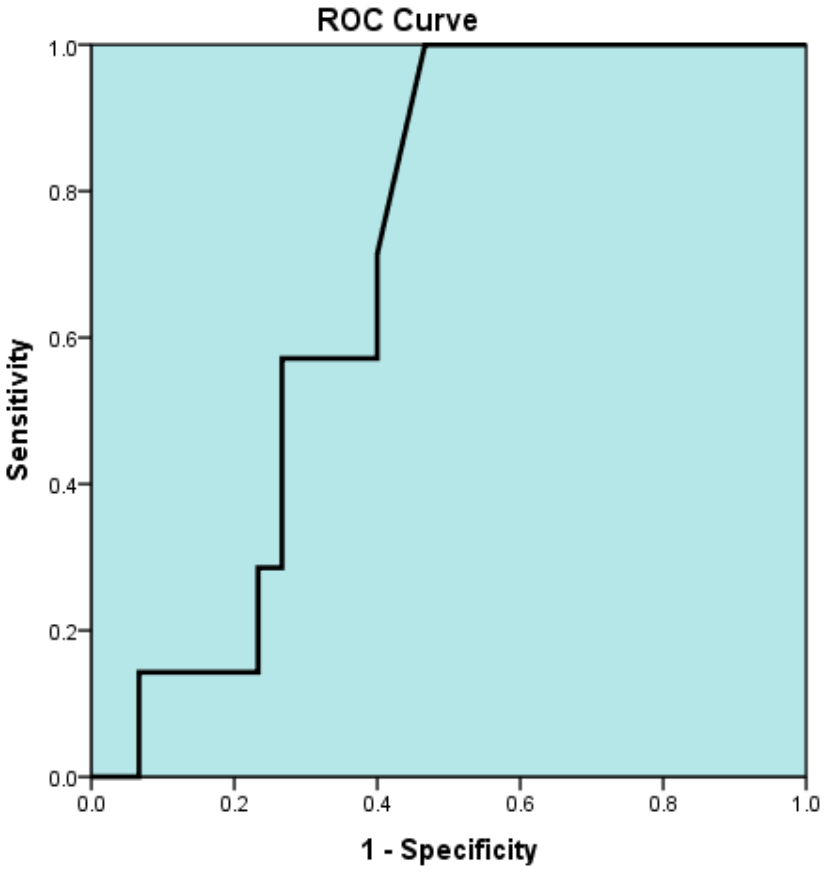


Figure 2. Receiver Operating Characteristic (ROC) curve plotting the mean total score on the SARS tool against the presence of a GTCS during their admission to the SEC.

ROC curve analysis indicates that the area under the curve is 0.7, and indicates that the SARS tool has good sensitivity (1) however with poor specificity (0.2).

As noted above, the *NoGTCS* group scored, on mean, lower than the *GTCS* group on Questions 2, 4, 5 and 11 on the SARS tool. Figure 3 shows the individual ROC curves for the mean scores for each of these questions.

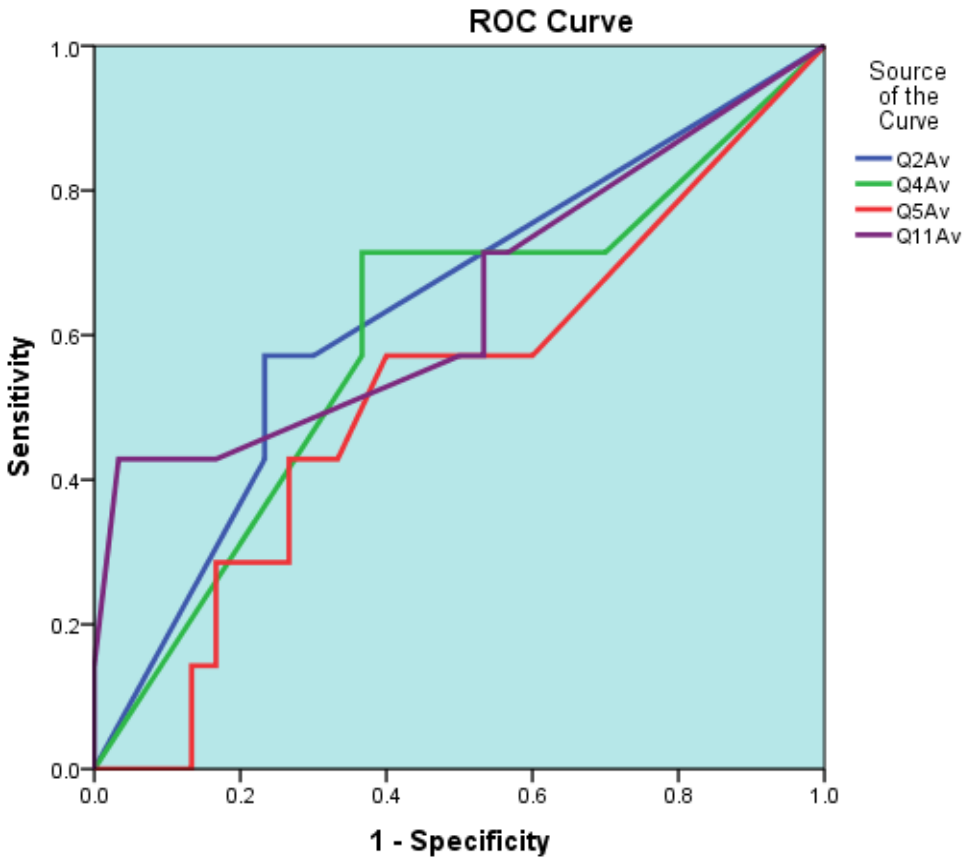


Figure 3. ROC curve analysis for Questions 2, 4, 5 and 11 on the SARS tool comparing NoGTCS and GTCS groups.

Question	Area Under the Curve
Q 2	0.638
Q 4	0.6
Q 5	0.524
Q 11	0.648

Table 6. ROC curve analysis for Questions 2, 4, 5 and 11 on the SARS tool comparing NoGTCS and GTCS groups.

ROC analysis suggests moderate sensitivity and specificity for questions 2, 4 and 11, and a small effect of question 5 (see Table 6). Table 7 summarises the ROC analysis for all other questions in the SARS tool (Q1, 3, 6, 7, 8, 9, 10) which shows that there was little difference between the groups on these questions, indicating poor sensitivity and specificity.

Variable	Area Under the Curve
Q 1	0.521
Q 3	0.467
Q 6	0.462
Q 7	0.433
Q8	0.557
Q9	0.467
Q10	0.531

Table 7. ROC curve analysis for Questions 1, 3, 6, 7, 8, 9 and 10 on the SARS tool comparing NoGTCS and GTCS groups.

Internal Consistency

The internal consistency of the SARS tool was calculated. Cronbach's Alpha was 0.561, indicating a poor level of consistency between items. A Cronbach's Alpha score of 0.70 or above is deemed acceptable. Table 8 summarises the Cronbach's Alpha result if each item was deleted.

Q	1	2	3	4	5	6	7	8	9	10
CA if deleted	0.419	0.460	0.618	0.450	0.363	0.717	0.293	0.599	0.521	0.383

Table 8. Cronbach's Alpha (CA), indicating the level of consistency between items, if each item was deleted.

Post Hoc Analysis

The results so far do not support our hypothesis that a higher score on the SARS tool predicts the occurrence of a GTCS. Post-hoc analysis was performed to determine if any aspects of our participant population indicated specific risk factors for experiencing a GTCS. Analysis was performed on the demographic data of our sample, including age,

gender, diagnosis, presence of a learning disability, presence of a comorbid health condition, and previous brain injuries. Although we are carrying out multiple comparisons, we have not applied a correction to the results as this is exploratory analysis which is intended to highlight factors which could be examined in future research.

Age

The age of the GTCS group (Mdn=31) did not significantly differ from the NoGTCS group (Mdn=39), U=57.5, ns, r=0.303, medium effect size.

Gender

A Fisher's Exact test revealed no significant effect of gender on patients experiencing a GTCS, p=1, φ=0.03, small effect size.

Diagnosis

We then explored if there was an impact of participants having a diagnosis of only epilepsy (ES) or epilepsy plus non epileptic seizures (ES+NES) on the occurrence of GTCSs. The 'unknown' data point was classed as an outlier and excluded in this analysis. A Fisher's Exact test revealed no significant effect of diagnosis on patients experiencing a GTCS, p=1 φ=0.04, small effect size.

Learning Disability

We looked at whether the presence of a Learning Disability impacted the likelihood of participants having a GTCS during their admission. There was no significant relationship between the diagnosis of a Learning Disability and the experience of a GTCS, Fisher's Exact p=0.383, φ=0.211, small effect size.

Other Health Conditions

We looked at whether having other diagnosed health conditions alongside epilepsy had an impact on experiencing a GTCS. When data are collected within the SEC, health conditions includes physical and mental health diagnoses. Firstly we looked at the impact of all diagnosed health conditions. A Fisher's Exact test revealed a significant effect of a comorbid health condition on the likelihood of experiencing a GTCS during admission, with those who do have a secondary diagnosis being less likely to have a GTCS, $p=0.029$, $\varphi=0.41$, medium effect.

We then excluded mental health sub-type conditions, including depression, anxiety and autism, and looked specifically at the group of individuals who had a diagnosed physical health condition (n=14). The significant effect remained indicating that a comorbid diagnosis of a physical health condition was a significant factor against experiencing a GTCS; Fisher's Exact $p=0.012$, $\varphi=0.422$, medium effect size. We then looked specifically at comorbid mental health diagnoses (n=6). A Fisher's Exact test showed that this was not significant, $p=1$, $\varphi=0.02$, small effect.

Brain Injury

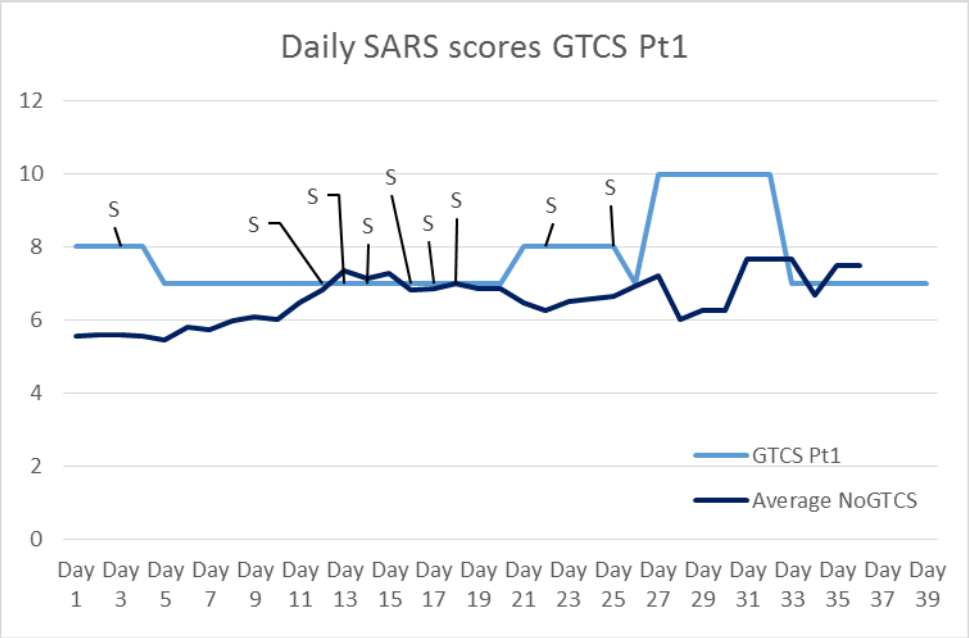
We looked at whether having a previously acquired brain injury was a factor in the experience of having a GTCS (n=3). A Fisher's Exact test revealed that this was not significant, $p=0.477$, $\varphi=0.109$, small effect.

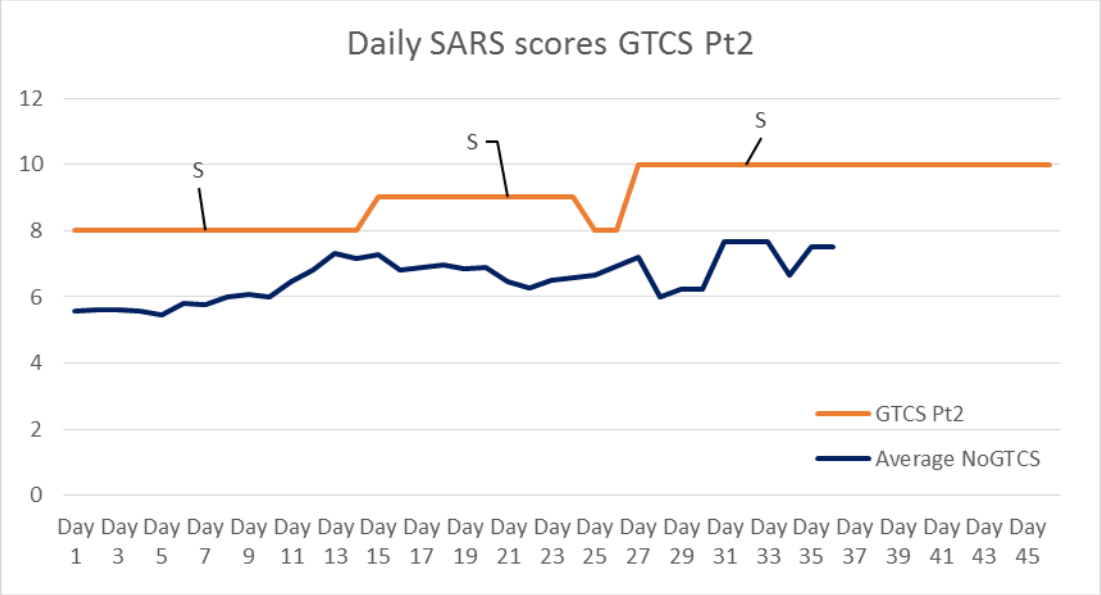
GTCS Group – Individual Participants

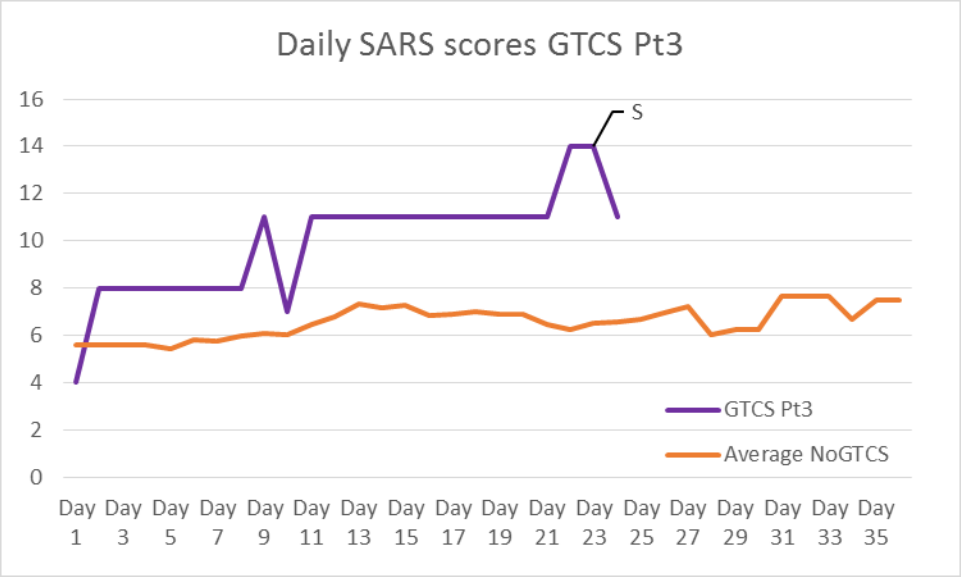
We then considered the pattern of SARS scores for each participant within the GTCS group to determine if the SARS tool gave an indication of their heightened levels of risk for the following day.

Figure 4 shows individual graphs for each participant within the GTCS group showing daily SARS scores and plotting the occurrence of seizures (marked 'S'). The graphs also

depict the mean daily SARS score obtained by the NoGTCS group. The length of admission to the SEC varied for each individual participant.






Daily SARS scores GTCS Pt3
16
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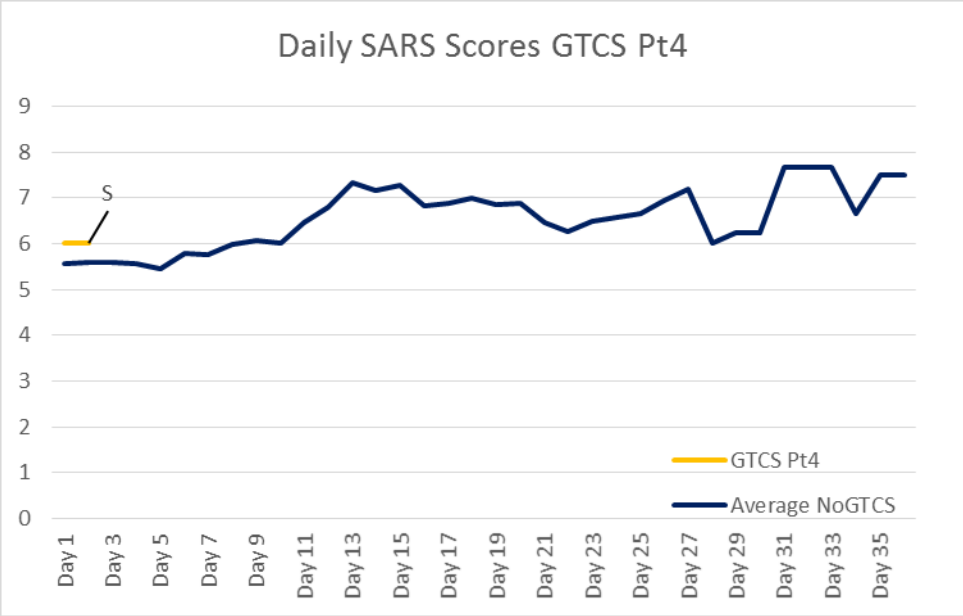
Day 33
Day 35


Daily SARS Scores GTCS Pt4
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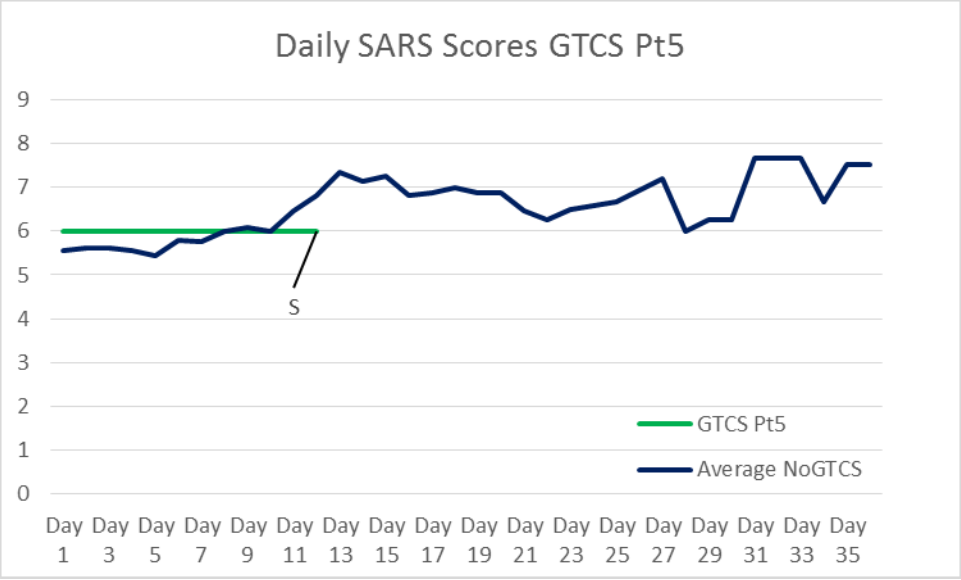
Daily SARS Scores GTCS Pt5
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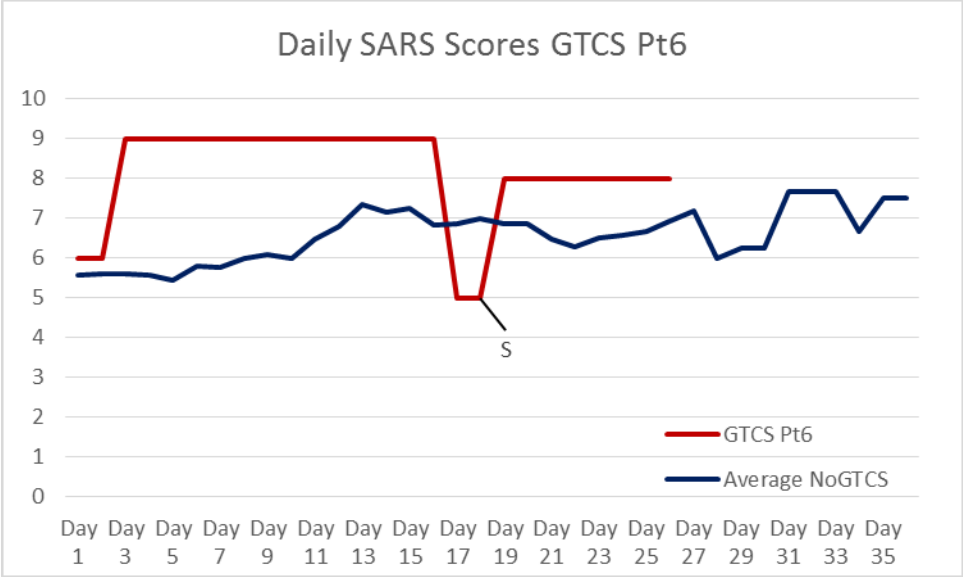

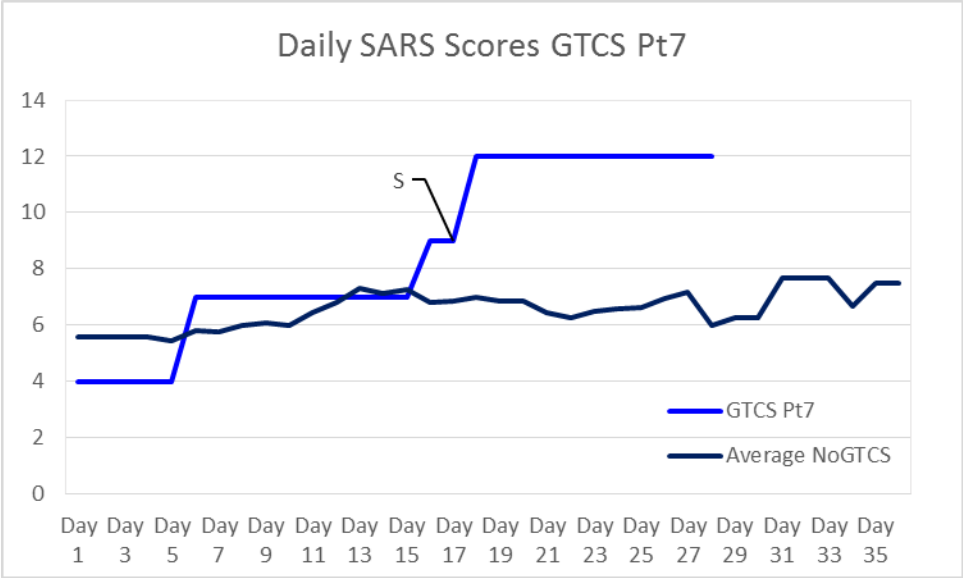

Figure 4. Graphs depicting daily SARS scores for each GTCS participant plotted against the overall mean daily SARS score for the NoGTCS group. GTCS occurrence is marked 'S'.

Table 9 summarises the SARS scores given the night before each individual in the GTCS group experienced a generalised seizure. In the case of those who experienced multiple seizures (participants 1 and 2), the mean score for the nights prior to seizure activity is shown. The mean SARS scores for all other nights where a GTCS was not experienced the following day are also given.

GTCS Participant	Mean score night before GTCS	Mean scores all other nights
1	7.3	7.8
2	9	9.09
3	14	9.74
4	6	6
5	6	6
6	5	8.28
7	9	8.56

Table 9. SARS scores for each participant in the GTCS group the night before GTCS and all other nights.

Table 9 shows that two participants had a higher SARS score the night before experiencing a GTCS compared to their mean scores on all other nights (Participants 3 and 7). Participant 1, 2 and 6 had lower SARS scores the night prior to a GTCS. Participants 4 and 5 had the same scores on average on all nights.

Discussion

Accurately predicting if and when a Generalised Tonic Clonic Seizure (GTCS) is going to occur could help to prevent injury or death. The current research sought to investigate whether the SARS tool accurately predicts when a seizure might occur.

In summary, our results indicate that the SARS tool does not sufficiently predict whether patients admitted to the SEC will experience a GTCS or not. We will now consider our individual results in terms of the previous literature and the future directions of risk assessment in inpatient epilepsy monitoring units.

Discriminating between the GTCS and NoGTCS groups

The purpose of the SARS tool is to identify those patients with epilepsy who are at greater risk of having a GTCS and are therefore at greater risk of injury or death. Our primary hypothesis was that higher total scores on the SARS tool would indicate higher GTCS occurrence. The results of our study do not support this hypothesis. There was no significant difference between groups in respect of the total SARS score obtained. There was also no significant difference between groups regarding the category scores (low/high) on the SARS tool. Therefore, our results indicate that the SARS tool does not effectively differentiate between patients who do experience a GTCS and those who do not.

Within our overall sample, we obtained a relatively high occurrence of GTCS activity (18.92%) compared to the percentage activity found in previous studies (10.2%)[4]. However, our sample size in the GTCS group was still small (n=7), and so we must interpret our results with caution. Also if we consider the incidence of GTCS in terms of the proportion of days (2.2%) this is very low, highlighting the challenge of trying to predict the occurrence of events that have a low base-rate.

Analysis looking at each question within the SARS tool indicated that none of these questions in themselves significantly differentiated between the two groups. Analysis on question 2 (confirmed GTCS within the past 3 months) had the highest effect size, however this was still small.

Cut off scores

Due to the high risk of serious injury or death in the epilepsy population, the SARS tool must err more on the side of higher sensitivity than specificity. It is ethically more preferable to provide higher levels of observation to an individual who may not have a GTCS than to inhibit further observations levels of a patient who does experience a GTCS and who may then not receive the rapid assistance required. No tool is likely to determine risk with 100% accuracy. ROC analysis indicated that the SARS tool, while having good sensitivity for detecting the likelihood of GTCS, also had poor specificity. Looking at individual scores, the lowest total SARS score reported on the night prior to a GTCS was 5. Therefore, the current instruction of scores 5+ requiring higher levels of observation appears to offer the most reasonable option for this population However it is important to note that this will result in a high number of false positives.

Calculations of internal consistency indicated poor consistency between the items of the SARS tool. On further analysis, it seems that the deletion of question 6 from the SARS tool (reduced Anti-Epileptic Drugs) to sub-therapeutic level would raise the Cronbach's Alpha score to a level which indicated good consistency. However, it is thought that reducing AEDs below the therapeutic threshold is a risk factor for GTCS [6] and so would not recommend deleting this item from the SARS tool at this stage.

Post Hoc Analysis

Post-hoc analysis was performed to determine if there were any factors which significantly differentiated the groups which may indicate features of risk which the SARS tool did not address. No difference was found for age, gender, epilepsy diagnosis, learning disability diagnosis, mental health conditions or brain injury. However, the

presence of a comorbid physical health condition proved to be a significant differentiating factor, with medium effect size. Our results suggest that poorer physical health decreases the likelihood of an individual with epilepsy experiencing a GTCS. It is understood that people with epilepsy have a higher comorbid chronic physical health conditions [10], however this comorbidity is not a factor which has been considered in previous research as decreasing risk of GTCS. It may be that individuals with poorer physical health are more cautious with their activities and self monitoring, so they are therefore more likely to seek assistance early and prevent GTCS. However, as the sample size of the GTCS group was small, we must interpret this result with caution. Future research could benefit from looking at this with higher numbers of participants.

Individual GTCS participants

The pattern of SARS scores was then screened for each participant within the GTCS group to determine if there were any other risk factors for GTCS highlighted. The purpose of the SARS tool is to inform when a patient's risk increases to a level where they may experience a GTCS. All participants within the GTCS group scored in the high risk category on the night before their GTCS. Only two participants showed an increase in their total SARS scores in the nights prior to their GTCS (participants 3 and 7). Three participants (2, 3, 7) obtained higher total SARS scores on the night before their GTCS in comparison to their mean scores across all other nights of their admission. Two participants obtained lowers SARS scores their night before their GTCS (1, 6). Two participants (4, 5) had stable SARS scores across their admission.

As one of the risk factors within the SARS tool is the occurrence of a confirmed GTCS within 3 months, this resulted in SARS scores increasing for two of the participants after they experienced a GTCS on the ward. However, although this raised their risk score, they did not go on to experience another GTCS during their admission.

Future developments of the SARS tool

The design of a risk screening tool for the occurrence of GTCS within an epilepsy population admitted to a VT unit has proven very difficult. Considering the low rates of occurrence of GTCS during VT admission we are trying to predict something very rare. The population admitted to these units present at a greater risk of GTCS in comparison to other epilepsy sufferers due to the very fact that they require referral to a specialist monitoring unit for their epilepsy management. However the actual incidence of GTCS during admittance is low. This has resulted in difficulties acquiring base rates for those at lower risk upon admission and also ceiling effects in terms of categorisation, with the majority of participants falling into the high risk category throughout their admission. This study suggests that it is a difficult task to differentiate an already specialised group of patients.

A further limitation of this study was the lack of qualitative data collected regarding the use of the SARS tool. Future studies may benefit from interviewing staff who are using the tool to look at their perceptions of both the implementation of the tool, how clinically useful they perceive it to be, and how much they rely on the scores to inform their levels of observation. Also, in regards to data analysis, there is a possible limitation in our data analysis. We decided to focus our analysis on the average SARS scores preceding the occurrence of a GTCS for our GTCS group. However, on reflection, it may useful to calculate average scores based on the SARS score in one week prior to a GTCS. It is possible that there may be a temporal bias in scores for those patient who had a longer admission to the SEC. However, this would not have been possible within the confines of our study due to the varying nature of the admission length of our participants. Future studies examining this may benefit from further thought on the temporal aspects of SARS scores and how this may impact our understanding of the relationship between SARS scores and seizure activity.

A possible helpful addition to the current SARS tool may be the inclusion of a self-assessment score relating to whether or not the service user feels that they may have a seizure in the next 24 hours. Haut et al. (2007, 2013) [13][14] suggested that individuals

with epilepsy may be able to accurately predict seizure occurrence. They examined seizure prediction diaries in which patients would self-rate the risk of having a seizure within a 24 hour period and found significant correlations between high self ratings and the actual occurrence of a seizure. This would be an interesting advancement for the current SARS tool. However, it should be noted that, due to the high prevalence rate of Learning Disabilities within the epilepsy population, not all service users may be able to complete this question.

It would be useful to further develop the SARS tool with consideration of our findings and in conjunction with previous research. It may be helpful to include questions relating to a history of sleep seizures and scoring demographic information, such as being young and/or male, as these are factors that have been highlighted as increasing risk of GTCS in previous research[6]. Other research highlights aspects such as alcohol intake, recent injury and depression as elevating risk factors[12]. These are aspects which may be noted within the current SARS tool under 'other risk factors' however the tool may benefit from noting these specifically. Although our study does not indicate age and gender as differentiating between groups, we must be mindful of our small sample size. This study suggested a possible negative relationship between GTCS and comorbid physical health conditions, therefore this is an important aspect to examine in the future development of the tool.

However, at this time we do not seem to know enough about specific risk factors to predict GTCS incidence with accuracy. The use of electronic monitoring devices which alert staff to unusual activity are useful in terms of quick intervention. At this time, devices such as bed alarms, audio feed and continuous camera recording, accelerometers, heart rate monitors, oxygen monitor and fall alarms are used in VT units or are in development. However there are limits to technology in the process of actual detection of GTCS and all systems require a human to be alerted and respond. Ideally, we want to combine these electronic systems with a risk assessment tool in order for staff to be able to fine tune their observations of these instruments as well as of the individual patient. In the detection of something with such low occurrence, a number of sensitive systems are required alongside a sense of predicted risk.

Completion Errors

During the data collection period, it was noted that some of the SARS tools had been incorrectly completed by nursing staff. This was noted on 46 occasions over 5 different patients and all mistakes were in relation to Question 1 (possible history of GTCS). A common mistake was that a score of 0 was awarded to this question, while giving 3 points to Question 2 regarding the patient experiencing a confirmed GTCS within the last 3 months. If a patient has experienced a confirmed GTCS then 2 points should always be obtained for the first question regarding suspected GTCS. It is likely that the ambiguous language in Question 1 has led to these mistakes. This highlights a training need for staff completing these risk assessment tools and also a need for staff to be vigilant about checking any score patterns that look improbable.

Conclusion

There is a need for effective risk assessment for people with epilepsy on admission to specialist VT monitoring units. However, this study suggests that the current SARS tool is not effective at predicting whether a patient admitted to a VT unit will experience a GTCS during their stay. This is an important tool which requires redevelopment and this study has made a number of suggestions as to how this may be done. New developments to the tool must continue to be studied in terms of their predictive validity.

Although we found that the SARS tool was not able to differentiate between inpatients who do experience a GTCS and those who do not, it is important to note that this does not mean that the tool does not work. This was a small preliminary study, and the low frequency of GTCS during the data collection period means that all results must be interpreted with caution. Also the presence of completion errors noted at the point of data collection raises concerns over the use of the tool at present, again highlighting the need for caution in interpretation.

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CHAPTER 3: ADVANCED CLINICAL PRACTICE I

REFLECTIVE CRITICAL ACCOUNT

REFLECTIONS ON MY PERSONAL DEVELOPMENT WITHIN CLINICAL PSYCHOLOGY

Abstract

This reflective account considers the course of training for Clinical Psychology, and the emotional journey associated with it, in relation to the Integrated Development Model (Stoltenberg, 1993). This account summarises the main phases which a trainee in Clinical Psychology would expect to encounter during their course of training. Phase one describes the beliefs and attitudes which a trainee would have at the start of their training when they would be considered a novice. Phase two describes an intermediary stage where the trainee begins to grow in confidence, however these feelings and beliefs have a tendency to fluctuate in regards to the most recent experience encountered. Phase three describes a more stable stage in which the trainee's confidence is growing and they become more reflective on themselves and process issues within clinical settings.

I have considered three main areas of clinical development which I have experienced through my training so far. These are ethical considerations, clinical practice, and communication. I have considered my journey through each of these, and how this interplays with the phases of the Integrated Development Model. This has allowed for reflections on personal development and also how these changes will inform my future practice.

CHAPTER 4: ADVANCED CLINICAL PRACTICE II

REFLECTIVE CRITICAL ACCOUNT

REFLECTIONS ON THE ROLE OF TEACHING AND TRAINING OTHERS IN CLINICAL PSYCHOLOGY

Abstract

This reflective account considers the personal development of my competence of teaching and training within my own training in Clinical Psychology. I have chosen to consider this development in the context of the Integrated Development Model (Stoltenburg, 1993).

I have considered each of the three stages of the model and how I have seen myself progress, and at times fluctuate, within this model in relation to my teaching and training of others. I have addressed a few examples of when I have delivered teaching and training to other staff members throughout various placements in my time as a Trainee Clinical Psychologist. I have reflected on the personal evolution which I have noticed across these different episodes and how I believe these have come to be. What began with an inwardly focused trainee who struggled to confidently deliver a powerpoint presentation, has developed into someone who is now able to lead a reflective practice group and actively understands that impact that their ways of working and sharing information can have on a staff team. This account has allowed, not only for reflections on my professional competence but also on my own personal development and how this has impacted my clinical practice, and will continue to do so.

Research Portfolio Appendices

Appendix 1.1: Instructions for Authors – Journal of Epilepsy and Behaviour

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TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.
TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.
TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.
Please do not:
• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;
• Supply files that are too low in resolution;
• Submit graphics that are disproportionately large for the content.

Color artwork
Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. **For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article**. Please indicate your preference for color: in print or online only. For further information on the preparation of electronic artwork, please see http://www.elsevier.com/artworkinstructions.
Please note: Because of technical complications that can arise by converting color figures to 'gray scale' (for the printed version should you not opt for color in print) please submit in addition usable black and white versions of all the color illustrations.

Color figures for exclusive use as **cover illustration** may be submitted by authors who are also submitting a manuscript for consideration. These figures should relate to the manuscript being submitted as well as the larger scope and focus of *Epilepsy & Behavior*.

Illustration services

Elsevier's WebShop (http://webshop.elsevier.com/illustrationservices) offers Illustration Services to authors preparing to submit a manuscript but concerned about the quality of the images accompanying their article. Elsevier's expert illustrators can produce scientific, technical and medical-style images, as well as a full range of charts, tables and graphs. Image 'polishing' is also available, where our illustrators take your image(s) and improve them to a professional standard. Please visit the website to find out more.

Figure captions
Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules.

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Web references

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

References in a special issue

Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

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If you manage your research with Mendeley Desktop, you can easily install the reference style for this journal by clicking the link below:
http://open.mendeley.com/use-citation-style/epilepsy-and-behavior
When preparing your manuscript, you will then be able to select this style using the Mendeley plug-ins for Microsoft Word or LibreOffice. For more information about the Citation Style Language, visit http://citationstyles.org.

Reference style

Text: Indicate references by number(s) in square brackets in line with the text. The actual authors can be referred to, but the reference number(s) must always be given.
List: Number the references (numbers in square brackets) in the list in the order in which they appear in the text.
Examples:
Reference to a journal publication:
[1] Van der Geer J, Hanraads JAJ, Lupton RA. The art of writing a scientific article. J Sci Commun 2010;163:51–9.
Reference to a book:
[2] Strunk Jr W, White EB. The elements of style. 4th ed. New York: Longman; 2000.
Reference to a chapter in an edited book:
[3] Mettam GR, Adams LB. How to prepare an electronic version of your article. In: Jones BS, Smith RZ, editors. Introduction to the electronic age, New York: E-Publishing Inc; 2009, p. 281–304.

Note shortened form for last page number. e.g., 51–9, and that for more than 6 authors the first 6 should be listed followed by 'et al.' For further details you are referred to 'Uniform Requirements for Manuscripts submitted to Biomedical Journals' (J Am Med Assoc 1997;277:927–34) (see also http://www.nlm.nih.gov/bsd/uniform_requirements.html).

Journal abbreviations source
Journal names should be abbreviated according to the List of Title Word Abbreviations: http://www.issn.org/services/online-services/access-to-the-ltwa/.

Video data
Elsevier accepts video material and animation sequences to support and enhance your scientific research. Authors who have video or animation files that they wish to submit with their article are strongly encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed. All submitted files should be properly labeled so that they directly relate to the video file's content. In order to ensure that your video or animation material is directly usable, please provide the files in one of our recommended file formats with a preferred maximum size of 150 MB. Video and animation files supplied will be published online in the electronic version of your article in Elsevier Web products, including ScienceDirect: http://www.sciencedirect.com. Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For more detailed instructions please visit our video instruction pages at http://www.elsevier.com/artworkinstructions. Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

AudioSlides
The journal encourages authors to create an AudioSlides presentation with their published article. AudioSlides are brief, webinar-style presentations that are shown next to the online article on ScienceDirect. This gives authors the opportunity to summarize their research in their own words and to help readers understand what the paper is about. More information and examples are available at http://www.elsevier.com/audioslides. Authors of this journal will automatically receive an invitation e-mail to create an AudioSlides presentation after acceptance of their paper.

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Elsevier accepts electronic supplementary material to support and enhance your scientific research. Supplementary files offer the author additional possibilities to publish supporting applications, high-resolution images, background datasets, sound clips and more. Supplementary files supplied will be published online alongside the electronic version of your article in Elsevier Web products, including ScienceDirect: http://www.sciencedirect.com. In order to ensure that your submitted material is directly usable, please provide the data in one of our recommended file formats. Authors should submit the material in electronic format together with the article and supply a concise and descriptive caption for each file. For more detailed instructions please visit our artwork instruction pages at http://www.elsevier.com/artworkinstructions.

Database linking
Elsevier encourages authors to connect articles with external databases, giving readers access to relevant databases that help to build a better understanding of the described research. Please refer to relevant database identifiers using the following format in your article: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN). See http://www.elsevier.com/databaselinking for more information and a full list of supported databases.

3D neuroimaging
You can enrich your online articles by providing 3D neuroimaging data in NIfTI format. This will be visualized for readers using the interactive viewer embedded within your article, and will enable them to: browse through available neuroimaging datasets; zoom, rotate and pan the 3D brain reconstruction; cut through the volume; change opacity and color mapping; switch between 3D and 2D projected views; and download the data. The viewer supports both single (.nii) and dual (.hdr and .img) NIfTI file formats. Recommended size of a single uncompressed dataset is maximum 150 MB. Multiple datasets can be submitted. Each dataset will have to be zipped and uploaded to the online submission system via the '3D neuroimaging data' submission category. Please provide a short informative description for each dataset by filling in the 'Description' field when uploading a dataset.

1.2 Quality Rating Score summary Table

Study	Methodology			Participants					Analysis			
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total
Addis et al (2007)	1	1	1	1	1	1	1	1	1	1	1	11
Herfurth et al (2010)	1	1	0.5	1	1	1	0	1	1	1	1	9.5
Lah et al (2006)	1	1	1	1	1	1	1	1	1	1	1	11
Metternich et al (2013)	1	1	0	1	0	1	0	0	1	1	1	7
Múnera et al (2014)	1	1	1	1	1	1	1	1	1	1	1	11
Narayanan et al (2012)	1	1	0	1	0	1	1	1	1	1	1	9
Park et al (2011)	1	1	1	1	0	1	0	1	1	0	1	8

Protzner et al (2013)	1	1	0	1	0	n/a (1)	1	1	1	0	1	8
Ricci et al (2015)	1	1	0	1	1	1	0	1	1	1	1	9
St-Laurent et al (2009)	1	1	1	1	0	1	0	1	1	0	1	8
St-Laurent et al (2011)	1	1	1	1	0	1	1	1	1	0	1	9
St-Laurent et al (2014)	1	1	0	1	0	1	1	1	1	0	1	8
Tramoni et al (2011)	1	1	0	1	1	1	1	1	1	0	1	9
Viskontas et al (2000)	1	1	1	1	0	1	0	1	1	0	1	8
Voltzenlogel et al (2006)	1	1	1	1	1	1	1	1	1	0	1	10
Voltzenlogel et al (2014)	1	1	1	1	1	1	1	0	1	1	1	10

Appendix 2.1: Instructions for Authors – Epilepsia

Epilepsia, **56**(3):329–339, 2015
Wiley Periodicals, Inc.

Epilepsia
The Journal of the International League Against Epilepsy

INSTRUCTIONS *for* AUTHORS

Epilepsia is the official journal of the **International League Against Epilepsy (ILAE)**. The Journal publishes original articles on all aspects of epilepsy, clinical and experimental, especially of an International importance. Manuscripts should be the work of the author(s), must not have been previously published elsewhere, and must not be under consideration by another journal.

If you have a question not addressed in these pages then contact the journal at epilepsia@epilepsia.com.

EDITORIAL POLICIES

(1) The Editors-in-Chief of *Epilepsia* invite manuscripts in all areas of epilepsy-related research, especially if useful for an international audience. Manuscript submission is free. As a general guide, manuscripts will be considered for publication if they contribute significant new findings to the field. The primary aim of *Epilepsia* is to publish innovative and high quality papers that provide clinical and/or basic science insights.

The Editors will make an initial evaluation of all manuscripts to determine whether they provide new important information and in the field, are in the proper format, and are appropriate for the Journal (editorial review). Reports are unlikely to be accepted for publication if they are not based in sound science and/or they provide only incremental knowledge of limited general usefulness. To assist authors in deciding whether to submit a manuscript to *Epilepsia*, we provide the following commonly encountered examples of reports which we are unlikely to publish:

(a) Papers that describe clinical features or epidemiology in a given region of the world that do not provide new insights into epilepsy not already published;
(b) Correlative studies where the sample size is too low to provide statistically sound findings;
(c) Genetic association studies in which the association has already been confirmed;
(d) Investigatory articles describing the application of a new technical variation which is not likely to have clinical utility or impact;
(e) Correlative clinical studies, which are conceived without clear hypotheses and the results of which are of little clinical utility;
(f) Basic research studies that are not grounded in epilepsy relevant hypotheses;
(g) Single group, before-after evaluations of therapeutic interventions and programs that do not include a control group;
(h) Small case series which largely replicate what is already known;
(i) Case reports (highly unlikely to be accepted unless they provide novel findings of theoretical or clinical importance).

Epilepsia will accept, review, and publish studies with negative results, provided that appropriate controls have been used, the study is adequately powered, and the results are important and or useful to others in there search community.

(2) Manuscripts describing original research, and passing the initial editorial screen, will be subject to external peer review. Acceptance of these manuscripts is never guaranteed. At least two reviews are generally obtained for these submissions; additional reviews may be sought at the discretion of the Editors. Appeals of rejection decisions will be considered by the Editors-in-Chief; decisions of the Editors-in-Chief are final.

(3) In the cover letter, authors should indicate that the material described in the manuscript is the work of the author(s), has not been previously published, except in abstract form, and that it is not simultaneously under consideration by any other journal.

(4) As a condition of publication, *Epilepsia* requires authors to transfer copyright to the ILAE. Authors will be asked to login into Author Services and complete the appropriate license agreement via Wiley Author Licensing Service.

(5) *Epilepsia* complies with recommendations of the International Committee of Medical Journal Editors (http://www.ICMJE.org). Authors are required to include a statement at the end of their manuscript affirming that the work described is consistent with the Journal's guidelines for ethical publication (see below). *Epilepsia* is a member of the Committee on Publication Ethics (COPE), and we adhere to itsprinciples (http://publicationethics.org/).

(6) Data reporting should follow appropriate checklists and guidelines (e.g., STROBE for observational trials; CONSORT for clinical trials), and other checklists should be consulted for other reports including diagnostic accuracy (STARD) or meta-analyses (PRISMA). Checklists can be downloaded from the following:
STROBE – http://strobe-statement.org
CONSORT – http://www.consort-statement.org/consort-statement/
STARD – http://www.stard-statement.org/
PRISMA – http://www.prisma-statement.org/

(7) For animal experiments, the authors need to state that the experiments have been performed in accordance with all applicable national and/or international guidelines/laws. The authors should also provide their allowance number for performing animal experiments when available and should add a statement indicating that the principles outlined in the ARRIVE guidelines and the Basel declaration (http://www.basel.declaration.org) including the 3R concept have been considered when planning the experiments.

(8) Authors are also required to provide full disclosure of any conflict of interest as a part of the submitted manuscript (see Disclosure of Conflicts of Interest in the Manuscript Format section under Manuscript Preparation). Manuscripts that do not conform to these guidelines will not be considered for publication. Discovery of or failure to comply will result in rejection of the manuscript, retraction of the published article, and/or a ban on future submissions by the author(s).

(9) In submitting a manuscript, the submitting/corresponding author must acknowledge that: a) all co-authors have been substantially involved in the study and/or the preparation of the manuscript; b) no undisclosed groups or persons have had a primary role in the study and/or in manuscript preparation (i.e., there are no "ghost-writers"); and c) all co-authors have seen and approved the submitted version of the paper and accept responsibility for its content. The Editors reserve the right to require authors to submit their original data for comparison with the manuscript's illustrations, tables, and results.

(10) Sometimes editors make mistakes. If an author believes an editor has made a decision in error we welcome an appeal. Please contact the editor and in your appeal letter, clearly state why you think the decision is a mistake and set out specific responses to any comments related to the rejection. An appeal does not guarantee a re-review.

TYPES OF MANUSCRIPTS

The following types of material may be considered for publication:

(1) **Peer-reviewed papers** (to be submitted by uploading online via Scholar One Manuscript Central http://mc.manuscriptcentral.com/epilepsia).

a. Critical Reviews and Commentaries. The Editors-in-Chief encourage submission of reviews and commentaries on topical and controversial issues. Authors planning/proposing such papers should contact the Editors-in-Chief at epilepsia@epilepsia.com before submitting their manuscripts. Authors can also approach one of *Epilepsia's* Associate Editors about possible reviews. While there are no strict length limits on this type of paper, manuscripts generally should be around 4-5000 words. Ample figures and tables are encouraged. Longer manuscripts will be considered at the discretion of the Editors-in-Chief, but justification should be provided by the authors.

b. Full-length Original Research Articles. These articles should be limited in length to 4000 words and no more than 6 figures and tables (combined). Additional figures and tables will be permitted at the discretion of the Editors or can be submitted as online only Supporting Information (which will be linked to the online version of the published article). Authors should aim for presenting material clearly and completely, in the most concise and direct form possible; the Introduction should be brief (typically less than 600 words), and the Discussion should be restricted to issues directly relevant to the Results (typically less than 1200 words).

c. Brief Communications. These articles including short studies, small series, case reports, etc. should describe previously unpublished material, including original research and/or clinical observations. The papers are limited generally to 1800 words (excluding the summary), 15 references, and no more than 2 figures and tables (combined). Please note that the Editors may use their discretion to request that brief communications be shortened to a length that they feel is appropriate, and may provide for a larger number of figures and tables if justified.

Brief Communications may be published online only (not in the print version of the journal) depending on their impact. They will appear in a specific issue in the electronic (online) version, and will be identified and described (Short Summary) in the Table of Contents of the printed version of that issue. The online versions will be dealt with by PubMed/Medline and other indexing/citation systems, exactly the same way as print articles; they will be referenced by their DOI number and date of online publication (which will continue to be approximately 35 working days following acceptance).

d. Controversy in Epilepsy: For emerging areas related to epilepsy care and research for which there is more opinion than high quality data, Epilepsia uses the Controversy series as a venue. Authors can propose a pro- and

con-position each limited to 2000 words. Contact the editors at epilepsia@epilepsia.com before submitting in this series.

(2) **Editorially-reviewed material** (to be submitted by email to the Editors-in-Chief at epilepsia@epilepsia.com, except letters and commentaries which should be submitted online at http://mc.manuscriptcentral.com/epilepsia)

Other contributions that do not report original research will be published at the discretion of the Editors-in- Chief, with only editorial review. Such material includes: workshop reports and conference summaries, obituaries, letters/commentary to the Editors (500 word limit, and only exceptionally figures or tables), special (brief) reports from ILAE Commissions or other working groups, and announcements. Such material will usually be published in **Gray Matters**.

(3) **Supplements** (to be submitted as directed by the Editors-in-Chief)

Supplements, including meeting abstracts, will be published only after advance arrangements are made with the Editors-in-Chief. Guidelines for preparing supplements are given below. Proposal for, and questions about supplements should be directed to one of the Editors-in-Chief (epilepsia@epilepsia.com). Such proposals must be explicitly approved by the Editors-in-Chief, who will also confirm the page rate charge for the proposed supplement.

(4) **Special reports:** In some cases, special reports from ILAE Commissions or other broadly constituted working groups will be published after peer review. The corresponding author of such papers should confer with the Editors-in-Chief to determine if the full manuscript willbe peer-reviewed, or whether only a short version will be considered for publication in *Epilepsia's* Gray Matters (see below).

MANUSCRIPT PREPARATION

General Style Guidelines

Manuscripts are to be submitted (and will be published) in English. Writers not fluent in English should seek assistance to ensure proper grammar and syntax, and to help generate a manuscript organization that facilitates reader understanding. Authors for whom English is a second language may choose to have their manuscript professionally edited before submission, to improve the English. A list of independent suppliers of editing services can be found at http://wileyeditingservices.com/en/. All services are paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication. The Editors will not re-write papers submitted in unacceptable English, and will return such manuscripts for revision before sending them out for review.

Use international non-proprietary (generic) names when referring to drugs; avoid proprietary (brand) names. All acronyms should be spelled out at first mention. Spell out numbers below 10 and all numbers that are used to begin a sentence; use Arabic numerals for numbers above 10 and for units of measure. Manuscript text should be double spaced with at least 1 inch margin on all sides using size 12 font. Word limits for each type of submission will generally be enforced unless there are good reasons not to do so. If manuscripts exceed these guidelines, authors should submit a cover letter explaining why the additional length is necessary.

Authors are encouraged to use the most recent terminology of seizures and epilepsy (Fisher et al., 2014) and epilepsy classification of the ILAE (Berg et al., 2010). Studies involving treatments should adhere to ILAE's classification of medically refractory epilepsy (Kwan et al., 2011).

Manuscript Format

a. Critical Reviews and Invited Commentaries

- **Title Page** (see Full-Length Original Research below)
- **Summary and Key Words**

  Reviews and commentaries should generally begin with a summary (less than 300 words) of the content. The summary (structured) should provide the reader with the main points of the paper, and be divided into Objective, Methods, Results, and Significance. The Summary should be followed by a list of 3-6 Key Words; please provide Key Words that will assist in the indexing of your article (i.e., make it easy for individuals who are searching PubMed to find your paper). Do not use words already incorporated into your title (those words are picked up automatically by the indexing service).

- **Body of review**

  There is no designated structure for the body of Reviews or Commentaries. Authors are encouraged, however, to use sub-headings to separate major sections and to facilitate clarity and to use figures and tables to illustrate the key issues of the document.

  Tables, figures, figure legends, references, acknowledgements, statement of compliance with the Journal's guidelines for ethical standards in publishing, disclosure of conflicts of interest, and Supplementary material as for *Full-Length Original Research* (see below)

b. Full-Length Original Research, Special Reports, and Brief Communications

- **Title Page**

  Include the following information: Full title of the manuscript which generally should be as concise and precise as possible; authors' names (first and last names,

middle initial when commonly used by that author); institutional affiliation for each author (use superscripted numbers after each author's name, and a corresponding superscripted number before each institutional affiliation); contact information for the corresponding author (name, address, telephone number, fax number, e-mail address); running title (no more than 40 characters and spaces in length); Key Words for use by abstracting services (same as following summary); number of text pages; number of words; number of references; number of figures; number of tables.

❑ **Summary and Key Words**

Provide a summary of no more than 300 words (200 words for Brief Communications). The summary for Full Length Original Research reports should consist off our sections, labeled: Objective; Methods; Results; Significance. This structured summary should concisely and specifically describe why and how the study was performed, the essential results, and what the authors conclude from the results. To promote brevity, authors may use phrases rather than complete sentences. The summary for Special Reports, Invited Commentaries, and Brief Communications is not structured, but should cover the same topics as the structured summary. The summary (structured or unstructured) should be followed by 3-6 Key Words (see above). A second short summary (less than 100 words) is required for Brief Communications that can be used in the print issue Table of Contents. Submit the second short summary as a Supporting Document.

❑ **Key Point Box**

Include 3 to 5 key bullet points that summarize your article after the main body of text. Please ensure each bullet point is no longer than 140 characters.(A key point box is not needed for Brief Communications). An example of a key point box can be found on the Epilepsia Scholar One Manuscripts website (http://mc.manuscriptcentral.com/Epilepsia); please click 'Instructions and Forms' at the top right-hand corner of the homepage.

❑ **Introduction**

State the objectives of the study clearly and concisely, and provide a context for the study by referring judiciously to previous work in the area. Do not attempt to present a comprehensive view of the field. Provide a statement about the significance of this research for understanding and/or treating epilepsy.

❑ **Methods**

Describe the research methods in sufficient detail that the work can be duplicated; alternatively, give references (if they are readily accessible) to previous comprehensive descriptions. Identify the statistical procedures that were used and the rationale for choosing a particular method, especially if it is not standard.

Reports of experimental studies on humans must explicitly certify that the research received prior approval by the appropriate institutional review body and that informed consent was obtained from each volunteer or patient. Studies involving animals must include an explicit statement that animal care and use conformed to institutional policies and guidelines. When animals are subjected to invasive procedures, details must be provided regarding the steps taken to eliminate/minimize pain and suffering, including the specific anesthetics, analgesics, or other drugs used for that purpose (amounts, mode of delivery, frequency of administration).

If extensive descriptions of methods are needed, provide basic information with in the text and submit supplementary information for online Supporting Information.

❑ **Results**

Results should be reported fully and concisely, in a logical order. Do not repeat methodological details from the Methods section. Where possible, use figures and/or tables to present the data in a clear and concise format. Do not repeat data in the text that are given in a table, but refer to the table. Provide textual explanations for all figures, with clear reference to the figure(s) under discussion. Descriptive information provided in figure legends need not be repeated in the text; use the text, however, to describe key features of the figures. When appropriate, give sample numbers, the range and standard deviation (or mean error) of measurements, and significance values for compared populations.

❑ **Discussion**

Provide an interpretation of the results and assess their significance in relation to previous work in the field. Do not repeat the results. Do not engage in general discussion beyond the scope of the experimental results. Conclusions should be supported by the data obtained in the reported study; avoid speculation not warranted by experimental results, and label speculation clearly. Discuss the significance of the data for understanding and/or treating epilepsy.

❑ **Statistical Methods**

The following guidelines assume familiarity with common statistical terminology and methods. We recommend that authors consult a biostatistician during the planning stages of their study, with further consultations during the analytical and interpretational stages.

1. Analysis guidelines:

- Use robust analytic methods when data are skewed.
- Use Kaplan Meier methods, Cox Proportional Hazards, and mixed models analyses for longitudinal data.
- Account properly for statistical outliers.

- Use exact methods as much as possible in analyses of categorical data.
- Use appropriate correction procedures to account for multiple comparisons, and conduct post-hoc comparisons with statistically appropriate methods.

2. Presentation guidelines:

- Report means accompanied by standard deviations; standard errors should not be used.
- Present results with only as much precision as is appropriate.
- Present confidence intervals, whenever possible, including in figures.
- Describe quantity of missingness and methods used for handling such missingness.
- In general, present two-sided p-values. P-values larger than 0.01 should be reported to two decimal places, those between 0.01 and 0.001 to three decimal places, and those smaller than 0.001 should be reported as $p<0.001$.
- In reporting clinical trials, include a flow diagram, a completed trial checklist, and trial registration information. The CONSORT flow diagram and checklist are recommended (http://www.consort-statement.org/).

❑ Acknowledgements

Acknowledge sources of support (grants from government agencies, private foundations, etc.); including funds obtained from private industry. Also acknowledge (consistent with requirements of courtesy and disclosure) participation of contributors to the study who are not included in the author list.

❑ Disclosure of Conflicts of Interest

In addition, each author should provide full disclosure of any conflicts of interest. One of the following sentences must be included at the end of the paper: either "Author A has received support from, and/or has served as a paid consultant for .... Author B has received support from.... The remaining authors have no conflicts of interest." Or "None of the authors has any conflict of interest to disclose." Note: Disclosure is needed for financial income/payment from commercial sources, the interests of which are relevant to this research activity. Please identify sources from which financial assistance/income was obtained during the period of the research activity and generation of the current report. Grants from government and/or private agencies should be identified in the Acknowledgements section.

❑ Ethical Publication Statement

All papers must include the following statement to indicate that the authors have read the Journal's position on issues involved in ethical publication (see below) and affirm that their report is consistent with those guidelines: "We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.".

❑ References

Authors are responsible for the accuracy of their references. References should follow a modified Vancouverstyle format. Citation of references in the text should be in superscript numbers (including those in figure legends and tables). Cite the end references in numerical order. The first three authors should be listed and followed by et al. Use journals' PubMed abbreviations in the reference list at the end of the paper (as opposed to journals' names being written out in full). Reference program patches are available on the Epilepsia Scholar One Manuscripts website (http://mc.manuscriptcentral.com/Epilepsia); please click 'Instructions and Forms' at the top right-hand corner of the homepage.

Number of references is limited to the following:
Full Length Original Research Paper – 40
Brief Communications – 15
Reviews – 80
Special Reports – 80

SampleReferences:

Journal Article

Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia 2010; 51: 676-685.

Journal article published electronically ahead of print version

Reilly C, Atkinson P, Das KB et al. Academic achievement in school-aged children with active epilepsy: A population-based study. Epilepsia Epub 2014 Oct 20.

Journal article In Press

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- **Figure legends**

Number each legend sequentially to conform to the figure number (e.g., Figure 1, Figure 2...). The legend should provide a brief description of the figure, with explanation of all symbols and abbreviations. Written permission to use non-original material must be obtained (from the original authors (where possible) and publishers) by the authors. Credit for previously published material (author(s), date, journal/book title, and publisher) must be included in the legend.

- **Tables**

Tables should be formatted as the authors wish the table to appear in print. Present all tables together at the end of the manuscript, with each table on a separate manuscript page. Each table should be given a number and a descriptive title. Provide notes and explanations of abbreviations below the table, and provide clear headings for each column and row. Do not duplicate data given in the text and/or in figures. Written permission to use non-original material must be obtained (from the original authors (where possible) and publishers) by the authors. Credit for previously published material (author(s), date, journal/book title, and publisher) must be included in the table notes.

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All figures should be prepared with care and professionalism. Submissions that do not comply with the following formatting requirements will be returned for correction and re-submission. Figures should be submitted as TIFF files in the size expected for final publication– approximately 3 inches (7-8 cm) for half column and 6 to 7 inches (15-17 cm)for double columns. Submit black and white figures with a minimum of 300 dpi (MRI scans) and for line drawings or figures that included imbedded text (bar graphs with numbers) at least 600 dpi. Complex figures (including photographs, micrographs, and MR-related images), either in color, in half-tones, or in black and white, should also be submitted in TIF format with a resolution of at least 600 dpi. We recommend saving the TIF files with LZW compression (an option when you 'save as' in packages like Photoshop), which will make the files smaller and quicker to upload without reducing the resolution/quality. Save each TIF file with a name that includes the first author's last name and the figure number as referenced in the text (e.g., Smith-fig1.tif). Provide clear labels on the ordinate and abscissa. Figures with more than one part should be combined by the authors in the correct orientation and labeled with A, B, C etc. When relevant, include calibration information. Label figures using Calibri font and be sure that all labels are large enough to be clearly legible when the figure is reduced to fit onto a journal page. The maximum size of any figure is 7x9 in (17 22.5 cm) and 40 mega pixels; the total number of pixels for each figure (i.e., height width) must be less than 40 megapixels otherwise the image will not convert to PDF for review. There is no charge for color figures. We strongly encourage authors to generate figures in color (to enhance clarity of presentation and aesthetic appeal), using the following color palette:

Color #	RGB Definition	CMYK Definition
#e4b8b4	228/184/180	0/25/15/9
#ce8080	206/128/128	0/50/30/18
#a30234	163/2/52	0/100/60/37
#511d24	81/29/36	42/85/67/60
#f1b682	241/182/130	0/29/50/4
#e37c1d	227/124/29	0/58/100/8
#ffdf76	255/223/118	0/11/64/0
#abb47d	171/180/125	13/0/47/27
#67771a	103/119/26	27/0/94/55
#a1c5cb	161/197/203	25/0/7/16
#5698a3	86/152/163	50/0/14/32
#00545f	0/84/95	100/0/28/64
#002f30	0/47/48	87/34/47/77
#bacfec	186/207/236	25/11/0/0
#0076c0	0/118/192	100/46/0/0
#002157	0/33/87	100/75/0/60
#7a5072	122/80/114	50/73/30/18

Photographs or videos of patients should not reveal patient identity; masking eyes and/or other identifiers is compulsory unless the eyes are essential to the meaning of the photograph or video. In addition, such photographs and videos must be accompanied by a letter saying that signed consent forms authorizing publication have been obtained for all identifiable patients, and that the consents will be maintained by the author for seven years or until the patient reaches 21 years of age, which ever is longer. Do not send Epilepsia the consent forms; U.S. Federal privacy rules prohibits ending signed consent forms to Epilepsia or Wiley-Blackwell Publishing without written permission from the patient to do so. A sample signed consent form can be found on the Epilepsia Scholar One Manuscripts website (http://mc.manuscriptcentral.com/Epilepsia); please click 'Instructions and Forms' at the top right-hand corner of the homepage.

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Supporting information, to be published online only, can be submitted for review. Such material may include: additional figures, large tables, videos, etc. that cannot be accommodated within the normal printed space allocation for an article–but provide important complementary information for the reader. As determined by the reviewers and Editors, supporting information will be posted on the Wiley Online Library Epilepsia server and directly integrated into the full-text HTML article. Explicit reference to the supporting information in the main body of the text of the article is recommended, and the material must be captioned at the foot of the text, below the reference list. Supporting information will be published as submitted and will not be corrected or checked for scientific content, typographical errors or functionality. Although hosted on Wiley Online Library, the responsibility for scientific accuracy and file functionality remains entirely with the authors. A disclaimer will be displayed to this effect with any supporting information published.

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Graphics – GIF; TIF (or TIFF); EPS; PNG; JPG (or JPEG); BMP; PS (postscript); embedded graphics (e.g. a GIF pasted into a Word file) are also acceptable.

Video–QuickTime; MPEG; AVI. All video clips must be created with commonly-used codecs, and the codec used should be noted in the supplementary material legend. Video files should be tested for playback before submission, preferably on computers not used for its creation, to check for any compatibility issues. Video clips are likely to be large; try to limit their size to less than 10 MB.

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❑ **Title**

Letters, workshop reports, etc. should be given a brief title. Letters should start with the opening *To the Editors*:

❑ **Authors and affiliations**

Provide authors' names (first and last names, middle initial when commonly used by that author); institutional affiliation for each author (use superscripted numbers after each author's name, and a corresponding superscripted number for each institutional affiliation); e-mail contact address for the corresponding author.

❑ **Body of submission**

Letters and commentaries should be restricted to 500 words or less, unless other wise allowed by the Editors. Figures and tables will be included only in exceptional cases. Gray Matters will not be used to publish case reports. Tables, figures, figure legends, references, acknowledgements, disclosure of conflicts of interest, ethical publication statement and Supporting Information–as for *Full Length Original Research* (see above).

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a. Text

Manuscripts should be prepared using a word processing program. Save text and tables as a Microsoft Word document. Place the lead author's name and the page number in the upper right hand corner of each page. Begin numbering with the Title Page as #1, and number pages consecutively including references, figure legends, and tables. Text (including acknowledgements, disclosure statement, and figure legends) and references should be double-spaced, and be composed in 12 point font (preferably Times New Roman). When generating a revised manuscript, identify the altered portions of the manuscript with highlighted text, underlined, colored or bold font to indicate where changes to the original version of the text have been made.

b. Tables, Figures, and Supporting Information

See above.

Appendix 2.2: Major Research project Proposal

MRP Proposal

Proposal Title: The Efficacy of a Seizure Assessment Risk Tool in Predicting Occurrence of Tonic-Clonic Seizures

Date of Submission/Version number: 7th April 2015 – Version 2

Abstract

Background

There is growing evidence that specific risk factors can be identified to help predict an individual's level of risk of serious injury or death as a result of their epilepsy. Previous studies have highlighted the prevalence of peri-ictal EEG suppression, which is characterised by a period of no brainwave activity around the time of a seizure, and incidence of Global Tonic Clonic Seizures, a seizure affecting the whole brain, as well as other risk factors such as polypharmacy, withdrawal from or changes to antiepileptic drugs, sleep seizures, age and gender, and alcohol consumption. The need for fast intervention from nursing staff has been indicated as being beneficial in avoiding serious injury or death when patients with epilepsy have generalised seizures accompanied by EEG suppression. Research has suggested that intervention should optimally occur within 50 seconds of EEG suppression commencing. At this time, there are no specific guidelines for risk assessment in regards to risk of incidence of Global Tonic Clonic Seizures or incidence of death or serious injury.

The William Quarrier's Scottish Epilepsy Centre (SEC) have developed a new risk assessment checklist based on various risk issues highlighted by previous research. Generalised seizures carry a serious risk of injury and/or death for epileptic patients. It is known any seizure activity is a risk factor for the occurrence generalised seizures and so the tool is used to calculate risk of a patient experiencing a seizure of any description. This checklist, known and the Seizure Risk Assessment Scoring tool (SRAS), has been being piloted within the SEC since September 2014.

Aims

This project will investigate the efficacy of this checklist in highlighting those patients admitted to the videotelemetry ward who are at risk of generalised seizure or epilepsy related injury or death.

Procedure

The Seizure Risk Assessment Scoring tool (SRAS) has been used in the SEC since September 2014. The tool provides scores on various conditions, such as medication withdrawal, seizure history, and experience of tonic clonic seizures, which are believed to increase a person's risk of having a generalised seizure. Data from this tool has been collected for 6 months on site for all patients admitted to the SEC. All of these scores will be collected and compiled in a database. We will compare these scores with the actual occurrence of individuals having seizures which will allow us to measure the efficacy of the tool and determine if it is effective at predicting the risk of someone having a seizure.

Application

We hope that the SRAS checklist will prove to be a viable tool for clinicians for risk assessment which can then be used to influence observation and staffing levels on an individual basis.

Background Information

Sudden Unexpected Death in Epilepsy (SUDEP) is one of the leading causes of death in individuals with refractory epilepsy and is of great concern to the epilepsy population and those involved in their clinical care (Shorvon and Tomson, 2011). There is growing evidence that specific risk factors can be identified to help predict an individual's level of risk of serious injury or death as a result of their epilepsy. Shankar et al. (2014) conducted an investigation into the factors which may have been associated with SUDEP and discovered that most of the individuals who met criteria for SUDEP had experienced an increase in seizure frequency and/or intensity within 6 months of their death. Semmelroch and colleagues (2012) performed a retrospective audit of patients undergoing EEG videotelemetry. They found that 10.2% of patients experienced at least one Global Tonic Clonic Seizure (GTCS), and of these 27% showed peri-ictal EEG suppression. They also discovered that if an individual experienced more than one GTCS they demonstrated more incidences of EEG suppression alongside other seizures. Lhatoo et al. (2010) had previously identified a link between prolonged post-ictal EEG suppression (duration longer than 50 seconds) and individuals with refractory epilepsy who are more at risk of SUDEP. This highlights the need for close monitoring and fast intervention from nursing staff to ensure that EEG suppression is not sustained for longer periods (>50s).

Shankar and colleagues (2013) also performed a literature review looking at risk factors associated with SUDEP. They found evidence that the following were well documented risk factors which should be considered when evaluating the risk of death of serious injury of an epileptic patient:

- Having uncontrolled generalised tonic-clonic seizures
- Not taking anti-epileptic drugs (AEDs) as prescribed
- Having tonic-clonic seizures that are not controlled by AEDs
- Having sudden and frequent changes to AEDs
- Being a young adult (in particular male)
- Having sleep seizures
- Having seizures when alone
- Drinking large amounts of alcohol

There have been a few studies investigating the risk and safety issues within video telemetry units across the United Kingdom. Kandler et al.(2013) looked at the incidence of adverse events, such as physical injury or respiratory difficulties which occurred during seizure activity in 27 different VT units over the period of one month. They found that these adverse events occurred in 12% (n=33) of seizures. However, they found that staff did not attend the patient in 44% (n=120) of cases.

Cole and colleagues (2010) developed and piloted a risk awareness checklist for individuals with epilepsy and a learning disability. Qualitative analysis of nursing staff who piloted the checklist reported that staff confirmed the need for a risk checklist and that they found this beneficial for reducing patients' risk of injury. This checklist was developed for individuals with learning disability dwelling in the community and was directed at the staff supporting them in the community.

The British Society for Clinical Neurophysiology published safety guidelines for video EEG telemetry admissions, which outline staffing levels and monitoring procedures.

However there are currently no explicit guidelines for risk assessment in regards to risk of incidence of GTCSs or SUDEP.

Given the high risk nature of the patients admitted to Videotelemetry Units due to their complex epilepsy presentations and the nature of treatment and exploratory procedures that are undertaken, the William Quarrier's Scottish Epilepsy Centre (SEC) developed a new checklist based on the findings of previous research (Ryvlin et al, 2013). This highlighted the main area of risk was having a generalised seizure or stopping medication which would in turn be more likely to lead to having a generalised seizure.

Generalised seizures carry a serious risk of injury and/or death for epileptic patients. It is known any seizure activity is a risk factor for the occurrence generalised seizures and so the tool is used to calculate risk of a patient experiencing a seizure of any description. The checklist is completed daily with each patient. This is firstly because there are things that are part of routine patient care which increase risk, such as reducing medications or sleep depriving. There may also be information gained that changes our perception of risk, such as a diagnosis or emergence of a different seizure type. This checklist, known and the Seizure Risk Assessment Scoring tool (SRAS), has been used within the SEC since September 2014, but its effectiveness has not been evaluated.

Aims

The aim of this study is to assess the effectiveness of the Seizure Risk Assessment Scoring tool (SRAS). We aim to assess if this tool is an accurate predictor of patients' risk of seizures.

Research Question

Does the current tool effectively predict the likelihood of seizure incidence within the Epilepsy Video Telemetry Unit?

Hypothesis

We hypothesise that increased scores on the Seizure Risk Assessment Scoring tool will correlate with higher incidence of seizure activity within the VT unit during the patients' stay.

Design

This is a single group correlational study.

Procedure

The SRAS is completed for each patient every night by one of the nursing staff in the SEC clinical team. The total score of the SRAS form then informs the levels of monitoring required for each patient for the next 24 hours. The forms are stored in the patients' medical notes and the same form is updated on each assessment. Seizure activity is recorded on a dedicated sheet at the front of the medical notes. The location, presentation and duration of each seizure is recorded by nursing staff, for example, seizure occurred in bedroom, lasted for 3 minutes, presented as jerking of both arms..

Data Collection

The SRAS tool has been implemented in the Scottish Epilepsy Centre since September 2014. The tool provides scores on a number of areas deemed to increase a person's risk of having a seizure. Each question has an allocated risk score (in brackets) and the total score, out of 27, of each of these areas determines the level of observation a patient should be under for approximately the following 24 hours.

- History of possible Generalised Tonic Clonic Seizure (GTCS) (2)
- Confirmed GTCS in <3 months on Optimal Treatment (3)
- Nocturnal Seizures (1)
- Outstanding diagnostic uncertainty (1)
- Reduced AED but on therapeutic dose (3)
- Reduced AED sub therapeutic level (4)
- AED withdrawn (no AED) (5)
- Non-Compliance with AED (1)
- Sleep deprivation (3)
- Breathing/Cardiac Issues (1)
- Any Other Risk (0-3) *e.g. falls, psychosis, wandering*
- Total SRAS Score

Total scores are calculated and categorised as follows:

0-2: Low risk; normal monitoring

3-4: moderate risk; increase monitoring

5+: high risk; highest level of monitoring

All of these scores will be collected and compiled in a database.

All patients have a record of seizure activity and injury held within their medical notes. The number and type of seizures will be collected for each individual. In addition, the following data will also be collected:

- Gender
- Age
- Reason for admittance to the SEC
- Diagnosis if applicable
- Duration of epilepsy

Sample Size

It is anticipated that we will collect data points from the months of September 2014 until March 2015. There are on average 8 patients screened using this tool each day. Therefore we anticipate that we will have around 1,500 data points for analysis, with data points being total risk scores as calculated through the SRAS. All individuals will be 18+ years old with a history of epilepsy. Individuals presenting with non epileptic attacks will be excluded.

Statistical Analysis

Data will be analysed using the Statistical Package for Social Sciences (SPSS). The data will be screened for outliers and hand checked for typing errors and abnormal data results. The data will be examined in a number of ways to explore the relationship between ratings on the SRAS and the likelihood of patients having seizures.

Initially, the full data set will be considered taking each SRAS category score as an individual data point. This will be done in an exploratory nature to better understand the data. We will use a Chi Square to look at the association between presence of a seizure (yes/no) and the corresponding SRAS category (low risk/moderate risk/high risk) which was reported the previous night. We can then use logistic regression to identify if the SRAS category does seem to predict the likelihood of a seizure at data point level.

As the data points are related due to many points being gathered from the same individual, we will then formally control for dependence by looking at the average scores for each person for the duration of their stay in the SEC and compare this to the number of seizures which they had. We will likely use a Fisher's test to determine if there is an overall association between these two variables. If the data is normally distributed, we will then perform a linear regression to establish the nature of that association.

Settings and Equipment

Data collection will take place in the Quarrier's Scottish Epilepsy Centre. The researcher will require access to the medical notes of individuals who have been risk assessed using the SRAS tool under supervision of the clinical team directly involved in patient care. Data will be collected from the medical notes, anonymised, and transferred

to a database. Statistical analysis will be performed using the information contained within this database.

All data will be held on an encrypted laptop provided by the University of Glasgow. Data analysis will also be conducted on this encrypted laptop to ensure the safe storage of sensitive information. Data will be backed up on an encrypted memory stick which will be held securely in a locked cabinet.

Health and Safety Issues

Participant Safety Considerations

There are no risks to patients caused by this project. Data has already been collected and patients will have no contact with the researcher for the duration of the data collection and analysis period.

Researcher Safety Considerations

The research setting is a clinical base which has procedures in place to minimise risk to staff and patients. These are thought to be adequate in the context of the proposed study. The researcher will have no direct contact with patients.

Ethics

All data will be held confidentially, and any data held electronically will be stored on an encrypted laptop provided by Glasgow University. All data will be anonymised and no patient identifiable data will be used during the course of the project. All of the data is routinely collected during a typical admission to the SEC and therefore patients will not be undergoing any additional contact or screening as a result of this project. No patients will be directly contacted by the researcher during this project, nor will they experience any change to their routine care. This proposal has been reviewed by the West of Scotland Research Ethics Service and deemed that it does not require NHS research ethics review. Permission will be sought from the Guardian of data at the SEC prior to accessing medical notes.

Financial Issues

As this data is routinely collected and monitored by staff this will incur no additional costs. Costs will be incurred mainly in regards to paper, printing and photocopying charges.

Timetable

Milestone	**Expected date**
MRP Proposal Submission	March 2015

Begin Data collection	April 2015
Begin Write up	May 2015
First Full Draft submitted	June 2015
Thesis Submission	July 2015

Practical Applications

Research has shown that both patients and clinicians would benefit from an effective risk assessment tool to help identify those individuals most at risk from experiencing seizures and subsequently epilepsy related injury and death. We hope to produce a tool which can be confidently used to risk assess all patients admitted to VT wards for EEG screening. This tool will also be used to inform staffing levels within a VT unit and also observation requirements for each individual patient to minimise risk and to ensure fast response to seizure activity.

References

References can be found in Chapter 2: Major Research Proposal

Appendix 2.3: Screening Assessment Risk Score (SARS) tool

Patient Name: **D.O.B.**

Review Daily and Update as Required

Date	*Seizures*				*Provocation*					*Other*		**Total SRAS Score**	*Risk Management*			Sign
	History of Possible GTCS (2)	Confirmed GTCS in <3 months on Optimal Treatment (+3)	Nocturnal Seizures (1)	Outstanding diagnostic uncertainty (1)	reducedAED but on therapeutic dose (3)	reducedAED sub therapeutic level (4)	AED withdrawn (no AED) (5)	sleep deprivation (3)	Non-Compliance With AED (1)	Breathing/ Cardiac Issues (1)	Any Other Risk (0-3) *e.g. falls, psychosis, wandering*		Care Plan No.	Additional Info	Risk Measure(S) **E** – Emfit, **15** – 15 min checks, **30** – 30 min checks,, **NM** – video on Nurse Monitor	

SEC SRAS Scoring Indicators	
0-4 low risk – normal monitoring **5+** high risk – highest level of observation	**5+** consider/confirm all precautions in place emfit, frequency of face to face check 15/30mins etc /(*fall monitor / 0^2 monitoring/cardiac /- not currently available)*

Appendix 2.4: Summary table of mean SARS scores for all participants

Ppts	Av. Total SARS	Mean score for each SARS question										
		Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
1	4.00	2.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00
2	6.00	2.00	0.00	1.00	1.00	1.00	0.00	0.00	0.00	0.00	1.00	0.00
3	6.00	2.00	3.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4	8.42	2.00	0.00	1.00	0.88	3.00	0.00	0.00	0.00	0.00	0.00	1.54
5	7.00	2.00	3.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6	8.74	0.30	3.00	0.89	0.00	3.00	0.00	0.00	0.00	0.00	0.00	1.56
7	8.54	2.00	3.00	0.96	0.00	0.00	0.00	0.00	0.00	0.00	1.00	1.58
8	5.00	2.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00
9	6.15	2.00	0.00	1.00	1.00	0.00	0.42	1.73	0.00	0.00	0.00	0.00
10	5.43	2.00	0.43	1.00	0.00	2.25	0.00	0.00	0.00	0.00	0.00	0.25
11	4.92	2.00	0.00	1.00	1.00	0.25	0.67	0.00	0.00	0.00	0.00	0.00
12	9.86	2.00	3.00	0.78	0.22	1.83	0.00	0.00	0.08	0.00	0.00	1.94
13	6.18	2.00	0.00	0.00	1.00	0.11	0.39	2.68	0.00	0.00	0.00	0.00
14	4.60	2.00	0.00	1.00	1.00	0.60	0.00	0.00	0.00	0.00	0.00	0.00
15	6.44	0.47	0.00	0.85	0.29	2.82	0.00	0.00	0.00	0.00	0.00	2.00
16	8.73	2.00	0.00	1.00	1.00	1.20	1.87	0.67	0.00	0.00	0.00	1.00
17	2.18	2.00	0.00	0.05	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00
18	9.29	2.00	0.00	1.00	1.00	1.29	3.00	0.00	0.00	0.00	0.00	1.00
19	8.12	0.32	3.00	1.00	0.00	1.80	0.00	0.00	0.00	1.00	0.00	1.00
20	4.14	2.00	0.21	1.00	0.93	0.00	0.00	0.00	0.00	0.00	0.00	0.00
21	4.90	2.00	0.00	1.00	0.10	0.30	0.00	0.00	0.00	0.00	0.60	0.90
22	4.43	2.00	0.00	0.00	0.43	0.00	0.00	0.00	0.00	0.00	1.00	1.00
23	4.00	2.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
24	4.11	0.00	0.00	0.00	0.56	2.00	0.56	0.00	0.00	0.00	0.00	1.00
25	5.00	2.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
26	5.80	0.00	0.00	1.00	0.90	0.90	0.00	3.00	0.00	0.00	0.00	0.00
27	10.00	2.00	3.00	1.00	0.00	3.00	0.00	0.00	0.00	0.00	0.00	1.00
28	5.50	2.00	0.00	1.00	0.92	0.54	0.04	0.00	0.00	0.00	1.00	0.00
29	5.00	2.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
30	4.00	0.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	1.00
31	7.69	2.00	3.00	1.00	0.10	1.13	0.00	0.00	0.00	0.00	0.00	0.46
32	9.09	2.00	3.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.65	2.43

33	9.92	2.00	1.75	0.00	1.00	1.88	1.33	0.00	0.38	0.00	1.00	0.58
34	6.00	2.00	3.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
35	6.00	2.00	0.00	1.00	1.00	0.00	0.00	0.00	0.00	0.00	1.00	1.00
36	8.15	2.00	0.00	1.00	0.62	1.62	0.00	0.00	0.00	0.00	0.00	2.00
37	8.57	0.93	1.18	0.00	1.00	2.46	0.00	0.00	0.00	0.00	0.00	3.00