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Doctoral Thesis:

Psychological characteristics related to epileptic and non-epileptic seizures

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Statement of word count for thesis sections

	Text	References, Tables, & Appendices	Total
Thesis Abstract	282	0	282
Literature Review	7,893	7,331	15,224
Empirical Paper	7,979	7,294	15,273
Critical Review	3,993	981	4,974
Ethics Section	2,353	5,891	8,244
Totals	22,500	21,497	43,997

Abstract

This thesis consists of a quantitative systematic review, a quantitative empirical research paper, and a reflective critical appraisal. The review included 16 published empirical research papers. It examined how psychological characteristics have been used to differentiate subgroups of people who experience non-epileptic seizures (NES) and contextualised subgroup differences in theories of NES aetiology. Results indicated that trauma experiences, alexithymia, and presence of intellectual disability were characteristics that were important in differentiating subgroups.

The aims of the empirical paper were to check data against hypotheses based on previous research, before comparing the psychological characteristics of people who reported experiencing NES and epileptic seizures (ESs). Data were collected via online surveys. NES subgroups were formed using cluster analysis of alexithymia and childhood trauma data. Subgroups were found to differ on childhood trauma, alexithymia, and adult attachment style.

There were parallels between the subgroups indicated in the review and empirical paper, which are explored further in the empirical paper discussion and critical appraisal. The empirical paper and systematic review emphasised the complexity of NESs and the importance of assessing and understanding individual differences in research and clinical settings. The alexithymia and adult attachment measures used in the empirical project may be useful as part of an assessment of individual differences. These measures could form a basis for psychological assessment and formulation for NES patients, and may help identify ES patients with attachment and/or alexithymia difficulties who may benefit from psychological assessment and therapy. The two research papers also make recommendations for research relating to treatments appropriate to the identified subgroup characteristics. The critical appraisal reflects on

the impact of mind-body dualism in the other two papers and discusses how such considerations may influence clinical practice.

Declaration

This thesis represents work undertaken for the Doctorate in Clinical Psychology at Lancaster University, Division of Health Research, from March 2014 to April 2016.

The work presented is the author's own, except where due reference is made. The work has not been submitted for the award of a higher degree elsewhere.

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Date:

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Firstly, I would like to thank the participants who completed the online survey and members of forums who supported the research. I would also like to recognise the support of the NHS organisations, charities, and support groups who assisted with recruitment.

I would like to express my gratitude to Dr Ian Fletcher (senior lecturer in research methods, Lancaster University) for his input and support throughout the process and Dr Jayne Martlew (Clinical Lead for the Neuropsychology Service, The Walton Centre) for her valuable contributions from a clinical perspective. I would like to recognise the contributions made by Dr Emma Eastoe (lecturer in statistics, Lancaster University) in her role as statistical consultant.

I would like to thank my friends and family for their support and belief in me, and especially my Dad for his help with proof reading.

Contents

Section Three: Critical Appraisal

Section Four: Ethics

Section One: Literature Review

The psychological characteristics of subgroups of adults who experience non-epileptic seizures: A systematic review.

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Word Count: 7,893 excluding tables, figures, references, & appendices

15,224 in total excluding author guidance of 7,135 words

This paper was prepared in accordance with the guidelines of the target journal Seizure. The journal guidance is included in Appendix A.

ABSTRACT

Purpose: To identify how people who have experienced non-epileptic seizures (NESs) have been split into subgroups, based on psychological characteristics, and to explore what these subgroups' reveal about the aetiology of NESs.

Methods: Systematic review of peer reviewed published literature. Empirical articles (n=16) were identified via a systematic search, using Academic Search Complete, AMED, CINAHL, MEDLINE, and PsycINFO databases and manual searching. Reported methods of differentiating subgroups and psychological characteristics that significantly differentiated these subgroups were reviewed.

Results: Investigators' methods of splitting their NES samples into subgroups fell into nine different categories. They examined a broad range of psychological characteristics and there was little consensus on subgroup attributes. However, there was evidence from four studies to support the existence of NES subgroups who have experienced more trauma, and more mental health difficulties than average for the overall NES groups. There were some indications of subgroups with intellectual disabilities, which were more likely to have environmental triggers for NESs, and subgroups who were described as 'over-controlled' in their emotion regulation.

Conclusion: The different subgroups outlined above may be consistent with integrated, behavioural, and psychodynamic theoretical models respectively. This research further establishes the complexity of NESs aetiology and emphasises the need for comprehensive psychological assessment and formulation of people experiencing NESs, in order to identify which theoretical model(s) are most useful in their therapy. Trauma, and alexithymia measures, and presence of intellectual disability and mental health problems may be useful to inform these formulations and could be used to identify subgroups in future research.

Key words:
Non-epileptic, subgroups, psychological characteristics, aetiology, systematic review.

Highlights for the journal are provided in Appendix B.

Introduction

Non-epileptic seizures (NESs) have been defined as episodes during which a person's behaviour and sensations resemble those during epileptic seizures (ESs) but without any abnormal electrical discharge in the brain [1]. The prevalence of people experiencing NESs in the general population is estimated to be between 1.5 and 4.9 per 100,000 [2]. Research has indicated that around 1 in 5 patients attending hospital due to a seizure, and 1 in 7 of those attending a 'first fit' clinic, experience NESs [3]. NESs is not a diagnosis in itself, and their complexity is reflected in the number of diagnostic labels with which they are associated. In the diagnostic and statistical manual of mental disorders, 5th edition (DSM-5) [4] they are considered a possible symptom of conversion disorder (functional neurological symptom disorder). They may also be part of a wider range of medically unexplained symptoms and labelled as somatic symptom disorder, or be part of a dissociative disorder and receive a label, such as depersonalization disorder. NESs have been referred to with many different names including, non-epileptic attack disorder (NEAD), pseudo seizures, and psychogenic non-epileptic seizures (PNESs). In this research the term 'non-epileptic seizures' is used, consistent with the International League Against Epilepsy (ILAE, 2015)[5] report.

Due to the similarity in appearance of ESs and NESs, concern about the accuracy of diagnosis has raised issues in relation to the risks posed to patients who are inappropriately prescribed medication with potentially severe side effects, demands on health services, and neglect of unrecognised psychological distress [6]. Differentiating between ESs and NESs can be difficult and costly for health services [7]. Research has indicated that the most reliable way to differentiate between ESs and NESs is video-electroencephalography [8]. However, even this is not entirely accurate [9], partly due to high levels of comorbidity of ESs and NESs, which Hoepner et al. [10] reported as 36% in a

sample of 114 people who experienced NESs. Therefore, it is important that clinicians understand the aetiology of NESs so that they are better equipped to recognise this difficulty and support patients.

Aetiology of NESs

At present, there is no consensus in the theoretical or empirical literature about the aetiology of NESs. They have been described as caused by psychological processes and contrasted with epileptic seizures (ESs) which are described as caused by physical processes [11]. However, this distinction is probably too simplistic as physiological differences, for example interictal abnormalities, have been noted in both ES and NES patients [12]. Research has suggested that patients see ESs and NESs as both psychological and physical conditions [13].

Some psychological models of functional symptoms, such as NESs, conceptualise symptoms as the result of emotions that are too difficult to process. According to a psychoanalytic perspective first proposed by Freud the underlying cause of the difficulty with processing emotions is trauma, often of a sexual nature [6]. A related theory was that NESs may be a dissociative response that provides relief from intolerable feelings, including the unpleasant anticipation of the seizure itself [14]. These models appear to be consistent with a neurological model of NESs in conversion disorder, which has suggested that emotion systems (the limbic system and densely connected areas) override the sensory and motor cortex to produce neurological symptoms [15]. This model has received support from functional magnetic resonance imaging (fMRI) studies, which have shown differences in the patterns of neurological activity between NES patients and controls[16, 17]. The psychological and neurological

models above appear to be describing a similar process at a different level of explanation.

An alternative model is provided by behavioural theory, which proposed that NESs are learned patterns of behaviours that enable a person to avoid responsibility and escape from stressful situations. The person may or may not be conscious of the reasons for their behaviour, and the pattern is proposed to be reinforced by the way others respond to them when they exhibit seizures [6]. In some ways, this behavioural model could be similar to the models linked to emotion processing above, as both avoid something difficult. However, it is different in terms of the process it is proposing. The emotion processing models seem to be describing a system that becomes emotionally overloaded producing seizures as a direct result, whereas the behavioural model is describing a system that is learning to use the seizures as a protective strategy. These two processes could happen within the same person in parallel; the seizures could initially be due to emotional overloading but then become a learnt behaviour due to their consequences having some benefit.

Bodde et al. [18] proposed a model of NES aetiology illustrating the interaction of risk factors on several levels. This model appears to incorporate the aforementioned psychoanalytic, neurological, and behavioural theoretical models into an integrative model, with similar features to a generic psychological formulation. Bodde et al.'s [18] model is reproduced in Figure 1. The model starts at level 1, with a cause, such as traumatic experiences. These causes interact with level 2, the person's emotional and neurological characteristics, and are shaped by factors at level 3 into seizures rather than other functional symptoms. Level 4 represents triggers of NESs and level 5 are factors, including coping strategies, which lead to maintenance of NESs.

<<INSERT FIGURE 1>>

To date, research studies do not support any one of the above aetiological theories exclusively. Previous reviews have found that empirical research has identified differences in a variety of psychological factors, when they compared people who experience NESs with those who have ESs or with control groups. These factors included experiences of abuse or trauma, difficulties with emotion regulation, primary or secondary gain (where the patient benefits in some way either consciously or unconsciously from the seizures), and experience of epilepsy (self or others) [18]. However, a lack of consistency in the findings has suggested, more recently, that people who experience NESs are not a homogenous group, but fall into subgroups with differing aetiologies [14, 18-20]. This may help explain the difficulties in research relating to appropriate treatments; a Cochrane review examined the evidence for treatment of NESs and found there was very little reliable evidence that could inform the choice of treatment [2].

Consequently, this review focussed specifically on NES subgroups, in contrast to previous reviews that considered people who experienced NESs as one group [6, 14, 18-23]. It used a systematic search strategy and quality appraisal, in order to reduce the risk of bias. Quantitative empirical research was reviewed in order to examine reported methods of subgroup differentiation and differences between subgroups on measures of psychological characteristics. This information about psychological characteristics was then related to NES theoretical models to explore what it revealed about NES aetiology.

Methods

The research question and search criteria for this systematic review were developed in a conjunction with a PICO analysis (Appendix C) in accordance with methods described by Cherry and Dickson [24]. Based upon the PICO analysis, it was

decided that the target population of studies for review related to adults who experienced NESs, and used quantitative measurement of psychological characteristics. The setting the research took place in was not restricted.

Identifying search terms

Two sets of search terms were identified by using thesauruses, searches on electronic database search engines, consulting key words in relevant articles, reading articles, and consulting a clinician who works with people who experience seizures. The PsycINFO thesaurus[25] and American Psychological Association (APA) glossary of psychological terms[26] were also consulted. However, they did not include entries for non-epileptic seizures. The terms related to a) subgroups and b) NESs. The main terms are given in Table 1. In the final search, the NES terms (except PNES and conversion disorder) were combined in turn with the words seizures, attacks, and convulsions; alternative spellings and spacing of words were included. See Appendix D for a full list of the search terms.

<<INSERT TABLE 1>>

The sets of search terms relating to NESs and subgroups were joined with 'AND'. As the number of search terms in the NES set exceeded the field length on the search engine, three separate searches were completed and the results were combined.

The Academic Search Complete, AMED, CINAHL, MEDLINE, and PsycINFO databases were searched between 01/08/2014 and 05/02/2016, using the EBSCO host, which automatically removes duplicates. In addition, relevant references from review articles and the studies included in the full text read were included for abstract reading. The process is summarised in Figure 2.

<<INSERT FIGURE 2>>

Inclusion and exclusion criteria

The results were not restricted by publication date because no previous reviews have specifically considered subgroups within the population of people who experience NESs. Peer reviewed published literature only was searched, in order to control for quality of research and adhere to review time constraints. The inclusion and exclusion criteria are shown in Appendix E. In addition to the details in Appendix E, a further table was developed to clarify what were included and not included as psychological characteristics. This list is included to enable replication because what constitutes a psychological characteristic is debatable. Examples of included psychological characteristics were personality measures, emotion processing characteristics, adult attachment style, mental health, and intelligence. Examples of excluded characteristics were gender, features of the seizures, and medication use; the full list is presented in Appendix F. Childhood attachment style was excluded as the review focussed on adults and adult characteristics. One study used 'active high speed referral' as the criteria for defining subgroups, this article was included, as the authors stated that they assumed referral speed was related to patient characteristics, as there had been no changes to referral criteria [27].

Quality of the reviewed literature

All except one of the articles identified for inclusion in this review used a cross-sectional design. Searches of published literature and key websites did not reveal any validated quality assessment tools specific to cross-sectional design, except one which was only available in Spanish [28], and the strengthening of the reporting of observational studies in epidemiology (STROBE) guidance and checklist [29, 30]. The STROBE checklist evaluates the quality of reporting in studies, not the methodological quality. Following a

trial quality analysis using STROBE it was decided to pursue a more comprehensive quality analysis tool that included consideration of possible sources of bias in the results. Therefore, the Downs and Black [31] checklist (Appendix G) was used to assess quality of the articles included in this review. This checklist includes sections on reporting and quality, and has been tested on cross-sectional studies and found to have good inter-rater agreement for total scores and specific domains [32].

Due to the studies mostly using cross sectional designs, not all the Downs and Black checklist items could be applied. For example, question 19, 'was compliance with the intervention/s reliable?' could not be applied, as there were no interventions in the cross sectional studies. However, the same set of 20 items was applied to each article. For the reporting section 9 out of 10 items were applied, for external validity 3 out of 3, for internal validity risk of bias 3 out of 7, for internal validity confounding 4 out of 6 and for power 1 out of 1 items were applied. All items had possible scores of 0 or 1 except for power, which had 0, 1, 2 or 3. The scores were calculated for each section of the Downs and Black checklist as well as an overall score (Appendix H). They were converted to percentages, by dividing the score by the total possible score for each section.

Scoring was completed following Downs and Black's recommendations with the exception of question 27 (Power). In order to assess the adequacy of study sample sizes and allocate a power score (0-3), minimum sample sizes were calculated using G*Power [33], that would enable reliable detection of small, medium, and large effect sizes. These were calculated for the tests relevant to this review i.e. those at a subgroup level. The calculations were based on Cohen's rules of thumb [34 35] with a power of 0.8 and the α error probability of 0.05. Power scores were allocated as detailed in Appendix I. For example, a study using a T-test to compare two NES subgroups, with a sample of 130

would score two, because its sample size is above the minimum (n=128) required to reliably detect a medium effect size using a T-test (table N.1).

The GRADE approach was then used to assess the quality of evidence across the studies [36].

Procedures

Titles and abstracts were read for the articles identified from searches and references in other literature. Where there was any uncertainly about inclusion of an article, the full text of it was examined. Reasons for exclusion were recorded throughout, and a summary of the reasons for not including articles at each stage is provided in Figure 2 and Appendix J. The most common reasons for exclusion at the abstract reading stage were that the articles related to secondary data only (n=20), that they did not include subgroups (n=17) and that the subgroups were not formed based on psychological characteristics (n=16). Appendix K lists articles that were included in the full-text reading but not included in the final review, and the reasons for their exclusion.

Following the initial full text read, included articles were re-read in order to extract data and complete the quality analysis. The quality analysis is provided in Appendix H, and a sample of the summary data extraction table in Appendix L. Data were extracted from each article relating to the: country in which the research took place, type of setting, methodology, sample type, sample number, key exclusion criteria, measures used, number of subgroups identified, and author's subgroup labels. In addition, a short summary, and notes on strengths and weaknesses of the study were made.

Studies that used factor or cluster analysis were then grouped together and their results compared, by extracting data on psychological factors that differentiated the subgroups. This included Cohen's d effect sizes (d), and odds ratios (OR). Studies that split their sample of people with NESs based on predetermined categories were grouped according to the type of category they used. For example, all studies using presence or absence of trauma to split their sample into subgroups were analysed together. Where studies used categories common to two or more studies, the results of psychological characteristics showing a significant difference between the subgroups were extracted and compared. Where a study used more than one method or category to differentiate subgroups, it was included in the analysis for each. Where effect sizes were not reported, they were calculated if sufficient data were provided to do so. Calculation used equations provided by Field[37]. Attempts were made to contact authors who did not provide sufficient information to calculate effect sizes. In order to compare effect sizes across studies, Cohen's rules of thumb were used to identify small, medium, and large effect sizes for each statistic as detailed in appendix H. Odds ratios (OR) less than one were converted using 1/OR for ease of comparison. In factor analysis factor loadings greater than 0.4 (explaining more than 16% of the variance) were considered important[37].

PRISMA reporting guidelines have been followed for this systematic review, and a PRISMA checklist[38] was completed (Appendix M).

Results

All the studies except one used a cross sectional design. This one exception used an experimental design [39]. Eight (50%) of the studies investigated differences between means of psychological characteristics for the study subgroups [27, 39-45] and one used

logistic regression [46] to compare subgroup characteristics. Two studies noted they used correlational approaches [27] or regression analyses [47] subsequent to tests comparing means of subgroups. Five studies used cluster or factor analysis with other tests [45, 48-51] and two studies did not use any statistical tests [52] at the subgroup level. Table 2 summarises the studies included in this systematic review. It is notable that the studies were all located in Europe or the USA. Sample sizes ranged from 20[52] to 288[46] with a mean of 110 and a median of 65.5. A large number of measures related to psychological characteristics were used, with one article reported using 11 in the same study[45].

<<INSERT TABLE 2>>

Study Quality Analysis

Table 2 includes the total quality score as a percentage and summarises effect sizes for each article, for detailed scoring see appendix H. The quality of studies varied; out of a possible score of 22 on each paper, the median was 14 (64%), with a range from 8 (36%) to 18 (82%). The majority of studies (81%) scored 67% or more (6 out of a possible 9 points) on the reporting section. Internal validity, risk of bias, was a strength overall, with all except one study scoring 2 or 3 out of a possible 3 points, indicating that the studies clearly described their measures and used appropriate statistical tests. Eight of the 16 studies (50%) scored zero for external validity [27, 40-42, 44, 45, 47, 52], largely due to samples taken from one specific specialist clinic and there being no information to help judge if the sample was representative of the entire population. None of the studies reported power calculations. Quality analysis of power indicated that none of the sample sizes were large enough to detect small effect sizes at the subgroup level. Four out of sixteen (25%) of the studies were able to detect a medium effect size or larger, four out of 16 (25%) were able to detect a large effect size or greater. Eight out of sixteen (50%) had insufficient power to detect a large effect size; two of these studies did not carry out any statistical tests at the subgroup level.

Effect sizes

Eight (50%) of the studies reported medium or large significant effect sizes for differences between subgroups on psychological characteristics (table 2). Three (19%) reported small to large effect sizes. These studies had comparatively large sample sizes (n=288[46], 288[41], 176[43]) and two of them appeared to use the same sample. It was not possible to calculate effect sizes for five (31%) studies because they did not do statistical tests at subgroup level or it was not possible to obtain sufficient data to

calculate effect sizes (table 2). Large effect sizes were reported for differences between subgroups in personality, mental health, learning disability, health related trauma experiences, cognitive functioning, and presence of environmental triggers. Medium effect sizes were reported for differences relating to personality measures, engagement in therapy, comorbid PTSD, comorbid epilepsy, trauma symptoms, somatization, and life complaints.

Subgroups

The studies used methods that fell into nine different categories to identify subgroups in their samples of people who experienced NESs. These methods and the subgroups are summarised in table 3. In ten studies[27, 39, 41-47, 53] (63%) the subgroups were decided in advance based on characteristics or experiences known to be associated with NESs, for example, comparing people who have reported experiencing sexual abuse with those who have not [43]. These predetermined characteristics fell into seven categories, trauma, personality disorders, dissociation, mental health, cognitive functioning, daily hassles, and referral speed. The first five were used by more than one study and are explored in subsequent sections.

In five studies (31%), subgroups were identified through cluster or factor analysis [45, 48-51] (one of these also used predefined groups[45]). One study used a points scoring system linked to mental health to allocate people to subgroups[40] and in another article it was unclear how subgroup membership was decided[52].

<<INSERT TABLE 3>>

Trauma

Seven (47%) of the studies split their sample of people who experienced NESs into subgroups based on whether or not they had experienced trauma. Table 4 summarises psychological characteristics which showed significant differences ($p<0.05$) between these subgroups, full details are located in Appendix N. Most significant differences were reported in only one study each, but avoidant behaviour[45, 47], self-harm[43, 46], and history of engaging with mental health support[43, 47] have each been reported in two studies, all of which were higher in subgroups who had reported experiencing trauma. Comorbid mood disorders or symptoms of mood difficulties associated with trauma experience have been reported in three studies[43, 44, 47]. The results indicated that those people with NESs who have experienced trauma, when compared to people with NESs who have not experienced trauma, had greater levels of personality difficulties (e.g. interpersonal difficulties $d\approx1.5$ [45]; tendency to blame $d\approx0.8$ [45]; demoralisation, sense of guilt, being a failure and helplessness $d=0.80$ [47]; and personality disorder diagnoses OR 7.9 [43]) and more mental health problems (e.g. self-harm OR 4.3 [43], OR 3.3 [46] and incidence of mood disorders [47], $d=0.86$, [44] OR 1.8 [43]). There were some indications that specific areas of cognitive functioning (processing speed $d\approx2$ [45] and delayed verbal semantic memory $d=1.1$ [42]) were worse for those who had experienced trauma. It appeared that those people with NESs who had reported experiencing sexual abuse were less likely to have a learning disability OR 0.15 (1/OR=6.67)[46] or to have experienced health related trauma OR 0.09 (1/OR=11.11)[46].

Bakvis at al. [39] did not find any significant differences between patients, with ($n=7$) and without ($n=11$) a sexual trauma history. They did report results approaching significance ($p=0.067$), for differences in basal diurnal cortisol rates, which indicated

that for those who had experienced trauma, the body's stress system may have been more activated at baseline, suggesting they were hyper vigilant for dangers.

Overall power in this group was mixed. Two studies had sufficient power (0.8) to reliably detect medium or greater effect sizes, two large or greater, and three insufficient to reliably detect a large effect size (Appendix H).

<<INSERT TABLE 4>>

Personality Disorders

Three of the studies split their sample of people who experienced NESs into subgroups based upon presence or absence of personality disorder [44], or type of personality disorder[52, 53]. Magaudda et al.[52] and Harden et al.[53] did not report any statistical tests comparing the psychological characteristics of the subgroups. Baillés et al.[44] reported that scores on the Paranoia (d=1.4) and Mania (d=0.66) subscales of the MMPI were significantly higher ($p<0.05$) for those with personality disorders (effect size calculated, using the stated standard deviation for those who did not have a personality disorder diagnosis). All three of these studies scored zero in the power section of quality analysis indicating that the likelihood of them missing a large effect size or smaller (type two errors) was outside of accepted limits (0.2 or 20%).

Dissociation

Two studies considered differences between subgroups based upon experiences of dissociation [44, 45]. Baillés et al. [44] did not find any significant differences when comparing presence and absence of dissociative experiences. Bodde et al. (2013) [45] reported significant differences, with medium effect size, between people having higher and lower dissociation tendency on measures of somatization ($r=0.35$, $p=.027$), life complaints ($r=0.41$, $p=0.012$) and tendency to blame others ($r=0.33$, $p=0.042$). Both these studies were underpowered as indicated by scoring zero in the power quality analysis.

Mental Health

Two studies split their NES groups according to measures related to mental health. Bodde et al. (2013) [45] used scores above and below zero on the psychopathology

scale of the short MMPI, and found no significant differences between these two groups. Baslet, Roiko and Prensky [40] reported that their subgroup labelled 'psychiatric burden' was significantly more likely to have experienced trauma than the 'neurological burden' ($p=0.013$, OR ∞) or 'no burden' ($p<0.001$, OR ∞) subgroups. The psychiatric burden group were also more likely to have a diagnosis of type B personality disorder than the neurological burden group ($p=0.018$, OR ∞) or the no burden group ($p=0.037$, OR 10). The psychiatric burden group were significantly more likely to have 'cognitive complaints' than the no burden group ($p=0.032$, OR 6). These two studies had sufficient power to be likely to detect large and above effect sizes. Baslet et al.'s [40] method for distinguishing subgroups was different to that used in other articles in that it involved a points system based on various symptoms or diagnoses agreed by the researcher clinicians.

Cognitive functioning

Four studies split their sample of people with NESs into subgroups based on their level of cognitive function [41, 45, 46, 52]. The studies considered different factors and the only common single factor was the increased likelihood of seizures having an environmental trigger in people who have a learning disability (OR 20.83 [46], OR 14.74 [41]). Details of differences found between subgroups in each study based on cognitive functioning are presented in Appendix O. Two of these studies had sufficient power to be likely to detect medium effect sizes [41, 46], the other two insufficient to detect large sizes.

Factor and cluster analysis

Table 5 provides a summary of the psychological factors that were reported to differ between subgroups identified through factor or cluster analysis; further details

are provided in Appendix P, Tables P.1 and P.2. The most common measures assessed either mental health [48-50] or alexithymia [48, 49, 51]. Analysis of power, in relation to ability to differentiate between subgroups, indicated that two of these studies had insufficient power to be likely to detect large effect sizes [50, 51], one would be likely to detect large effect sizes and above[48] and the other medium effect sizes and above[49].

<<INSERT TABLE 5>>

Discussion

The purpose of this review was to establish how people who experience NESs have been split into subgroups, and what these subgroups' psychological characteristics indicate about NES aetiologies. The 16 reviewed studies have used methods falling into nine different categories to split their samples into subgroups. These methods included cluster analysis and predetermined characteristics, such as trauma experience. The studies compared their subgroups on a diverse range of psychological characteristics including cognitive abilities, mental health, coping strategies, and personality.

There were few significant findings for some methods of splitting the samples, such as those based on dissociation or personality disorder. However, the studies in these areas were all underpowered. Therefore, it is possible there were differences between subgroups that were not detected (type II errors).

There was congruence for some psychological characteristics between subgroups formed in more than one way. For example, when subgroups were formed based on presence or absence of trauma, three studies indicated that those who had experienced trauma had significantly more mental health problems (table 4), and when subgroups were formed based on presence or absence of mental health problems, Baslet et al. [40] reported that those with more mental health difficulties were more likely to have experienced trauma. Mental health and trauma experience were also differentiating factors in the studies that used factor or cluster analysis, although they were not considered together in any of the studies. These results were consistent with each other, and indicated that those people with NESs who report trauma experiences are likely to have worse mental health than those who do not. Two studies also indicated that experiences of trauma were associated with problematic coping strategies such as avoidant behaviour and blaming (table 4).

There is a degree of concordance between Bodde et al.'s[18] model (figure 1) and these subgroups with trauma experiences, increased mental health problems, and problematic coping strategies. Experiences of trauma (level 1 – psychogenic causation), are associated with increased mental health problems (level 2 – emotional 'make-up') and coping strategies that may maintain the NESs (level 5 – 'prolongation').

Contrarily, there were subgroups of people in the studies that assessed trauma, who were not reporting a history of trauma, appeared to have fewer mental health problems, fewer detrimental coping strategies and experience NESs. These subgroups would appear inconsistent with the psychodynamic theory of NES aetiology, which has proposed trauma as a causal factor. Possible reasons include: (1) Many of these people may have experienced some type of trauma but under reported it, or it may have been of a type not assessed by the measures used in the research. For example, the TEC used by Bakvis at al. [39], and Bodde et al. (2013) [45] assessed sexual, physical and emotional trauma, but not health related trauma. (2) The aetiology of the subgroup(s) that did not report trauma could be different.

Duncan and Oto (2008a) [46] (n=288) identified that people who experienced NESs and reported having experienced sexual abuse (n=94) were less likely to have reported health related trauma. They also noted that health related trauma was not related to self-harm or other medically unexplained symptoms whereas sexual abuse was related to these factors. None of the other studies assessed medical trauma specifically except for Myers et al. (2014) [42] who reported that nine of their sample of people with NESs (n=66) had experienced medical trauma. Baillés et al. [44] may have included medical trauma as they included car accidents (n=3) and other traumas (n=4), in their sample (n=30). Myers et al. (2014) [42] and Baillés et al. [44] did not analyse differences between groups of people who had experienced different types of trauma. While we need to be

cautious drawing conclusions from a single study, Duncan and Oto's (2008a) [46] data may indicate that people who have developed NESs after experiencing health related trauma may have different psychological characteristics to those who have developed seizures following other types of trauma.

Many of the studies found significant differences on personality measures, such as alexithymia, shyness, and avoidant behaviour. It is difficult to compare the findings relating to personality across the different studies in the review due to the studies having used different measures, and different methods for identifying subgroups [44, 45, 47, 49, 50]. However, alexithymia and emotion regulation are closely related concepts[54]. Considering, emotion regulation and alexithymia together they are reported to show a significant difference between subgroups in three studies that used factor or cluster analysis (table 5). These findings indicate that alexithymia is an important area of difference between NES subgroups.

When Reuber, Pukrop, Bauer, Derfuss and Elger [49] made a comparison between their subgroups of patients with NESs and healthy controls, one subgroup, whom they described as similar to borderline personality disorder (n=43, 51% of sample), scored significantly higher on most measures of personality pathology. However, a second group (n=37, 44% of sample), whom they described as over-controlled, scored significantly lower or had no significant differences from healthy controls (n=100) on most measures (e.g. anxiousness, self-harm and suspiciousness), except for compulsivity, on which they scored significantly higher. Reuber et al. [49] suggested that this indicates a group that are over-controlled in their emotion regulation, perhaps separating themselves from their own feelings to an extent that they are unaware of them. Uliaszek, Prensky and Baslet [48] reported that one of their subgroups scored significantly lower than controls on some aspects of emotion regulation, which could be

consistent with Reuber et al.'s [49] suggestion of an over-controlled group. However, Brown et al. [51] reported slightly higher scores compared to epilepsy controls for their cluster with lower emotional dysregulation scores, although there was no significant difference. While we need to be cautious about these findings, future research should consider the possibility of a subgroup of people who are over-controlled or similar to normal in their emotion regulation, as part of NES aetiology. The aetiology of this group could be consistent with a psychodynamic perspective on NESs, that they are linked to repression of emotions. Whether or not some members of this subgroup have experienced trauma, which is also being repressed, and hence not reported, could be an avenue for future research.

Theoretically, alexithymia is related to disruption in childhood attachment relationships[55]. Cassidy suggested that emotion regulation style is an adaptive response that the child develops in relation to their caregiver's style of interaction[55]. For example, if the child is repeatedly rejected they minimise their emotions to avoid further rejection and decrease their need for emotional closeness. Childhood attachment may be disrupted by trauma or abuse, which prevents the child's emotions being contained and mirrored, a process proposedly essential to development of emotion regulation skills[56]. Therefore, it would be expected that there would be a relationship between trauma, attachment, and alexithymia for NES patients. This is not evident in this review. However, on further examination, none of the studies that measured trauma included specific alexithymia or emotion regulation measures. A related finding was that Uliaszek[48] reported scores on the CERQ blaming others scale were significantly higher (d=0.8) for those NES patients who had experienced trauma. This scale was described as representing an emotion regulation strategy. This indicates that relationships between trauma, attachment, and alexithymia warrants further study.

Studies that have used cognitive function to differentiate subgroups have shown little consensus, despite reports of many significant findings, and several having sufficient power to reliably detect medium effect sizes. This appears to be due to the studies examining a diverse range of psychological characteristics with few common to more than one study. In addition, people with intellectual disabilities account for a relatively small proportion of the overall NES sample (9% in Duncan and Oto's study[41]) and they were excluded from several studies (table 2); therefore, the available evidence is reduced.

Differences in cognitive abilities were reported in relation to subgroups formed by splitting based on trauma experience and factor or cluster analysis. Duncan and Oto (2008a) [46] indicated that reporting trauma was less likely for people who had a learning disability. This may be due to under reporting of traumas in people with learning disabilities, perhaps due to cognitive impairments and communication difficulties that make it difficult for them to do so, or it could mean that the aetiology is different for this group. Their aetiology may fit better with the behavioural model described in the introduction, aetiology section, which proposes that rather than having a psychogenic causation associated with trauma, NESs are a behaviour that is reinforced by the environment, including the responses of others. This would be consistent with the two studies that suggested seizures were more likely to have an environmental trigger in people who have a learning disability [41, 46].

Analysis of the reviewed articles suggests there is evidence for three subgroups of adults who experience NES: [1] A subgroup who have experienced trauma, elevated mental health difficulties, and more problematic coping strategies. This subgroup appears consistent with Bodde et al.'s [18] integrated model. [2] A subgroup with 'over-controlled' emotion regulation, which may be consistent with a psychoanalytic model of

repression of emotion. [3] A subgroup who have intellectual disabilities and are more likely to have environmental triggers for NESs, consistent with a behavioural model.

Clinical Implications

The above subgroups and associated models may be useful to help understand individual presentations. It is clear that the aetiology of NESs is complex. It is likely that more than one of these aetiologies could apply to any one individual, and that different treatments will be effective for different individuals. Therefore, comprehensive psychological assessment and formulation of each individual's circumstances will be vital to identifying appropriate treatment strategies. Recommendations for psychometrics to include in assessment are a trauma measure that includes health and other types of trauma as well as, sexual, physical, and emotional abuse; an alexithymia or emotion dysregulation measure; and possibly personality and adult attachment measures. Many of the measures used in the studies were very long and probably impractical to have as part of a battery for clinical use. For example, the MMPI-2 has 567 items. However, others such as the TAS-20 (20 items) and the DERS (36 items) may be more feasible. It is also suggested to include assessment of intellectual ability; mental health; coping strategies; and potential benefits that could maintain seizures.

Another important point in clinical practice is that the absence of trauma reporting does not exclude NESs. For some people the aetiology may not be related to trauma or it may be a type of trauma not targeted by most measures used clinically. For example, health related trauma is often not targeted by measures, as the questions usually focus on childhood trauma and sexual events, due to their hypothesised role in NES aetiology. It is therefore important that clinicians assess for a broad range of

traumas and recognise that presentations related to different types of trauma may be varied.

The aetiology of NESs may be consistent with a behavioural model for some people, and indicators for this may be presence of a learning disability, seizures linked to environmental triggers, and responses of others that reinforce the behaviour (probably inadvertently). Aetiology associated with over-controlling of behaviour and emotion, consistent with psychodynamic theory, may be indicated by near normal or lower than normal scores on emotional dysregulation or alexithymia measures, and fewer indicators of mental health distress.

Based on individual formulations, the suggestions for appropriate treatments outlined in the further research section below may be appropriate for research in a clinical setting.

Strengths and Limitations of the reviewed literature

The variety of methods reviewed studies have used to form subgroups and the diverse range of psychological characteristics they have considered, made comparing psychological factors across the studies difficult and while there were many reported significant differences between subgroups, there appears to be little consensus. Part of the reason for this may be that some studies were measuring related factors but with different names. For example, the DERS, used to measure emotional dysregulation, contains a subscale about difficulties engaging in goal directed behaviours [48], which may be similar to self-directedness in the TCI[45].

Using the GRADE approach [36] the body of evidence reviewed was given a quality rating of low, indicating that there is risk of bias across the studies. Some studies found large effect sizes, which could have upgraded the quality rating, as they were strengths.

However, the inconsistency of results was a downgrading point; therefore, the standard rating of low quality for observational studies was allocated. One reason for inconsistency may be the differing inclusion criteria for the studies. For example, many of the studies excluded people who have learning disabilities and those who have comorbid ESs and NESs. Very few studies reported what proportions of people were excluded, which is a further limitation.

While many studies achieved high scores in their reporting and internal validity, power was a limitation as 50% of the studies scored zero in the power quality analysis. This means many differences between clusters may not have been detected. Most of the studies used small sample sizes, and tests of differences between means, which may make it difficult to represent the complexity of NES aetiology. This could be due to recruitment being a challenge, given that incidence is relatively low in the population, and treatment is via specialist clinics. Few of the studies examined the relationship between variables within clusters. External validity of the studies was a limitation, which has implications for the generalisability of findings from the review. This was often due to studies selecting a sample from one specific specialist clinic. This could be resolved in future research by recruiting across more than one clinic or research site.

Strengths and limitations of this review

As Schwan, Hingray, Laprevote, Vignal, & Maillard [57] identified, NESs are important in both neurology and psychology. They suggested that research should be undertaken collaboratively across the two disciplines. The searches used in this review identified a range of articles that were aimed at neurologists, psychologists, psychiatrists or any epilepsy practitioners. Therefore, it would have been preferable if

this literature review had been undertaken with the support of a neurologist. However, this was not possible within the study constraints.

A strength of this review was the systematic approach to reviewing the literature. A limitation is that it included only published literature, which is well known to be biased towards significant findings[58, 59]. In addition, the review considered only the significant findings from the studies. This excluded results that may have contradicted significant findings or added to understanding by suggesting variables that are not related to each other. Given that, many of the studies were underpowered, there is a high likelihood of type two errors across this review. Therefore, a lack of significant findings in a particular area should not be interpreted as indicating that differences are not present. This recommendation is particularly relevant to the personality disorder and dissociation sections, due to all the studies in these sections being underpowered.

In future, it would be useful to consider qualitative findings to gain a greater depth of understanding about the aetiologies suggested by the quantitative research. For example, by exploring patient and/or clinician perspectives on how NESs have developed for individuals and relating this to NES theoretical models. However, before this could take place there would need to be more qualitative research in the area, as very few studies (n=5) were excluded from this review due to not being quantitative.

The quality analysis in this review lacked confirmation by a second rater; therefore, there is increased risk of bias in the results. A second reviewer will repeat a sample of the ratings and compare results prior to submitting the paper for publication.

In terms of the generalisability of the findings from this review, the studies include a range of samples from the USA and Europe, findings that were common to more than one study may be cautiously generalised in the USA and Europe. Further research would be necessary to establish generalisability outside this region. Many

studies excluded people with a dual diagnosis of epilepsy and NESs. Therefore, it would not be appropriate to generalise to this population.

Further research

It would be useful for attempts to be made to develop consistency in research methods and measures for this area of research, so that results from different studies can be compared and contrasted more easily. As NES presentation is complex, it would be helpful if studies used larger sample sizes and sophisticated statistical techniques. This would enable the examination of the relationships between variables, within clusters, for example, using correlation or regression analyses.

Alexithymia and trauma experience were frequently indicated to differentiate subgroups and due to their theoretical link, it would make sense to consider both these factors in future research. These factors could be used to differentiate subgroups, perhaps using cluster analysis as this enables subgroups to be formed using more than one variable. Given the theoretical relationship between trauma, alexithymia, and attachment, it is suggested that an attachment measure should also be included in future research.

In order to identify appropriate treatments for NESs, as identified by Martlew et al. [2], further research is needed. Given the possibility identified in this review that the aetiologies of NES subgroups may be consistent with different theoretical models, it is likely that research into treatments will need to consider subgroups that need different treatment approaches. Trans-diagnostic research regarding difficulties with alexithymia has found treatments, such as Dialectical Behavioural Therapy (DBT), improved emotion regulation and were successful [60]. This could be considered for people with NESs who report difficulties with emotion regulation.

Those people with who have trauma as a key part of their formulation may benefit from therapy such as CBT for trauma or EMDR. Baslet, Dworetzky, Perez, Dworetzky, and Oser [61] suggested that mindfulness-based therapy may be appropriate for people who experience NESs as it targets recognition and acceptance of emotional states. They completed a small (n=6) pilot with promising results in the reduction of seizure frequency. Further research could investigate the use of this therapy (which is also part of DBT) for those people whose aetiology includes overregulation of emotion. For people for whom a behaviour model of aetiology seems most appropriate, research may wish to focus on behaviourally based interventions, such as changing the environment, altering demands put on the person and positive reinforcement of behaviours other than the seizures.

Conclusion

The literature covered a broad range of psychological characteristics associated with the aetiology of NESs. Many significant differences between subgroups of people who experienced NESs were reported, but there was a lack of consistency, which made it difficult to identify psychological characteristics of subgroups. However, there was evidence of a subgroup of people, who reported experiencing trauma, having more mental health problems, and problematic coping strategies, consistent with Bodde et al.'s [18] integrated model. Evidence for the characteristics of other subgroups is less clear. There is some indication of a group who have intellectual disabilities and are more likely to have environmental triggers for seizures, whose aetiology is more consistent with a behavioural model. There is also the possibility of a group that are over-controlled in their emotion regulation and behaviour, which may be linked to psychodynamic theories of NESs being linked to repression of emotion. Subgroups can

be formed using a variety of characteristics; trauma experience, alexithymia, and intellectual ability seem most likely to be effective and relevant to treatment. It is suggested that cluster or factor analysis of these measures is used to identify subgroups. The inconsistency and complexity of the reviewed empirical research indicates a complicated picture and the aetiologies discussed are unlikely to be mutually exclusive. This emphasises the importance of comprehensive assessment and formulation of people with NESs, in order to understand their individual aetiology, and treatment that is likely to be helpful. Alexithymia and trauma measures are likely to be informative in the formulation process.

Research involving larger samples, using consistent methods and measures capable of exploring relationships between variables, and qualitative research would be beneficial. It is suggested that research needs to consider how subgroups can be managed within the study design, prior to further investigation of their aetiology and efficacy of treatment strategies.

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Figures

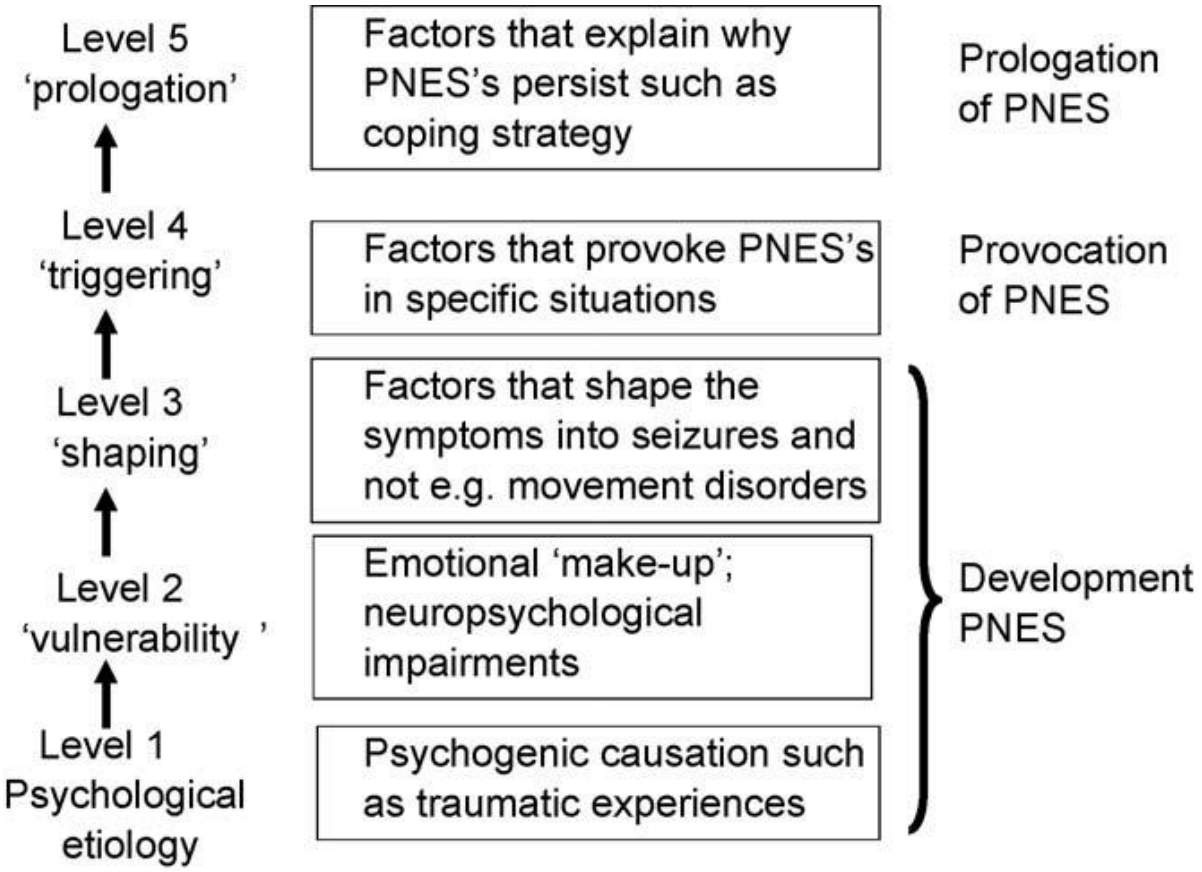

Figure 1. Bodde et al.'s [18] model of NESs

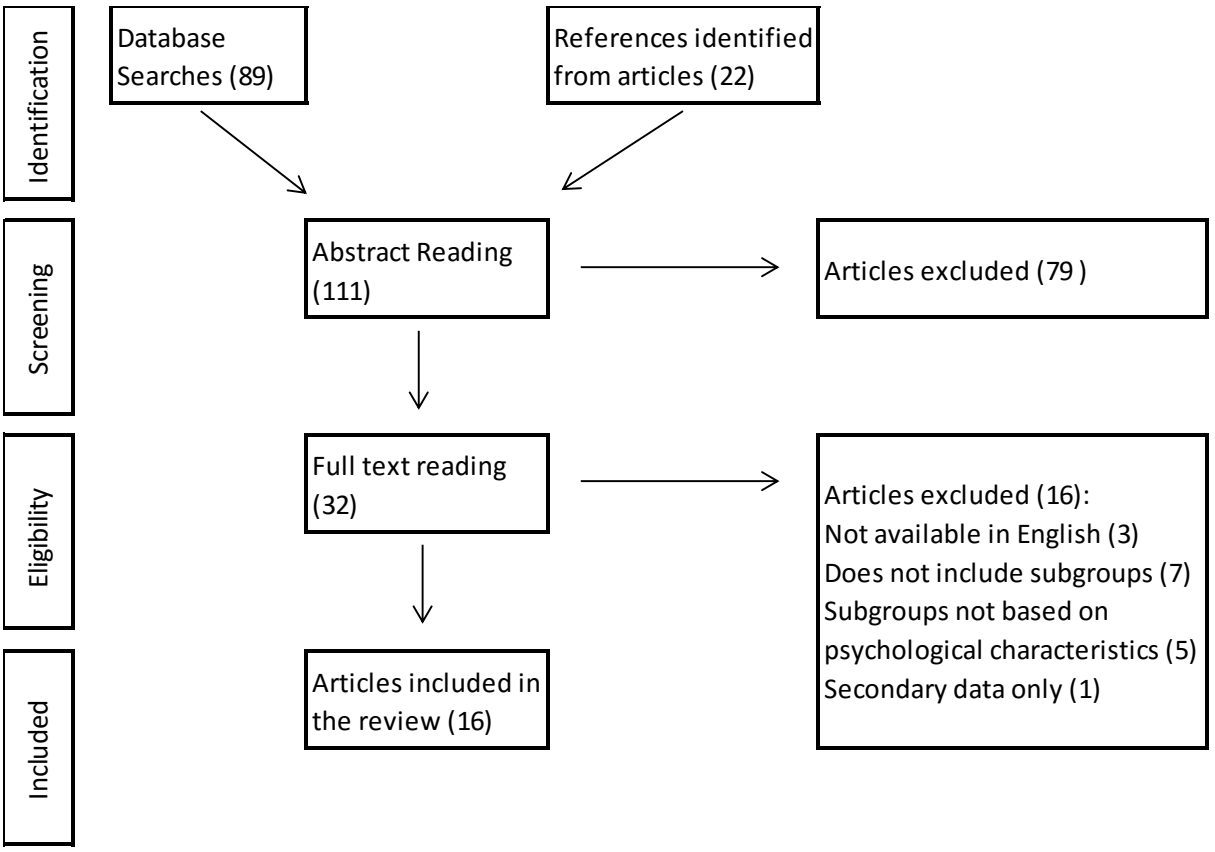

Figure 2. Summary of process for identifying articles included in the review

Tables

Table 1. Main terms in the final search

Terms related to NESs	Term related to subgroups
Psychogenic, pseudo epileptic, functional, stress related, hysterical, psychosomatic, somatic, somatoform, somatization, dissociative, non-organic, conversion disorder, psycho-physiological, PNES	Subcategories, subgroups, distinct groups, clusters

Table 2. Summary of key characteristics and quality scores of included studies

First author, year & reference	Country	Sample	Measures used	Total Quality Score	Range of significant relevant effect sizes reported/calculated	For details see
Baillés (2004) [44]	Spain	30 NESs, comorbid ESs/ other neurological disorders excluded	MMPI, SCID	48%	d=0.66 to 1.4 (medium to large)	Appendix N and personality disorder section of results
Bakvis (2010) [39]	Netherlands	18 NESs, 19 healthy controls	TEC, cortisol and a-amylase levels	73%	Insufficient data to calculate relevant effect sizes.	
Baslet (2010) [40]	USA	44 NES patients split into 3 groups	BDI-II, Seizure characteristics and semiology, DFI, DES, medical/ neurological/ psychiatric history, PHQ-15	76%	OR 6 to ∞[a] (medium to large)	Mental health section of results
Bodde (2012) [27]	Netherlands	90 NESs included from age 12 years	History, seizure semiology	48%	Insufficient data to calculate relevant effect sizes.	

First author, year & reference	Country	Sample	Measures used	Total Quality Score	Range of significant relevant effect sizes reported/calculated	For details see
Bodde (2013) [45]	Netherlands?	40 NESs, excluded LD and major psychiatric comorbidity, appears to be from the same clinic as Bodde (2012) [32], but unclear if there is any overlap in the samples.	CERQ, CVST, DIS-Q, EPCL, MMPI (short Dutch version), RPM, SDQ-20, TCI (short Dutch version), TMT, TEC, UCS,	62%	d=0.7 to 2 (medium to large) r=0.35 (medium)	Appendix N Appendix O
Brown (2013) [51]	UK	51 NESs, response rate of 18.7%, moderate/severe LD excluded	DERS, GAD-7, PHQ-9, RSQ, SDQ, TAS	67%	r= 0.49 to 0.67 (medium to large)	Appendix P, Table O.2
Cragar (2005) [50]	USA	184 adults with NESs, 18 excluded due to comorbid epilepsy/ other diagnoses	Neuropsychological tests, medical history, MMPI-2, NEO-PI-R	62%	d=0.85 to 1.99 (large)	Appendix P, Table O.2
Duncan (2008)a [46]	Scotland	288/289 NESs	Non-standard measures relating to history and characteristics	67%	OR 3.30 to 20.83 (small to large)	Appendix N, Appendix O
Duncan (2008)b [41]	Scotland	263 NESs without LD, 25 NESs with LD, appears to be same sample as Duncan (2008)a [40]	Non-standard measures relating to history and characteristics	76%	OR 3.45 to 14.74 (small to large)	Appendix O
Harden (2009) [53]	USA	32 ESs, 16 NESs	SCID-II	57%	No statistical tests at subgroup level	

First author, year & reference	Country	Sample	Measures used	Total Quality Score	Range of significant relevant effect sizes reported/calculated	For details see
Magaudda (2011) [52]	Italy	20 NESs split into subgroups	Non-standard measures relating to cognitive function, seizure semiology and psychiatric co-morbidity	38%	No statistical tests at subgroup level	
Myers (2013) [47]	USA	61 NESs, IQ>70, Passed effort testing (TOMM)	Cognitive battery, MMPI-2RF, TOMM	62%	OR 5.13 to 6.56 (medium to large) d= 0.78 to 3.6 (medium to large)	Appendix N
Myers (2014) [42]	USA	79 to 63 NESs , IQ>70, sample appears be largely comprised of same people as Myers (2013) [39]	BNT, CVLT, CVMT, D-KEFS, MCI, TOMM, TSI-2, WASI, WMS-II	71%	d=0.57 to 1.75 (medium to large)	Appendix N
Reuber (2004) [49]	Germany	100 healthy controls, 64 ESs, 85 NESs	DAPP-BQ (German version)	71%	No statistical tests comparing subgroups to each other	
Selkirk (2008) [43]	Scotland	176 NESs, Comorbid ESs excluded	PNES severity scale	86%	OR 1.42 to 7.88 (small to large)	Appendix N
Uliaszek (2012) [48]	USA	70 NESs	History, DASS, DERS, DFI, PHQ-15, QOLIE-31, BDI-II, DES	81%	d=0.85 to 2.29 (large)	Appendix P, Table O.2

?: location was not stated but assumed from author affiliations,
d=Cohen's d,
[a] Odds ratios calculated using 2 x 2 contingency tables
BDI: Beck Depression Inventory,
BNT: Boston naming test,
CERQ: cognitive emotion regulation questionnaire,
CVLT: California verbal learning test,
CVMT: continuous visual memory test,
CVST: computerised visual searching task,

DAPP-BQ: Dimensional Assessment of Personality Pathology - Basic Questionnaire,
DASS: depression, anxiety, and stress symptoms scale,
DERS: difficulties in emotion regulation scale,
DES: dissociative experiences scale,
DFI: disruption of functioning index,
DFI: disruption of functioning index,
DIS-Q: Dissociation Questionnaire,
D-KEFS: Delis-Kaplan executive function system,
EPCL: everyday problem checklist,
ESs: people who experience epileptic seizures,
GAD-7: generalised anxiety disorder,
LD: people who have a learning/intellectual disability,
MCI: memory complaint inventory,
MMPI: Minessota Multiphasic Personality Inventory,
NEO-PI-R: NEO Personality Inventory – Revised,
NESs: people who experience non-epileptic seizures,
PHQ: patient health questionnaire,
QOLIE-31: Quality of life in epilepsy inventory,
RPM: Raven's progressive matrices,
RSQ: relationship scales questionnaire,
SCID: structured clinical interview for DSM disorders,
SDQ: somatoform dissociation questionnaire,
TAS: Toronto alexithymia scale,
TCI: temperament and character inventory,
TEC: traumatic experiences checklist, BDI-II:
TMT: trail making test, UCS: Utrecht coping scale,
TOMM: test of memory malingering,
TSI: trauma symptom inventory,
UCS: Utrecht coping scale,
WAIS-R: revised Wechsler adult intelligence scale,
WASI: Wechsler abbreviated scale of intelligence,
WMS: Wechsler memory scale.

Table 3. Summary of subgroups described in the articles

Article first author and reference	Number of subgroups	Labels given to subgroups by the article authors
Baillés (2004) [44]	2 in 3 different ways	Presence vs. absence of traumatic experiences; Presence vs. absence of personality disorder; Presence vs. absence of dissociative disorders
Bakvis (2010) [39]	2	PNES without sexual trauma vs. PNES with sexual trauma
Baslet (2010) [40]	3	Psychiatric burden vs. neurological burden vs. no burden
Bodde (2012) [27]	2	Active high-speed referral group vs. the rest of the group
Bodde (2013) [45]	2 in 5 different ways	Patients with no trauma vs. patients with trauma; Higher vs. lower dissociation tendency; Extremely high number of complaints on daily hassles vs. the remaining patients; Average of higher on RPM vs. below average; Psychopathology <0 vs. >0 on subscale psychopathology of the short MMPI;
	4 by factor analysis	Psychotrauma subgroup vs. high vulnerability somatization subgroup vs. high vulnerability sensitive personality problem subgroup vs. high vulnerability somatization subgroup with a low cognitive level
Brown (2013) [51]	2 by cluster analysis	High levels of emotional dysregulation and alexithymia vs. relatively normal dysregulation and alexithymia
Cragar (2005) [50]	3 by cluster analysis	Depressed neurotic vs. somatic defender vs. activated neurotic
Duncan (2008)a [46]	3 suggested	Patients with sexual abuse vs. patients with LD vs. patients with health-related trauma
Duncan (2008)b [41]	2	Patients with LD vs. patients without LD
Harden (2009) [53]	6	Personality disorders types A, B, C in different combinations
Magaudda (2011) [52]	3 unclear how formed	Group 1 pharmacoresistant epilepsy, normal cognition, and comorbid anxiety and vs. or depressive disorders vs. group 2 patients, the epilepsy is associated with mental retardation and dependent personality traits vs. Group 3 patients have epilepsy, normal cognition, comorbid cluster B personality disorders and anxiety disorders, and psychic trauma

Article first author and reference	Number of subgroups	Labels given to subgroups by the article authors
Myers (2013) [47]	2 in 2 different ways	With trauma history vs. without trauma history, PTSD likely vs. PTSD not likely
Myers (2014) [42]	3	PTSD vs. trauma but not PTSD vs. no trauma or PTSD
Reuber (2004) [49]	4 by cluster analysis	Cluster 1, similar to borderline personality disorder vs. cluster 2, over controlled vs. cluster 3 similar to avoidant personality disorder vs. cluster 4, outlier
Selkirk (2008) [43]	2	Sexual abuse history reported vs. no sexual abuse history reported
Uliaszek (2012) [48]	2 by cluster analysis	Highly emotion dysregulated vs. low emotion dysregulated

LD: Learning disability, PTSD: Post traumatic stress disorder

Table 4. Psychological characteristics showing a significant difference between subgroups, comparing people with NESs who have reported trauma with those who have not reported trauma experiences

Psychological characteristic	Baillés (2004) [38]	Bakvis (2010) [30]	Bodde (2013) [37]	Duncan (2008)a [40]	Myers (2013) [39]	Myers (2014) [35]	Selkirk (2008) [36]
Avoidant behaviour +			√		√		
Coping strategies involving blame +			√				
Demoralisation, sense of guilt, being a failure and helplessness +					√		
Shyness or interpersonal difficulties +			√				
Self-directedness -			√				
Self-harm +				√			√
Health related trauma -				√			
Incidence of bipolar or mood disorders or symptoms +	√				√		√
Incidence of PTSD or symptoms of trauma +					√		
Incidence of personality disorder diagnosis +							√
History of engaging in psychotherapy or referral to mental health services +					√		√
Processing speed -			√				
Delayed verbal semantic memory function -						√	
Self-reported memory difficulties +						√	
Presence of learning disability -				√			

+: factor is increased with experience of trauma, -: factor is decreased with experience of trauma, √: study found a significant difference

Table 5. Summary of psychological factors upon which differences between clusters were indicated in each article using cluster or factor analysis

	Bodde (2013) [37]	Cragar (2005) [44]	Reuber (2004) [42]	Brown (2013) [43]	Uliaszek (2012) [41]
Experiences of trauma	√				
Reporting of everyday problems	√				√
Self-blame	√				
Somatization	√				
Emotional dysregulation or alexithymia			√	√	√
Interpersonal difficulties or avoidance			√		
Mental health (depression, paranoia, obsessive compulsive, mania, psychosis)		√	√		√
Cognitive abilities (processing speed, memory, IQ,)	√	√			

SEIZURE - EUROPEAN JOURNAL OF EPILEPSY

AUTHOR INFORMATION PACK

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DESCRIPTION

Seizure - European Journal of Epilepsy is an international journal owned by Epilepsy Action (the largest member led epilepsy organisation in the UK). It provides a forum for papers on all topics related to **epilepsy** and **seizure disorders**.

Seizure focuses especially on **clinical** and **psychosocial** aspects, but will publish papers on the basic sciences related to the condition itself, the differential diagnosis, natural history and epidemiology of **seizures**, as well as the investigation and practical management of seizure disorders (including drug treatment, neurosurgery and non-medical or behavioural treatments).

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INTRODUCTION

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Seizure is keen to publish focused reviews, especially on the latest developments in particular fields or on topics which are currently debated by clinicians and researchers. Authors are welcome to approach the Editor-in-Chief with their idea for a focused review prior to submission. Focused reviews should be preceded by an abstract. Focused reviews should be 1,500-2,500 words, and include no more than
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Appendix B. Journal Highlights

- Published empirical research has split NES patients into subgroups in nine ways
- Subgroups indicated behavioural, psychodynamic, and integrated models
- Individual psychological assessment and formulation is recommended
- Future research should take account of subgroups within the NES sample
- Measures of alexithymia, trauma, and attachment are likely to be useful

Appendix C. Developing the research question

Table C.1

PICO analysis

Review Question	How have researchers split people who experience NESs into subgroups and what does this reveal about the psychological mechanisms of NES aetiology?
Population	Adults who experience NESs
Intervention	Measurement of psychological factors including trauma history
Comparator	Comparison between subgroups, or subgroups and overall group or controls
Outcomes	Psychological characteristics
Setting	Any setting
Study design	Primary quantitative research

Appendix D. Search terms

Table D.1

Final Search Terms

Terms related to NESs	Term related to sub-categories
Part 1: Psychogenic non-epileptic seizures, Psychogenic non epileptic seizures, psychogenic nonepileptic seizures, pseudoepileptic seizures, pseudo epileptic seizures, non-epileptic seizures, non epileptic seizures, nonepileptic seizures, functional seizures, pseudo seizures, stress related seizures, stress-related seizures, stressrelated seizures, psychogenic seizures, hysterical seizures, psychosomatic seizures, somatic seizures, somatoform seizures, somatization AND seizures, somatisation AND seizures, dissociative seizures, non-organic seizures, non organic seizures, nonorganic seizures, conversion disorder AND seizures, psycho-physiological seizures, psycho physiological seizures, psychophysiological seizures	Subcategories, sub-categories, sub categories, subgroups, sub-groups, distinct groups, sub groups, cluster, clusters, clustering
Part 2: Psychogenic non-epileptic attacks, Psychogenic non epileptic attacks, psychogenic nonepileptic attacks, pseudoepileptic attacks, pseudo epileptic attacks, non-epileptic attacks, non epileptic attacks, nonepileptic attacks, functional attacks, pseudo attacks, stress related attacks, stress-related attacks, stressrelated attacks, psychogenic attacks, hysterical attacks, psychosomatic attacks, somatic attacks, somatoform attacks, somatization attacks, somatisation attacks, dissociative attacks, non-organic attacks, non organic attacks, nonorganic attacks, conversion disorder AND attacks, psycho-physiological attacks, psycho physiological attacks, psychophysiological attacks	
Part 3: Psychogenic non-epileptic convulsions, Psychogenic non epileptic convulsions, psychogenic nonepileptic convulsions, pseudoepileptic convulsions, pseudo epileptic convulsions, non-epileptic convulsions, non epileptic convulsions, nonepileptic convulsions, functional convulsions, pseudo convulsions, stress related convulsions, stress-related convulsions, stressrelated convulsions, psychogenic convulsions, hysterical convulsions, psychosomatic convulsions, somatic convulsions, somatoform convulsions, somatization AND convulsions, somatisation AND convulsion, dissociative convulsions, non-organic convulsions, non organic convulsions, nonorganic convulsions, conversion disorder AND convulsions, psycho-physiological convulsions, psycho physiological convulsions, psychophysiological convulsions, pseudoseizures, PNES	

Where AND terms were nested within the search terms, these were placed in brackets then the search terms were combined into sets using 'OR'.

Appendix E. Inclusion and exclusion criteria

Table E.1

Inclusion and exclusion criteria

Inclusion Criteria	Point applied
Available in English	Search engine, abstract and full text reading
Peer reviewed	Search engine
Non-epileptic seizures as main topic	Abstract or full text if unclear
Relates to subgroups of people who experience NESs based on psychological characteristics including trauma history	Abstract or full text if unclear
Quantitative primary research	Abstract or full text if unclear
Exclusion Criteria	
Includes only secondary data	Abstract or full text if unclear
Relates to NESs in children only	Abstract or full text if unclear
Considers only demographic subgroups	Abstract or full text if unclear

Appendix F. Included and excluded psychological characteristics

Table F.1

Clarification of included and excluded characteristics

Included	Not included
All personality measures	Gender
Emotion processing	Seizure semiology (appearance and features)
Adult attachment style	Childhood attachment style
Intelligence	Comorbid diagnosis of Epilepsy
Measures of anxiety, depression or other distress	Medication
Current mental health diagnosis	Age of onset
Trauma history	

Appendix G. Downs & Black checklist

Checklist for measuring study quality

Reporting

1. *Is the hypothesis/aim/objective of the study clearly described?*

yes	1
no	0

2. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*
   If the main outcomes are ®rst mentioned in the Results section, the question should be answered no.

yes	1
no	0

3. *Are the characteristics of the patients included in the study clearly described ?*
   In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case-control studies, a case-de®nition and the source for controls should be given.

yes	1
no	0

4. *Are the interventions of interest clearly described?*
   Treatments and placebo (where relevant) that are to be compared should be clearly described.

yes	1
no	0

5. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*
   A list of principal confounders is provided.

yes	2
partially	1
no	0

6. *Are the main ®ndings of the study clearly described?*
   Simple outcome data (including denominators and numerators) should be reported for all major ®ndings so that the reader can check the major analyses and conclusions. (This question does not cover statistical tests which are considered below).

yes	1
no	0

7. *Does the study provide estimates of the random variability in the data for the main outcomes?*
   In non normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or con®-dence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes.

yes	1
no	0

8. *Have all important adverse events that may be a consequence of the intervention been reported?*
   This should be answered yes if the study demonstrates that there was a comprehen-sive attempt to measure adverse events. (A list of possible adverse events is provided).

yes	1
no	0

9. *Have the characteristics of patients lost to follow-up been described?*
   This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that ®ndings would be unaVected by their inclusion. This should be answered no where a study does not report the number of patients lost to follow-up.

yes	1
no	0

10. *Have actual probability values been reported(e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?*

yes	1
no	0

External validity

All the following criteria attempt to address the representativeness of the ®ndings of the study and whether they may be generalised to the population from which the study subjects were derived.

11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*
    The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sam-ple. Random sampling is only feasible where a list of all members of the relevant

population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as unable to determine.

yes	1
no	0
unable to determine	0

12. *Were those subjects who were prepared to par-ticipate representative of the entire population from which they were recruited?*
The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source popula-tion.

yes	1
no	0
unable to determine	0

13. *Were the staV, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?*
For the question to be answered yes the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.

yes	1
no	0
unable to determine	0

Internal validity - bias

14. *Was an attempt made to blind study subjects to the intervention they have received ?*
For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.

yes	1
no	0
unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

yes	1
no	0
unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

yes	1
no	0
unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for diVerent lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls ?*
Where follow-up was the same for all study patients the answer should yes. If diVerent lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where diVerences in follow-up are ignored should be answered no.

yes	1
no	0
unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.

yes	1
no	0
unable to determine	0

19. *Was compliance with the intervention/s reliable?*
Where there was non compliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the eVect of any misclassi®cation was likely to bias any association to the null, the question should be answered yes.

yes	1
no	0
unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*

For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the ques-tion should be answered as yes.

yes	1
no	0
unable to determine	0

Internal validity - confounding (selection bias)

21. *Were the patients in diVerent intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?*
For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and case-control studies where there is no information concerning the source of patients included in the study.

yes	1
no	0
unable to determine	0

22. *Were study subjects in diVerent intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?*
For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.

yes	1
no	0
unable to determine	0

23. *Were study subjects randomised to intervention groups?*
Studies which state that subjects wererandomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no be-cause it is predictable.

yes	1
no	0
unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staV until recruitment was complete and irrevocable?*
All non-randomised studies should be answered no. If assignment was concealed from patients but not from staV, it should be answered no.

yes	1
no	0
unable to determine	0

25. *Was there adequate adjustment for confound-ing in the analyses from which the main ®nd-ings were drawn?*
This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the diVerent treatment groups was not described; or the distribution of known confounders diVered between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the eVect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the ®nal analyses the question should be answered as no.

yes	1
no	0
unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
If the numbers of patients lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow-up was too small to aVect the main ®ndings, the question should be answered yes.

yes	1
no	0
unable to determine	0

Power

27. *Did the study have suYcient power to detect a clinically important eVect where the probabil-ity value for a diVerence being due to chance is less than 5%?*
Sample sizes have been calculated to detect a diVerence of x% and y%.

	Size of *smallest* intervention group	
A	$<n_1$	0
B	$n_1 \pm n_2$	1
C	$n_3 \pm n_4$	2
D	$n_5 \pm n_6$	3
E	$n_7 \pm n_8$	4
F	n_8+	5

Appendix H. Table H.1. Article quality scores on the Downs and Black checklist [31]

Question no. / Article	Baillés (2004)[44]	Bakvis (2010)[39]	Baslet (2010)[40]	Bodde (2012)[27]	Bodde (2013)[45]	Brown (2013)[51]	Cragar (2005)[50]	Duncan (2008) a[46]	Duncan (2008) b[41]	Harden (2009)[53]	Magaudda (2011)[52]	Myers (2013)[47]	Myers (2014)[42]	Reuber (2004)[49]	Selkirk (2008)[43]	Uliaszek (2012)[48]
1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	1
2	1	1	1	0	1	1	1	1	1	0	0	1	1	1	1	1
3	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
4	1	1	1	0	1	1	1	0	1	1	0	1	1	1	1	1
5	0	1	1	0	0	1	1	1	1	0	1	0	1	1	0	0
6	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1
7	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1
8	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
9	0	1	1	1	1	0	0	0	1	1	0	0	0	1	1	1
10	0	1	1	1	1	0	0	1	1	1	0	1	1		1	0
Reporting score	**6**	**9**	**9**	**4**	**7**	**7**	**5**	**6**	**9**	**6**	**5**	**7**	**8**	**7**	**8**	**7**
Percentage	**67%**	**100%**	**100%**	**44%**	**78%**	**78%**	**56%**	**67%**	**100%**	**67%**	**56%**	**78%**	**89%**	**78%**	**89%**	**78%**
11	0	0	0	0	0	1	1	1	0	0	0	0	0	1	1	1
12	0	0	0	0	0	0	0	1	0	1	0	0	0	1	1	1
13	0	1	0	0	0	1	1	0	0	0	0	0	0	1	1	0
External validity	**0**	**1**	**0**	**0**	**0**	**2**	**2**	**2**	**0**	**1**	**0**	**0**	**0**	**3**	**3**	**2**
Percentage	**0%**	**33%**	**0%**	**0%**	**0%**	**67%**	**67%**	**67%**	**0%**	**33%**	**0%**	**0%**	**0%**	**100%**	**100%**	**67%**
14	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
15	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
16	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
17	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Question no. / Article	Baillés (2004)[44]	Bakvis (2010)[39]	Baslet (2010)[40]	Bodde (2012)[27]	Bodde (2013)[45]	Brown (2013)[51]	Cragar (2005)[50]	Duncan (2008) a[46]	Duncan (2008) b[41]	Harden (2009)[53]	Magaudda (2011)[52]	Myers (2013)[47]	Myers (2014)[42]	Reuber (2004)[49]	Selkirk (2008)[43]	Uliaszek (2012)[48]
18	0	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1
19	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
20	1	1	1	0	1	1	1	0	0	1	0	1	1	1	0	1
Internal validity - bias	**2**	**3**	**3**	**2**	**3**	**3**	**3**	**2**	**2**	**3**	**1**	**3**	**3**	**2**	**2**	**3**
Percentage	**67%**	**100%**	**100%**	**67%**	**100%**	**100%**	**100%**	**67%**	**67%**	**100%**	**33%**	**100%**	**100%**	**67%**	**67%**	**100%**
21	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
22	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1
23	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
24	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
25	0	1	1	0	0	1	1	0	0	0	0	0	1	0	0	1
26	0	1	1	1	1	0	0	0	1	0	0	0	0	0	1	1
Internal validity - confounding	**2**	**3**	**4**	**3**	**3**	**2**	**3**	**2**	**3**	**2**	**2**	**2**	**3**	**1**	**3**	**4**
Percentage	**50%**	**75%**	**100%**	**75%**	**75%**	**50%**	**75%**	**50%**	**75%**	**50%**	**50%**	**50%**	**75%**	**25%**	**75%**	**100%**
27	0	0	0	1	0	0	0	2	2	0	0	1	1	2	2	1
Power	**0**	0	0	1	0	0	0	2	2	0	0	1	1	2	2	1
Percentage	**0%**	**0%**	**0%**	**33%**	**0%**	**0%**	**0%**	**67%**	**67%**	**0%**	**0%**	**33%**	**33%**	**67%**	**67%**	**33%**
Total Score	**10**	**16**	**16**	**10**	**13**	**14**	**13**	**14**	**16**	**12**	**8**	**13**	**15**	**15**	**18**	**17**
Percentage	**45%**	**73%**	**73%**	**45%**	**59%**	**64%**	**59%**	**64%**	**73%**	**55%**	**36%**	**59%**	**68%**	**68%**	**82%**	**77%**

Appendix I. Quality scoring for question 27 (power)

Table I.1. Minimum sample sizes and quality scores for statistical tests

Test type	Detectable effect size [62]		Minimum sample size[63, 64]	Quality score allocated
Difference between 2 means (T-test)	d=0.2	small	788	3
	d=0.5	medium	128	2
	d=0.8	large	52	1
	d>0.8		<52	0
Difference between 2 groups (Mann-Whitney test)	d=0.2	small	824	3
	d=0.5	medium	134	2
	d=0.8	large	54	1
	d>0.8		<54	0
ANOVA repeated measures (5 measurements) between factors (3 groups). Corr among rep measures 0.5.	f=0.1	small	582	3
	f=0.25	medium	96	2
	f=0.4	large	42	1
	f>0.4		<42	0
ANOVA one way (3 groups)	f=0.1	small	969	3
	f=0.25	medium	159	2
	f=0.4	large	66	1
	f>0.4		<66	0
Regression models (1, 2, 3, 4, 5, 6 predictors) [a]	R^2=0.02	small	387,476,539,590, 635, 667	3
	R^2=0.13	medium	55,68, 77, 85, 92, 98.	2
	R^2=0.26	large	25, 31, 36, 40, 43, 46	1
	R^2>0.26			0
X^2	w=0.10	small	785	3
	w=0.30	medium	88	2
	w=0.50	large	32	1
	w>0.50		<32	0
Fisher's exact test	OR=1.68	small	1.68	3
	OR= 3.47	medium	124	2
	OR= 6.71	large	68	1
	OR>6.71		<68	0

[a] Taken from Field[37] p. 314

Appendix J. Summary of reasons for article exclusion

Table J.1

Reasons for article exclusion at each stage

Reason	No. excluded at abstract read	No. excluded at full text read
Related to children only	6	
Not available in English	2	3
Irrelevant topic	13	
Does not include subgroups	17	7
The subgroups were not based on psychological characteristics including trauma history	16	5
Not quantitative research	5	
Secondary data only	20	1
Total excluded	79	16

Appendix K. Excluded articles

Table K.1

List of articles excluded during full-text reading

1st Author, year & reference	Title	Reason(s) for exclusion after full text reading
Asadi-Pooya (2013)[65]	Demographic and clinical manifestations of psychogenic non-epileptic seizures: The impact of co-existing epilepsy in patients or their family members.	Sub categories related to comorbid epilepsy/ family history of epilepsy not psychological characteristics
Asmussen (2009)[66]	Differences in self-reported depressive symptoms between patients with epileptic and psychogenic nonepileptic seizures.	Subgroups based on Male/female not psychological characteristics.
Beghi (2015)[67]	Psychogenic non-epileptic seizures: So-called psychiatric comorbidity and underlying defense mechanisms.	Secondary data only
Brown (1991)[68]	Characteristics of patients with nonepileptic seizures.	The results do not include analysis at subgroup level. Reference is made to heterogeneity in the discussion, but the analysis is qualitative only.
Duncan (2006)[69]	Late onset psychogenic nonepileptic attacks.	Subgroups related to age of onset not psychological characteristics
Grimaldi (2010)[70]	Anxiety and depression in psychogenic movement disorder and non-epileptic seizures: A prospective comparative study.	Does not include any analysis at sub-group level
Drake (1992)[71]	Neuropsychological and psychiatric correlates of intractable pseudoseizures.	Does not include any analysis at sub-group level.
Hill (2011)[72]	Neuropsychological characteristics of nonepileptic seizure semiological subgroups.	Clusters are related to seizure semiology not psychological characteristics
Hubsch (2010)[73]	Psychogenic non-epileptic seizures: clinical classification based on the video-EEG analysis of 145 seizures.	Not a full article, insufficient information, abstract only, full text not available in English

1st Author, year & reference	Title	Reason(s) for exclusion after full text reading
Locke (2006)[74]	Relationship of Indicators of Neuropathology, Psychopathology, and Effort to Neuropsychological Results in Patients with Epilepsy or Psychogenic Non-epileptic Seizures.	Regression analysis of relationship between cognitive functioning and various other measures including psychopathology. Not really subgroups as such, maybe useful for discussion
Martinović (2000)[75]	Diagnosis and classification of psychiatric disorders in patients with pharmacoresistant epilepsy.	Full text not available in English
Pintor Pérez (2002)[76]	Psychiatric disorders, personality and traumatic experiences in conversion non-epileptic seizure patients.	Not available in English
Ramchandani (1993)[12]	Evaluation of pseudoseizures: A psychiatric perspective.	Includes subgroups which are based on semiology not psychological factors
Reuber (2011)[77]	Psychogenic nonepileptic seizure manifestations reported by patients and witnesses.	Does not include any analysis at subgroup level
Rosenberg (2000)[78]	A comparative study of trauma and posttraumatic stress disorder prevalence in epilepsy patients and psychogenic nonepileptic seizure patients.	Does not include any analysis at sub-group level
Scévola (2013)[79]	Psychiatric disorders in patients with psychogenic nonepileptic seizures and drug-resistant epilepsy: A study of an Argentine population.	Does not include any analysis at sub-group level

Appendix L. Data extraction

Table L.1

Sample of summary data extraction during full text reading

1st Author and year	Title	Reasons/ summary after full text read	Country	Setting	Methodology	Sample type, number, and comments	Overall opinion
Baillés (2004)[44]	Psychiatric disorders, trauma, and MMPI profile in a Spanish sample of non-epileptic seizure patients.	Range of comorbid psychiatric diagnosis found. Heterogeneity of personality profiles on the Minnesota Multiphasic Personality Inventory (MMPI). Elevated mania scores associated with presence of trauma and personality disorder, elevated paranoia with presence of personality disorder	Spain		comparison of mean MMPI scores between groups	30 PNES confirmed via video-electroencephalography, comorbid epilepsy/ other neurological disorders excluded	Results need to be interpreted cautiously as p values were not reported, the sample was small, and the data analysis appears to have been exploratory.

1st Author and year	Title	Reasons/ summary after full text read	Country	Setting	Methodology	Sample type, number, and comments	Overall opinion
Bakvis (2010)[39]	Basal hypercortisolism and trauma in patients with psychogenic non-epileptic seizures		Netherlands	Tertiary epilepsy centre	Comparisons of mean levels of cortisol in saliva between groups and within participants at different times. Also after administering a drug. Mixed design experiment	18 PNES, 19 Healthy controls advertised though newspaper	A well-written article, experiment seems well designed, sample size small but analysis seems reliable. Out of my area of expertise, as it was a neurological article, but it was written in a way that was easy to understand.

Appendix M. PRISMA 2009 checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1.1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1.3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1.5-1.9
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	1.9-1.10
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n/a
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	1.10-1.14
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	1.12
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	1.80
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	1.16-1.17
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	1.16-1.17
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	1.16-1.17

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	1.14-1.15
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	1.16 - 1.17
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n/a

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	1.16
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	1.13
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	1.17-1.29
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	1.20
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	1.17-1.29
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	1.36-1.37
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	1.30-1.41
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	1.36-1.39

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	1.39-1.41
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	n/a

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix N. Subgroups based on trauma experience

Table N.1

Details of significant differences reported between subgroups with and without trauma experiences

Article	Item	Item description	Direction	Effect size (confidence interval)	P value
Baillés (2004)[44]	MMPI Mania sub-scale	Indicating elated unstable mood, excitement, restlessness and inflated self-esteem[80]	Greater with trauma	d=0.86[a]	<0.05
Bodde (2013)[45]	CERQ blaming others	Emotion regulation strategy of cognitively putting the blame onto others	Greater with trauma	d=0.8[b]	0.018
	Short MMPI negativism	Items that indicate passive avoidant behaviour, bearing grudges and feeling dissatisfied	Greater with trauma	d=2 [b]	0.049
	Short MMPI shyness	Indicates feelings of shyness and interpersonal difficulties	Greater with trauma	d=1.5 [b]	0.006
	DISQ-1	Subscale of the Dissociation Questionnaire relating to identity confusion and depersonalization	Greater with trauma	d=1 [b]	0.019
	Short TCI harm avoidance	A dimension of personality based on the psychobiological theory of personality	Greater with trauma	d=0.7 [b]	0.027
	Short TCI self-directednesss	As above	Less with trauma	d=0.8 [b]	0.024
	CVST rt	Processing speed	Slower with trauma	d=2 [b]	0.011
Duncan (2008)a[46]	Predictors of reporting sexual abuse	Female gender	More likely with reported sexual abuse	OR 6.02 (2.50-14.49)	<0.001
		Learning disability	Less likely with reported sexual abuse	OR 0.15 (0.03-0.73) 1/OR=6.67	0.019
		self-harm	More likely with reported sexual abuse	OR 3.30 (1.73-6.33)	<0.001

Article	Item	Item description	Direction	Effect size (confidence interval)	P value
		health related trauma	Less likely with reported sexual abuse	0.09 (0.01-0.71) 1/OR=11.11	0.023
Myers (2013)[47]	Psychotherapy engagement	Engaged in psychotherapy presently or in the past	More likely with trauma	OR= 5.13[c]	0.009
	Mood/bipolar disorder	Diagnosis of comorbid mood/bipolar disorder	More likely with trauma	Insufficient information to calculate	0.005
	PTSD	Diagnosis of comorbid post-traumatic stress syndrome	More likely with trauma	OR=6.56	0.04
	TSI-2	The trauma symptom inventory, includes anxious arousal, depression, anger, intrusive experiences, defensive avoidance, dissociation, somatic concerns, dysfunctional sex behaviour, impaired self-reference, & tension reduction behaviours	All scales higher with trauma	d=3.6[a] for dysfunctional sexual behaviour to d=0.78[a] for anxious arousal	0.000 for defensive avoidance, to 0.045 for dysfunctional sex behaviour
	MMPI RCd Demoralization subscale of the Minnesota Multiphasic Personality Inventory-2RF	Higher scores indicate a person functioning with reduced efficiency and competence; a sense of guilt, failure, helplessness and desperation, distraction and being overwhelmed; (who may avoid or collapse under everyday stresses.[80])	Higher with trauma	d=0.80[a]	0.028
Myers (2014)[42]	Welscher Memory Scale- III logical memory II	A test of delayed verbal semantic memory administered by a professional, higher scores indicate better functioning	Lowest scores with PTSD, then with trauma but no PTSD, highest scores with no trauma	No trauma – trauma without PTSD d=0.57[a] No trauma – trauma with PTSD d=1.10[a]	0.032

Article	Item	Item description	Direction	Effect size (confidence interval)	P value
	Memory Complaints Inventory total	A self-report measure with broad range, relating to verbal and visual memory, higher scores indicate worse functioning	PTSD group significantly higher than: Trauma no PTSD, and group without trauma	 d=1.56[a] d=1.75[a]	0.0001
Selkirk (2008)[43]	Indicators of mental ill health	Previous referral to mental health services	Higher with reported sexual abuse	OR 2.03 (1.56-2.63)	<0.0001
		History of any mental health problem	Higher with reported sexual abuse	OR 1.42 (1.24-1.64)	<0.0001
		History of depression	Higher with reported sexual abuse	OR 1.79 (1.36-2.35)	0.0001
		History of deliberate self-harm	Higher with reported sexual abuse	OR 4.25 (2.47-7.30)	<0.0001
		Diagnosis of personality disorder	Higher with reported sexual abuse	OR 7.88 (1.76-35.33)	0.0012

[a] Effect size calculated from stated means and standard deviations, using the standard deviation for no trauma subgroup; [b]Cohen's d effect size estimated from graph of Z scores, as figures were not reported; [c]Odds ratio determined using Wilson's 'Practical meta-analysis effect size calculator'[81]. OR: odds ratio with 95% confidence interval in brackets.

Appendix O. subgroups based on cognitive functioning

Table O.1

Psychological factors showing significant differences between subgroups based on level of cognitive functioning

Study	Factor subgroups are determined by	Significant differences between subgroups	Effect size (confidence interval)	p
Bodde (2013)[45]	Global cognitive level (RPM)	Those scoring below average on the RPM scored significantly: lower on 'persistence' higher on 'positive refocusing' on the TCI	 r=0.35 r=0.35	 0.03 0.043
Duncan (2008)a [46]	Predictors of learning disability	Male gender Comorbid epilepsy Environmental triggers Pseudostatus	OR 3.40 (1.22-9.49) OR 5.61 (1.71-18.87) OR 20.83 (5.35-83.33) OR 3.77 (1.35-10.35)	0.019 0.005 <0.001 0.012
Duncan (2008)b[41]	Presence or absence of learning disability (LD)	Likelihood of having comorbid epilepsy 36% compared to 8.7% for those without LD More likely to be on anti-epileptic medication Less likely to have reported sexual abuse More likely to have identified environmental triggers for the seizures	OR 5.87 (2.33-14.76) OR 3.85 (1.40-10.57) OR 0.29 (0.08 – 1.00) 1/OR=3.45 OR 14.74 (4.83-43.31)	<0.001 0.005 0.038 <0.001
Magaudda (2011)[52]	Presence of mild learning disability	No statistical tests done, but case data seems to indicate aetiology of NESs more likely to be associated with a reduction in epileptic seizures		Not available

OR: odds ratio; CI: 95% confidence interval

Appendix P. Subgroups based on factor and cluster analysis

Table P.1

Factor loadings above 0.4 for subgroups identified by factor analysis

Article	Factor	Factor loadings
Bodde (2013)[45]	Factor 1, Psychotrauma subgroup	TEC 0.586, SDQ-20 0.800, EPCL total complaints 0.661, CERQ self blame 0.511
	Factor 2, high vulnerability somatization subgroup	TEC -0.650, Short MMPI somatization 0.663, CVST -0.417, EPCL total complaints 0.569
	Factor 3, high vulnerability sensitive personality problem subgroup	Short TCI novelty seeking 0.746, CVST 0.401, CERQ self blame 0.693
	Factor 4, high vulnerability somatization subgroup with a low cognitive level	Short MMPI somatization 0.654, CVST 0.639

See Table 4 in results for abbreviations

Table P.2

Psychological characteristics upon which significant differences between groups were found following cluster analysis

Article	Clusters	Measures upon which significant differences were found between clusters	Effect sizes
Cragar (2005)[50]	Depressed neurotic/ somatic defender/ activated neurotic	MMPI-2 (scales F, K, 2, 6, 7, 8, 9, 0), intellectual ability, memory ability, language ability, visual spatial ability	d=0.85 to 2.47
Reuber (2004)[49]	Cluster 1, similar to borderline personality disorder/ cluster 2, over controlled/ cluster 3 similar to avoidant personality disorder/ cluster 4, outlier	No statistics on differences between clusters, only comparisons with healthy controls	n/a
Brown (2013)[51]	Cluster 1, high levels of emotional dysregulation and alexithymia/ Cluster 2, relatively normal emotional dysregulation and alexithymia	All subscales of DERS other than awareness, TAS difficulty identifying and described feelings subscales	r= 0.49 to 0.67
Uliaszek (2012)[48]	Highly emotion dysregulated/ low emotion dysregulated	DERS total score DASS (anxiety, depression, stress), BDI-II, DES, PHQ-15, QOLIE-31	d=0.85 to 2.29[a]

[a]Cohen's d effect sizes calculated using the f or t statistic and cluster n[81].

Section Two: Empirical Paper

Relationships between early life events, individual differences, and seizures

Liz Tallentire

Doctorate in Clinical Psychology

Division of Health Research, Lancaster University

Word Counts: 7,979 excluding title page, tables, figures, references, and Appendices

15,273 in total excluding author guidance of 7,370 words

Presented in the style of the journal Epilepsia, see Appendix A for author guidelines

SUMMARY

Objectives: To identify subgroups of people who experience non-epileptic seizures (NESs) and examine their psychological characteristics in comparison to each other and those people who experience epileptic seizures (ESs).

Methods: 316 people who reported experiencing ES, NES, or both epileptic and non-epileptic seizures (ES+NES) consented to take part via an online survey. Following initial exploratory data analysis (n=278), a cluster analyses (n=114) was implemented to split those who experienced NESs into subgroups based on their trauma and alexithymia scores. Further exploratory analysis then compared the NES subgroups (n=49, 21, 44) to each other and to the ES group (n=119) by testing for differences between group means and correlations.

Results: Consistent with previous research, the overall NES group compared to the ES group, had a significantly higher mean trauma score and seizure frequency, and seizures had a greater impact on their quality of life. Clustering of the NES group identified three clusters which differed significantly on trauma, attachment, and alexithymia measures. There were also significant differences when comparing correlations between psychological characteristics for each cluster and the epilepsy data.

Significance: This research emphasises the importance of assessment and formulation of individual differences in both ES and NES presentations. Assessing experiences of trauma, attachment, and alexithymia is likely to be helpful, in future research and in clinical settings. Further research to test whether the subgroup characteristics in this research are supported and to assess the efficacy of therapeutic interventions informed by the psychological characteristics of each subgroup is suggested. If further research is congruent with this study, it may form the basis of a means of allocating people who experience seizures to appropriate psychological assessment and therapeutic pathways.

Key words

Epilepsy, non-epileptic, attachment, alexithymia, childhood trauma, subgroups

Epilepsy or epileptic seizures (ES) are caused by abnormal bursts of electrical impulses in the neurons of the brain; these bursts alter the functioning of the brain and body. Symptoms vary; they may include, altered perception, being unresponsive, losing consciousness, and convulsions[1]. The unusual electrical activity in the brain associated with ES can usually be detected using an electroencephalogram (EEG)[1]. Non-epileptic seizures (NES) have similar symptoms and appearance to ES, but they are not associated with unusual electrical activity in the brain or with other somatic causes, such as acute infections[2-5]. Alternative names for NES include, non-epileptic attack disorder (NEAD), psychogenic non-epileptic seizures (PNES), and dissociative episodes[3, 6]. A meta-analysis of the incidence of epilepsy internationally reported a median incidence of 50.4 per 100,000 people per year (interquartile range 33.6–75.6)[7]. Estimates of the prevalence of NES have varied between 1.5 and 4.9 per 100,000 people in the general population and 25 to 30 in every 100 people referred to tertiary epilepsy centres[6]. Some people experience ESs and NESs; comorbidity has been reported at a prevalence of 5 to 40 in every 100 people in samples of people who have experienced NESs[3, 8].

Both ES and NES can be very distressing for people who experience them; they are associated with a poorer quality of life and increased risk of psychological difficulties, such as, depression, anxiety, and personality disorders[4, 9-15]. Financial costs are large; one study estimated the direct and indirect cost of epilepsy across the European Union's 25 member countries to be €15.5 billion (€33 per capita) in 2004[16]. The main treatment for epilepsy is anti-epileptic medication, and in severe cases, surgery is considered. However, several studies have reported success in reducing ES frequency using psychological therapies, such as CBT[41-43]. Treatments for NES have focussed on psychological therapy, such as cognitive behavioural therapy (CBT), and

psycho-education; a Cochrane review found little reliable evidence to support choice of treatment for NES[6]. Despite treatments for ESs focusing on medical intervention and NESs psychological intervention a study indicated that patients perceived ES and NES as both psychological and physical[44].

NES that are unrecognised or mistaken for epilepsy present a significant issue because of the risk of potentially severe side-effects of unnecessary anti-epileptic medication or other inappropriate intervention, such as surgery, and the neglect of the actual psychological difficulties that may be causing the seizures[15]. Unrecognised NESs also presents a significant cost to health services; for example, one hospital in Ireland estimated the cost of to be €20,995.30 per year per patient[17]. Differentiating between ES and NES is difficult and costly[18-20] and is further complicated by comorbidity and the heterogeneity of NES aetiologies[19, 21-24].

This heterogeneity has been explored by those such as Brown et al.[25] and Reuber et al.[22]. They used cluster analysis and were successful in identifying NES subgroups. For example, Brown et al. identified a subgroup with elevated levels of psychopathology, somatisation and alexithymia, and a subgroup with relatively normal levels of alexithymia, but high somatisation and depression scores[25]. Reuber identified three subgroups that differed on measures of personality and emotion dysregulation[22]. Differences have been identified between subgroups on a variety of psychological characteristics; for example, personality difficulties[26, 27], mood disorders[10, 28], reporting of everyday problems[23, 27] and cognitive abilities[21, 27]. Trauma reporting and emotion regulation have been identified frequently as variables that can differentiate subgroups [22, 23, 25-27].

Understanding the psychological characteristics typical of different seizure types and clusters is important, as they may help clinicians to be alert to unmet psychological

needs and prompt further exploration of seizure types, where atypical characteristics are present. It may also inform interventions upon which further research is based. This study investigated trauma experience, seizure frequency, quality of life, adult attachment style, and alexithymia. Their relevance to NESs and ESs will be discussed below.

Literature reviews have frequently reported that having a history of trauma is more common for people who experience NES than for those who experience ES[2, 19, 29]. Lally et al.[30]reported that the number of categories of reported trauma correlated significantly and positively with seizure frequency for people who experienced NES. This evidence suggests that trauma history and seizure frequency will be worthy of further investigation. Corrallo et al.[31] suggested that quality of life (QoL) is also important to consider in relation to seizure patients.

Bowlby's[32] attachment theory proposed that the way a child relates to their main caregiver shapes the way they relate to others throughout life, through the process of forming an internal working model of that relationship. This develops into an attachment style, which Bowlby[32] described categorically as secure, anxious resistant or anxious avoidant. Later, in social psychology, Brennan, Clark and Shaver[33] developed this categorical understanding, and conceptualised adult attachment style as consisting of two major dimensions, attachment anxiety and attachment avoidance. People scoring high on attachment anxiety would be expected to fear others abandoning them and to need approval from others. Those scoring high on attachment avoidance would be expected to avoid getting close to others and be very self-reliant. People scoring low on both dimensions would correspond to Bowlby's secure category and Brennan, Clark and Shaver[33] suggested they would be able to easily form supportive adult relationships.

Quinn, Schofield, and Middleton[34] proposed the theory that experiences of trauma, in the context of an attachment relationship that is not validating, form the basis of one aetiology of NES. This suggests that a child who experiences trauma and is cared for by parents who do not recognise, acknowledge and cope with the child's thoughts and feelings, would be more likely to develop NES than a child who experiences the same trauma but is emotionally supported by their parents. However, adult attachment styles have not been widely studied in relation to NES. Only one study, with a small sample size, has found that people who experienced NES (n=17) were significantly more likely to have a fearful adult attachment style than those who had epilepsy alone (n=26)[35]. In the same study the results were not significant for secure, dismissing, or preoccupied attachment categories[35]. Another study found no significant differences in attachment styles for those experiencing ES and NES[36]. However, the investigators reported reliability issues with the particular attachment measure employed in the study.

The personality characteristic, alexithymia, relates to recognising and describing feelings, as well as interacting with others[37]. The concept is related to the broader concept of emotion regulation[38]. High levels of alexithymia indicate a person has difficulties with identifying, describing and sharing their emotions. Research has reported mixed results in relation to alexithymia and seizures; Kaplan et al.[39] reported that people who experienced NES had higher levels of alexithymia than those who experienced ES, whereas, Bewley et al.[40] reported similar levels of alexithymia in people with ES and NES, both being significantly higher than controls. In addition to Bewley et al.'s[40] research, other indicators suggest a relationship between psychological characteristics and ES. For example, Harden et al.[9] reported that 75% of their sample of

people diagnosed with epilepsy (n=16) met criteria for a diagnosis of personality disorder (n=12).

Theoretically, the concept of emotion regulation is closely linked to childhood attachment style. Cassidy[45] proposed that emotion regulation style is an adaptive response, which the child develops in order to manage and maintain the attachment relationship with their caregiver. Cassidy[45] suggested that when a caregiver repeatedly rejects a child, the child develops an avoidant attachment style and minimises their emotions in order to avoid further rejection. When a caregiver is unavailable or inconsistently available, the child develops an anxious attachment style and maximises their feelings in order to increase the chances of getting a response from the caregiver. Research, consistent with this theory, has identified a link between adult attachment style and alexithymia. For example, low levels of alexithymia, indicating no problems with emotion processing have been associated with secure adult attachment style in a student sample[46]. Fearful or anxious adult attachment style has been linked to high levels of alexithymia in young men with mood disorders[47]. A combination of both anxious and avoidant attachment strategies, and over and under regulation of emotion has been reported in a study subgroup of people who were diagnosed with both somatoform disorder and personality disorder[48]. The authors proposed that this was consistent with a disorganized attachment style, which has been associated with childhood adversity[48, 49].

In relation to NES, a comprehensive review in 2009 identified a lack of studies that obtained sufficiently large sample sizes to achieve an appropriate level of power[3]. Five studies have considered psychological characteristics and used cluster or factor analysis to account for NES heterogeneity[21-23, 25, 27]. None of these studies considered alexithymia, attachment, and trauma together.

Consequently, in order to address the gaps in the current literature, this study aimed to collect data from a relatively large sample of NES and ES participants on their trauma experience, seizure frequency, quality of life, adult attachment style, and level of alexithymia. In order to achieve the desired sample size it used a cross sectional survey design and online recruitment. It was hoped that this study would increase understanding of the differences in psychological characteristics of people who experience ESs and those subgroups that experience NESs. This understanding may help clinicians differentiate between seizure presentations and identify psychological therapies that may be appropriate in further clinical research.

Research aims

In order to achieve a larger sample size this study used self-reporting of seizure type, which has not been used in previous research. Therefore, it was important to check the data against hypotheses based on previous research before completing the main analysis. It was hypothesised that people who experienced NESs compared to people who experienced ESs would on average, (H1) report more episodes of childhood trauma, (H2) report higher levels of seizure frequency, and (H3) report lower quality of life.

Following this initial assessment of the data to ensure they matched hypotheses from previous research, the aims of the main analyses were (1) to identify NES subgroups and (2) to compare mean scores and correlations of psychological characteristics between NES subgroups and those people who have experienced ESs using exploratory analysis.

Method

Design

The study used a cross sectional survey design.

Ethics

The study gained ethical approval via NHS ethics proportionate review, Research Ethics Service reference number 15/NW/0110; details of the application are included in section four.

Participants

Participants were over 18 years of age and identified themselves as experiencing ES and/or NES. Inability to understand the instructions and measures in English language was an exclusion criterion, because not all measures were available in alternative languages.

Measures

Participants were asked to self-report their demographic details, seizure type (ES and/or NES) and seizure frequency, followed by the measures (Appendix B) presented in the order below.

Impact of Seizures

The revised Liverpool impact of epilepsy scale (RLIOES) was used to assess quality of life. It has 12-items and asks participants about the impact of seizures on aspects of life, such as health and relationships. Responses are on a 5-point Likert scale from 'very much for the better' to 'very much for the worse'. The RLIOES was scored

according to the method outlined by Crossley, Jacoby, & Baker[50]. The measure has possible scores ranging from -24 to +24, with negative scores indicating a detrimental effect on quality of life and positive scores indicating a positive effect on quality of life. It was chosen over other more general measures of quality of life because it asks specifically about the impact of seizures on quality of life. It was reported to have good reliability and acceptable validity[50] with Cronbach's α of 0.83.

Attachment

The experiences in close relationships short form (ECR-SF)[51] was used to measure adult attachment anxiety and avoidance, based on Brennan, Clark and Shaver's dimensional model of attachment[33]. The ECR-SF contains 12 statements about how a person generally feels in relationships. Six items form the attachment anxiety dimension and six items the attachment avoidance dimension. The participant rates their level of agreement on a 7-point scale, from 'strongly agree' (1), to 'strongly disagree' (7). The presentation order of the ECR items was randomised as recommended by the authors and it was scored in accordance with the methods used in its development and validation[51]. Possible scores ranged from 6 to 42 for each dimension; higher scores indicated increased levels of attachment anxiety or avoidance. The ECR short form has been reported to have good reliability and validity with Cronbach's alpha values between 0.77 and 0.86 for the anxiety scale and 0.78 and 0.88 for the avoidance scale[52, 53].

Alexithymia

The Toronto Alexithymia scale (TAS-20) was used to assess levels of alexithymia[54]. The TAS-20 consists of 20 statements about emotions, sensations, and

interpersonal interactions. The measure has a three-factor structure, labelled as difficulty identifying feelings, difficulty describing feelings, and externally-oriented thinking. Responses are on a five-point Likert scale from strongly disagree (1) to strongly agree (5). Scoring was completed according to instructions provided by the author; scoring involved reverse scoring five items before adding up the score for each subscale and the total score. Missing items, up to a maximum of 3 in the total score and 1 in each subscale, were replaced by the mean of the other items. Possible total scores range from 20 to 100, with greater than or equal to 61 described as high alexithymia and lower than or equal to 51 described as low alexithymia[55]. The TAS-20 has been used with clinical and non-clinical populations[56, 57]; it has been validated using internet administration and found to have good cross-cultural validity for the difficulty identifying feelings and difficulty describing feelings factors[58, 59]. The TAS-20 is reported to be reliable and to have factorial validity, with a Cronbach's α of 0.86[60]. This measure was chosen in preference to other measures of alexithymia because it has a comprehensive evidence base, including online presentation and international samples.

Childhood Trauma

The Early Trauma Inventory Self Report- Short Form (ETISR-SF)[61, 62] was used to enquire about experiences of trauma prior to the age of 18 years. It has 29 items, asking about experiences of different traumas, arranged into four domains of physical, emotional, sexual abuse, and general trauma. Responses are, yes or no. Scoring was completed by summing the number of yes responses in each domain, and calculating the overall sum, as recommended by Bremner, Bolus, and Mayer[61]. The possible range for the total score was from 0 to 29, with higher scores indicating more different types of childhood trauma were reported. An overall score was calculated for those with no

more than 4 items missing, the score for each subscale was calculated if no more than 1 item in the scale was missed, with the exception of the dissociation sub-scale which has two items. The dissociation subscale was only scored if both items were completed. Bremner[61] tested the ETISR-SF using a sample of healthy controls and people with psychiatric disorders, including abuse history. Bremner[61] reported acceptable validity and internal consistency with Cronbach's α of 0.95; another study reported excellent reliability[63]. This scale was chosen because it includes a range of trauma types, including emotional abuse, and it has been used with clinical populations.

Procedures

The study was promoted to potential participants through online forums and health clinics that were likely to be accessed by people who experience ES and/or NES, between the dates of 2nd February 2015 and 13th March 2015 (Appendix C). The online data collection closed on 16th March 2015. Participants were asked to pass on information about the study to others who may be interested.

Participants accessed information about the study and completed the questionnaires via an online survey hosted by Lancaster University (see Appendix D for examples of information presented to participants). Data were collected anonymously: anonymity was important as previous research has indicated that it increased the likelihood of reporting childhood traumas[64].

Statistical Analysis

The analysis was completed using IBM SPSS statistics 22.0.01 and the R: language and environment for statistical computing[65]. Figure 1 reports details of the numbers of participants with missing data who were excluded or included in score

calculations; Appendix E includes this data for the subscales of the TAS-20 and ETISR-SF. The stages of analysis are described below. Details of the specific tests used are in Appendix F. Tests were administered using pairwise exclusion for missing data. The analysis was exploratory therefore; a Bonferroni correction was not applied.

<<INSERT FIGURE 1>>

Exploratory data analyses (EDA) included three groups: (1) those who experienced ES only (n=119), (2) those who experienced NES only (n=131), and (3) those who experienced both ES and NES (ES+NES, n=28). The cluster analyses were applied to group 2, NESs only. Consistent with the research aim of contrasting differences in psychological characteristics NES subgroups and the ES group, subsequent analyses focussed on the subgroups, formed from group 2, and group 1.

Exploratory data analysis (EDA)

EDA involved considering exclusion of outliers and small n categories. Outliers were examined for unusual patterns of responses, but none were removed from the analyses at this stage. Group means and frequencies for demographics and total scores on all the measures were compared across the ES, NES, and ES+NES groups. Due to non-normal distributions, comparisons were checked using permutation tests for the seizure frequency and trauma data. Effect sizes for differences between group means were calculated using the mean and standard deviation for the epilepsy group.

Cluster analysis

The NES group was clustered on the childhood trauma (total score) and alexithymia (total score) measures as these variables have been found to differentiate subgroups of NES patients in previous research (see part 1). The clustering method used was agglomerative hierarchical cluster analysis, using Ward's method and the squared Euclidean distance measure. Cluster analysis[66] was chosen because it allowed the clustering to incorporate more than one variable at once and negated the need for the researcher to set arbitrary cut off values. Hierarchical methods were chosen because the number of clusters was unknown.

Clustering is sensitive to differences in scale[66]; therefore, the trauma and alexithymia scores were standardised using Z-scores. As Ward's method is sensitive to outliers[67], nearest neighbour cluster analysis was used to identify them[68] by examination of the dendrogram (appendix G). Case numbers 150 and 220 were removed prior to Ward's method clustering. The cluster analysis was then repeated, using average linkage within groups, and the results compared.

Comparison of cluster and epilepsy data means

Mean age and total scores on all measures were compared across the three NES clusters, obtained from the cluster analysis, and the ES only group, using the same methods as the EDA.

Comparison of correlations within clusters and epilepsy data

In order to investigate the relationships between variables and how these differed between the NES clusters and ES group, correlations within NES clusters were examined and compared to those for the ES group.

Power calculation

The power calculation was based on the ability to detect differences in mean scores when comparing the NES subgroups and ES group, post clustering. Based on there being a maximum of three NES subgroups, therefore a total of four groups, of equal size, assuming a medium effect size (f=0.25), alpha error probability of 0.05 and a power of 0.8 the minimum sample size was 180[65].

Results

All participants completed the survey online; no paper copies were received. A total of 313 participants consented to take part. Figure 1 illustrates the numbers of

participants providing a full data set for each section of the survey. The 60 included with missing data on the trauma measure relate mainly to the last two questions, which read 'If you responded "YES" for any of the above events, answer the following…' It appears that most participants had interpreted this as relating to the section immediately before this question about sexual abuse, as 59 out of 60 of the people who did not answer the dissociation questions had answered no to all the sexual abuse questions. Seven out of 60 had responded negatively on the whole trauma survey.

Participants who had not entered any data on the first survey were excluded leaving an initial sample size of 288. From this initial sample (n=288), the highest dropout was between the revised Liverpool impact of epilepsy scale (RLIOES) (survey 1) and the experiences in close relationships short form (ECR-SF) (survey 2), at this point n=25 (9%) provided a complete data set for the RILOES but not for the ECR-SF.

Cronbach's alpha values were 0.88 for the RLIOES, 0.73 for ECR-SF anxiety, 0.83 for ECR-SF avoidance, 0.87 for the TAS-20, and 0.90 for the ETISR-SF; indicating that internal reliability was at least acceptable for all measures.

Exploratory data analysis

Gender, country, and seizure occurrence

In the sample (n=288), 119 (41.3%) of the participants indicated they experienced ES only; 131 (45.5%) NES only; 28 (9.7%) ES+NES; and 10 (3.5%) were unsure about one or both seizure types. The data from the 10 participants who were unsure about their seizure type was excluded from further analyses. Table 1 summarises the categorical variables for the participants included in the exploratory data analysis (n=278).

<<INSERT TABLE 1>>

The distributions of gender ($\chi^2(2)=7.18$ p=0.03) and whether or not seizures were reported in the last year (p<0.001, Fisher's exact test) were significantly different across the ES, NES and ES+NES groups. The percentage of males in the ES (16.0%) and ES+NES (17.9%) groups were similar. The NES group had a smaller proportion of males (6.1%) than the ES group (χ^2 (1) = 6.29, p=0.01) and the ES+NES group (p=0.055, Fisher's exact test). The odds ratio indicated that the odds of being male were 2.9 times greater in the ES group than the NES group. The percentage of people experiencing seizures in the last year in the ES group (72.3%) was significantly smaller than the NES group (93.1%, χ^2 (1) = 19.41, p<0.001) and smaller (approaching significance) than the ES+NES group (85.7%, χ^2 (1) = 3.27, p=0.053). The odds of having seizures in the last year were 5.20 times greater in the NES group than the ES group.

Clinically it was expected that people with ESs may not currently experience seizures, due to antiepileptic medication. However, it was more unusual for people with NESs not to have experienced seizures in the last year. Therefore, this NES group were investigated to assess any possible bias they may introduce. The group was relatively small (n=9) and their mean scores were not significantly different to the rest of the NES group on any of the measure total scores or their age (p>0.25). Therefore, they were included in the analysis as it seemed unlikely they would have a significant impact on the results.

Age, seizure frequency, childhood trauma, adult attachment, alexithymia, and impact of seizures

Table 2 provides the descriptive statistics for each group of participants. Subscale data are provided in Appendix H, Table H.1, and Appendix I.

<<INSERT TABLE 2>>

The differences between the groups' mean ages were statistically significant (F=6.01, p=0.003). However, the mean (32.43, 36.85, 38.04) and median (30, 36, 38.5) ages of the three groups all fell within 30 and 40 years, and their ranges were similar (18-66, 18-61, & 19-62). Therefore the groups were, to all intents, comparable. Post hoc tests (Appendix J) indicated that the epilepsy group had a significantly lower mean total childhood trauma score (5.48) than the NES group (9.78, d=0.85, p<0.001) or the ES+NES group (12.57, d=1.40, p<0.001). The NES and ES+NES groups did not differ significantly (p=0.06). The epilepsy group also had significantly lower mean seizure frequency (15.21 per month, d=0.33, p=0.02) and less impact of seizures (-8.69, d=0.98, p<0.001) when compared to the NES only group who had mean seizure frequency of 41.05 per month and mean impact of seizures score of -14.58.

Summary of seizure type groups

The EDA considered three groups of participants; those who experienced ESs only, NESs only, and both types of seizures (ESs+NESs). The ES+NES group was much smaller (n=28) and not all of them provided sufficient data to include in analyses, therefore they were excluded from subsequent analyses.

Cluster analysis

The graph of the agglomeration schedule (n=114) showed a relatively sharp increase on step 111 (Appendix K) indicating a three cluster solution. Clustering based on Ward's method and within groups average linkage, produced a similar pattern of results, the main difference being the boundary between clusters 1 and 2, which was at a lower level of alexithymia using Ward's method (Appendix L). However post-hoc tests

showed that the solution under Ward's method gave subgroups that were both more distinct and theoretically more sensible.

With reference to the whole NES group, cluster 1 included those with low to medium childhood trauma and medium to high alexithymia, cluster 2 low to medium childhood trauma and low to medium alexithymia, cluster 3 medium to high childhood trauma and medium to high alexithymia. The clusters are illustrated in Figure 2.

<<INSERT FIGURE 2 >>

Comparison of NES clusters and the ES group

Categorical data is provided in table 3, the only significant categorical difference between clusters was gender ($p=0.04$, Fisher's exact test). The differences between means across the three NES clusters and ES group were significant for all variables in Table 4 ($p<0.001$ to 0.004). The means are illustrated in Figure 3, subscale data is in Appendix H, Table H.2. Post hoc test results are provided in Table 5. Differences between the groups' mean ages were only significant ($p=0.01$) for the difference between cluster 3, mean 38.25 (standard deviation 10.46) and epilepsy data, 32.45 (10.68), and all means were between 30 and 40 years. With reference to tables 4 and 5, and figure 2 it can be seen that cluster three is characterised by significantly higher scores than some or all of the other groups in childhood trauma reporting, alexithymia, and attachment anxiety. All the NES groups have significantly greater negative impact of seizures than the ES group. With the exception of impact of seizures, cluster 1 is quite similar to the epilepsy group. Cluster 2 is characterised by significantly lower scores than some or all of the other groups in attachment anxiety, attachment avoidance, and alexithymia.

<<INSERT TABLE 3>>

<<INSERT TABLE 4>>

<<INSERT FIGURE 3>>

<<INSERT TABLE 5>>

Comparison of correlations within clusters and epilepsy data

Results of the correlation analyses are given in Table 6. Notable points were that attachment anxiety and avoidance were correlated significantly and positively with each other in all groups (range r= 0.25 to 0.51). Correlations between attachment avoidance and alexithymia were also similar across the groups and were close to medium effect size, although those in clusters 2 and 3 were not significant. It was also notable that in cluster 3 there was only one significant correlation, and for many comparisons r was close to 0, whereas in the ES group the correlations between, alexithymia and impact of seizures ($r=-0.38$, $p<0.001$), alexithymia and attachment anxiety ($r=0.28$, $p=0.004$), alexithymia and attachment avoidance ($r=0.34$, $p<0.001$), were significant and close to a medium effect size. Permutation tests for significance of differences between correlations are located in Appendix M.

Cluster 2 had several large significant correlations and several medium correlations that were insignificant. Insignificance of medium correlations is likely to be related to the sample size (n=22).

<<INSERT TABLE 6>>

Discussion

Summary of results

The EDA results showed significant differences between the three groups of people who experienced seizures (ESs only, NESs only, or ESs+NESs) in terms of their age, gender, seizure occurrence, seizure frequency, impact of seizures score, and childhood trauma total score. As hypothesised, when the whole group with NESs were compared to those with ESs, childhood trauma reporting was greater (H1), seizure frequency was higher (H2), and impact of seizures was greater (scores more negative) (H3). These results support the viability of this dataset, which is also examined in the following demographics section.

The cluster analysis, comparisons of means, and correlation analyses provide information relating to the research aim of comparing the psychological characteristics of NES subgroups and the ES group, which will be explored in subsequent sections.

Demographics

In this study 17.6% of the people who reported experiencing NES reported also having ES; other studies have reported 5 to 40%[3, 8]. The reported mean age (36.85 years) of the NES group was similar to that reported in other studies[29] (mean 33.1 years, range 25-38.7 years, n=15, for studies relating to adults). The percentage of females (93.9%) in the NES only group was towards the higher end of the range (64-100%) reported in previous studies[19, 29]. The percentage of females in the ES only group (84.0%) was higher than expected (around 50%)[69]; this may be due to the method of recruitment, which was largely through online support groups, as Mo, Malik, and Coulson[70] reported females make more use of online discussion forums than males.

Epilepsy group

The mean alexithymia score for the epilepsy data (57.31) is approximately 1 standard deviation higher than the mean reported from a community sample in previous research using the same measure (n=1933)[60]. It is possible that levels of alexithymia have been inflated in this group due to inaccurate self-reporting of seizure type i.e. people who are experiencing NESs reporting they have ESs only. However, elevated levels of alexithymia in an ES group have been previously reported in research that did not rely on self-reporting of seizure type[40]. A medium negative correlation was found between total alexithymia score and impact of seizures for the ES group ($r=-0.38$, $p<0.001$), indicating that if they have more problems with emotion regulation, their epilepsy has a greater impact on their quality of life. One possible explanation for both these observations could be that epilepsy has an impact on the brain's ability to process emotions, so more severe epilepsy, which results in a greater impact on quality of life, also increases alexithymia. This would be consistent with previous research linking seizure control with emotion processing[71]. However, alexithymia did not correlate significantly with seizure frequency in the epilepsy group; this may indicate that at least part of the difference in impact of epilepsy scores is due to levels of alexithymia that are not the result of epilepsy but of other factors. From a psychological perspective the correlation between alexithymia and impact of epilepsy could mean that for those people who have epilepsy and have emotion processing difficulties, coping with the emotions that arise as a result of having seizures, e.g. anxiety, embarrassment, and sadness, may be more difficult, which then means the seizures have a greater impact on quality of life. Whatever the cause of elevated alexithymia levels in some people with ESs; intervention to improve emotion-processing skills could help improve their quality of life, which is consistent with research that has found psychological interventions

helpful for people with ES[41-43].

Cluster one

Cluster 1 had a mean trauma score (5.39) slightly above that reported previously for a non-clinical sample (mean 3.4, SD 3.1, n=83)[61]. This cluster seems similar in many ways to the epilepsy group. For example the mean scores on Figure 3, the correlation between seizure frequency and total childhood trauma score, and the pattern of correlations between the adult attachment and alexithymia variables in Table 6. They did differ significantly (p=0.006) on the correlation between childhood trauma and adult attachment anxiety, which was medium (0.42) for cluster 1 and virtually zero (-0.02) for the epilepsy group.

Cluster 1's mean total scores were quite similar to cluster 3. The only significant difference was childhood trauma (d=2.12, p<0.001), which was lower in cluster 1. However, there were more differences in the correlations, notably those between adult attachment anxiety, alexithymia, and childhood trauma total score, which were medium (or close to) and significant (or close to) in cluster 1 but near to zero in cluster 3. The differences between these correlations were significant except for alexithymia and childhood trauma (p=0.34, Table M.3).

Given the similarity of cluster 1 to epilepsy data and cluster 3 one possible explanation is that the aetiology is similar to cluster 3 but the childhood trauma scores are lower as they have experienced traumas not identified by the ETI-SF. The ETI-SF only asks about trauma before age 18 and therefore may miss traumas occurring in adulthood, which may to include health related traumas. However, the childhood trauma measure in cluster 1 does seem to be important as it correlates with adult

attachment anxiety, alexithymia, and seizure frequency. Perhaps in this cluster the childhood trauma was key to the development of NESs, hence its association with other characteristics, whereas in cluster 3 traumas happened within the context of already disrupted attachment relationships. This cluster appears consistent with Bodde et al.'s[3] model of NES aetiology, which suggests that psychogenic causation, such as trauma, combines with emotional 'make up', in this case alexithymia and attachment anxiety to produce NESs.

Cluster two

Cluster 2 seems distinct from the other two clusters and the epilepsy data, with mean alexithymia total score approximately 0.7 standard deviations below that reported from a community sample (n=1933)[60]. Cluster 2's adult attachment anxiety ($d=1.19$, $p<0.001$), adult attachment avoidance ($d=0.77$, $p=0.004$), and total alexithymia ($d=2.09$, $p<0.001$) scores were significantly lower than cluster 3's. Cluster 2's adult attachment avoidance and total alexithymia scores were also significantly lower than cluster 1's or the epilepsy data. This cluster had a mean trauma score (5.71) slightly above that reported in previous research for a healthy sample (3.5, SD 3.3, n=83). These scores may lead us to think that this group was similar to a non-clinical population in terms of attachment and alexithymia. As identified in the introduction, low levels of alexithymia have been associated with secure attachment styles[46]. However, this group is clearly distressed by seizures, as indicated by an impact of seizures average score higher than that of cluster 1 and significantly higher ($d=1.13$, $p<0.001$) than that of the epilepsy group.

This cluster appears consistent with clusters found in other research[22, 23], which have been described as over-controlled. Reuber et al.[22] suggested such groups could

represent people who separate themselves from their feelings to the point that they are unaware of their distress. This would be consistent with the psychodynamic theory that NESs are connected to repression of emotions. It is not consistent however, with Cassidy's theory described in the introduction that links minimisation of emotions with rejection and avoidant attachment style, as this group scored lower than the other groups on adult attachment avoidance. Perhaps, instead of becoming avoidant of attachment, this group have become indifferent to it, and do not value attachments with others, therefore having lower adult attachment anxiety and avoidance than would be expected. This idea would need to be explored with further research.

The large correlation between adult attachment avoidance and adult attachment anxiety ($d=0.51$, $p=0.02$) in cluster 2 was notable. We need to be cautious about interpretation due to the small sample size ($n=21$) and exploratory nature of the correlation analysis. A meta-analysis of the correlations between ECR attachment avoidance and anxiety reported that the dimensions were correlated, with a range of -0.22 to 0.68[72]. This was based on the longer version of the measure used in this study and the revised version (ECR-R). They also reported that older and non-university samples had higher correlations. For the ECR-SF, Wei et al. [51]reported correlations of 0.25, 0.19, and 0.28 in the validation research studies. The correlations in this study seem larger, especially for cluster 2. However, other studies using clinical samples have reported higher correlations, such as 0.97 ($n=82$, $p<0.01$) in a group with obsessive compulsive disorder symptoms[73]. This could indicate that in clinical samples adult attachment avoidance and anxiety are more likely to be correlated, perhaps due to both being associated with abuse and trauma.

Cluster three

Cluster 3 was characterised by a similar pattern of means to the epilepsy data and cluster 1; most were elevated slightly further, and the childhood trauma score was significantly elevated (2.1 standard deviations above epilepsy data). This cluster with higher adult attachment anxiety, alexithymia, and childhood trauma scores than the other groups could be consistent with the NES aetiology proposed by Quinn, Schofield, and Middleton described in the introduction. They suggested that NESs might develop due to a child experiencing trauma, in the context of attachment relationships that do not provide emotional support. Experiences of trauma and alexithymia[74, 75] are also common in those diagnosed with borderline personality disorder. A related finding in borderline personality disorder (BPD) and somatoform disorder research was that potentially traumatizing experiences, instigated by a primary care giver, were associated with alexithymia (under regulation of affect) and severity of BPD symptoms[75].

Cluster 3 also had a higher attachment avoidance (mean 18.8) than that reported in a sample of undergraduate students (15.0, SD 6.4, n=65) in the measure validation research[51]. Dijke and Ford[48] reported a similar finding of elevated adult attachment avoidance and anxiety for a subgroup of their study who were diagnosed as having somatoform disorder and borderline personality disorder.

Due to the similarities identified in the previous two paragraphs, it may be useful to explore further evidence-based therapeutic approaches for treatment of personality disorders for people in this cluster, an idea also suggested by Reuber[22]. These techniques include mentalization-based therapy; and mindfulness, and emotion regulation training, such as dialectical behavioural therapy (DBT) [76-79].

Cluster 3 showed a distinct lack of significant correlations of seizure frequency, impact of seizures, and total childhood trauma scores with the adult attachment and alexithymia variables, despite being one of the larger clusters (n=44). This may be because once a certain amount of childhood trauma has been experienced, further trauma does not increase difficulties, or perhaps as suggested above, the high levels of childhood trauma, attachment anxiety and alexithymia indicate disrupted attachment relationships, where children are not protected from experiencing traumas or supported emotionally. This attachment relationship context could be the key factor in developing NESs rather than the childhood trauma, which could be thought of as secondary.

Cluster summary

Clusters 1 and 3 have some similarities. However, it is suggested that trauma may have a pivotal role in NES development in cluster 1 whereas disrupted attachment relationships may be key in cluster 3 and trauma secondary. Cluster 2 warrants further research and its aetiology may be linked to psychodynamic theories regarding repression of emotions. Alexithymia was an issue for all groups except cluster 2.

Clinical implications

The results are consistent with previous research indicating increased mean levels of alexithymia in groups of people with ESs and subgroups with NESs. This suggests that interventions, such as DBT that have been reported to reduce alexithymia in BPD[80] and transdiagnostic[81] research could be explored in clinical research for those with ESs and/or NESs. Mindfulness, which is one aspect of DBT has been investigated in a small (n=12) pilot of NES patients and found to be feasible and warrant further

studies[82]. A randomised controlled study found that in the mindfulness treatment group compared to the social support controls, significantly more people showed clinical improvement in quality of life, they also had a significant reduction in seizure frequency, and depression and anxiety symptoms[83]. Techniques, such as DBT and mindfulness may help people to learn to express and manage difficult emotions. For people who have NESs that may be related to trauma this may be a useful starting point enabling them to go on to explore, with a therapist, their emotions surrounding their traumatic experiences. However, given the heterogeneity of the NES population, for example the existence of a subgroup with low alexithymia, it would be important to assess individual differences, to aid formulation, before recommending such treatment. The ETI-SF, TAS-20, and ECR-SF are short easily administered scales that could be useful in differentiating NES clusters and identifying people with ESs who have emotion regulation difficulties. The low number of incomplete responses to these surveys (n=1, n=1, n=4 respectively) indicated that they are acceptable to participants.

These measures could also help identify the pattern of high childhood trauma, alexithymia, and adult attachment difficulties characteristic of cluster 3. For this group, the possible impact of adult attachment issues on treatment should be considered, as this is known to affect treatment effectiveness[84]. Therapeutic approaches that incorporate attachment could be useful, such as mentalization-based therapy or cognitive analytic therapy[85-87]. People who score slightly lower on childhood trauma measures, with elevated alexithymia scores, could be consistent with cluster 1. This may indicate a presentation in which trauma is key to the development of NESs. This possibility could be explored with psychological assessment and formulation. People with this presentation may benefit from interventions to address the psychological

difficulties associated with the traumatic event(s), such as cognitive behavioural therapy (CBT) for trauma or eye movement desensitisation reprocessing (EMDR)[88, 89].

The above points emphasise the importance of assessing individual differences for both NES and ES patients. The identified measures could be used alongside psychological assessment and formulation for all NES patients and ES patients where emotion regulation and/or attachment difficulties are indicated. This would increase the likelihood of identifying appropriate treatments.

Further research

In order to explore the hypothesised differences in NES aetiology it would be useful to conduct mixed methods research, using the measures to identify people with characteristics similar to each subgroup and then explore their experiences, perhaps through formulation with a clinical psychologist, using a qualitative methodology to gain greater understanding of their NES aetiology from a psychological perspective. It would be particularly useful to explore the subgroup which has low alexithymia and attachment scores in order to investigate the possibility of repression of emotions being a factor in their NES aetiology.

It is suggested that future research relating to treatments for NESs and ESs considers the individual differences in adult attachment and alexithymia, and the possible impact on appropriate treatment. As well as different types of trauma, such as health related trauma, trauma in adulthood, and whether or not the primary care giver is involved in the trauma.

Given the exploratory nature of the data analysis in this study, researchers may like to use the findings to formulate hypotheses that can be tested. For example, by collecting a sample of data and clustering it based on alexithymia and childhood trauma

scores to assess if the same pattern of means is reproduced.

Strengths and weaknesses

A potential weakness of this research is the use of self-reporting of seizure type, and self-report measures. Self-report measures have been widely used in previous studies relating to ESs and NESs, but no other published studies appear to have relied on self-reporting of seizure type. Scrag, Brown, and Trimble[90] found that people who experience medically unexplained symptoms were less accurate in their reporting of their past diagnoses than others. This could be a reason for some of the outliers in the data. From a clinical perspective, related to a desire for medical explanations, it seems the most likely that ESs would be reported when in fact the person has NESs. Therefore the group most likely to be affected would be the ES group and it is unlikely this issue has affected the NES data. While the use of self-reporting may have introduced some inaccuracy, the similarities of findings in this research to previous data, e.g. the association of trauma, higher seizure frequency, and poorer quality of life with NES, supports that this is a viable way to collect data for this population. The use of self-reporting allowed the deployment of online recruitment. This had advantages in terms of access to a relatively large worldwide sample and ease and efficiency of data collection for both participants and researchers. A disadvantage was that the sample was biased towards a greater proportion of females, which could have implications for generalisability.

The sampling procedures were convenience/snowballing, most of the data analysis was exploratory, and the sample consisted of mostly British and American people. The necessary ability to understand the questions is likely to have excluded some people with intellectual disabilities. Therefore, a high degree of caution is

indicated in applying these results to other populations, especially to males, and people with intellectual disabilities.

This research uses the epilepsy group as reference group, for example when displaying means in Figure 2 and for calculation of effect sizes. The epilepsy group, however, is not truly a control group, as, due to the effects of ESs on the brain discussed above, they are not representative of the general population. Due to relevant scale norms not being available for all the measures, future research may wish to consider recruiting a control group, representative of the general population, in order to estimate effect sizes when comparing to a non-clinical population.

Conclusion

Comparison with previous research indicates that alexithymia (emotion processing) was a difficulty for many people in the sample; this suggests that further research, regarding activities aimed at reducing alexithymia would be useful. It will be important to assess individuals, both in research and clinical treatment, as cluster analysis indicates NES subgroups differ on childhood trauma, alexithymia, and adult attachment and one NES subgroup had lower alexithymia scores than was previously reported in a community sample[60]. The measures used in this research could be useful, and acceptable, to use alongside psychological formulation in clinical and research settings. In clinical settings, it is suggested that psychological formulation will be useful for those with NESs and those with ESs who have elevated alexithymia and/or adult attachment scores. This will help consider the individual differences and identify appropriate diagnosis, treatments, and support. Further clinical research is recommended to explore the effectiveness of treatments, such as DBT, for people with ESs or NESs who have elevated alexithymia. For those with elevated attachment anxiety

and/or avoidance, alexithymia and childhood trauma scores (cluster 3), especially if psychological formulation indicates that attachment relationships may be key to the development of NESs, it may be useful to explore therapies with an attachment focus, such as mentalization based therapy and cognitive analytical therapy. For those people with lower childhood trauma scores who are experiencing alexithymia difficulties (cluster 2), especially if psychological formulation indicates trauma is key to the development of NESs, therapy specifically addressing the trauma, such as CBT or EMDR may be useful to investigate.

This research alongside further academic and clinical research could lead to the development of therapeutic pathways appropriate for subgroups of people who experience NESs and ESs taking into account their individual differences.

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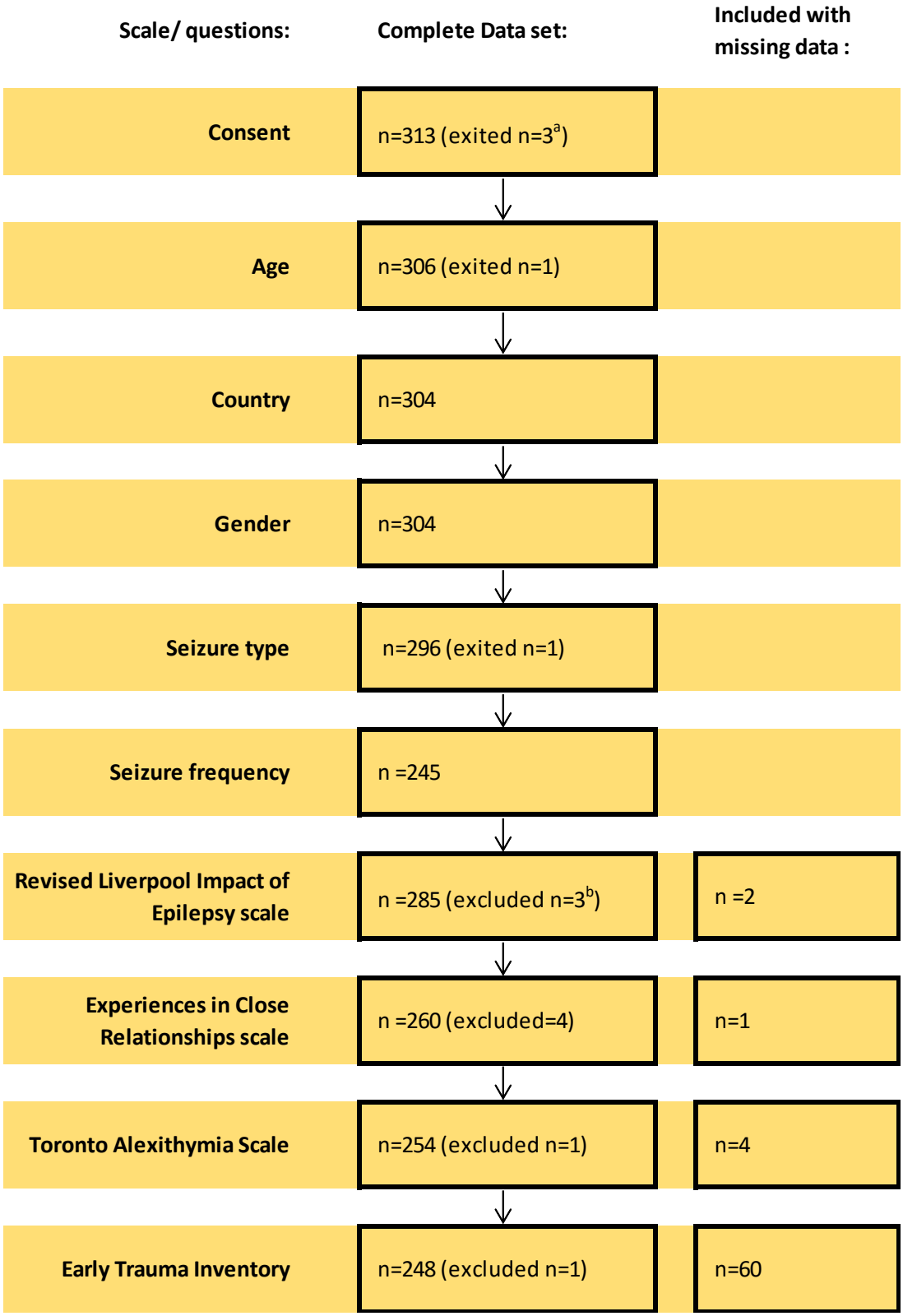

[a]Exited by survey logic; [b]Excluded due to missing data

Figure 1. Numbers of participants; providing a full data set for each question or scale, exited or excluded, and included with missing data

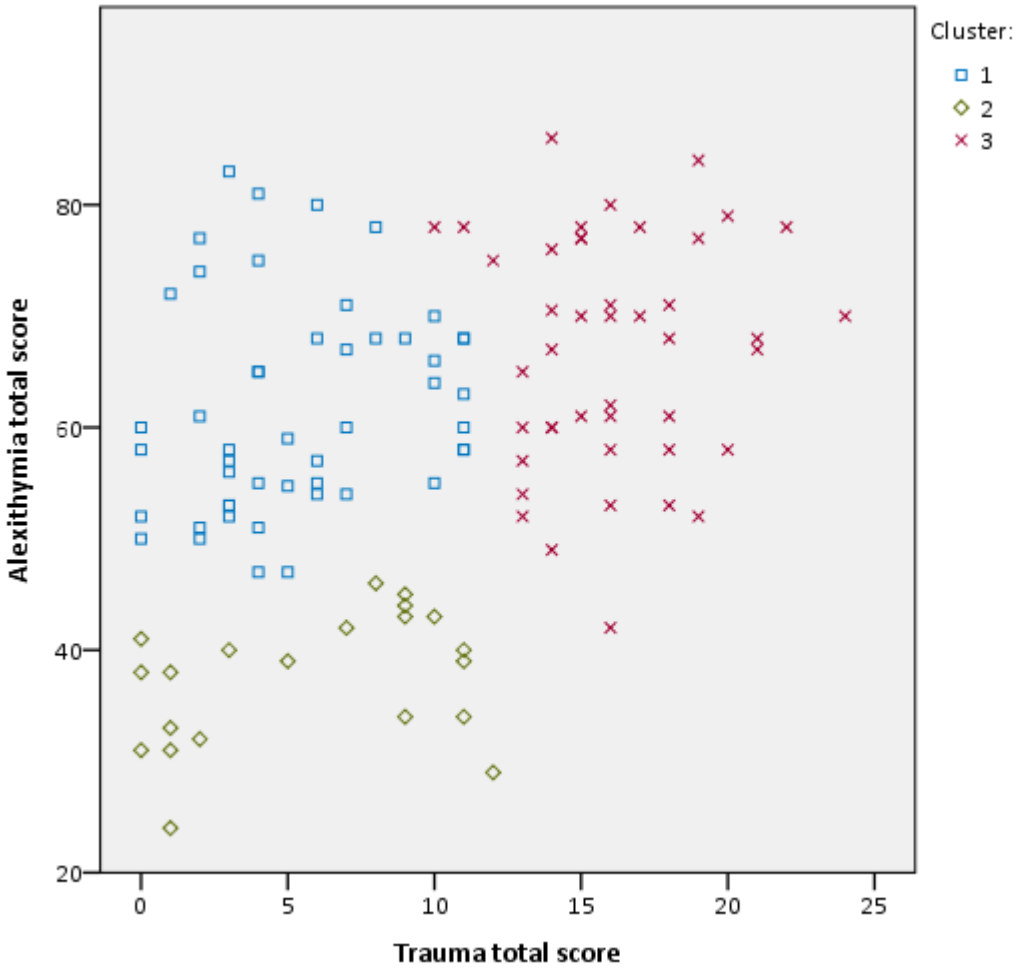

Figure 2. Illustration of NES clusters

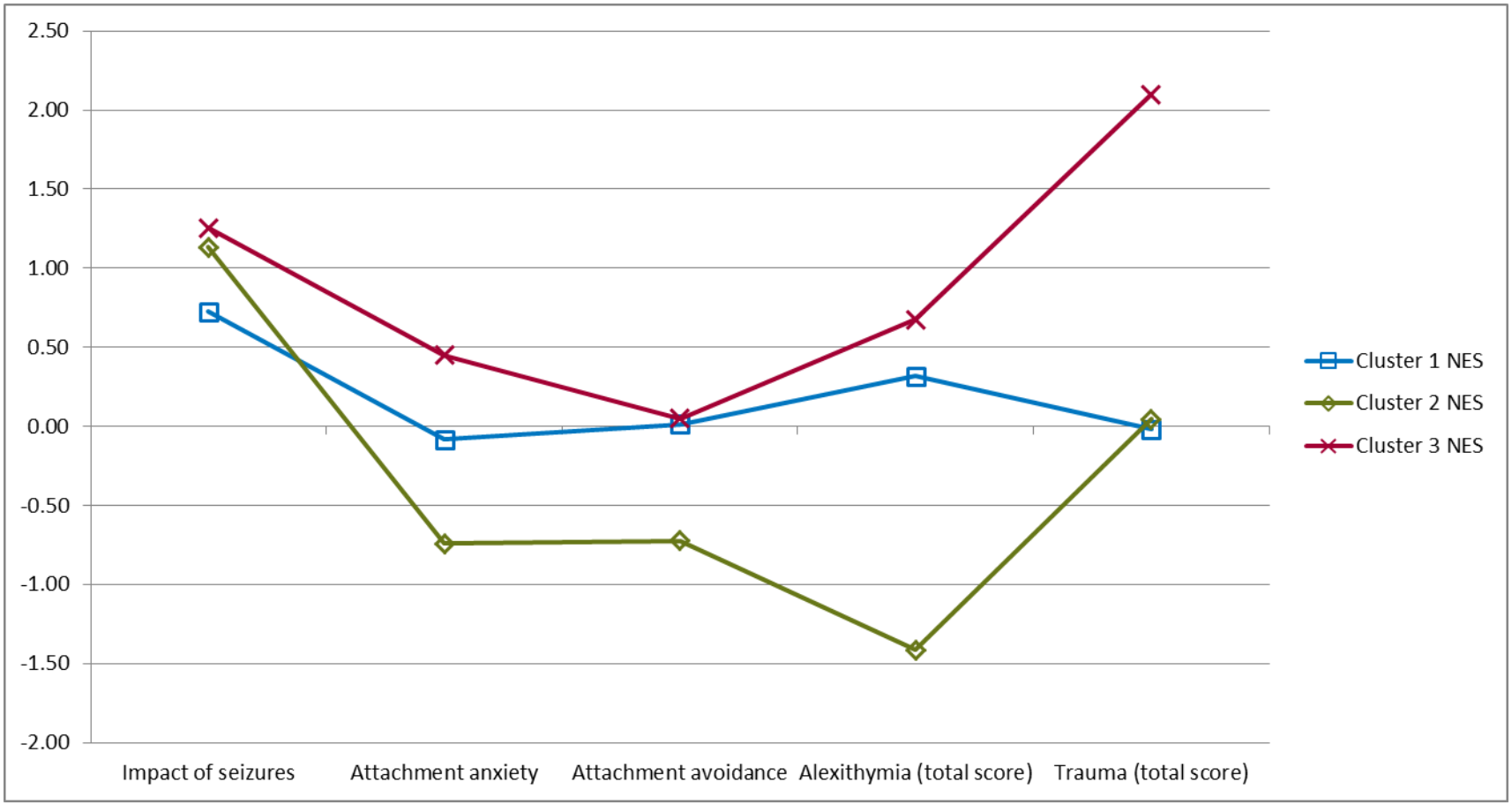

Figure 3. Chart illustrating means for each NES cluster expressed in standard deviations of difference from epilepsy data means

Tables

Table 1. Numbers of participants reporting ES only, NES only, or ES+NES within each category

	Gender*:		**Country:**			**Seizure occurrence***:**		
Group	**Male**	**Female**	**UK and NI**	**USA**	**Other**	**In the last year**	**Over a year ago**	**Not sure**
ES only (n=119)	19 (16.0%)	100 (84.0%)	104 (87.4%)	10 (8.4%)	5 (4.2%)	86 (72.3%)	33 (27.7%)	
NES only (n=131)	8 (6.1%)	123 (93.9%)	94 (71.8%)	28 (21.4%)	9 (6.8%)	122 (93.1%)	9 (6.9%)	
ES+NES (n=28)[a]	5 (17.9%)	23 (82.1%)	22 (78.6%)	5 (17.9%)	1 (3.6%)	24 (85.7%)	3 (10.7%)	1 (3.6%)

* Differences between the three groups significant at $p<0.05$; ** significant at $p<0.01$; *** significant at $p<0.001$.

Table 2. Descriptive statistics for each seizure type group in the study

	Demographics:		**Childhood trauma:**	**Adult attachment:**		**Alexithymia:**	**Seizures:**	**Impact of seizures:**
	Age in years**		Total score***	Attachment anxiety	Attachment avoidance	Total score	Seizure frequency*	Total score***
ES only	32.43 (10.68)[a]	n=119[b]	5.48 (5.06)	22.57 (6.82)	18.35 (8.19)	57.31(13.14)	15.21(77.53) n=86	-8.69 (6.04)
NES only	36.85 (11.01)	n=131	9.78 (6.35)	22.37 (8.23)	17.43 (7.26)	58.79 (14.43)	41.05(76.18)	-14.58(6.42)
ES + NES	38.04 (12.77)	n=28	12.57 (7.02)	23.46 (5.44)	20.67 (7.23)	61.36 (14.02)	20.88 (24.37)	-11.11(9.16)

[a] Values given are sample mean (sample standard deviation); [b] n varied slightly due to missing data, where there was a large variation from the stated n this is reported next to the data; * Differences between the three group means significant at $p<0.05$, ** differences significant at $p<0.01$; *** significant at $p<0.001$.

Table 3. Numbers of participants in each cluster within each category

	Gender*:		**Country:**			**Seizure occurrence:**	
Group	**Male**	**Female**	**UK and NI**	**USA**	**Other**	**In the last year**	**Over a year ago**
NES cluster 1 (n=49)	7(14.3%)	42(85.7%)	40(81.6%)	5(10.2%)	4(8.2%)	44(89.8%)	5(10.2%)
NES cluster 2 (n=21)	0	21(100%)	14(66.7)	7(33.3%)		21(100%)	
NES cluster 3 (n=44)	1(2.3%)	43(97.7%)	30(68.2%)	13(29.5%)	1(2.3%)	41(93.2%)	3(6.8%)

* Differences between the three groups significant at $p<0.05$;

Table 4. Descriptive statistics for each NES cluster, and the ES group

	Demographics:		**Childhood trauma:**	**Adult attachment:**		**Alexithymia:**	**Seizures:**		**Impact of seizures:**
	Age in years**		Total score***	Attachment anxiety**	Attachment avoidance**	Total score***	Seizure frequency		Total score***
Cluster 1	35.63(11.48)[a]	n=49[b]	5.39 (3.41)	22.00(8.32)	18.47(7.65)	61.77(9.41)	33.28(64.14)		-13.06(7.22)
Cluster 2	39.38 (10.51)	n=21	5.71 (4.47)	17.52(6.93)	12.43(6.49)	37.43(5.90)	63.43(79.31)		-15.52(5.14)
Cluster 3	38.25 (10.46)	n=44	16.09(2.99)	25.64(7.60)	18.77(6.56)	66.81(10.43)	39.29(93.43)		-16.26(5.93)
Epilepsy only (0)	32.45 (10.68)	n=119	5.48 (5.06)	22.57 (6.82)	18.35 (8.19)	57.31(13.14)	15.21(77.53)	n=86	-8.69 (6.04)

[a]Data displayed, sample mean (sample standard deviation); [b]n varied slightly due to missing data, where there was a large variation from the stated n this is reported next to the data; *differences between the group means significant at $p<0.05$, **significant at $p<0.01$; *** significant at $p<0.001$.

Table 5. Effect sizes and confidence intervals of post hoc tests comparing means of the NES clusters, and the ES group

Age in years			
	Cluster 2	Cluster 3	Epilepsy
Cluster 1	0.35 (-1.06, 0.36)[a]	0.24 (-0.80, 0.31)	0.30 (-0.17, 0.77)
Cluster 2		0.11 (-0.59, 0.80)	0.65 (0.01, 1.29)
Cluster 3			0.54 (0.09, 1.00)*
Childhood trauma total score			
	Cluster 2	Cluster 3	Epilepsy
Cluster 1	0.06 (-0.65, 0.52)	2.12 (2.46, 1.77)***	0.02 (-0.38, 0.34)
Cluster 2		2.05 (2.63, 1.47)***	0.05 (-0.54, 0.64)
Cluster 3			2.10 (1.75, 2.45)***
Attachment anxiety			
	Cluster 2	Cluster 3	Epilepsy
Cluster 1	0.66 (-0.10, 1.41)	0.53 (-1.17, 0.10)	0.08 (-0.61, 0.44)
Cluster 2		1.19 (1.93, 0.45)***	0.74 (1.40, 0.08)*
Cluster 3			0.45 (-0.06, 0.96)
Attachment avoidance			
	Cluster 2	Cluster 3	Epilepsy
Cluster 1	0.74 (0.15, 1.32)*	0.04 (-0.51, 0.43)	0.01 (-0.42, 0.45)
Cluster 2		0.77 (1.34, 0.21)**	0.72 (1.26, 0.19)**
Cluster 3			0.05 (-0.35, 0.46)
Alexithymia total score			
	Cluster 2	Cluster 3	Epilepsy
Cluster 1	1.73 (1.38, 2.08)***	0.36 (-0.74, 0.03)	0.32 (-0.03, 0.66)
Cluster 2		2.09 (2.47, 1.71)***	1.41 (1.75, 1.07)***
Cluster 3			0.67 (0.30, 1.05)***
Impact of seizures			
	Cluster 2	Cluster 3	Epilepsy
Cluster 1	0.41 (-0.26, 1.08)	0.53 (-0.07, 1.12)	0.72 (1.23, 0.22)***
Cluster 2		0.12 (-0.52, 0.76)	1.13 (1.70, 0.57)***
Cluster 3			1.25 (1.72, 0.79)***

[a]Data given for all entries is Cohen's d effect size based on standard deviation of epilepsy only data (95% confidence interval).

Table 6. Correlations of childhood trauma, adult attachment, impact of seizures and seizure frequency in each NES cluster and the ES group

		Alexithymia total score	Childhood trauma total score	Adult attachment anxiety	Adult attachment avoidance	Impact of seizures
Childhood trauma total score	Cluster 1	0.26 (-0.02, 0.50)[a]				
	Cluster 2	0.28 (-0.24, 0.74)				
	Cluster 3	0.07 (-0.20, 0.36)				
	Epilepsy	0.11 (-0.08, 0.29)				
Adult attachment anxiety	Cluster 1	0.40 (0.13, 0.62)**	0.42 (0.18, 0.61)**			
	Cluster 2	0.36 (-0.06, 0.70)	0.22 (-0.29, 0.66)			
	Cluster 3	-0.06 (-0.38, 0.30)	0.02 (-0.27, 0.30)			
	Epilepsy	0.28 (0.10, 0.43)**	-0.02 (-0.24, 0.17)			
Adult attachment avoidance	Cluster 1	0.38 (0.15, 0.57)**	-0.10 (-0.40, 0.24)	0.37 (0.11, 0.60)**		
	Cluster 2	0.30 (-0.11, 0.68)	-0.19 (-0.62, 0.31)	0.51 (0.11, 0.79)*		
	Cluster 3	0.28 (-0.01, 0.55)	-0.16 (-0.46, 0.18)	0.30 (0.03, 0.53)*		
	Epilepsy	0.34(0.16, 0.51)***	0.10 (-0.09, 0.31)	0.25 (0.07, 0.42)**		
Impact of seizures	Cluster 1	-0.13 (-0.37, 0.18)	-0.29 (-0.54, 0.02)*	-0.16 (-0.42, 0.14)	-0.12 (-0.40, 0.19)	
	Cluster 2	0.00 (-0.48, 0.41)	0.59 (0.17, 0.8.)**	-0.30 (-0.63, 0.09)	-0.40 (-0.76, 0.11)	
	Cluster 3	-0.03 (-0.35, 0.33)	-0.21 (-0.50, 0.07)	0.13 (-0.24, 0.49)	-0.06 (-0.38, 0.28)	
	Epilepsy	-0.38(-0.55, -0.16)***	-0.02 (-0.20, 0.16)	-0.28 (-0.48, -0.07)**	-0.19 (-0.34, -0.03)	
Seizure frequency	Cluster 1	0.03 (-0.28, 0.37)	0.32 (-0.01, 0.58)*	0.05 (-0.26, 0.37)	-0.13 (-0.45, 0.22)	-0.45 (-0.69, -0.11)**
	Cluster 2	-0.05 (-0.45, 0.39)	0.27 (-0.28, 0.66)	-0.22 (-0.65, 0.22)	-0.24 (-0.65, 0.28)	-0.07 (-0.54, 0.40)
	Cluster 3	-0.06 (-0.38, 0.25)	0.04 (-0.29, 0.37)	-0.15 (-0.43, 0.14)	-0.03 (-0.31, 0.24)	-0.19 (-0.51, 0.16)
	Epilepsy	0.17 (-0.05, 0.37)	0.23 (-0.02, 0.45)*	-0.07 (-0.28, 0.13)	0.05 (-0.18, 0.27)	-0.36 (-0.55, -0.15)**

[a]Data given for each item are: Spearman's rho (bootstrap BCa 95% confidence interval); * Correlation significant at p<0.05; ** significant at p<0.01; *** significant at p<0.001.

Appendix A

Journal guidance

Epilepsia

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 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 with- out 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 con- trol 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 the research 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 maybe 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 its principles (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). A completed checklist should be submitted with their protocols as a supporting document. 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/
PRIMSA – 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 substantively 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 upload- ing 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 consult with the Editors-in-Chief before submitting the 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 4000 words and no longer than 6000 words, with no more than 5 to 7 figures/tables (combined). Longer manuscripts will be considered at the discretion of the Editors-in-Chief.

b. Full-length original research articles. These articles should be limited in length to 4000 words and no more than 6 figures and tables. Additional figures and tables 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 1500 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 (unless more are approved by the Editors-in-Chief prior to manuscript acceptance), 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.

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).

(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 submit- ted 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 will be 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://authorservices.wiley.com/bauthor/english_language.asp. 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 s 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 12 fonts. 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 covering letter explaining why the additional length is necessary.

Authors are encouraged to use the most recent terminology of seizure 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.

  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 figures; number of tables.

❑ Summary and Key Words

Provide a summary of no more than 300 words (200 words for Brief Communications). The summary of Full-Length Original Research reports should consist of four 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.

❑ 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 review 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 within 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 analy- ses 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 deci–mal 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. 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 Vancouver style 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 the journals' names being written out in full).

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

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
Faure JB, Akimana G, Carneiro JE, et al. A comprehensive behavioral evaluation in the lithium-pilocarpine model in rats: Effects of carisbamate administration during status epilepticus. *Epilepsia* Epub 2013 May 11.

Journal article In Press
Battino D, Tomson T, Bonizzoni E,et. al. Seizure control and treatment changes in pregnancy: Observations from the EURAP epilepsy pregnancy registry. *Epilepsia* (in press 2013)

Letter
Marucci, G. Commentary on the new ILAE classification system for focal cortical dysplasias. *Epilepsia* 2012; 1:219–220. Letter

Published Abstract
Noe, K, Drazkowski, J. Safety of Long-Term Video EEG Monitoring. *Epilepsia* 2008; 59 (Suppl. 7):1.125. Abstract

Book
Shorvon, S. Handbook of the treatment of epilepsy. Oxford: Blackwell Publishing; 2005

Chapter in a Book
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Online
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❑ **Figure legends**

Number each legend sequentially to conform to the figure number (e.g., Figure1, 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

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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 for half column and 6 to 7 inches 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. Scale bars should be applied to photomicrographs of histology and relevant figures. Label figures using Calibri font and be sure that all labels are large enough to be clearly legible. The maximum size of any figure is 17 × 22.5 cm and 40 megapixels; 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	CMYK Definition	RGB Definition
Yellow	0/11/65/0	255/222/117
Orange	0/58/100/8	227/124/29
Red	0/100/60/37	163/1/52
Green	27/0/95/55	103/119/24
Green-blue	100/0/28/65	0/83/94
Blue	100/46/0/0	0/118/192

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c. Gray Matters

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  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 otherwise 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, 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.

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All manuscripts should be submitted with a cover letter, addressed to the Editors-in-Chief, which explains why the manuscript should be published in *Epilepsia*. In particular, authors should identify novel findings, innovative approaches, and important insights that would make the manuscript of particular value to the broad readership of *Epilepsia*.

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Most supplements require external sponsorship. When a supplement proposal is presented to the Editors-in-Chief, they will fix appropriate fees. Supplement costs may be negotiated with the Editors-in-Chief and the publisher's supplement representative. The Editors-in-Chief may choose to publish a supplement of particular academic and clinical value without external sponsorship.

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(Continued on next page)

Epilepsia's POSITION ON ISSUES INVOLVED IN ETHICAL PUBLICATION (CONT.)

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The authors should include within the manuscript an explicit statement indicating that the submitted study was approved by the relevant research ethics committee or institutional review board (IRB).When the study involves human participants (including material from human subjects), authors should also provide assurance that appropriate consent was obtained. When studies involve animal subjects, authors should provide methodological details about steps taken to minimize pain/discomfort. Such papers must contain a statement that affirms that the experimental protocols were approved by the institutional animal care and use committee (IACUC).

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Authors are expected to proof-read their articles carefully before returning page proofs for publication. They should make needed corrections at this time. We recognize that it is only human to err occasionally, and the Journal is committed to correcting mistakes when those errors affect the interpretation of data or information presented in an article.

(Continued on next page)

Epilepsia's POSITION ON ISSUES INVOLVED IN ETHICAL PUBLICATION (CONT.)

Such corrections will be published in the form of an Erratum, and linked to the original article electronically. Errors that result from author oversight in the proofing process, and that do not affect data interpretation, will not be corrected.

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[redacted]

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Appendix B. Questions and Measures

Early life events, individual differences, and seizures

Survey Questions

How old are you? [ ] years

What Country do you live in? [ ]

What gender are you? (Please circle one)

male female transgender other gender prefer not to say

Have you experienced seizures, attacks, or fits?

yes, in the last year | yes, over a year ago | never | not sure

IF yes, approximately how often do you experience these seizures, attacks, or fits? Enter the approximate number of times per month in the box: [ ]

Do you have a diagnosis of **epilepsy**? If your doctor has told you your seizures are **epileptic** answer yes, see information sheet for further information.

yes no not sure

Do you have **non-epileptic** seizures? Non-epileptic seizures may be called PNES, functional seizures, non-epileptic attack disorder (NEAD) or conversion disorder. See information sheet for further information.

yes no not sure

If you are unsure if you have epilepsy or non-epileptic seizures, write in the box below any names your seizures, fits, or attacks have been given:

[ ]

[redacted]

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Revised Liverpool Impact of Epilepsy Scale

We would like to know how much you feel the attacks you have had affect your everyday life. For each item listed, please ring the number which shows <u>best</u> how you feel.

Thinking about the attacks you have had,
do you feel they have affected for better or worse :

	Very much for the better	Somewhat for the better	No difference	Somewhat for the worse	Very much for the worse	Does not apply
a) Your relationship with your spouse/partner?	1	2	3	4	5	6
b) Your relationship with other close member of your family	1	2	3	4	5	6
c) Your social life and social activities?	1	2	3	4	5	6
d) Whether or not you are able to work in paid employment?	1	2	3	4	5	6
e) The kind of paid work you can do?	1	2	3	4	5	6
f) Your health overall?	1	2	3	4	5	6
g) Your relationships with friends?	1	2	3	4	5	6
h) The way you feel about yourself?	1	2	3	4	5	6
i) Your plans and ambitions for the future?	1	2	3	4	5	6
j) Your standard of living?	1	2	3	4	5	6
k) Whether or not you are able to drive?	1	2	3	4	5	6
l) The level of your independence	1	2	3	4	5	6

[redacted]

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Experiences in Close Relationship Scale-Short Form (ECR-S)

Instruction: The following statements concern how you feel in romantic relationships. We are interested in how you generally experience relationships, not just in what is happening in a current relationship. Respond to each statement by indicating how much you agree or disagree with it. Mark your answer using the following rating scale:

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Slightly Disagree	Neutral	Slightly Agree	Agree	Strongly Agree

1.	My desire to be very close sometimes scares people away.	
2.	I do not often worry about being abandoned.	
3.	I am nervous when partners get too close to me.	
4.	I want to get close to my partner, but I keep pulling back.	
5.	It helps to turn to my romantic partner in times of need.	
6.	I usually discuss my problems and concerns with my partner.	
7.	I find that my partner(s) don't want to get as close as I would like.	
8.	I worry that romantic partners won't care about me as much as I care about them.	
9.	I need a lot of reassurance that I am loved by my partner.	
10.	I turn to my partner for many things, including comfort and reassurance.	
11.	I try to avoid getting too close to my partner.	
12.	I get frustrated if romantic partners are not available when I need them.	

Wei, M., Russell, D. W., Mallinckrodt, B., & Vogel, D. L. (2007). The experiences in Close Relationship Scale (ECR)-Short Form: Reliability, validity, and factor structure. *Journal of Personality Assessment, 88,* 187-204.

[redacted]

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According to the wishes of the author, the Toronto Alexithymia Scale is not reproduced here, however a small sample of questions are included as examples.

Using the scale provided as a guide, indicate how much you agree or disagree with each of the following statements by circling the corresponding number. Give only one answer for each statement.

Circle 1 if you STRONGLY DISAGREE
Circle 2 if you MODERATELY DISAGREE
Circle 3 if you NEITHER DISAGREE NOR AGREE
Circle 4 if you MODERATELY AGREE
Circle 5 if you STRONGLY AGREE

	Strongly Disagree	Moderately Disagree	Neither Agree nor Disagree	Moderately Agree	Strongly Agree
1. I am often confused about what emotion I am feeling.	1	2	3	4	5
2. It is difficult for me to find the right words for my feelings.	1	2	3	4	5
12. People tell me to describe my feelings More.	1	2	3	4	5

[redacted]

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This questionnaire asks about childhood trauma, including sexual abuse. If you find this distressing, please feel free to leave out some or all of these questions.

Early Trauma Inventory Self Report-Short Form (ETISR-SF)

J. Douglas Bremner, Emory University School of Medicine, Atlanta GA

Part 1. General Traumas. Before the age of 18

1. Were you ever exposed to a life-threatening natural disaster?	YES	NO
2. Were you involved in a serious accident?	YES	NO
3. Did you ever suffer a serious personal injury or illness?	YES	NO
4. Did you ever experience the death or serious illness of a parent or a primary caretaker?	YES	NO
5. Did you experience the divorce or separation of your parents?	YES	NO
6. Did you experience the death or serious injury of a sibling?	YES	NO
7. Did you ever experience the death or serious injury of a friend?	YES	NO
8. Did you ever witness violence towards others, including family members?	YES	NO
9. Did anyone in your family ever suffer from mental or psychiatric illness or have a "breakdown"?	YES	NO
10. Did your parents or primary caretaker have a problem with alcoholism or drug abuse?	YES	NO
11. Did you ever see someone murdered?	YES	NO

Part 2.Physical Punishment.Before the age of 18

1. Were you ever slapped in the face with an open hand?	YES	NO
2. Were you ever burned with hot water, a cigarette or something else?	YES	NO
3. Were you ever punched or kicked?	YES	NO
4. Were you ever hit with an object that was thrown at you?	YES	NO
5. Were you ever pushed or shoved?	YES	NO

Part 3.Emotional Abuse.Before the age of 18

1. Were you often put down or ridiculed?	YES	NO
2. Were you often ignored or made to feel that you didn't count?	YES	NO
3. Were you often told you were no good?	YES	NO
4. Most of the time were you treated in a cold, uncaring way or made to feel like you were not loved?	YES	NO
5. Did your parents or caretakers often fail to understand you or your needs?	YES	NO

Continued on the next page

[redacted]

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Part 4.Sexual Events. Before the age of 18

1. Were you ever touched in an intimate or private part of your body (e.g. breast, thighs, genitals) in a way that surprised you or made you feel uncomfortable? ..... YES NO
2. Did you ever experience someone rubbing their genitals against you?..... YES NO
3. Were you ever forced or coerced to touch another person in an intimate or private part of their body? ..... YES NO
4. Did anyone ever have genital sex with you against your will? ..... YES NO
5. Were you ever forced or coerced to perform oral sex on someone against your will?..... YES NO
6. Were you ever forced or coerced to kiss someone in a sexual rather than an affectionate way? ..... YES NO

If you responded "YES" for any of the above events, answer the following for the one that has had the greatest impact on your life. In answering consider how you felt at the time of the event.

1. Did you experience emotions of intense fear, horror or helplessness?..... YES NO
2. Did you feel out-of-your-body or as if you were in a dream? ..... YES No

Appendix C

Table C.1. List of organisations and sectors the study was promoted through

Contact Organisation	Sector
[redacted]	NHS
[redacted]	Facebook group
[redacted]	Facebook page
[redacted]	Facebook page
[redacted]	Facebook page
[redacted]	Facebook page
[redacted]	Charity
[redacted]	Facebook group
[redacted]	Facebook page
[redacted]	Facebook group
[redacted]	Facebook forum
[redacted]	Facebook group
[redacted]	NHS
[redacted]	NHS

[redacted]

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Appendix D

Participant information Sheet

Relationships between early life events, individual differences, and seizures

Who are the researchers?

The main researcher is Liz Tallentire. She is training to be a clinical psychologist. This study is part of her doctoral thesis at Lancaster University.

Two people are supervising this study:

- Dr Ian Fletcher, Senior Lecturer, Lancaster University, and
- Dr Jayne Martlew, Consultant Clinical Neuropsychologist at the Walton Centre, Liverpool.

What is the study about?

This study is investigating the relationship between early life events, individual differences, and seizures. It will consider seizure type, seizure frequency, and impact of seizures. The researchers hope this will increase understanding of the relationship between what happens to people in their early lives, the way they process emotions, how they relate to others, and their seizure experiences. In future, this may help professionals to identify people who are more likely to have different types of seizures.

Why have I been approached?

You may be someone who experiences epileptic or non-epileptic seizures, or both. Seizures are also called fits, convulsions, or attacks. They may be given a name other than epileptic or non-epileptic, for example, epilepsy, NEAD, conversion disorder, or functional seizures. If you are unsure, please see the list below for full details of names of seizures that are relevant

[redacted]

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to this study.

Do I have to take part?

NO. You do not have to take part. This survey is not related to your health care. There will be no consequences if you choose not to take part.

Who can take part?

To take part you must:

- Experience epileptic and/or non-epileptic seizures (see list below if unsure)
- Be over 18 years old
- Be able to understand the questions in English

How do I take part?

There are two ways to take part:

1. Complete the survey online
2. Complete the survey on paper and send it using the freepost address

Instructions for each way of taking part are below:

1. If you would like to take part online go to http://tinyurl.com/SeiRes15

   Or scan the QR code on the right, using your mobile phone
2. If you would like to complete the study on paper and do not already have a pack:
   a. If you have seen the study advertised in a health clinic they may have packs available
   b. If a member of your care team provided you with information about the study they may be able to give you a pack

Can I think about it?

Yes, please take some time to think about this. The planned close date for the study is **16th March 2015**

If I have any questions about the survey who do I contact?

You can contact Liz in any of the following ways

Email her at l.tallentire@lancaster.ac.uk

Write to her at:

Liz Tallentire, DClinPsy,
Furness Building,
Lancaster University
LA1 4YG

Phone the research mobile

07508 375 657 (UK)

0044 7508 375 657 (international)

What if I need help to take part

You can have someone help you to take part, but the answers must be your own. So for example, it is **OK** for someone to read the questions out to you, and you tell them what to put. You need to be able to understand the questions in English; it is **not OK** to translate questions, as this could affect the results.

What will taking part involve?

You will be asked to answer some basic questions about yourself e.g. age, how often you have seizures and the country you live in. Then you will be asked to complete some questionnaires about how your seizures affect your life, how you relate to other people, how you manage feelings, and your childhood experiences.

This may take 10 to 15 minutes.

Will my data be confidential?

[redacted]

During the survey, the researchers will not ask you for any identifying information. Therefore, your data will be anonymous to the researchers; they will not know who sent it. You have the option of providing an email or postal address to receive a summary of the study results. If you choose to do this, the researchers will not link your email or postal address to your questionnaire data.

How will my data be stored?

All data will be stored electronically using password protection on the Lancaster University Secure file store. The researchers will delete email and postal address lists once they have sent information about the results of the study. Lancaster University will store securely anonymous survey data for 10 years following the end of the study.

What will happen to the results?

After Liz has used the results in her thesis, the researchers may also use them to write an article in a journal. Liz will do a presentation about the study to her colleagues at the university. She may also do other presentations, for example, at conferences. It will not be possible to identify you in the results.

Are there any risks?

It is possible that asking you about your experiences will remind you of difficult feelings or times in your life. If you think you will find the questions distressing, please do not participate. If you find that you become distressed when filling in the questionnaires please stop. In the pack, there will be information on sources of support.

Can I change my mind?

Yes, up to the point when you send information to the researchers. At the end of each page on the electronic form, or when you post paper questionnaires, you are sending information.

[redacted]

It will not be possible to remove information you have already sent, because the information is anonymous, so the researchers will not know which your information is.

You can stop completing the questions at any point.

Do I have to answer all the questions?

You may miss out questions, for example if you find them too distressing or you do not understand them.

Are there any benefits to taking part?

There is no direct benefit to taking part. However, you will be contributing to research that may help develop understanding and treatments for people who experience seizures.

Who has approved this study?

An NHS Research Ethics Committee has approved this study.

What if I have a complaint

If you have a complaint about this study, you would like to discuss informally, please contact Dr Jane Simpson, Research Director at Lancaster University.

You can contact Jane in any of the following ways

Email her at j.simpson2@lancaster.ac.uk

Write to her at:

Dr Jane Simpson
Furness Building
Lancaster University
LA1 4YG

Phone Jane on 0044 1524 592 858

[redacted]

If you would like to make a formal complaint, please contact:

Professor Roger Pickup by email r.pickup@lancaster.ac.uk

or by post

Prof R Pickup
Biomedical Sciences
Lancaster University
LA1 4YG

[redacted]

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List of possible names for seizure types relevant to this study.

You only need to read this list if you are unsure whether your seizure type is relevant to this study.

In any of these names, the term seizure may be replaced with fit, attack, or convulsion. Please note that sometimes these terms may be used in relation to either epileptic or non-epileptic seizures. The use of one of these terms does not imply that your seizures are definitely of the associated type. Some of the terms are outdated, they are included here for reference, and not because the researchers think they are appropriate to use.

Terms usually associated with epileptic seizures	**Terms usually associated with non-epileptic seizures**
Epilepsy Complex partial seizure Partial seizure Generalized seizure Grand-mal Petit mal Myoclonicseizure Tonic seizure Tonic-clonic seizure Focal seizures Absence seizures	Psychogenic seizures Pseudoepileptic seizures Pseudo seizures Functional seizures Stress-related seizures Hysterical seizures Somatoform/ somatic seizures Dissociative seizures Non-organic seizures Hysterical seizures Psychophysiological seizures Non-epileptic attack disorder (NEAD) PNES Conversion disorder (with seizures)

Appendix E

Table E.1. Summary of participants with missing data and actions taken

Scale or sub-scale	Max number of missing items allowed	No of participants who viewed the scale who were excluded	No of cases with missing data that were scored	How missing data was treated
Revised Liverpool Impact of epilepsy scale	6	3	2	Item scored 0
Experiences in Close Relationships Anxiety	1	4	1	Replaced with mean of completed items
Experiences in Close Relationships avoidance	1	4	0	
Toronto Alexithymia Scale total score	3	1	4	Replaced with mean of completed items
Toronto Alexithymia Scale difficulty identifying feeling	1	2	2	Replaced with mean of completed items
Toronto Alexithymia Scale difficulty describing feelings	1	1	1	Replaced with mean of completed items
Toronto Alexithymia Scale externally-oriented thinking	1	1	3	Replaced with mean of completed items
Early Trauma Inventory total score	4	1	60	Item scored as 0
Early Trauma Inventory general trauma	1	1	0	
Early Trauma Inventory physical punishment	1	1	0	
Early Trauma Inventory emotional abuse	1	1	0	
Early Trauma Inventory sexual events	1	1	2	Item scored as 0
Early Trauma Inventory dissociation	0	98	0	

Appendix F. Details of statistical tests and analyses

Exploratory data analysis

Group means were compared using ANOVA, Kruskal-Wallis, Welch, and Brown-Forsythe. Levene's test was used to check for homogeneity of variance. Post hoc tests used Games-Howell. EDA established that seizure frequency and trauma subscale scores were not normally distributed.

Frequencies were compared using Pearson chi-square tests. Results associated with expected cell counts less than 5 in more than 20% cells, or less than 1 in any cell were checked with Fisher's Exact tests.

Where the assumption of normality was broken for ANOVA i.e. for childhood trauma and seizure frequency data, Asymptotic K-Sample Fisher-Pitman permutation tests were used via the COIN package in R [91]. Post hoc tests used the same test with code adapted from Mangiafico's[92] to assess each possible comparison.

Cluster analysis

Ward's method is sensitive to outliers[93] therefore these were removed by examining the dendrogram produced using nearest neighbour cluster analysis. Ward's method proceeds by combining the two clusters that have the smallest sum of the squares of error within clusters. In order to determine the number of clusters in the solution the agglomeration schedule was examined for sharp increases, which indicated clusters that were quite different being amalgamated. Average linkage within groups uses the smallest average distance between all possible pairs of cases in the resulting combined cluster.

Comparison of means

For some variables the assumption of equal variances was broken therefore, for ease of reference, robust tests were consulted for all variables. The mean and standard deviation for the epilepsy group were used to calculate effect sizes. Robust tests for comparisons of means were Welch, Brown-Forsythe and Games-Howell. Permutation tests were used as for the EDA.

Correlation analysis

As some variables were not normally distributed and had small sample sizes, for ease of presentation, Spearman's rho correlations were used for all variables. The correlations were compared across clusters and epilepsy data using permutation tests.

Correlation results were checked following the removal of outliers (case numbers 186, 243, & 113), which did not alter them significantly. Scatter plots were examined and there was no evidence of issues likely to affect the correlation such as non-linearity.

Effect sizes

Cohen's d effect sizes were calculated using the standard deviation for the ES group. This statistic is also sometimes called Glass's delta Δ. Effect size descriptors for Cohen's d were based on Cohen's rules of thumb: 0.2 small, 0.5 medium, and 0.8 large[94].

The following effect size descriptors were used for correlations, based on recommendations by Cohen[94]; small, 0.10; medium, 0.30; and large, 0.50.

Appendix G. Section of the dendrogram for nearest neighbour linkage using squared Euclidean distance based on the childhood trauma and alexithymia total scores

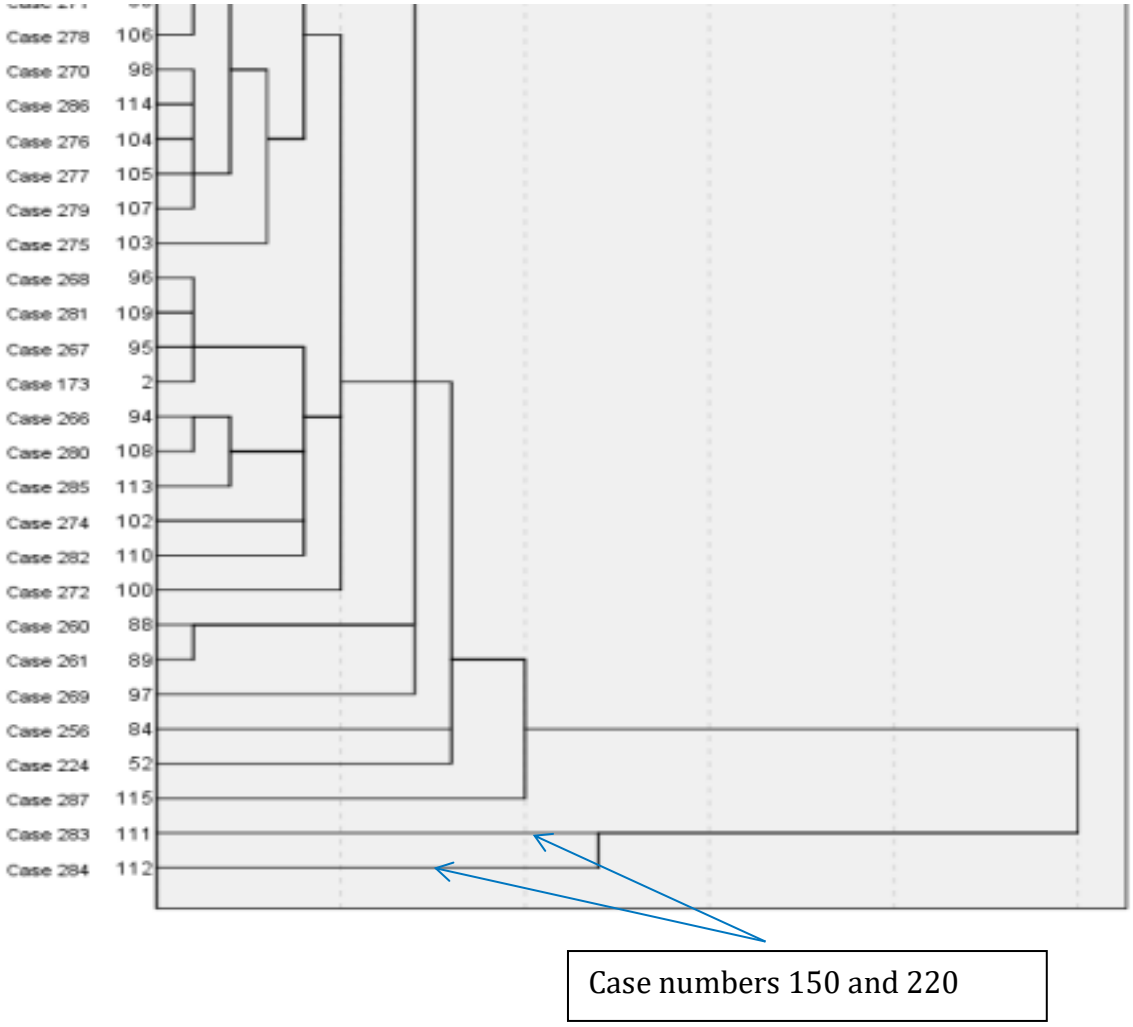


Figure G.1. Section of dendrogram for nearest neighbour cluster analysis

Appendix H. Results tables for subscales

Table H.1. Subscale descriptive statistics for each seizure type group in the study

	ES only $\bar{x}$ (SD)	NES only $\bar{x}$ (SD)	ES+NES $\bar{x}$ (SD)
Childhood trauma:			
general trauma	2.09(1.80)	2.87 (2.02)	3.74 (2.07)
physical punishment	1.21(1.51)	1.93 (1.69)	2.87 (1.63)
emotional abuse	1.55(1.78)	2.52 (1.91)	2.70 (1.92)
sexual events	0.46 (1.19)	1.70 (2.09)	2.13 (2.51)
Alexithymia:			
difficulty identifying feelings	21.98 (6.73)	23.68 (7.38)	24.59 (7.16)
difficulty describing feelings	14.96 (4.87)	15.41 (5.21)	16.50 (4.84)
externally-oriented thinking	20.37 (4.88)	19.71 (5.10)	20.27 (4.96)

Table H.2. Subscale descriptive statistics for each NES cluster

	Cluster 1 $\bar{x}$ **(SD)**	**Cluster 2** $\bar{x}$ **(SD)**	**Cluster 3** $\bar{x}$ **(SD)**
Childhood trauma:			
general trauma	1.98 (1.63)	2.24 (2.12)	4.07 (1.74)
physical punishment	1.18 (1.33)	0.57 (0.87)	3.23 (1.26)
emotional abuse	1.53 (1.60)	1.43 (1.78)	3.98 (1.13)
sexual events	0.41 (0.76)	1.10 (1.81)	3.30 (2.10)
Alexithymia:			
total score	61.77(9.41)	37.43(5.90)	66.81(10.43)
difficulty identifying feelings	24.16(5.75)	14.24(4.79)	28.25(4.96)
difficulty describing feelings	16.51(4.32)	8.62(2.71)	17.75(4.08)
externally-oriented thinking	21.10(3.66)	14.57(2.54)	20.84(5.77)

Appendix I

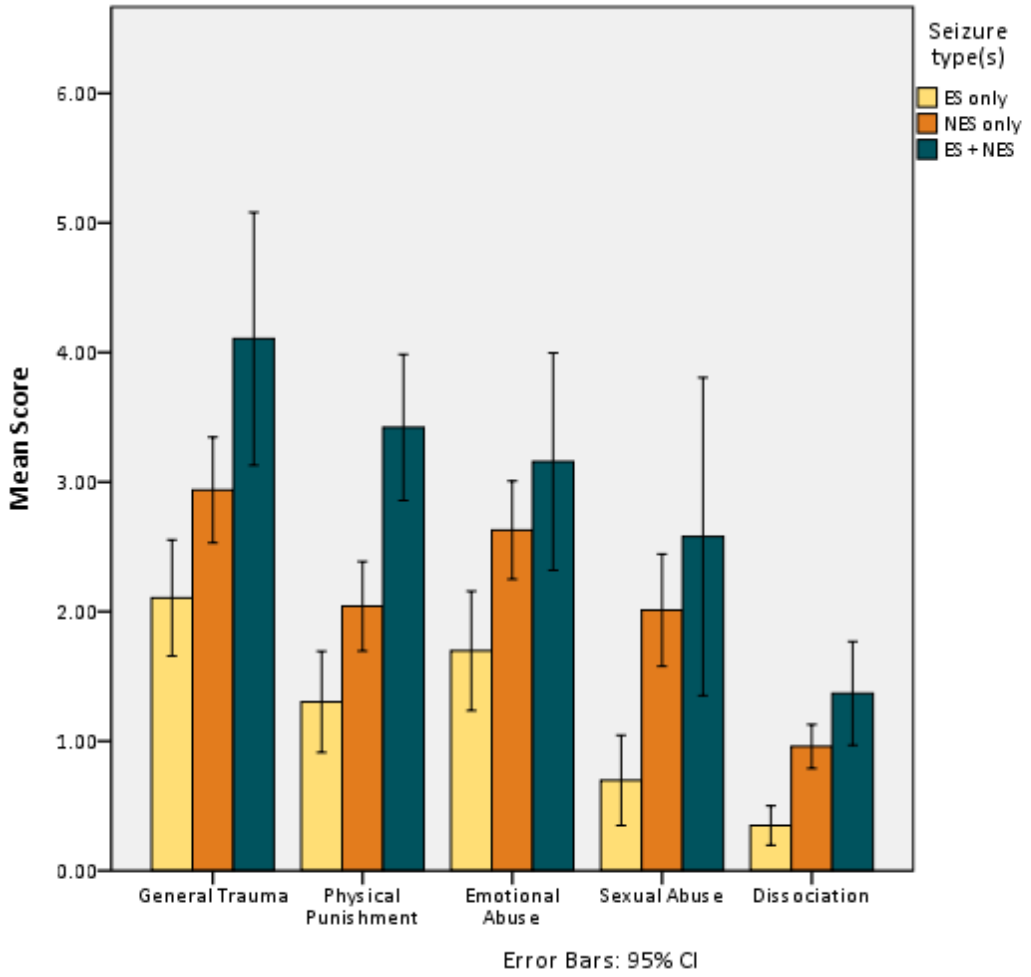


Figure I.1. Chart showing mean scores on childhood trauma subscales by seizure type(s)

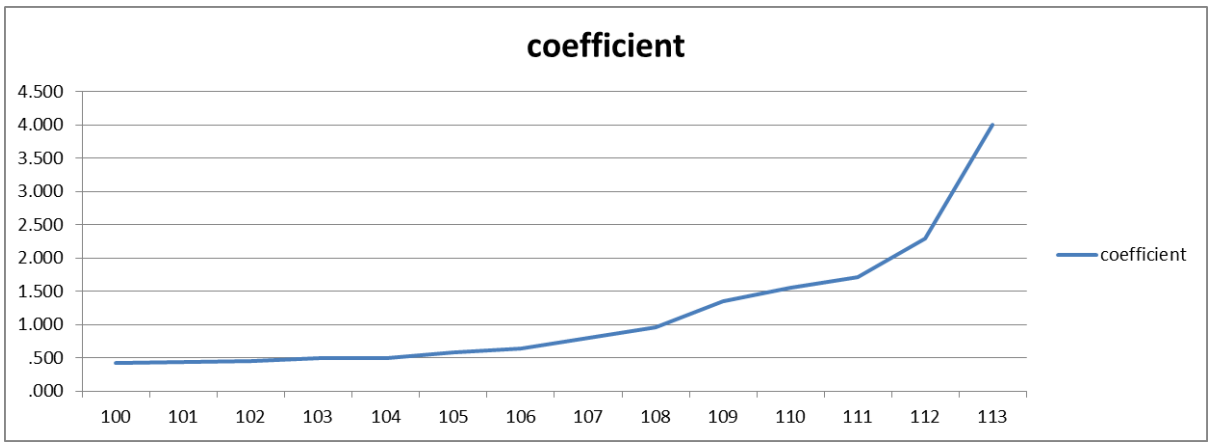
Appendix J. Post hoc tests ES vs. NES vs. ES+NES

Table J.1 Effect sizes, confidence intervals, and significance of post hoc tests

Variable	Comparison		Effect size (CI)[a]	p
Age	ES only	NES only	-0.41 (-0.72,-0.11)**	0.004
		ES + NES	-0.52 (-1.12,0.07)	0.09
	NES only	ES + NES	-0.11 (-0.71,0.48)	0.89
Childhood trauma (total score)	ES only	NES only	-0.85(-1.21,-0.49)***	<0.001
		ES + NES	-1.40(-2.16,-0.64)***	<0.001
	NES only	ES + NES	-0.55 (-1.32,0.22)	0.06
Adult attachment anxiety	ES only	NES only	0.03 (-0.32,0.38)	0.98
		ES + NES	-0.13 (-0.59,0.33)	0.77
	NES only	ES + NES	-0.16 (-0.64,0.32)	0.70
Adult attachment avoidance	ES only	NES only	0.11 (-0.19,0.41)	0.65
		ES + NES	-0.28 (-0.78,0.22)	0.36
	NES only	ES + NES	-0.40 (-0.88,0.09)	0.13
Alexithymia (total score)	ES only	NES only	-0.11 (-0.44,0.22)	0.71
		ES + NES	-0.31 (-0.92,0.30)	0.44
	NES only	ES + NES	-0.20 (-0.81,0.42)	0.71
Seizure frequency	ES only	NES only	-0.33 (-.066, 0.00)*	0.02
		ES + NES	-0.07 (-0.37, 0.23)	0.72
	NES only	ES + NES	0.26 (0.00, 0.52)	0.20
Impact of seizures	ES only	NES only	0.98(0.67,1.29)***	<0.001
		ES + NES	0.40 (-0.35,1.16)	0.40
	NES only	ES + NES	-0.57 (-1.33,0.18)	0.16

[a]Effect sizes are cohen's d calculated using the epilepsy data standard deviations, *The mean difference between the groups is significant at the 0.05 level. CI 95% confidence interval

Appendix K. Agglomeration schedule for cluster analysis using Ward's method



Figures along the bottom indicate the steps in the process

Figure K.1. Illustration of agglomeration schedule

Appendix L. Illustration of average linkage clustering

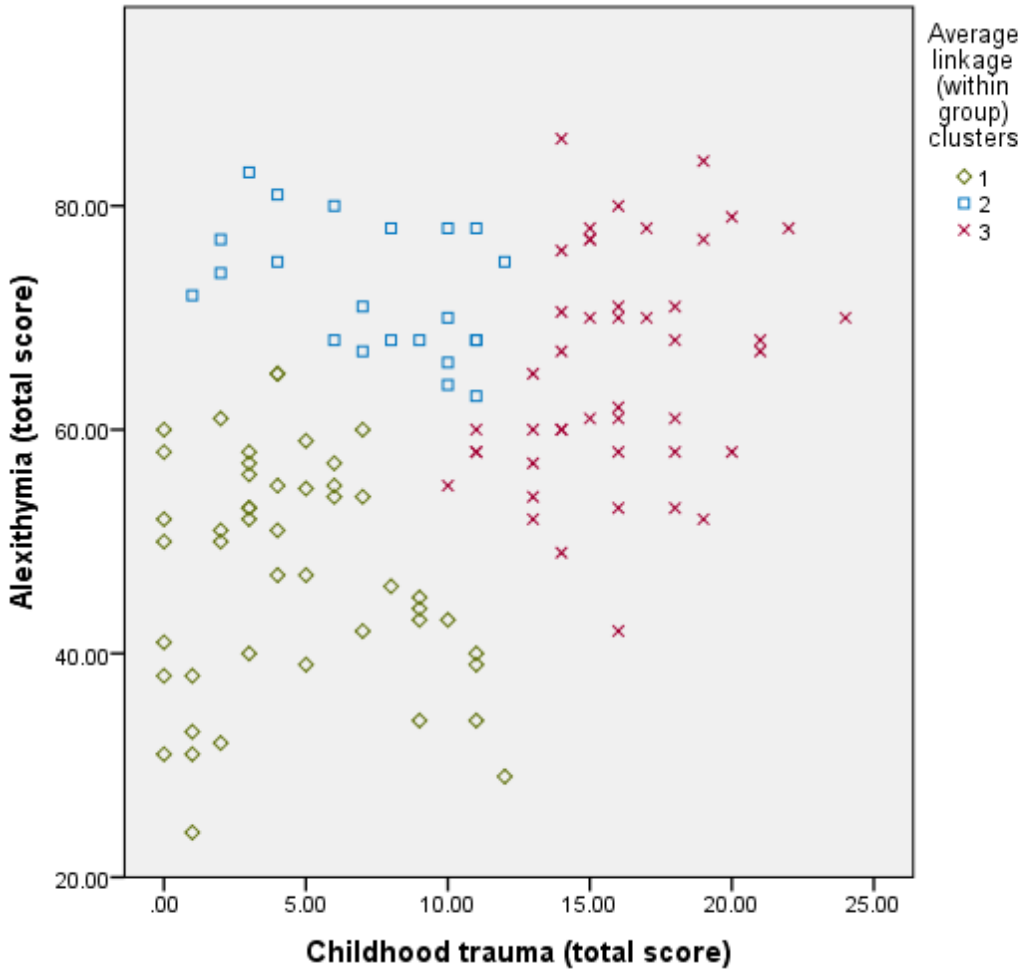


Figure L.1 Illustration of clusters formed via average linkage within groups

Appendix M. Permutation tests for significance of differences between correlations

Each permutation test compares the observed difference between correlations with the differences between correlations for 1000 group permutations. Each permutation has the same group sizes as the original groups. These permutations are drawn from a combined pool of pairs of observations from the two groups being compared. This is based on the null hypothesis that the correlations are the same in both groups.

Table M.1. Comparing cluster 1 and the ES group correlations

Correlation of characteristics	Observed difference between correlations	P-value from permutation test
Childhood trauma and attachment anxiety	0.45	0.006

Table M.2. Comparing cluster 3 and the ES group correlations

Correlation of characteristics	Observed difference between correlations	P-value from permutation test
Alexithymia and impact of seizures	0.35	0.03
Alexithymia and attachment anxiety	0.33	0.06
Alexithymia and attachment avoidance	0.06	0.80

Table M.3. Comparing cluster 1 and cluster 3 correlations

Correlation of characteristics	Observed difference between correlations	P-value from permutation test
Attachment anxiety and alexithymia	0.46	0.04
Alexithymia and childhood trauma	0.19	0.34
Attachment anxiety and childhood trauma	0.41	0.05

Section Three: Critical Appraisal

Mind-body dualism: an illusion?

A critical reflection on the impact of dualism on this research

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Word Count: 3,993 excluding tables, figures, references, & appendices

4,974 in total

In this critical appraisal, I will focus on the theme of mind-body dualism, which has arisen repeatedly in this research. I will first explain the concept of mind-body dualism and my reasons for attending to it, before summarising my results, and critically reflecting on the design, implementation, interpretation, and dissemination of my literature review and empirical research.

My interest in mind-body dualism is in its early stages. Therefore, this will not be a comprehensive review of the literature. It reflects my thoughts regarding my limited, reading and experience to date and its implications for my research.

The concept of mind-body dualism refers to thinking of the mind and body as two separate entities. It dates back to the concept of Cartesian dualism introduced by Descartes in the seventeenth century, who thought of the world as consisting of 'mind' and 'matter'[1]. He proposed that the mind, thoughts, feelings, etc., is qualitatively different from the physical body and that the physical body is part of matter along with inanimate objects. Dualism has been a topic of much debate among philosophers. The separation of the mind and body may be a natural assumption as we grow to realise that our thoughts, feelings, and dreams, cannot be directly observed by other people, unlike our physical body[2]. It also means beliefs, such as afterlife and reincarnation, can exist, as it allows the mind to exist independently of the body. However, this perception has been questioned for many years; one alternative is the concept of physicalism, which suggests that it is possible to explain all functions of the mind in terms of the physical sciences (if science was advanced enough),which is essentially a positivist view of the mind[3]. Advances in neuropsychology, and functional magnetic imaging (fMRI) may provide support for the physicalist perspective. For example, evidence has been proposed for a semantic control network operating across several brain regions [4]. Several researchers have suggested that consciousness could be a by-product of

preconscious brain activity and that control over our own actions could be an illusion[5]. This is a topic of much debate. An alternative concept is that of the 'lived-body' in which the mind and body are part of a system that forms our conscious being; its intention is to self-develop. It does this through a range of strategies, including organic processes and behaviours. Difficulties (diseases) arise through a combination of these processes, not through a process that is either purely physical (matter) or of the mind, as in the Cartesian dualism approach[6].

In Western medicine, organisation of our services and training into separate physical and mental health departments is consistent with dualism. Mehta[7] proposed that medicine is in crisis, due to its definition of illness through the lens of Cartesian dualism, which has self-defeating consequences. Gold[6] suggested that patients' interactions with doctors in this system encourage them to think of the body as an object, which needs to be 'repaired' by the doctor. In clinical settings, one example where this is evident is in relation to pain. Patients with diagnoses such as chronic pain often go from one physician to another searching for a medical diagnosis that they feel would justify their pain. An explanation related to the mind appears less acceptable than a medical diagnosis; despite fMRI studies indicating that emotional and physical pain activate the same areas in the brain[8, 9].

This Cartesian dualism in services and training persists, despite evidence suggesting other approaches would be more effective. This evidence includes: the success of cognitive behaviour therapy, wherein the basic model includes thoughts, feelings, behaviours and physical feelings, and therapy involves identifying links and cycles between these elements; the recognition of many conditions, such as, irritable bowel syndrome, shingles, psoriasis, non-epileptic seizures (NESs), and other functional diagnoses, as both physical and psychological; and evidence that conditions that are

thought of as physical, such as cancer, are influenced by people's beliefs. For example, beliefs that cancer is incurable have been found to decrease the likelihood of survival from cancer as they affect behaviours, such as treatment compliance [10]. The current organisation of services and training is even more surprising when you consider that the most frequently quoted definition of health as "a complete state of physical, mental and social well-being, and not merely the absence of disease or infirmity" was defined by the World Health Organisation, in 1948[11]. Issues are also reflected through patient complaints; a study found that 99% of patients were satisfied with an apology and an explanation[12]. They suggested that this indicates the main problem was communication skills, which were lacking due to the disproportionate attention that is given to biomedical and technical skills[12].

However, not all medicine is arranged according to dualism. Chinese medicine is more holistic in its approach; underpinned by beliefs that imbalance in the body's organs can lead to physical and emotional symptoms[13]. There is also evidence that few people hold entirely dualistic beliefs. For example, in a sample of 180 US residents only 1 was categorised as strongly dualistic, whereas 15 were strongly physicalist and 60 had roughly equal beliefs in physicalism and dualism[14]. Some authors have stated the opinion that dualism should be abandoned as it is not helpful for patients[15]. An experiment designed to test the effects of patients being primed with physicalism or dualism found that those primed with dualism were less likely to engage in healthy behaviours, and more likely to make decisions that could compromise their health[2]. Fotopoulou has argued that dualism in terms of psychogenic and neurogenic explanations for confabulation and delusion has been unhelpful, and that combining these fields of study allows a greater understanding of the relationship between cognition and emotion[16].

Seizures (both epileptic and non-epileptic) produce symptoms that would be traditionally associated with the mind or the body. For example, associated with the body are convulsions, eye movements, and incontinence; associated with the mind are changes in behaviour, emotions, and perception. This means that seizure research naturally crosses the hypothetical mind- body divide. One study reported that patients see both epileptic and NESs as both physical and psychological[17]. Despite this evidence, neurologists are reported to view NESs as largely psychological and epileptic seizures as largely physical[17]. This view can be problematic for NES patients as they may feel like they are not believed and it is 'all in the mind' i.e. imaginary[18, 19]. The view is also apparent in the treatments and research relating to the two conditions, which have emphasised the physical for epilepsy (medication, surgery) and the psychological for NESs (psychotherapy, education). However, the limited research that has been completed outside of this dichotomy has had some positive results, e.g. psychological therapy that reduced epileptic seizure frequency[20, 21]. Many people who work in the field of functional symptoms (including NESs) view them as being both neurological and psychological. For example, Dr Jon Stone, a consultant neurologist specialising in functional disorders, describes them as 'symptoms that exist at the interface between brain and mind'[18]. This quote reflects the difficulty we have in conceiving the brain and mind as being part of one system; it is a 'lived-body' explanation that makes use of Cartesian dualism to make the concept understandable. Using models that move away from Cartesian dualism, such as a biopsychosocial model in explaining NESs to patients, has been found to be helpful for most people[22]. The non-epileptic seizure treatment (NEST) group[23] have trialled a communication strategy for sharing the diagnosis of NESs with patients, which emphasises the combination of the reality of physical symptoms associated with psychological stresses. The NEST group reported this

strategy to be successful[23]; Following the consultation, 86% of patients acknowledged that psychological factors were at least a contributing factor in their seizures[23].

The term 'psychological' is unclear; it originally referred to a study of the mind[24], and this is likely to be how it is used in lay language. However, the definition has expanded to include behaviour; and its origins in biology and philosophy[24] are evident as it includes the anatomy of the brain amongst other biological topics. This is a particularly important area for neuropsychologists who often consider the impact of brain damage on individual's cognitive and emotional processing. Many neuropsychologists are trained in the interpretation of neuroimaging data[25]. It has been suggested that brain imaging in research attracts greater interest and funding as it conflicts with mind-body dualism[26]. A research study aimed to investigate this possibility, using a population taken from an online database of people who have signed up to do human intelligence tasks, which found that beliefs about dualism did not predict interest in articles using fMRI and suggested this refuted the above hypothesis[14].

Given the pervasiveness of mind-body dualism, despite evidence that it is not helpful, especially for people with symptoms such as NESs, it is not surprising that the theme arose repeatedly during my research. I therefore decided it was important to reflect on mind-body dualism and chose it as a focus for this critical appraisal. In the next sections, I will summarise my results, and consider the strengths and limitations of this research with regard to mind-body dualism.

Summary of results

The results of my literature review indicated three possible types of subgroups of adults who experience NESs: [1] A subgroup who had trauma experiences, elevated mental health problems and problematic coping strategies, consistent with Bodde et

al.'s integrated model[27]. [2] A subgroup that may be over-controlled in their emotion regulation, which could be linked to psychodynamic theory of emotion repression. [3] A subgroup with intellectual difficulties who are more likely to have environmental triggers for seizures, consistent with a behavioural model.

Through my cluster analysis in the empirical research I identified 3 clusters: [C1] Cluster 1 had a relatively low number of reported childhood trauma categories associated with elevated attachment anxiety and alexithymia. [C2] Cluster 2 was the most distinct from the other clusters and epilepsy data. It had lower mean alexithymia scores than reported in a community sample (n=1933)[28] and lower attachment anxiety and avoidance than the other clusters and the ES group. This cluster is consistent with subgroups in Reuber et al.'s[27] research and similar those in Brown et al.'s[29] results. [C3] Cluster 3 was quite similar to cluster 1 with slightly greater elevation of attachment anxiety and alexithymia and a much higher score on the childhood trauma measure.

The subgroups I suggested in the literature review and the clusters I identified in the empirical paper do not correspond directly. Cluster 3 in the research paper appears to be congruent with the subgroup [1] consistent with Bodde et al.'s model. Cluster 1 may also be congruent with this integrated model, as although childhood trauma was lower in this group than cluster 3, it did seem to play an important role. I suggested that in cluster 1 trauma may be pivotal to development of non-epileptics seizures and therefore correspond to 'level 1 psychogenic causation' in Bodde et al.'s [27] model (Section 1, Figure 1, p1.52). However, in cluster 3 the trauma may be secondary to a disrupted attachment relationship, the relationship being the main psychogenic causation.

Cluster 2 in the empirical paper appears consistent with the 'over-controlled' subgroup [2] from the literature review, as indicated by lower than normal levels of

alexithymia. There was no evidence of a subgroup [3] with characteristics resembling the behavioural model identified in the literature review. This is probably because people with intellectual disabilities may not have been able to understand or access the study and there was no assessment of seizure triggers.

The recommendations made in the literature review regarding the use of cluster analysis based on trauma and alexithymia were demonstrated to be effective in identifying subgroups. The empirical paper was successful in identifying acceptable and effective measures for this purpose.

Both papers provide further evidence for the complexity of NES aetiology, consistent with previous research and specifically the need to consider subgroups in research and clinical settings. This emphasises the need for assessment and formulation of individual differences in order to identify appropriate support. The papers go further by suggesting specific measures that could be used for this purpose and therapeutic interventions appropriate for further research, based on subgroup characteristics.

The impact of mind body dualism on this research

The subsequent sections evaluate this research's design, implementation, analysis and interpretation, across the literature review and the empirical paper, in relation to the issues of mind-body dualism described above.

Design

Mind-body dualism had an impact on the design of both my literature review and empirical project. In the literature review I chose to exclude studies that looked at differences based on the physical characteristics of seizures, such as Hill and Gale's[30] study, which considered the neurocognitive functioning of groups based on seizure

semiology. Neurologists more often write articles, such as this considering observable and measurable features, whereas neuropsychologists are less likely to include these features. My concerns about the effect of mind-body dualism were evidenced fairly early in the process of conducting this research, as illustrated by this excerpt from my research journal

> *Thinking about…articles that are neurology based or psychology based and how different they seem. Many neurology articles seem to focus on observable differences, although not all. Where psychological ones [articles] do not seem to consider these [observable differences] at all. It seems silly not to consider both [physical and psychological]*

Given the view I am expressing in this article it seems surprising that I went on to exclude observable characteristics from my literature review and largely from my empirical project. One clue to my reason for this perhaps was apparent in the next line of my journal, which stated 'I wonder how this would fit with thesis criteria, of what I bring as a psychologist?' Here I am questioning how including both these aspects would fit with my view of what a psychologist should bring. I go on to state

> *Perhaps what I bring as a psychologist is an ability to step back and bring a challenge to my own profession, rather than accepting the way things are done. We're not in an ivory tower.*

Reflecting on this statement, I think the amount I have achieved in this is limited within the context of the research. However, my decision to write the critical appraisal on this topic reflects a desire and willingness to make this challenge by starting with myself.

Reflecting on the decision to exclude articles based on seizure semiology, and thus most of the articles written by neurologists, I think that there were a number of reasons for this decision. Some of the reasons were pragmatic, e.g. to reduce the number of articles to a manageable level. Other reasons were deeply affected by mind-body dualism. For example, the training route for a neurologist is via medical school before

specialising in neurology, so they have an in depth knowledge of the human body. My training involved undergraduate psychology degree, which included a modest amount of biology, followed by doctoral level training which is largely focussed on psychotherapy. These completely different training routes mean that articles written by neurologists can be very difficult for me, as a trainee clinical psychologist, to understand. However, I do wonder whether I was slightly over concerned about this. From my notes, it seemed an overheard conversation was significant. The conversation related to the dangers of using literature from outside your area of expertise. In fact, I have studied a substantial amount of literature relating to neurology and I took an optional extra course at undergraduate level on 'biology and the brain', I have completed a neuropsychology placement and have participated in teaching on various related topics as part of doctoral training. I did acknowledge in my literature review that it would have been better to do this research collaboratively with a neurologist, a view that is also held by Schwann et al.[31]. However, the very need for collaboration is underpinned by the mind-body dualism that separates our training into, physical and psychological approaches. This is particularly unhelpful when addressing difficulties, such as seizures, which are (arguably) the result of the lived-body system that is both physical and psychological.

The design of my empirical project was perhaps less affected by mind-body dualism; the concepts of alexithymia and attachment both have broad theoretical and evidence bases, which could be considered consistent with a lived-body perspective. For example, neuroimaging studies have found that people with different levels of alexithymia have differing patterns of neural activity in the brain in response to emotional stimuli[32] and attachment theory is linked to evolution[33]. Experiences of trauma could also be thought of as something that affect the lived-body, or to use the

Cartesian terms mind (e.g. feeling afraid) and body (e.g. physical injury). However, one participant made me question the effects of dualism on my design when they emailed saying they were surprised I did not ask more about the characteristics of their seizures (semiology). Reflecting on this I realised that I had few questions relating to this, only seizure frequency, and I wondered about my reasons for this. I think part of my reason was keeping the study design and number of questions as minimal as possible, but I also had an assumption that these factors would not be related to experiences of trauma, alexithymia, and attachment. Inherent in this assumption is the separation of the mind and body. If we view seizures as produced by a lived-body then there is no reason why these factors should not be related, and in fact one study (n=272) found that combining both seizure characteristics (duration and years since first seizure) with the conversion subscale of the personality assessment inventory, resulted in a model that achieved 84% correct classification of seizure type (epileptic or non-epileptic)[34].

Implementation

I experienced difficulties at various points in the research, it often felt like it was complex, and getting people to help was challenging. At various points, I wondered whether this was connected with the physical/psychological divide, as I had not had this experience when carrying out previous research. I think at some points it was. For example, when I was questioned about why it was relevant to ask people with epilepsy about their emotions. However, I think there were also other reasons for this difficulty. For example, the fact that I was approaching a number of different NHS services in different areas of the country meant that I needed approval from each different research and development (R & D) departments. The practicality of communicating with several different R & D departments at once was quite difficult to manage and I

needed to keep clear records of my progress with each one; see sample in Appendix 1. I noted in my journal on 25th Feb 2015 that it would have been 'better to have had more involvement [of R&D departments] from the start'. I did have some of them involved much earlier in the process and the implementation was much less problematic with these organisations. The fact that my study included questions about childhood trauma was also something that understandably made people anxious and perhaps made them hesitant about implementing the project.

Analysis and interpretation

An area that I think was less affected by mind-body dualism was the data analysis as there are many examples of similar data analysis methods being applied to variables that would be traditionally associated with the body[35] or those that would be traditionally associated with mind[36], and some that consider both[34]. However, as I mentioned in my literature review it was interesting that there was little qualitative research in this area. Qualitative research is common in other areas of psychological study, and would use very different analysis methods. I wonder whether my choice to use quantitative analysis in this area of research was sub-consciously influenced by a mind-body dualism that saw this as an area closer to medicine (the body) and therefore associated it with quantitative methods.

Another strength of this research was that I was aware of mind-body dualism and reflected on it throughout, which made me alert to how it may be influencing my research. My psychological training, which includes many models that attempt to move away from the dualistic perspective, such as cognitive behavioural therapy and the biopsychosocial model, was also helpful in interpreting the results. It means that whilst I was considering how the findings related to each other and to other literature I was

open minded to relationships between physical and psychological characteristics. Also, that when I think about psychological characteristics, such as attachment and alexithymia, I am not thinking about them as purely related to the mind, rather as features of the lived-body, and being made up of elements that, from a Cartesian perspective, would include both mind and matter.

Dissemination

One strength of this area of research is that it provides a forum for literature from different disciplines to converge, journals, such as Epilepsia include neurology, psychology, neuropsychology, molecular biology, and neurochemistry. This enables people from different disciplines to consider how their work relates to each other.

Future research

I believe that it is important that future researchers consider the influence of mind-body dualism on their design, implementation, interpretation, and dissemination. The pervasiveness of dualism makes it difficult, or perhaps impossible, to move away from its influence altogether, but reflecting on this issue and working collaboratively across disciplines is likely to help. This is particularly important in areas of research, such as seizures that fall between the dualistic categories of mind and matter, and this has been recommended by others, such as, Schwan et al.[31]. It could also be useful to include such consideration in other areas of research, as it may lead to advances, as we break down the illusion of mind-body dualism.

An important area of research, I recommended in the research papers, was the assessment of therapeutic interventions appropriate to individual psychological characteristics. I suggested using alexithymia and attachment measures alongside

individual formulations to allocate people to subgroups who receive different treatments. Possible therapies are detailed in the research papers and they included behavioural therapy, mindfulness, emotion regulation training, and psychodynamic approaches. This research could be undertaken through collaboration of a research team involving psychologists, neurologists, psychiatrists, and non-epileptic and epileptic seizure patients. I hope that such collaboration would reduce the influence of mind-body dualism and I would also recommend that specific attention is paid to the influence of dualism from the outset, especially during the design phase. It would be important to consider how the research would interact with other aspects of treatment, such as medication.

Clinical implications

Increased awareness and a critical approach to mind-body dualism may lead to different ways of practicing clinically perhaps through joined up working or broader training. There is evidence of this already happening. For example some clinics for functional neurological symptoms are starting to provide joint appointments with a neurologist and neuropsychologist present, and many areas of medical training include elements of psychology.

Conclusion

Mind-body dualism is pervasive in our society and health services, despite much criticism and evidence suggesting that perceiving our mind and body as qualitatively different can be unhelpful in a health context. Seizures, especially NESs are not consistent with dualism. This can lead to difficulties for patients, doctors, and researchers. Based on my limited knowledge at this point, I suggest that the concept of

lived-body provides an alternative, and potentially more helpful, way of thinking about ourselves. This may be particularly helpful for people experiencing functional difficulties, such as NESs. This research has been affected by the pervasive nature of dualism, but also had some strengths in terms of my alertness to the impact of mind-body dualism, and that I have had training in models that are more consistent with a lived-body concept.

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Contact Organisation[a]	Sector	Status	Contact Notes				Notes re numbers
********Partnership NHS Foundation Trust	NHS	20/1/15 agreed to support, send sponsorship, final R&D form and REC approval when available. 26/1/15 only REC approval outstanding. 28/1/15 all docs now sent. R&D approval received	Initial contact email sent	17/1/15 follow up email sent	20/1/15 emailed R&D with main docs. 26/1/15 All rec submission docs, final R&D form and sponsorship sent. 28/1/15 rec approval sent	11/2/15 emailed R&D asking if any updates 24/2/15 further prompt sent	2 people asked, 1 pack given out
********** NHS Foundation Trust	NHS	2/2/15 await go ahead to contact R&D	Initial contact email sent, interested, requested details of measures	17/1/15 email sent to ask if decision made about supporting project	28/1/15 email sent with REC approval and asking re support 11/2/15 prompt sent		
********* NHS Foundation Trust	NHS	4/2/15 waiting to hear back from R&D 11/2/15 awaiting response from R&D 12/2/15 awaiting response from R&D 17/2/15 R&D approval received	Initial contact email sent, requested details of measures	17/1/15 follow up email sent to confirm if able to support	28/1/15 email sent with REC approval and asking re support 4/2/15 email received to say they will chase R&D	9/2/15 queries from R&D re PIC/research site responded to 12/2/15 feedback that issue re R&D form resolved, CV sent as requested	7 packs given out

[a] Names have been removed

Section four: [1]Ethics

Liz Tallentire

Doctorate in Clinical Psychology

Division of Health Research, Lancaster University

Word Count: 2353 excluding form text & appendices
8,244 in total excluding form text

[1] The participant information sheet and measures were also including in the ethics application, please see these documents in Section 2, appendices B and D

Health Research Authority
National Research Ethics Service

NRES Committee North West - Liverpool Central
3rd Floor
Barlow House
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7818
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27 January 2015

Ms Liz M. Tallentire
Trainee Clinical Psychologist
Lancashire NHS Trust
Doctorate in Clinical Psychology
Department of Health Research
Lancaster University
LA1 4YG

Dear Ms Tallentire

Study title:	**Relationships between early life events, individual differences, and seizures**
REC reference:	**15/NW/0110**
IRAS project ID:	**166247**

The Proportionate Review Sub-committee of the NRES Committee North West - Liverpool Central reviewed the above application on 27 January 2015.

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

Ethical opinion

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

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

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

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

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

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

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

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

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

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

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

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

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

Ethical review of research sites

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

The members had no ethical issues with this application.

Approved documents

The documents reviewed and approved were:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Poster Advert]	1	22 December 2014
Copies of advertisement materials for research participants [Card with Link]	1	22 December 2014
Copies of advertisement materials for research participants [Online Forum Advert]	1	25 November 2014
Covering letter on headed paper [Covering Letter]	1	14 January 2015
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employers Liability]	1	01 August 2014

Letter from sponsor [Sponsorship Letter]	1	21 January 2015
Other [Gant Chart]	1	14 October 2015
Other [Review Process Evidence]	1	26 June 2014
Other [Online Survey Format Illustration]	1	25 November 2014
Other [Professional Indemnity Insurance]	1	04 August 2014
Other [Public Liability Insurance]	1	04 August 2014
Participant information sheet (PIS) [PIS Online Version]	1	22 December 2014
Participant information sheet (PIS) [PIS Paper Version]	1	22 December 2014
Participant information sheet (PIS) [Thank you and Support Information]	1	25 November 2014
REC Application Form [REC_Form_22012015]		22 January 2015
Research protocol or project proposal [Protocol]	1	22 December 2014
Summary CV for Chief Investigator (CI) [CV Liz Tallentire]	1	14 January 2015
Summary CV for supervisor (student research) [CV Ian Fletcher]	1	16 August 2014
Validated questionnaire [Questionnaires Pack]	1	25 November 2014

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

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

After ethical review

Reporting requirements

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

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

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

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

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

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

15/NW/0110	**Please quote this number on all correspondence**

Yours sincerely

Mrs Julie Brake
Chair

Email: nrescommittee.northwest-liverpoolcentral@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

"After ethical review – guidance for researchers"

Copy to: *Ms Debbie Knight*
Dave Watling, The [redacted] *NHS Foundation Trust*

NRES Committee North West - Liverpool Central

Attendance at PRS Sub-Committee of the REC meeting on 27 January 2015

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mrs Julie Brake	Specialist Diabetes Nurse / Chair	Yes	
Mrs Hannah Chambers	Lay Member	Yes	
Mr Fotios Polydoros	Statistician	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mrs Carol Ebenezer	REC Manager

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please enter a short title for this project (maximum 70 characters)
Early life events, individual differences, and seizures V1

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
(●) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation?	( ) Yes	(●) No
b) Will you be taking new human tissue samples (or other human biological samples)?	( ) Yes	(●) No
c) Will you be using existing human tissue samples (or other human biological samples)?	( ) Yes	(●) No

3. In which countries of the UK will the research sites be located? *(Tick all that apply)*

- [x] England
- [ ] Scotland
- [ ] Wales
- [ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- (●) England
- ( ) Scotland
- ( ) Wales
- ( ) Northern Ireland
- ( ) This study does not involve the NHS

4. Which review bodies are you applying to?

- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] National Information Governance Board for Health and Social Care (NIGB)
- [ ] National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D offices, the CI must create Site-Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

5. Will any research sites in this study be NHS organisations?

(●) Yes ( ) No

5a. Are all the research costs and infrastructure costs for this study provided by an NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC) or NIHR Research Centre for Patient Safety & Service Quality in all study sites?

( ) Yes (●) No

If yes, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP).

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) support and inclusion in the NIHR Clinical Research Network (CRN) Portfolio? Please see information button for further details.

( ) Yes (●) No

If yes, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP) and you must complete a NIHR Clinical Research Network (CRN) Portfolio Application Form immediately after completing this project filter and before completing and submitting other applications.

6. Do you plan to include any participants who are children?

( ) Yes (●) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

( ) Yes (●) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the NIGB Ethics and Confidentiality Committee to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

◉ Yes ○ No

Please describe briefly the involvement of the student(s):
Chief investigator is a doctoral student on the Clinical Psychology Doctorate at Lancaster University

9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?

◉ Yes ○ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Research administering questionnaires/interviews for quantitative analysis or mixed methodology study

NHS Health Research Authority

Application to NHS/HSC Research Ethics Committee

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Early life events, individual differences, and seizures V1

Please complete these details after you have booked the REC application for review.

REC Name:
NRES Committee North West - Liverpool Central

REC Reference Number:
15/NW/0110

Submission date:
22/01/2015

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Relationships between early life events, individual differences, and seizures

A2-1. Educational projects

Name and contact details of student(s):

Student 1

	Title	Forename/Initials	Surname
	Ms	Liz M.	Tallentire
Address	Doctorate in Clinical Psychology, Furness Building		
	Divison of Health Research		
	Lancaster University		
Post Code	LA1 4YG		
E-mail	l.tallentire@lancaster.ac.uk		
Telephone			
Fax			

Give details of the educational course or degree for which this research is being undertaken:

Name and level of course/ degree:
Doctorate in Clinical Psychology

Name of educational establishment:
Lancaster University

Name and contact details of academic supervisor(s):

Academic supervisor 1

	Title	Forename/Initials	Surname
	Dr	Ian	Fletcher
Address	Clinical Psychology		
	Division of Health Research		
	Lancaster University		
Post Code	LA1 4YG		
E-mail	i.j.fletcher@lancaster.ac.uk		
Telephone	01524 593301		
Fax			

Please state which academic supervisor(s) has responsibility for which student(s):
Please click "Save now" before completing this table. This will ensure that all of the student and academic supervisor details are shown correctly.

Student(s)	**Academic supervisor(s)**
Student 1 Ms Liz M. Tallentire	☑ Dr Ian Fletcher

A copy of a current CV for the student and the academic supervisor (maximum 2 pages of A4) must be submitted with the application.

A2-2. Who will act as Chief Investigator for this study?

- (●) Student
- ( ) Academic supervisor
- ( ) Other

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Ms	Liz M.	Tallentire
Post	Trainee Clinical Psychologist		
Qualifications	BSc Psychology, MA Leadership and Management		
Employer	Lancashire NHS Trust		
Work Address	Doctorate in Clinical Psychology		
	Department of Health Research		
	Lancaster University		
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* Personal Telephone/Mobile	07539294316
Fax	

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.

	Title	Forename/Initials	Surname
	Ms	Debbie	Knight
Address	Research Support Office,		
	B58 Bowland Main,		
	Lancaster University,		
Post Code	LA1 4YT		
E-mail	ethics@lancaster.ac.uk		
Telephone	01524 592605		
Fax			

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	
Sponsor's/protocol number:	
Protocol Version:	1
Protocol Date:	
Funder's reference number:	
Project website:	

Additional reference number(s):

Ref.Number Description	Reference Number

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

A5-2. Is this application linked to a previous study or another current application?

○ Yes ◉ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, this summary will be published on the website of the National Research Ethics Service following the ethical review.*

This research will investigate the link between early experiences, individual differences, and seizures. It will consider whether a person having particular early experiences, such as, being emotionally neglected or physically abused is associated with specific individual differences and seizures. The individual differences the research will consider are processing of emotions and the way people relate to others. Processing of emotions includes a person being able to recognise their own emotions and describe them. The way people relate to others is how much a person avoids or is anxious about close relationships with others. In relation to seizures, the research will include, type of seizure, how often they happen, and how much impact the person reports seizures have on their daily life. Seizure type in this research is epileptic (due to unusual electrical activity in the brain) or non-epileptic (not due to unusual electrical activity in the brain).
Participants will anonymously complete questionnaires about each of the factors described above. They will fill in questionnaires online and send them electronically; or on paper and send them in the post. The researchers will then work out scores based on the questionnaires. These scores will be analysed using statistical tests, in order to look for relationships between them, which represent relationships between the above factors.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, R&D office or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

Potential participants may be distressed due to experiencing seizures. One of the questionnaires may highlight possible childhood issues. The consent form will provide information about the topics the questions will cover so that people have opportunity to make an informed decision about whether they would like to participate or not. Participants will not receive individual feedback on their answers, and sign-posting to appropriate services will be provided.

A6-3. Proportionate review of REC application *The initial project filter has identified that your study may be suitable for proportionate review by a REC sub-committee. Please consult the current guidance notes from NRES and indicate whether you wish to apply through the proportionate review service or, taking into account your answer to A6-2, you consider there are ethical issues that require consideration at a full REC meeting.*

(●) Yes - proportionate review ( ) No - review by full REC meeting

Further comments (optional):

The researchers are applying for proportionate review as in accordance with point four of 'is my study suitable for Proportionate Review' on the HRA guidance (link below), the sensitive questionnaires have been validated and widely used with the proposed population or very similar populations (see protocol measures section for details). In addition, all sensitive information will be anonymous.
http://www.hra.nhs.uk/documents/2014/05/pr_website_v_ 5_15_05_2014.pdf

Note: This question only applies to the REC application.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- [ ] Case series/ case note review
- [ ] Case control
- [ ] Cohort observation
- [ ] Controlled trial without randomisation
- [x] Cross-sectional study
- [ ] Database analysis

- [ ] Epidemiology
- [ ] Feasibility/ pilot study
- [ ] Laboratory study
- [ ] Metanalysis
- [ ] Qualitative research
- [x] Questionnaire, interview or observation study
- [ ] Randomised controlled trial
- [ ] Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

The principle objective of the research is to identify how early experiences, individual differences and seizures are related to each other.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

N/A

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Previous research has found that certain childhood experiences, particularly traumatic ones, are associated with experiencing particular types of seizure in later life. Research also indicates that people, who experience trauma in childhood, are more likely to have difficulty processing emotions and to be more anxious and/or avoidant of close relationships. Other studies have found that difficulty processing emotions is associated with certain types of seizures and how often they occur. Therefore, it makes sense to consider these factors in one study, in order to investigate how they relate to each other for people who experience seizures.

Understanding more about how these factors relate to each other for people who have different types of seizure may help to identify people who are more likely to experience particular seizure types. Understanding the relationships between factors will also help to identify appropriate treatments. This is important, to be able to reduce the distress caused by seizures, as well as the potential harm to patients and cost to health services of inappropriate treatments.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

The project will be advertised to potential research participants using a variety of methods, which will include:
Adverts on online support forums for relevant groups;
Contacting support groups in person or via email to ask them to advertise the project to members;
Asking health clinic staff to inform potential participants about the research and provide them with packs if requested. The packs will contain the participant information sheet, questionnaires and support information; and
Displaying posters in relevant health clinics.

The advertisement will explain the options for participation, which are via online survey, or paper forms in the post.

For online participation a link will be included in adverts to direct the person to an online survey site. This site will provide full details of what the study involves and a consent form, to enable the person to make an informed decision about whether they would like to participate or not.

The paper packs and online site will include the same information with slight adaptions (as shown on the attached documents).

For all methods of participation the same information will be collected, including gender, age, seizure frequency, country of residence, and responses to the questionnaires (see attached documents). No identifying information will be collected as part of the survey. A page will be included thanking participants for taking part and providing contact details of support organisations. Participants will have the option to give their email or postal address if they would like

to receive a summary of the overall finding of the research. The email/postal address will be kept separate from the questionnaire data and will not be linked with it. In the paper version participants will be requested to post back their email/ postal address, if provided, separately from their completed questionnaires.

Participants will be asked to share information about the study with anyone else they think may be interested and eligible to participate.

Data from the electronic survey system will be imported directly to statistical analysis software. Data from paper versions will be entered onto the electronic statistical software by the researchers or their administrative support. Statistical tests will then be carried out on the anonymous data by the researchers.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- [x] Design of the research
- [ ] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results
- [ ] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
Members of the 'P.N.E.S awareness' support group for people who experience non-epileptic seizures have been consulted in relation to the design of the study, by asking five volunteers to feedback on the participant information sheet and adverts. The feedback received was positive; an additional link was added to the support information based on a suggestion from one of these reviewers.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Adults over the age of 18 years
Who experience epileptic and/or non-epileptic seizures

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Unable to understand the level of English language required to complete the measures

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Reading the participant information sheet and	1	0	3	Potential participant via the online survey site or

consent information			minutes	in the paper pack
Completing demographic questions	1	0	1 minutes	Participant via online survey site or paper form.
Completing measures (Details of measures are given in the protocol)	1	0	10 mins	Participant via online survey site or paper form.
Thank you and support information	1	0	1 minute	Participant via online survey site or paper form.

A21. How long do you expect each participant to be in the study in total?

15 - 20 minutes

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

Risk of becoming distressed due to answering questions about childhood experiences. Minimised by:
making it clear participants should stop answering questions if they become distressed,
including support information, and
providing a link to exit the survey and access support information on every page of the online version.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

(●) Yes ( ) No

If Yes, please give details of procedures in place to deal with these issues:

The survey does not include open questions therefore it is unlikely that disclosures will occur. Some questionnaires include sensitive topics, however the survey will be anonymous, which reduces issues relating to this.

A24. What is the potential for benefit to research participants?

There will be no direct benefit.

A26. What are the potential risks for the researchers themselves? *(if any)*

None

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Potential participants may be identified in several ways:
self-identification following viewing an advertisement,
identification by a member of their healthcare team who makes them aware of the study,
identification by their membership of a relevant forum or support group through which they receive study advertising, or
being forwarded the information by another participant.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

○ Yes ◉ No

Please give details below:

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

◉ Yes ○ No

If Yes, please give details of how and where publicity will be conducted, and enclose copy of all advertising material (with version numbers and dates).

Publicity will be conducted via online forums, support groups, and at relevant health clinics.

A29. How and by whom will potential participants first be approached?

This will include:
by a professional who works with the person face to face, or over the phone,
by viewing a poster/ advert in a clinic or other location, or online,
by another participant who forwards them information about the study.

A30-1. Will you obtain informed consent from or on behalf of research participants?

◉ Yes ○ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

For the paper version consent will be inferred from the fact that they have posted the survey forms back to the researcher. Guidance from the British Psychological Society suggests that participants may be less likely to read participant information for online surveys. Therefore, for those participating electronically, a page will include tick boxes to draw attention to key study information and a button to click to indicate consent. No identifying details will be collected during the consent procedures.

If you are not obtaining consent, please explain why not.

N/a

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

○ Yes ◉ No

If No, how will it be recorded?

It will be recorded electronically by the online survey system, in the case of paper forms it will be inferred from the act of posting the forms to the researcher.

A31. How long will you allow potential participants to decide whether or not to take part?

They will have the option to think about the participant information sheet and come back to it at any time whilst the study is still open for data collection. The participant information sheet will include a planned close date and the option to print information.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or

written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

As not all measures have been tested in languages other than English, translation is not available as this would compromise the validity and reliability of the data.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ○ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ○ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.
- ◉ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

As the research team will not be in direct contact with the participants during data collection they will be unable to monitor capacity. However, it seems unlikely that capacity will change in the time that it takes to complete the surveys.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?*(Tick as appropriate)*

- ☐ Access to medical records by those outside the direct healthcare team
- ☑ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☑ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☐ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☐ Use of audio/visual recording devices
- ☑ Storage of personal data on any of the following:
  - ☐ Manual files including X−rays
  - ☐ NHS computers
  - ☐ Home or other personal computers
  - ☑ University computers
  - ☐ Private company computers
  - ☐ Laptop computers

Further details:

The only personal data that will be collected is a list of email/postal addresses, if participants wish to give them, so that

the researchers can send them a copy of the overall results.

In the case of postal participation, participants will be asked to send their email/postal address in a separate envelope to the survey data. Online this information will be collected with a separate survey so that it is not linked to the questionnaire data.

Where I have ticked 'University computers' above this refers to the university secure server and not individual computers.

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

The researchers will not link the email/postal addresses and the rest of the survey data. Also see A37 above.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The non-identifiable personal information i.e. demographics and responses to measures will be accessible to the research team and any person standing in for or replacing a member of the research team.

The list of email/postal addresses to send out a summary of the study will be available to the research team but will not be linked to any other study data.

Storage and use of data after the end of the study

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ◉ 3 – 6 months
- ○ 6 – 12 months
- ○ 12 months – 3 years
- ○ Over 3 years

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

○ Yes ◉ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

○ Yes ◉ No

Please give details, or justify if not registering the research.

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

- ☑ Peer reviewed scientific journals
- ☐ Internal report
- ☑ Conference presentation
- ☐ Publication on website
- ☐ Other publication
- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☑ Other (please specify)

As part of a doctoral thesis

A53. Will you inform participants of the results?

◉ Yes ○ No

Please give details of how you will inform participants or justify if not doing so.
Participants will have the option of providing an email/postal address so that the research team can send them a summary of the results.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

- ☐ Independent external review
- ☐ Review within a company
- ☐ Review within a multi−centre research group
- ☑ Review within the Chief Investigator's institution or host organisation
- ☑ Review within the research team

☑ Review by educational supervisor

☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
Review took place in initial stages with members of the research team (see attached form). The academic supervisor and research officer for Lancaster University have checked this application and all supporting documents.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

☐ Review by independent statistician commissioned by funder or sponsor

☐ Other review by independent statistician

☐ Review by company statistician

☐ Review by a statistician within the Chief Investigator's institution

☐ Review by a statistician within the research team or multi−centre group

☑ Review by educational supervisor

☐ Other review by individual with relevant statistical expertise

☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Dr	Ian	Fletcher
Department	Division of Health Research		
Institution	Lancaster University		
Work Address	Clinical Psychology		
	Division of health research		
	Lancaster University		
Post Code	LA1 4YG		
Telephone	01524 593301		
Fax			
Mobile			
E-mail	i.j.fletcher@lancaster.ac.uk		

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Impact of seizures

A58. What are the secondary outcome measures? *(if any)*

Seizure frequency and type (epileptic or non-epileptic)

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:
Total international sample size (including UK): 98
Total in European Economic Area:

Further details:

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

The sample size above is the minimum recommended to achieve an appropriate level of power (0.8) in the statistical calculations (regression analysis). This is based on the expectation that the effect sizes (impact) of the mediators will be medium, as this has been indicated in other research. It also takes into account the fact that there will be six variables, including the demographic questions. The figure is obtained from the graphs given on page 314 of Field's (2013) book, 'discovering statistics using IBM SPSS statistics', see protocol for full reference.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Data will be analysed using statistical analysis software such as IBM SPSS. The main analysis is planned to be regression analysis, if appropriate it may also include analysis of mediators and moderators. Tests will be carried out to assess appropriateness of regression analysis. Should regression analysis be inappropriate due to insufficient number of participants, or other issues, alternate appropriate tests will be carried out, such as, tests for correlation between measures, and tests for significance of differences between means for different groups.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co–applicants, protocol co–authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Dr	Jayne	Martlew
Post	Consultant Clinical Neuropsychologist		
Qualifications	BSc, MPhil, Doctorate in Clinical Psychology		
Employer	The [redacted] NHS Foundation Trust		
Work Address	Lower Lane Fazakerley Liverpool		
Post Code	L9 7LJ		
Telephone	0151 529 5693		
Fax			
Mobile			
Work Email	Jayne.Martlew@thewaltoncentre.nhs.uk		

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- ○ NHS or HSC care organisation
- ◉ Academic
- ○ Pharmaceutical industry
- ○ Medical device industry
- ○ Local Authority
- ○ Other social care provider (including voluntary sector or private organisation)
- ○ Other

Commercial status:

If Other, please specify:

Contact person

Name of organisation	Lancaster University
Given name	Debbie
Family name	Knight
Address	Research Support Office,
Town/city	B58 Bowland Main,
Post code	LA1 4YT
Country	UNITED KINGDOM
Telephone	01524 592605
Fax	
E-mail	ethics@lancaster.ac.uk

Is the sponsor based outside the UK?

○ Yes ◉ No

Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.

A65. Has external funding for the research been secured?

- ☐ Funding secured from one or more funders
- ☐ External funding application to one or more funders in progress
- ☑ No application for external funding will be made

What type of research project is this?

- ◉ Standalone project
- ○ Project that is part of a programme grant
- ○ Project that is part of a Centre grant
- ○ Project that is part of a fellowship/ personal award/ research training award
- ○ Other

Other – please state:

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

○ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title	Forename/Initials	Surname
		Dave	Watling
Organisation	The [redacted] NHS Foundation Trust		
Address	Lower Lane		
	Fazakerley		
	Liverpool		
Post Code	L9 7LJ		
Work Email	dave.watling@thewaltoncentre.nhs.uk		
Telephone	01515295667		
Fax			
Mobile			

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/01/2015
Planned end date: 30/05/2015
Total duration:
Years: 0 Months: 4 Days: 30

A71-2. Where will the research take place? *(Tick as appropriate)*

- ☑ England
- ☑ Scotland
- ☑ Wales
- ☑ Northern Ireland
- ☑ Other countries in European Economic Area

Total UK sites in study

Number of sites anticipated in the Community

Does this trial involve countries outside the EU?
◉ Yes ○ No

- ☑ USA
- ☑ Other international (please specify)

Anyone with internet access may choose to complete the online measures

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? *Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:*

☑ NHS organisations in England	1
☐ NHS organisations in Wales	
☐ NHS organisations in Scotland	
☐ HSC organisations in Northern Ireland	
☐ GP practices in England	
☐ GP practices in Wales	
☐ GP practices in Scotland	
☐ GP practices in Northern Ireland	
☐ Social care organisations	
☐ Phase 1 trial units	
☐ Prison establishments	
☐ Probation areas	
☐ Independent hospitals	
☐ Educational establishments	
☐ Independent research units	
☐ Other (give details)	

One site is lead for R& D, other sites will be participant identification centres.

Total UK sites in study: 1

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:* in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland**

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (NHS sponsors only)

☑ Other insurance or indemnity arrangements will apply (give details below)

Lancaster University legal liability cover will apply.

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)

☑ Other insurance or indemnity arrangements will apply (give details below)

Lancaster University legal liability cover will apply.

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

☐ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

☑ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Lancaster University legal liability cover will apply.

Please enclose a copy of relevant documents.

[redacted]

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Research site		Investigator/ Collaborator/ Contact	
Institution name	THE [redacted] NHS FOUNDATION TRUST	Title	
Department name		First name/ Initials	Liz M.
Street address	LOWER LANE	Surname	Tallentire
Town/city			
Post Code	L9 7LJ		
Participant Identification Centre(PIC)-Collaborator/ Contact			

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.

9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.

11. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

(●) Chief Investigator

( ) Sponsor

- ○ Study co-ordinator
- ○ Student
- ○ Other – please give details
- ○ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☑ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Ms Elizabeth TALLENTIRE on 16/01/2015 11:51.

Job Title/Post:	Trainee Clinical Psychology
Organisation:	Lancaster University
Email:	l.tallentire@lancaster.ac.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

6. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by An authorised approver at ethics@lancaster.ac.uk on 21/01/2015 17:34.

Job Title/Post:	Research Support Officer
Organisation:	Lancaster University
Email:	s.c.taylor@lancaster.ac.uk

D3. Declaration for student projects by academic supervisor(s)

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.

2. I undertake to fulfil the responsibilities of the supervisor for this study as set out in the Research Governance Framework for Health and Social Care.

3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.

4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

Academic supervisor 1

This section was signed electronically by Dr Ian Fletcher on 16/01/2015 13:09.

Job Title/Post:	Senior Lecturer
Organisation:	Lancaster University
Email:	i.j.fletcher@lancs.ac.uk

Relationships between early life events, individual differences, and seizures

Epileptic seizures are associated with atypical electrical activity in the brain, seen during electroencephalography (EEG). Non-epileptic seizures appear similar when observed, but the changes in electrical activity are not seen on the EEG (Hubsch, Baumann, & Maillard, 2010). Differentiating between these types of seizures can be difficult, but it is important, in order to help people to access appropriate treatment; the most reliable way to differentiate has been found to be video-electroencephalography (Cragar, Berry, Fakhoury, Cibula, & Schmitt, 2002). The task of differentiating is made difficult by high levels of comorbidity of epileptic and non-epileptic seizures. For example Hoepner et al. (2014) reported that 36% of their sample of 114 people who experienced non-epileptic seizures also had epileptic seizures. This causes complications for the use of EEG for differential diagnosis, as people may receive a diagnosis of epileptic or non-epileptic seizures when in fact they experience both. Therefore, understanding how early life events and individual differences interact in relation to seizure type is important to be able to increase understanding of the aetiologies of different seizure types, to improve recognition of individual differences that may be contributing to seizure experiences, and to indicate specific psychological therapies that can target these individual differences.

Research has established a link between childhood traumatic experiences and seizure type; high rates of traumatic experiences, particularly childhood trauma and abuse, are associated with non-epileptic seizures (Bodde et al., 2009; Cragar et al., 2002; Fiszman, Alves-Leon, Nunes, D'Andrea, & Figueira, 2004). Trauma history has also been associated with seizure frequency for people who have non-epileptic seizures but not for people who have epileptic seizures (Lally, Spence, McCusker, Craig, & Morrow, 2010). It is also important to consider the impact seizures have in a person’s life, which Corallo et al. (2013) said gives a clearer indication of the health of a patient. Therefore, this research will consider

the seizure outcomes of seizure type, seizure frequency, and impact of seizures on a person's life. This research will examine the relationship between these seizure outcome measures and childhood trauma. This research will also consider how individual differences in adult attachment styles, and emotion processing (alexithymia), influence the relationship between childhood trauma and seizure outcomes.

Bowlby (1988) proposed that the type of attachment relationship a child has with their main caregiver shapes the way that person relates to others throughout life (their attachment style). Bowlby suggested that the child forms an internal working model based on repeated experiences of the way the caregiver responds to the child's communication of their internal state or emotion, e.g. crying. Brennnan, Clark, and Shaver (1998, cited in Wei, Russell, Mallinckrodt, & Zakalik, 2004) developed a two-dimensional model of adult attachment style, consisting of attachment anxiety and attachment avoidance. In their model, high levels of attachment anxiety represent an excessive need for approval, and fear of rejection from others; high levels of attachment avoidance indicate excessive self-reliance and fear of being close to others in relationships. They suggest that people with low levels of attachment anxiety and avoidance are able to form secure attachments in their adult relationships.

Research indicates that adult attachment style mediates the relationship between trauma and various psychological difficulties. For example, a study found that adult attachment was a mediator between childhood abuse (especially psychological) and current symptomology including trauma related symptoms (Muller, Thornback, & Bedi, 2012). Another study found that attachment anxiety partially mediated the relationship between experiences of violence in relationships or sexual victimisation and posttraumatic symptoms (Sandberg, Suess, & Heaton, 2010); and Dimitrova et al. (2010) found that attachment mediated the relationship between experiences of child and adolescent sexual abuse and psychopathology.

Understanding the relationship of attachment to distress is important because adult attachment style has been recognised to impact on therapy outcomes and it has been suggested that therapy should be adapted to consider different styles (Jellema, 2000). Theoretically, Quinn, Schofield and Middleton (2008) propose that trauma, in the presence of non-validating attachment experiences, is one pathway which leads to the development of non-epileptic seizures. Attachment has not been widely studied in relation to non-epileptic seizures. Brown et al. (2013) did consider it, and did not find a significant difference in attachment style between two subgroups of people experiencing non-epileptic seizures and a group who experience epileptic seizures. However, they had difficulties with the sub-scale reliability of their attachment measure (Brown et al., 2013). A different measure will be used in this study, which has a strong theoretical basis and extensive reliability and validity data (Brenning, Van Petegem, Vanhalst, & Soenens, 2014; Picardi, Martinotti, Paci, Simi, & Caroppo, 2011; Wei, Russell, Mallinckrodt, & Vogel, 2007).

The concept of Alexithymia refers to a difficulty with the ability to recognise and describe feelings and external orientation of behaviour (R. Michael Bagby, Parker, & Taylor, 1994). Alexithymia has been identified as a mediator between trauma related predictors and various indicators of distress including: between trauma and diagnosis of personality disorder (Gaher, Hofman, Simons, & Hunsaker, 2013); between childhood emotional maltreatment and somatic complaints in young adults (Smith & Flannery-Schroeder, 2013); between childhood maltreatment and self-injurious behaviours (Paivio & McCulloch, 2004)

People who experience non-epileptic seizures have been found to have higher levels of alexithymia than those who experience epileptic seizures (Kaplan et al., 2013). A relationship between trauma symptoms and alexithymia has also been suggested for people who experience non-epileptic seizures (Myers, Matzner, Lancman, Perrine, & Lancman, 2013).

The concepts of alexithymia and emotion regulation are closely related (Gratz & Roemer, 2004). Cassidy (1994) proposes that the child develops their style of emotion regulation as an adaptive response to the way their caregiver interacts with them, and that the style of emotion regulation serves the function of maintaining the relationship with their caregiver. They also suggest that a child, who has experienced repeated rejection from their caregiver, and therefore, has an avoidant attachment style, minimises their emotions in order to avoid further rejection. However, a child whose caregiver has been unavailable or inconsistently available, and has developed an ambivalent or anxious attachment style, maximises their feelings, in order to increase the likelihood of getting a response from the caregiver.

Given this proposed link between childhood attachment style and emotional regulation, it is not surprising that research has found a relationship between adult attachment style and alexithymia. For example, low levels of alexithymia have been associated with a secure adult attachment style (Hexel, 2003). High levels of alexithymia have been associated with a fearful or anxious style of attachment (Troisi, Argenio, Peracchio, & Petti, 2001). Emotional competence, including alexithymia, has been indicated as a mediator or link between childhood psychological maltreatment and adult attachment style (Kapeleris & Paivio, 2011). Kapeleris and Paivio (2011) suggested that the reason for this link is that psychological abuse or neglect in childhood means that the child does not develop the skills to understand and manage their emotions, which makes it more difficult for them to relate to others in adulthood.

This research will investigate the relationships between the predictors: childhood trauma, alexithymia and adult attachment style, and the outcomes: seizure type, frequency and impact of seizures. Initially this will involve regression analyses to investigate the relationships between variables. If viable, this research may go on to investigate complex

models of the relationship between childhood trauma and seizure outcomes, such as, alexithymia and/or adult attachment style acting as mediators.

Hypothesis

The research hypothesis is that higher levels of childhood trauma will be associated with higher levels of alexithymia, adult attachment anxiety, and avoidance; seizure type of non-epileptic; increased seizure frequency; and greater impact of seizures.

Method

This research will use self-report questionnaires, a method which other researchers in the area have used. For example, Kaplan et al. (2013) used self-report questionnaires to ask people with epileptic or non-epileptic seizures about childhood trauma, alexithymia, and psychological defence strategies. Van Merode et al. (2004) used self-report measures of symptoms, childhood trauma, dissociative experiences, anxiety and coping. Lehavot and Simpson (2014) used a self-report online survey to ask female war veterans, a group who like those with non-epileptic seizures have elevated levels of depression, PTSD and trauma, about childhood trauma, assault, PTSD and depression symptoms. These researchers have not reported any ethical issues arising from the use of self-report measures.

Chase, Beatty and Ondersma (2011) found that reporting of childhood trauma is increased when participants are able to be completely anonymous. Therefore, no identifiers will be collected.

Participants

Researchers will recruit participants via advertising on online forums such as the PNES awareness discussion forum ("P.N.E.S. Awareness Discussion Forum," 2014), contacting support groups, such as Epilepsy Action (Epilepsy Action, 2014), advertising in

relevant clinics, such as NHS epilepsy clinics, and other appropriate locations. Other people, such as NHS staff, promoting the research on behalf of the researchers may also recruit participants indirectly. Inclusion criteria are:

- adults over the age of 18,
- who identify themselves as experiencing epileptic and/or non-epileptic seizures.

Exclusion Criteria

- level of English insufficient to understand the instructions and measures

  It is not possible to offer translation as not all measures are available in other languages and translation would be likely to impact on reliability and validity of measures.

Design

The study will use a quantitative cross sectional survey design. It will use convenience and snowball sampling.

Materials

This research will use the Qualtrics online survey platform and/or printed copies of the same materials to provide information, obtain consent and collect data. The study will use SPSS (or similar software) to the analyse data.

Measures

Demographic Questions

Participants will be asked their age, gender, and county of residence.

Childhood Trauma

The Early Trauma Inventory Self Report- Short Form (ETISR-SF), is available free

(D. Bremner, 2004, 2009). It has 29 items, on a trial; the ETISR-SF took 3 minutes to complete. It consists of four domains, which are physical, emotional, sexual abuse, and general trauma. It has been tested for validity using a large sample of 288 people, which included healthy controls (28%) and people with a variety of psychiatric disorders including PTSD, depression and borderline personality disorder, 11% of the sample had a psychiatric disorder with a history of abuse (J. D. Bremner, Bolus, & Mayer, 2007).

Attachment

The experience in close relationships (ECR) short form has 12 items, and it assesses attachment anxiety and attachment related avoidance. Its factor structure, reliability and validity has been assessed (Wei et al., 2007). Its validity has been tested using clinical and non-clinical populations, including patients with drug-resistant epilepsy (Alessandri et al., 2014; Wongpakaran & Wongpakaran, 2012)

Alexithymia

The Toronto Alexithymia scale (TAS-20) has 20 items, and costs £35 (Taylor, 2014). Its factor structure, reliability and validity has been assessed (Wei et al., 2007). It has been validated for use in a wide variety of clinical and non-clinical populations including somatoform disorders (which are related to non-epileptic seizures) and psychiatric inpatients, as well as using internet administration (Bach & Bach, 1996; R. M. Bagby, Ayearst, Morariu, Watters, & Taylor, 2014; Caretti et al., 2011)

Seizure Frequency and type

The seizure type part of the outcome will be identified by participants' self-reports of experiencing epileptic, and/or non-epileptic seizures. For the seizure frequency part of the outcome participants will be asked to report the number of seizures they experience in a

month.

Impact of seizures

The revised Liverpool impact of epilepsy scale is a measure of the impact of seizures on daily life. It has 12 items and the researcher estimates it to take 2-3 minutes to complete. The scale has been found to have good reliability and acceptable validity (Crossley, Jacoby, & Baker, 2012).

Expected completion time of measures

Table 1, below summarises the measures and expected completion times

Measure	**Items**	**Expected completion time**
ECR-short form	12	3 minutes, based on test completion by researcher
TAS-20	20	4 minutes, estimate by researcher
ETISR-SF	29	3 minutes, based on test completion by researcher
Revised Liverpool impact of epilepsy scale	12	3 minutes estimate by researcher
Demographic questions, seizure type & frequency	8	2 minutes, estimate by researcher
Total	**81**	**15 minutes**

Procedure

The researchers will contact NHS and private clinics, support groups, and online forums that people who experience epileptic and/or non-epileptic seizures are likely to be in contact with, and ask if they are willing to support with the recruitment of participants. Following gaining any necessary ethical and R&D approval for each setting, the researcher will provide them with materials in order to promote the study. This will include posters,

electronic adverts, participant information sheets, and printed study packs. The way the clinic, forum or support group supports recruitment will be at their discretion. This may range from allowing the researcher to display posters or electronic adverts, to giving out or posting packs to potential participants. This would not involve the researchers having access to any personal information or records related to potential participants.

The adverts and posters will explain the options available to participants if they wish to take part. The options will be to complete the survey online, or on paper.

Potential participants wishing to access the survey online will access the Qualtrics site via a link, which will give details of the research on a participant information page, enabling them to give informed consent if they wish to participate. The Qualtrics survey site will guide them through several pages including basic demographics and questions about their seizures. People who answer these questions in a way that indicates it is not appropriate for them to participate will be given explanation of this and then transferred directly to the support information, end of study page. This will happen if a person indicates they do not understand the participant information, they are under 18 or do not experience seizures. Those who are not redirected will then progress onto completing the measures. The support information, end of study page will include the contact details of relevant support groups and other sources of assistance, should the participant become distressed. There will also be a link to exit directly to this page from every page of the study. The host survey site will collect data anonymously, and store it electronically and securely.

Participants wishing to take part using paper forms will access a printed pack including the same information as on the survey site. The researcher will provide relevant contacts with copies of the printed pack to pass on to potential participants, packs will be left alongside posters, and potential participants will have the option to print out their own pack from the survey site. The information in the postal pack will be adapted to explain that

posting the forms to the researchers will indicate consent, thus negating the need to collect any identifiers on consent forms. The pack will include a freepost address in order for participants to return their questionnaires to the researcher.

Participants will be asked to pass on information about the research to others who may be interested.

Proposed analysis

The researchers will complete regression analyses on the data. The researcher may use other types of statistical analyses on the anonymous data instead of, or in addition to the regression analysis depending on data obtained and number of participants. Following the regression analyses the researchers will consider using the data to test more complex models, for example, mediation models, using structural equation modelling.

Power calculation

This research expects to find medium effect sizes (0.39) as studies considering childhood trauma, alexithymia and attachment have found medium to large effect sizes (Carpenter & Chung, 2011; Paivio & McCulloch, 2004). Including the demographic variables there are six predictors. Therefore, based on tables provided by Field (2013, p. 314) the minimum sample size to achieve a power of 0.8 (80% chance of rejecting the null hypothesis if it is false), and a medium effect size is 98.

Practical issues (e.g., costs/logistics)

The sponsor, who will also cover costs related to printing of research materials by the researchers, and freepost return address, will meet the cost of £35 for the use of measures.

Ethical concerns

Some of the people this study aims to recruit are likely to be people who experience high levels of distress in their lives. It is possible that completing measures related to their life experiences and emotions may remind people of their distress. In order to address this issue, prior to starting the measures, potential participants will be given an explanation of the types of questions they will be asked so they can make an informed decision about whether they would like to participate or not. In addition, the researchers will not give any individual feedback on responses. Participants will be made aware they can stop completing the measures or miss out questions at any point. A debriefing screen or sheet highlighting relevant support organisations e.g. Samaritans will be provided.

Timescale

See attached Gant Chart for timescales.

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Thank you, results, forwarding, and support information

Thank You!

Thank you for completing the survey, the time you have spent is appreciated. The researchers hope it will lead to improvements for people who experience epileptic and non-epileptic seizures.

Results

If you would like the researchers to send you a copy of the overall results of the study, please fill in the tear off slip, and send it **in a separate envelope to your questionnaires.**

Forwarding the study

If you know anyone else who experiences epileptic and/or non-epileptic seizures and may want to participate, the researchers would appreciate it, if you pass on details about the survey.

A poster is included in the pack for you to pass on as you wish

Support Information

You may find the following support sources helpful:

- Talking to someone you know and trust
- Contacting the NHS on 111 (UK)
- Speaking to your doctor or other health professionals
- Calling the Samaritans (UK and ROI)
    - http://www.samaritans.org
    - 08457 90 90 90 * (UK)

- 116 123(ROI)

- Calling the Epilepsy Society Helpline 01494 601 400 (UK)

For further information and support related to epileptic and non-epileptic seizures, the following websites may be helpful:

Epileptic seizures:

NHS Choices: http://www.nhs.uk/conditions/Epilepsy

Epilepsy Society http://www.epilepsysociety.org.uk

Epilepsy Action https://www.epilepsy.org.uk/

Non-epileptic seizures:

Information about non-epileptic seizures http://www.nonepilepticattacks.info

Information about functional symptoms including seizures (click on blackouts / attacks) http://www.neurosymptoms.org

Information on the epilepsy society website

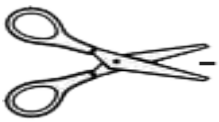
http://www.epilepsysociety.org.uk/non-epileptic-seizures

NEAD Trust Facebook page

https://www.facebook.com/pages/NEAD-Trust/101554536567742

PNES awareness facebook discussion forum

https://www.facebook.com/groups/153086878071352/



I would like to be sent a copy of the results of the study.

Please send it to (name and email or postal address):

_____

_____

Please return this form, **in a separate envelope to your questionnaires,** to:

Liz Tallentire, FREEPOST: RTAU-SYXU-YCZZ, Clinical Psychology,

Furness College, Bailrigg, LANCASTER, LA1 4YG

[redacted]

Health Research | Lancaster University

Do you experience seizures?

Would you like to help increase understanding about seizures and their impact on people's lives?

Then you may want to take part in my research

Hello, my name is Liz Tallentire and I'm in my final year of training as a clinical psychologist

My research involves completing a short anonymous survey. If you are interested in participating and would like to know more take a card below with the link,
pick up a pack from ...(insert detail)
or go to www.....(insert link)

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

4.50

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

[redacted]

Health Research | Lancaster University

For more information about my seizure research go to www………….(insert link)

or scan this code with your mobile

Thank you
Liz Tallentire
Trainee Clinical Psychologist

22/12/14 V1

Online Forum advert

Hello, my name is Liz Tallentire and I'm in my final year of training as a clinical psychologist at Lancaster University, UK. I'm looking for people who have experienced seizures to take part in my research. I'm aiming to increase understanding about seizures and their impact on people's lives. The research involves completing a short anonymous survey. Please click here if you are interested in participating and would like to know more. (link to online survey site to be included)

Below are some screen shots illustrating what the survey will look like online. The separate file 'Online Survey Questions' illustrates the text for each question, but not the formatting. Not all questions will be displayed to all potential participants. Survey logic and flow will be used to divert people whose answers indicate they should not take part and to hide irrelevant questions and information. There may be some minor adjustments to the online survey, for example, the order of questions on the Experiences in Close Relationships questionnaire will be altered to match the printed version.

[redacted]

Health Research | Lancaster University

What country do you live in?

What Gender are you?

- Male
- Female
- Transgender
- Other Gender
- Prefer not to say

0% 100%

<< Back Next >>

If you become distressed or you want to exit the survey for any other reason

click here to exit

Survey Powered By Qualtrics

[redacted]

Health Research | Lancaster University

We would like to know how much you feel the attacks you have had affect your everyday life. For each item listed, please click the option which shows best how you feel.

Thinking about the attacks you have had,
do you feel they have affected for better or worse :

	Very much for the better	Somewhat for the better	No difference	Somewhat for the worse	Very much for the worse	Does not apply
a) Your relationship with your spouse/partner?	●	●	●	●	●	●
b) Your relationship with other close members of your family?	●	●	●	●	●	●

Area of work/ deadline	Jun-14	Jul-14	Aug-14	Sep-14	Oct-14	Nov-14	Dec-14	Jan-15	Feb-15	Mar-15	Apr-15	May-15	Jun-15	Jul-15	Aug-15	
Literature review section:																
Reviewing Literature for critical review	m	m	m	h							**Key:**					
Write up literature review section				m	h	h	h									
1st draft deadline						14th					**Demands on time**					
2nd draft deadline							19th									
Research paper section:											**L = low**					
Reviewing literature for introduction/protocol				m							**M = medium**					
Prepare ethics application, protocol and other documents				h	h						**H = High**					
Submit to university to check and then NHS ethics					31st						**number = date of deadline or event**					
Set up online survey system					h	h										
Promote project to support groups, nhs and other services							*	h	h							
Data collection							*	m	m							
Analyse data									h	h						
Write up research paper introduction and methods						m										
1st draft deadline for intro and methods							5th									
Write up research paper results and discussion										h	h					
1st draft deadline for results and discussion											10th					
2nd draft deadling for whole empirical paper												1st				
Critical appraisal:																
Write critical appraisal										h	h	m				
1st draft deadline											24th					
Submit papers for publication														m	m	
* start as soon as ethical approval received																

CURRICULUM VITAE

Name:	
Liz Tallentire	
Present appointment:	
Trainee Clinical Psychologist	
Address:	
26 Bainbridge Road, Sedbergh, Cumbria, LA10 5AU	
Telephone number:	**Email address:**
07539 294316	l.tallentire@lancaster.ac.uk
Qualifications:	
MA Leadership and Management in Integrated Children's Services (2011) BSc (Hon) Psychology (2005) Diploma Life Sciences (2005) Level 5 Certificate Supervision Skills (2010) NVQ Level 3 Promoting Independence (2003) CACHE Level 3 Diploma Support Work in Schools (Pilot)(Parent Support) (2008) Level 4 module Preparing to Teach in the Life-long Learning Sector (2010) 'A' Levels: Mathematics, Further Mathematics, Biology, Chemistry, General Studies	
Professional registration:	
Previous and other appointments:	
Volunteer Psychology Assistant 2010 - 2012 Principal Family Worker 2011 - 2012 Supported Lodgings Provider 2009 – 2012 Parent Support Adviser Coordinator 2008 – 2011 Parent Support Adviser 2007 – 2008 Day Service Worker Level 2 Qualified 2001 - 2007 Home Care Assistant 1999 - 2000	
Research experience:	
I successfully completed a study as part of my current course, which involved working with, and interviewing people who live in a secure service for people with learning disabilities. Because of this study, I have spoken at several conferences including the International Conference on the Care and Treatment of Offenders with an Intellectual or Developmental Disability. I completed mixed methods service evaluation research as part of my post as Parent Support Adviser Coordinator. I have carried out research as part of my undergraduate and masters qualifications.	
Research training:	
I am in the final year of my doctorate in clinical psychology; this course has included teaching on research skills. My Masters Qualification included taught modules on research philosophy and methodology as well as completion of research for the dissertation. My undergraduate degree also involved practical and taught research elements.	
Relevant publications:	
In my role as Parent Support Adviser Coordinator I have completed the following reports which have been disseminated: Parent Support Adviser Coordinator Evaluation (2010) PSA Coordinators Locality Report Durham Dales (2009) Parent Support Adviser Coordinator Supervision Evaluation (2009)	
Signature:	**Date:**
Liz Tallentire	14/01/15

Dr Ian Fletcher CV

Current post - Senior Lecturer in Clinical Psychology, Lancaster University

Doctorate in Clinical Psychology, Division of Health Research
Furness College, Lancaster University LA1 4YG

Research Interests
Health provider-patient communication, cancer, migration and health, attachment, emotional intelligence.

Qualifications
PhD. University of Manchester, 2006
MSc. Applied Psychology, University of Manchester, 2001
BSc (Hons) Psychology, University of Central Lancashire, 1995

External examiner
Staffordshire & Keele University, Doctorate in Clinical Psychology

Reviewer
National Institute for Health Research (NIHR) - applications
Patient Education and Counseling - journal
BMC Medical Education - journal
Clinical Ethics – journal
Personality & Individual Differences - journal

Research Grants
2007 €57000 'An eye for quality – the patient as a research partner'
International study (Belgium, Italy, Netherlands, and UK)
Funder: Netherlands 'Patient Oriented Research' charity
2010 £95000 'Can high-quality evidence-based information about emotional reactions to cancer empower patients to manage their emotional problems more effectively? A pilot study.' Funder: Liverpool PCT
2011 £5000 'Cultural health beliefs of the Chinese community in Merseyside'
Funder: Knowledge Exchange, University of Liverpool
2012 £20000 'Pathways to health among Chinese populations in Liverpool and Manchester'
Funder: Liverpool PCT

Publications

Cherry MG, Fletcher I, O'Sullivan (2013) The influence of medical students' and doctors' attachment style and emotional intelligence on their patient–provider communication. *Patient Education and Counseling;* doi.org/10.1016/j.pec.2013.05.010

Cherry G, Fletcher I, O'Sullivan H (2013) Exploring the relationships between attachment, emotional intelligence & communication. *Medical Education;* 47: 317-325

Baker P, Beesley H , Dinwoodie R, Fletcher I, Ablett, J, Holcombe, C, Salmon, P (2013) 'You're putting thoughts into my head': a qualitative study of the readiness of patients with breast, lung or prostate cancer to address emotional needs through the first 18 months after diagnosis. *Psycho-Oncology*; 22: 1402-1410 2

Mazzi M, Bensing J, Rimondini M, Fletcher I, van Vliet L, Zimmermann C, Deveugele M (2013) How do lay people assess the quality of physicians' communicative responses to patients' emotional cues and concerns? An international multicentre study based on videotaped medical consultations. *Patient Education and Counseling*; 90: 347-353

Mazzi M, Rimondini M, Deveugele M, Zimmermann C, Moretti F, van Vliet L, Deledda G, Fletcher I, Bensing J (2013) What do people appreciate in physicians'communication? An international study with focus groups using videotaped medical consultations. Health Expectations; doi: 10.1111/hex.12097

Huntley CD, Salmon P, Fisher PL, Fletcher I, Young, B (2012) LUCAS: A theoretically informed instrument to assess clinical communication in objective structured clinical examinations. *Medical Education;* 46: 267-276

Cherry G, Fletcher I, Shaw N, O'Sullivan H, Shaw N (2012) What impact do structured educational sessions to increase emotional intelligence have on medical students? BEME Guide No.17. *Medical Teacher*; 34: 11-19

Moretti F, Fletcher I, Mazzi M, DeVeugele M, Rimondini M, Geurts C, Zimmermann C, Bensing J (2011) GULiVER—travelling into the heart of good doctor–patient communication from a patient perspective: study protocol of an international multicentre study. *European Journal of Public Health*; doi:10.1093/eurpub/ckr071

Bensing J, Deveugele M, Moretti F, Fletcher I, Zimmermann C, van Vliet E, Van Bogaert M, Rimondini M (2011) How to make the medical consultation more successful from a patient's perspective? Tips for doctors and patients from lay people in the United Kingdom, Italy, Belgium and the Netherlands. *Patient Education and Counseling*; 84:287-293

Moretti F, van Vliet L, Bensing J, Deledda G, Mazzi M, Rimondini M, Zimmermann C, Fletcher I (2011) A standardized approach to qualitative content analysis of focus group discussions from different countries. *Patient Education & Counseling*; 82:420-428

Fletcher I, Mazzi M, Nuebling M (2011) When coders are reliable: the application of three measures to assess inter-rater reliability/agreement with doctor-patient communication data coded with the VR-CoDES. *Patient Education & Counseling*; 82:341-345

Fletcher I, Leadbetter P, Curran A, O'Sullivan H (2009) A pilot study assessing emotional intelligence training and communication skills with 3rd year medical students. *Patient Education & Counseling*; 76:376–9

Pitceathly C, Maguire P, Fletcher I, Parle M, Tomenson B, Creed F (2009) Can a brief psychological intervention prevent anxiety or depressive disorders in cancer patients? A randomised controlled trial; *Annals of Oncology*, 20:928–34

Connor M, Fletcher I, Salmon P (2009) The analysis of verbal interaction sequences in dyadic clinical communication: A review of methods. *Patient Education & Counseling*; 75(2):169-177

Kitchener HC, Fletcher I, Roberts C, Wheeler P, Almonte M, Maguire P (2008) The psychosocial impact of human papillomavirus testing in primary cervical screening—a study within a randomized trial. *International Journal of Gynecological Cancer*; 18:743-8

Lancaster Doctorate in Clinical Psychology

Thesis feedback form

The purpose of this form is to record feedback on the discussions from the thesis presentation day. Please complete the details for the form as soon as possible after your presentation and email it to a member of the presentation panel for approval. The staff member will then forward it to the research coordinator.

You are then encouraged to share this with your field supervisor (if appropriate) and your research support person in order to develop your proposal. Please remember that it is not the role of the presentation panel to 'approve' or otherwise your proposal. The aim of the presentation panel is to provide feedback on the proposal and discuss practical and ethical issues. You will need to consider how to respond to these points when discussing your proposal further with your supervisors.

Trainee name	Liz Tallentire
/Date of presentation	26/3/14
Research team members present	Ian Fletcher, Craig Murray
Title of proposed thesis: Predictors relevant to seizure experience	
Field supervisor's name and contact details (if appropriate)	

Necessary changes/actions: These suggestions must be taken forward in order for the project to be viable.
Further discussions: These recommendations are optional and should be discussed with your academic supervisor.

<table>
<tr><td colspan="2"><u>Comments on Thesis content area</u>
There was a discussion around whether the literature review Liz wishes to complete in order to inform a model she can then test using multiple regression analysis could be used as the literature review for the thesis.
Ian F thought this would be OK as it would be publishable in its own right and would be to be quite broad and include Medically Unexplained Symptoms more generally due to lack of literature.
There was discussion of the clinical relevance of the study; Liz hopes this will contribute to identifying appropriate psychological support for people affected by these experiences. It may also contribute to understanding of non-epileptic seizures and their identification being more accurate and/or cost effective.</td></tr>
<tr><td>Necessary changes/action:
I will need to come up with a question for my literature review, which will be separate from the research question for the empirical part.
I was thinking of:
What are our understandings and evidence about how non-epileptic seizures develop and are maintained? This would be a mixed methods literature review (action not discussed in review session)</td><td>Further considerations:</td></tr>
<tr><td colspan="2"><u>Comments on Thesis methodology</u>
Liz asked for advice on her plans to complete literature review in order to develop a model as no suitable one seems to be available which she can then test.
Ian F explained. Two options available a) model (theory) driven b) exploratory. Also possible to try a) first and then do b) if this does not work
Ian suggests literature review could be completed alongside empirical part, predictors can be identified beforehand, and then the literature review can inform how these are likely to interact.</td></tr>
<tr><td>Necessary changes/action:</td><td>Further considerations:</td></tr>
<tr><td colspan="2"><u>Comments on analysis</u>
none</td></tr>
<tr><td>Necessary changes/action:</td><td>Further considerations:</td></tr>
<tr><td colspan="2"><u>Comments on practical and ethical issues</u>
Ian prefers Liz to have an external field supervisor</td></tr>
<tr><td>Necessary changes/action:
Liz to discuss possibility with the people she has identified. Ideally field supervisor to be someone working in NHS who has contact with people who experience seizures.</td><td>Further considerations:</td></tr>
</table>

☐ Please put a tick in this box if it is decided that the project must be brought back to another peer review

ZURICH
MUNICIPAL

To Whom it may Concern

Your reference

Our reference MH

Date 04/08/2014

Professional Indemnity Insurance To whom it may concern

Zurich Municipal
1 East Parade
Leeds
LS1 2BQ
Phone 0113 242 7742
Mobile 07730 735 395

http://www.zurich.com

Dear Sirs

This is to confirm that the Lancaster University have Professional Indemnity cover in place with ourselves with effect from the 1st of August 2014, the policy is renewable on the 31st of July, 2015. Cover will be in place until at least 31st July 2017.

The Policy Number is NHE07CA04-0013. Cover is in place with a limit of Indemnity of at least £1m.

Please do not hesitate to contact me should you require any additional information.

Yours Sincerely

M I Horsfield
Assistant Sales Manager Education.

ZURICH®
MUNICIPAL

Certificate of Employers' Liability Insurance(a)

(Where required by regulation 5 of the Employers' Liability (Compulsory Insurance) Regulations 2008 (the Regulations), a copy of this certificate must be displayed at all places where you employ persons covered by the policy or an electronic copy of the certificate must be retained and be reasonably accessible to each employee to whom it relates).

Policy No.	NHE-07CA04-0013
1. Name of policy holder	Lancaster University
2. Date of commencement of insurance policy	1st August 2014
3. Date of expiry of insurance policy	31st July 2015

We hereby certify that subject to paragraph 2:

1. The policy to which this certificate relates satisfies the requirements of the relevant law applicable in Great Britain, Northern Ireland, the Isle of Man, the Island of Jersey, the Island of Guernsey and the Island of Alderney **(b)**

2. **(a)** the minimum amount of cover provided by this policy is no less than £5 million **(c)**

Signed on behalf of Zurich Insurance plc (Authorised Insurer).

Signature

S. Lewis

Stephen Lewis

Chief Executive Officer Zurich Insurance plc, UK Branch.

Notes

(a) Where the employer is a company to which regulation 3(2) of the Regulations applies, the certificate shall state in a prominent place, either that the policy covers the holding company and all its subsidiaries, or that the policy covers the holding company and all its subsidiaries except any specifically excluded by name, or that the policy covers the holding company and only the named subsidiaries.

(b) Specify applicable law as provided for in regulation 4(6) of the Regulations.

(c) See regulation 3(1) of the Regulations and delete whichever of paragraphs 2(a) or 2(b) does not apply. Where 2(b) is applicable, specify the amount of cover provided by the relevant policy.

ZURICH
MUNICIPAL

To Whom it may Concern

Your reference

Our reference MH

Date 04/08/2014

Public Liability Insurance To whom it may concern

Zurich Municipal
1 East Parade
Leeds
LS1 2BQ
Phone 0113 242 7742
Mobile 07730 735 395

http://www.zurich.com

Dear Sirs

This is to confirm that the Lancaster University have Public Liability cover in place with ourselves with effect from the 1st of August 2014, the policy is renewable on the 31st of July, 2015. Cover will be in place until at least 31st July 2017.

The Policy Number is NHE07CA04-0013. Cover is in place with an indemnity Limit of at least £15m

Please do not hesitate to contact me should you require any additional information.

Yours Sincerely

M I Horsfield
Assistant Sales Manager Education.

Research and Enterprise Services Division | Lancaster University

Applicant name: Liz Tallentire
Supervisor: Dr Ian Fletcher
Department: DHR

16 January 2015

Dear Liz and Ian,

Re: Relationships between early life events, individual differences, and seizures

The University of Lancaster undertakes to perform the role of sponsor in the matter of the work described in the accompanying grant application. The sponsor as we understand it assumes responsibility for monitoring and enforcement of research governance. As principal investigator you will confirm that the institution's obligations are met by ensuring that, before the research commences and during the full term of the grant, all the necessary legal and regulatory requirements in order to conduct the research are met, and all the necessary licenses and approvals have been obtained. The Institution has in place formal procedures for managing the process for obtaining any necessary or appropriate ethical approval for this grant. Full ethical approval must be in place before the research commences and should be reviewed at all relevant times during the grant.

Yours sincerely,

Fiona Aiken,
University Secretary,
Chair, University Research Ethics Committee.

Cc Sarah Taylor, Secretary, UREC.

Lancaster University
Research and Enterprise
Services Division

Lancaster University
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