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The impact of receiving a diagnosis of Non-Epileptic Attack Disorder (NEAD): A systematic review.

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Abstract

Background: Clinicians have reported observations of the immediate cessation of non-epileptic attacks after the diagnosis of NEAD is presented.

Objective: The purpose of this systematic review was to examine the impact of receiving a diagnosis of NEAD.

Search strategy: A literature search across the databases Medline, PsycINFO, EMBASE, and CINAHL, and additional hand searching, identified 6 original studies meeting criteria for the review.

Selection Criteria: Included studies were original peer-reviewed articles investigating the impact of receiving a diagnosis of NEAD on adult populations with at least one outcome measured pre and post-diagnosis.

Analysis: The studies were assessed for methodological quality, including biases. This assessment was developed to include criteria specific to research regarding NEAD and diagnosis.

Results: Six identified studies, with a total of 153 NEAD participants, examined the impact of receiving a diagnosis on seizure frequency. Two of the six also examined the impact on health-related quality of life. The findings were inconsistent, with approximately half the participants experiencing seizure reduction or cessation post-diagnosis. Diagnosis appeared to have no significant impact on health-related quality of life. The overall evidence lacked quality, particularly in study design and statistical rigour.

Conclusions: Mixed results and a lack of high quality evidence was found. Concerns are considered regarding the appropriateness of seizure frequency as the primary outcome measure and the use of epilepsy control groups. Indications for future research include: measuring more meaningful outcomes, using larger samples and power calculations, and ensuring consistent and standard methods for communicating the diagnosis and recording outcomes.

Keywords: Diagnosis, Non-Epileptic Attack Disorder, Prognosis, Psychogenic Non-Epileptic Seizures, Systematic Review.

1. Introduction

Non-epileptic attack disorder (NEAD) is the diagnostic term for people who experience non-epileptic attacks [1], also commonly referred to as Psychogenic Non-Epileptic Seizures (PNES). Although many terms have been used historically [2], in this review the terms non-epileptic attacks and NEAD will be adopted. Non-epileptic attacks have been defined as: episodes of altered behaviour which resemble epileptic seizures but are absent of the characteristic clinical and electrographic features of epilepsy [3].

Whilst epilepsy is caused by excessive discharges in the brain, Non-epileptic attacks (when other physiological causes are ruled out) are considered to have psychological causes [4]. Although there is no universally accepted theory [5], attacks are widely thought to occur in response to overwhelming distress triggered by difficult situations, thoughts, and emotions [6]. With NEAD patients mainly entering neurology services, the involvement of psychology has been delayed. With growing clinical and academic interest [7], it is anticipated that theoretical understanding and clinical implications will develop.

It has been estimated that 20% - 30% of patients in neurology clinics for suspected epilepsy actually have NEAD [8,9]. Due to the topographical similarities, NEAD is often misdiagnosed as epilepsy, leading to inappropriate and potentially damaging treatment with antiepileptic drugs [10]. It takes an average of seven years before a revised NEAD diagnosis is reached [11]. To remedy this much of the research effort has focused on developing and validating a robust method for the differential diagnosis of NEAD [12]. The method of diagnosis considered the gold standard for sensitivity and specificity involves video-electroencephalogram (V-EEG) monitoring, whereby the electroencephalogram (EEG) records brainwave activity which is considered in conjunction with the clinical characteristics of the seizures observable on the video [13,14]. However, to complicate diagnosis and appropriate treatment, research using V-EEG data suggests that NEAD is co-morbid in up to 10% of epilepsy patients [15,16]. Research into treatment for NEAD has only recently received the attention of systematic reviewers, concluding that high quality evidence for effective treatments is lacking [17,18].

With comprehensive psychological theories and treatments yet to be established, clinicians often lack a good understanding of NEAD [19]. Consequent inadequate (potentially stigmatising) explanations to the patient can lead to confusion, anger, and disagreement with the diagnosis. Such reactions were associated with a poorer prognosis in terms of attack frequency and severity, and quality of life [19]. To provide clinicians with an adequate and non-stigmatising explanation for patients, several protocols have been developed [20-22].

1.1. Rationale

Within the literature, receiving a NEAD diagnosis is often referred to as the first stage of treatment [23-25]. This appears based on observations by clinicians that diagnosis can be interventive. Over the years clinicians have observed the communication of the diagnosis to result in the immediate cessation of attacks in some patients, negating the need for further treatment [e.g. 10,26]. To the author's knowledge research has not attempted to explain this phenomenon, or the difference between those whose attacks cease and those whose attacks continue. As with many aspects of NEAD, theory development has fallen short, with categorisation taking its place [27-29].

Being aware of the reports that receiving a diagnosis can reduce/eliminate seizures, neurologists may be more considered with their communication of the diagnosis, seeing it as a possibly effective therapeutic task. On the other hand, it may perpetuate the historic perception of non-epileptic attacks being considered factitious/malingering [30].

As the role of neurology post-diagnosis is yet to be widely agreed and implemented [31], these reports may serve to support services decisions to discharge patients from neurology upon diagnosis and offer no follow-up or formal pathway into psychology services. This lack of agreement on the role of neurology post-diagnosis is one factor contributing to the slow progress in establishing standard and effective management for patients [32].

With the reports of diagnosis having a positive impact being well known and perhaps influential, it is important to consider the evidence as a whole before any conclusions should be made.

1.2. Aims

This review aims to synthesise the evidence regarding the impact of receiving a diagnosis of NEAD. The purpose of this review is to ascertain what the diagnosis impacts on, and whether the evidence is sufficient to draw any specific conclusions regarding the therapeutic effect of diagnosis.

2. Method

2.1. Searching

As previously noted the variation in terminology used in place of non-epileptic attacks and NEAD necessitated a comprehensive and inclusive search approach. Also, due to the paucity of literature in this area, historically used terms now deemed pejorative, such as hysterical seizures, and terms encompassing many phenotypes, such as somatoform disorders, were also included. For searching the databases, groups of terms relevant to two specific elements of the question were combined: non-epileptic attacks and NEAD; and diagnosis and outcome.

Electronic searches were as follows:

- CINAHL (1981 to July, week 3, 2014);
- EMBASE (1980 to 2014 Week 29);
- Medline (1947 to July week 3, 2014); and
- PsycINFO (1910 to July week 3, 2014).

The chosen databases include research literature from social science, nursing, and medical professions. Covering this range of disciplines was necessary due to the changing conceptualisation and continued variation in the management of NEAD patients. For full search strategies see supplementary information (online only). Additionally, the reference lists of included studies and several relevant reviews [5,38,39] were hand searched.

2.2. Selection

In order to meet the aims of the review, a priori inclusion and exclusion criteria were developed.

Literature was included if it:

- Was original research.
- Included adult participants.

- Explored the impact of receiving a diagnosis of NEAD (or one of its other known terms) with the requirement that seizures with psychogenic non-epileptic origin rather than other medical causes were identified.
- Included one or more outcome measure with data recorded/collected pre and post diagnosis.
- Was written in English (due to the constraints of the study translation was not possible).

Literature was excluded if it:

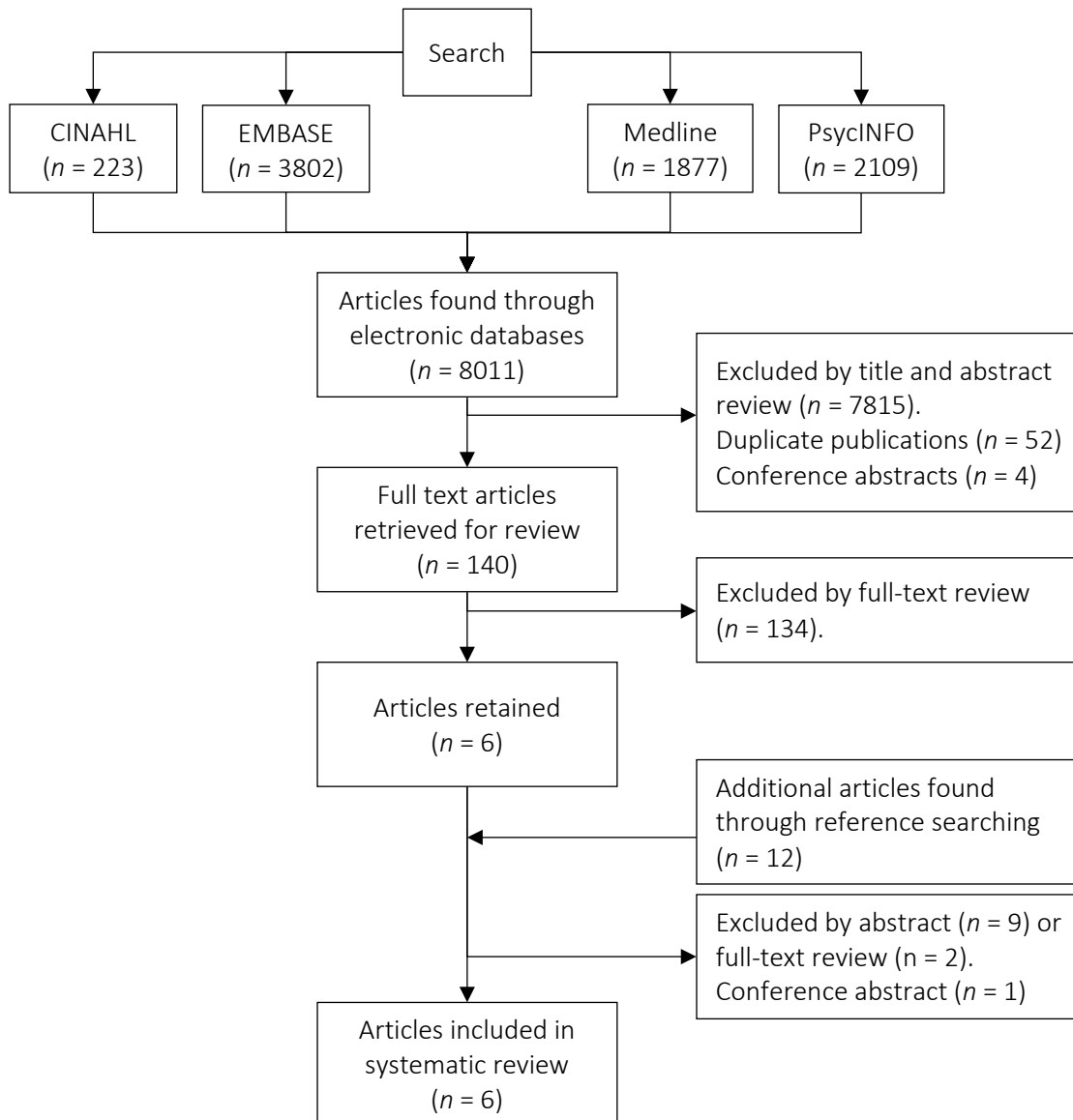
- Did not specify that the diagnosis was the only 'intervention' before outcome data was collected, or if active treatment/intervention was reported following the delivery of the diagnosis and before follow-up data was collected.
- Was not published in a peer-reviewed journal.
- Was not an article length representation of the study (required to assess quality).

A total of 8,011 articles were identified. The first author reviewed the titles and abstracts of articles for relevance. Articles were excluded at this stage for obvious violations of the inclusion criteria including: unrelated subject matter, papers other than original research and research with non-NEAD populations e.g. other somatoform disorder types. 196 papers remained after this process, 144 after duplicates were removed.

Some articles remained due to the information in the abstract not allowing suitability to be determined, or because no abstract was immediately accessible. Four publications were found to be conference abstracts and were therefore excluded. The authors reviewed full texts for the remaining 140 articles to determine eligibility. Further papers were excluded for the obvious violations of inclusion criteria and other reasons including: active treatment before follow-up, presence of treatment not specified, retrospective data collection, and baseline data collected post-diagnosis.

Hand searching of the six included studies [26,33-37] and relevant reviews [5,38,39] identified 12 additional potential studies, with three remaining after the initial abstract sift. Of these, one was a conference abstract and two were excluded when the full-text was reviewed.

2.3 Summary of search and selection process



3. Results

3.1. Data abstraction

General characteristics were abstracted from the six studies, including: publication year, sample size, outcomes measured, and method of analysis. Additional characteristics relating to the sample and the control group (if applicable) were also recorded. Finally, the findings of each study were abstracted and summarised. All abstracted data are detailed in Table 1.

3.2. Outcomes measured

3.2.1. Seizure frequency¹

Seizure frequency was measured in all of the studies but included a variety of methods of measuring/recording frequency. Three of the six studies recorded frequency of seizures in numerical form [26,35,36]. Three of the studies used a ranking system of seizure frequency (e.g. none, rare, or regular; monthly, weekly, or daily) [33,34,37]. The method of recording was less clear post-diagnosis; with most studies reporting whether seizure frequency had ceased fully, increased, decreased, or remained the same.

3.2.2. Health-related Quality of Life

Health-related quality of life was measured in two of the six studies [35,37], both using Quality of Life In Epilepsy inventories, QOLIE-31 and QOLIE-10 [40,41]. The QOLIE-31 is a measure of life satisfaction specific to patients with seizures although not specifically non-epileptic seizures. Scores range from 15-100 with a higher overall score representing better health-related quality of life. Within the measure are seven subscales: seizure worry, overall quality of life, energy/fatigue, emotional well-being, cognitive functioning, social life, and medication effects. Psychometric testing using a sample of 304 adults with epilepsy found the lowest internal consistency on the social functioning subscale (0.77) and the highest on the cognitive functioning subscale (0.85) [40]. The QOLIE-10 was found to be highly correlated with the QOLIE-31 concluding that it could be used as a time saving alternative [41].

¹ Seizure frequency will be the term used when reporting directly on reviewed studies, this is to ensure reporting accuracy and also due to the use of epilepsy control groups in some of the studies.

Table 1. Characteristics of included studies

Primary author Publication year Reference	Sample with NEAD			Control group [N, event type, sex, mean age (range)]	Methodology Design Analysis	Outcomes measured	Data collection points	Key findings
	<i>N</i>	<i>Sex</i>	<i>Mean age (range)</i>					
Duncan 2011 [33]	54	44F, 10M	32.6 (NR)	None	Quantitative Prospective audit Inferential statistics*	Seizure frequency	Baseline (pre), 3months (post), and 6 months (post)	24/54 (44%) immediate cessation post diagnosis.
Farias 2003 [26]	22	14F, 8M	40.36 (NR)	10, ES, 4F 6M, 37.10 (9.64)	Quantitative Repeated measures Inferential statistics	Seizure frequency	24 hours either side of diagnosis	21/22 (95%) reduced including 18/22 (82%) total cessation, 3/22 (13%) 50% reduction.
Scheepers 1994 [34]	27	20F, 7M	NR	None	Quantitative Retrospective audit Descriptive statistics	Seizure frequency	Pre and post diagnosis	12/27 (44%) increase in frequency, 15/27 (56%) reduction or same frequency.
Thompson 2013 [35]	19	11F, 8M	33 (18-66)	NR (sample of 19 split), NEAD, NR	Quantitative RC pilot Inferential statistics	HRQoL, Seizure frequency and intensity	Baseline (pre) and 6-8 weeks (post)	No significant differences in seizure frequency or HRQoL pre and post, or between intervention and control group.
Wyllie 1991 [36]	20	17F, 3M	34 (25-56)	Comparison group of 18 children	Quantitative Repeated measures Inferential statistics*	Seizure frequency	Baseline (pre) and 1 year, 2 year and 3 year (post)	4/20 (20%) immediate cessation post diagnosis.
Zhang 2009 [37]	11	8F, 3M	43 (33-53)	41, ES, 22F 19M, 39 (28-50)	Quantitative Repeated measures Inferential statistics	HRQoL and Seizure frequency	Baseline (pre) and 6-16 months (post)	Improvements in HRQoL but not statistically significant. Significant reductions in seizure frequency.

Notes – F, female; M, male; NR, not reported; ES, epileptic seizures; RC, randomised control; * inferential statistics were used in the analysis but not for seizure frequency related to impact of diagnosis; HRQoL, health-related quality of life.

3.3. Key findings

3.3.1. Impact of diagnosis on seizure frequency

All of the reviewed studies provided data regarding the effect of the diagnosis on seizure frequency. Of the three studies where the primary aim was not to investigate the impact on diagnosis [33,35,36], two reported levels of seizure cessation post-diagnosis [33,36]. Mixed results were reported with seizure cessation in 24/54 participants (44%) in one study [33] and 4/20 (20%) in the other [36]. The third study [35] which primarily aimed to assess the impact of a brief educational intervention on engagement with further treatment, used a diagnosis only control group and reported no significant difference in seizure frequency post diagnosis.

Of the two studies with epilepsy control groups, one reported a significant reduction in seizure frequency in both the NEAD and epilepsy groups [37]. The other [26] reported no change in seizure frequency in the epilepsy control group and a significant reduction in the NEAD group. Specifically, seizures reduced in 21/22 participants (95%), with complete cessation in 18 (82%) and a 50% reduction in seizure frequency for the remaining 3 (13%). It was not reported whether the seizures increased or remained the same in the final participant.

In the final study, which retrospectively reviewed the case notes of NEAD patients [34], it was reported that in 12/27 patients (44%) seizure frequency increased post diagnosis and in the other 15 patients (56%) seizure frequency stayed the same or decreased. However, this study included 15 patients with co-morbid epilepsy and NEAD and did not differentiate the changes in these patients and those with only NEAD.

3.3.2. Impact of diagnosis on health-related quality of life

Both of the studies which investigated the impact of diagnosis on health-related quality of life [35,37] found no significant difference (positively or negatively) pre- to post-diagnosis.

3.4. Assessment of Methodological Quality

A meta-analysis was deemed inappropriate for combining and contrasting the results of the studies due to the heterogeneity of the measurement of seizure frequency [42]. Also, as will be later discussed, the quality of the studies raises a concern that an average result across the studies would not be meaningful. Instead, a narrative framework is used to describe the similarities and differences of findings.

A domain-based quality evaluation tool was specifically developed for this review (see supplementary materials, online only). The developed tool incorporated elements of the Critical Appraisal Skills Programme (CASP) [43] and also considered previous (systematic) reviews relevant to NEAD populations [17,18].

The use of arbitrary cut-off scores in quality assessment tools have been criticised as important quality elements can be masked by the overall score and quality

label [44]. Also, single elements of quality can be more important than others in answering posed questions [45]. Therefore, this review adapted the tool developed by the Cochrane Collaboration [42], whereby shades represent levels of quality/bias. Although usually separated within Cochrane reviews, here, quality and bias are combined. No shading signifies low quality/high risk of bias, light shading represents, moderate quality/moderate risk of bias, and dark shading signifies high quality/low risk of bias.

In order to assess the inter-rater reliability of the quality appraisal tool, 50% of the studies (selected at random) were independently rated by two authors (JB and NM). The mean kappa coefficient across items was .75, indicating 'substantial' agreement overall [46].

The individual and synthesised assessment of quality can be seen in Table 3 and Table 4 respectively. Final ratings (presented in Table 3) represent scores agreed between the authors after independent appraisals and discussion of discrepancies. Table 4 displays the results of the synthesis of the quality and bias of the evidence as a whole. The overall quality and bias is considered by examining how many of the studies were judged as high quality for each criteria.

Table 2. Results of Quality Appraisal

Study	Design		Participants								Diagnosis		Outcomes		Statistics		Reporting
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Duncan 2011 [33]	+	+	++	N/A	++	++	+++	+++	+++	++	+++	+	+++	N/A	+	+	+
Farias 2003 [26]	+	+++	++	++	++	++	+++	+++	+++	+	+++	+++	+++	N/A	+++	+	+++
Scheepers 1994 [34]	+	+	++	N/A	++	+++	+++	+	N/A	N/A	++	++	+	N/A	+	+	+++
Thompson 2013 [35]	+	+	++	N/A	++	+++	+++	+++	+++	+	+++	++	++	++	+++	+	+++
Wyllie 1991 [36]	+	+	+++	N/A	++	+++	+++	+++	+	+	+++	++	+++	N/A	+++	+	+++
Zhang 2009 [37]	+	+++	+++	+++	++	+++	+++	+++	++	+++	+++	+++	+	++	+++	+	+++

Key

+ Low quality/High risk of bias

++ Moderate quality/Moderate risk of bias

+++ High quality/Low risk of bias

Table 3. Synthesis of quality of evidence

Criteria	Overall quality of evidence			
1. Power calculation				
2. Control group				
3. Demographics				
4. Matched controls				
5. Representative sample				
6. Inclusion and exclusion				
7. Take-up rate				
8. Confounding variables				
9. Attrition rate				
10. Attrition comparison				
11. Diagnostic method				
12. Diagnosis delivery				
13. Outcome measures				
14. Standardised measures				
15. Statistical analysis				
16. Effect size				
17. Reporting bias				
	25%	50%	75%	100%

3.4.1. Results of Quality Assessment

As can be seen in Table 2 the quality between and within the studies is mixed. Five of the studies reported all relevant demographics for the sample but in one study age was not reported [34]. However, in one of the five studies [35] the full sample was split into an experimental and control group but the numbers and demographics of each group were not reported.

Power is the ability of a statistical test to detect a true effect of an intervention (in this case the delivery of the diagnosis) [47]. When adequate power is established the risk of a Type II error is low. Type II errors are false negatives where an effect exists but is not detected [47]. None of the studies reported power calculations. As sample sizes were small it is likely that they do not fully represent all of the population (people with NEAD), and this means the findings are unlikely to approximate population outcomes [47]. Additionally attrition rates may have impacted on the representativeness of the sample in some studies [26,36]. Take-up rates were reported, and found to be high, in four studies [34-37]; but were not reported in two studies [26,33].

The statistically significant outcomes in the studies suggest that a difference exists but without conducting a meta-analysis it is unclear how robust such findings were to Type I errors. Type I errors are false positives, where an effect is detected but it can be attributed to chance [47]. Additionally, with no studies reporting effect size the magnitude of the differences was unclear [47]. This is particularly important when considering how effective interventions compare to each other [48]. Also, whilst four studies used inferential statistics to calculate the difference between pre and post measures [26,35-37], two only used descriptive statistics [33,34]. These were studies in which investigating the outcome of diagnosis was not the primary aim of the research.

Four of the studies accounted for possible confounding variables in their design by using strict inclusion and exclusion criteria [26,33,35,36], one study identified participants with co-morbid ES and NEAD and accounted for this in the design and analysis [37]. One study [34], included patients with co-morbid epilepsy and NEAD and did not differentiate when reporting changes in seizure frequency (which would have been possible due to the study having all individual data available retrospectively).

With regard to NEAD research in particular, five of the six studies [26,33,35-37] used the gold standard method for diagnosis, V-EEG monitoring [13,14]. The other study [34] used EEG data without a video overlay which is used to differentiate observable characteristics of seizures [14]. This was also the study which included co-morbid epilepsy and NEAD patients, which is perhaps an artefact of the method of diagnosis used being less specific. The delivery of the NEAD diagnosis was mixed in terms of a clear description but it was made clear in all but one study [33] that participants received the same diagnostic communication. Two of the studies [26,37] reported using a standard well-regarded framework for the communication of the diagnosis [20]. The two studies which used control groups used matched controls of patients who were diagnosed with epilepsy (ES) [26,37].

Seizure frequency was the main outcome and there are no standardised measures for recording this. The two studies which measured quality of life [35,37] used a tool standardised for an epilepsy population, the QOLIE [40, 41]. As previously described, seizure frequency was operationalised differently in the studies. Three were considered to have operationalised the outcome to be measured objectively and clearly [26,33,36], including the two studies where only cessation or continuation of seizures were measured post diagnosis [33,36]. Two studies were considered to use less objective ways of measuring seizure frequency including ranking methods open to bias [34,35]. One study was considered to use a method open to bias and subjectivity which was different at pre and post diagnosis data collection points [37].

Finally, five of the six studies reported in the results and discussion all data/measures described in the method [26,34-37]. One study collected data which was then not analysed/reported on in the results or discussion [33].

3.4.2. Synthesis of quality

As can be seen in Table 3, the overall evidence is not of a high standard with only four criteria being considered high quality/low bias in over 75% of the studies. The criteria reaching this standard were: take-up rates, reporting of data, diagnostic method, and controlling/adjusting for potential confounding variables. What can be judged and is of particular concern are the two criteria where low quality was identified in all studies. Power calculations and reported effect sizes are crucially important in drawing conclusions about presence and magnitude of impact [47]. Therefore the impact of receiving diagnosis may only be minimal and the accuracy of the results suggesting any impact is also questionable.

4. Discussion

This review explored the impact of receiving a diagnosis of NEAD. Six papers were included [26,33-37] to assess the evidence-base and the extent to which receiving a NEAD diagnosis impacts on non-epileptic attack frequency and to a lesser extent health-related quality of life.

Quality assessment tools have typically been developed to assess the quality of randomised controlled trials and other specific research designs [49,50], and there is no consensus on which is the best tool [42]. For these reasons and the specific potential quality issues in this area of research, namely varying diagnostic methods, a domain-based quality evaluation tool was specifically developed for this review.

Results found inconsistencies in the impact of receiving a diagnosis of NEAD. This may be influenced by the employment of heterogeneous methods of recording non-epileptic attacks. Also the quality of the research in terms of design and statistical rigour was highly questionable. This heterogeneity and lack of appropriate quality makes it difficult for any conclusions to be drawn regarding the impact of a NEAD diagnosis on attack frequency or health-related quality of life.

Specifically it has been reported that receiving a diagnosis of NEAD can reduce/cease attacks [10,26]. No proposed explanation or theory for why this

may occur or why it happens in some people and not others was found in the current literature. Although difficult to calculate due to the heterogeneous methods of recording and reporting, approximately half of participants included in the studies in this review were found to experience a reduction or cessation in non-epileptic attacks post diagnosis. The wide range of reported levels of cessation (20-82%) raises questions about what may moderate response. The inconclusive, variable results and lack of quality found in this review indicate that further research is required. Health-related quality of life was measured in two of the six studies, finding no statistically significant changes in pre and post-diagnosis measures [35,37].

Without further investigation, it is difficult to conclude whether receiving a diagnosis of NEAD has any impact, positive or negative.

4.1. Limitations

4.1.1. Limitations of this review

The criteria for this review meant that studies must administer measures before and after the diagnosis of NEAD is delivered. This may have led to the exclusion of qualitative research regarding the personal experience and impact of receiving a diagnosis. It is advised that when further research is available which enables conclusions to be made about the objective impact of receiving a NEAD diagnosis, considering qualitative accounts of the impact may support the generation and testing of hypotheses regarding the mechanism of impact.

Strict criteria were imposed on the literature in order to identify studies that would be able to answer the question: What is the impact of receiving a diagnosis of NEAD? Strict criteria applied to a well-researched area would enable the identification of high quality, specific studies which would increase the chance of the question being answered. However, the NEAD research pool remains small and at this time heterogeneous and poor quality studies mean that many questions are yet to be answered. Searching grey literature in any similar reviews in the future may provide more studies for consideration.

Numerous papers were excluded as they reported collecting baseline data immediately after the diagnosis of NEAD was delivered (see Table 1.). It was felt that these studies would not answer the question regarding the impact of receiving a diagnosis. Also, numerous studies were excluded if there was no definitive statement of whether active treatment was implemented prior to follow-up data being collected (see Table 1.). This may be an error in reporting rather than conduct.

With regard to quality assessment, in this review and generally, many items may reflect assessment of reporting rather than conduct [49]. Studies that did not report take-up rates may have concealed the rates to avoid selection bias criticism. Alternatively, take up rates may not be reported if standard service data was used and all participants were included as part of their service/treatment.

The synthesis of the quality assessment was based on the system developed by the Cochrane Collaboration [42] intended to review large amounts of studies. Using this system in the current review with only six studies may be less useful.

4.1.2. Limitations of the included studies

The scarcity of research is illustrated by the fact that investigating the impact of diagnosis was not the primary aim in half of the included studies [33,35,36]. Small sample sizes (11-54) were not surprising given the infancy of research into NEAD, it is suggest that the increasing interest in NEAD [7] will enable larger scale research to be undertaken in the future.

Overall the methodological quality of the selected studies was poor. The lack of statistical rigour was apparent across all studies within this review, which limited the ability to draw conclusions. The different methods of recording attack frequency meant that it was difficult to synthesise the findings. The heterogeneity of the studies meant that a meta-analysis to calculate and synthesise effect sizes was not indicated [42].

Although there was consistency with all studies measuring seizure frequency as an outcome, it has been proposed that attack frequency, specifically attack cessation, should not be the primary outcome measured [51]. One study found no significant differences in the employment and benefit status of NEAD participants whose attacks ceased and whose attacks continued. In addition to this, in all participants who remained unemployed (attack free and continued attacks), there was no significant difference in psychopathology (anxiety and depression) [51]. Research has also found that quality of life improved in only 50% of participants whose attacks had ceased [52]. Furthermore, there was no significant correlation between quality of life and attack frequency overall. A study in this review supported the need for further consideration of meaningful outcomes [37]; statistically significant reductions in seizure frequency were found whereas the HRQoL did not show statistically significant improvement. There is also research which has found that cessation of non-epileptic attacks can result in their 'replacement' with other 'conversion' type symptoms [53]. This limitation can be further generalised to studies of treatment efficacy which also use seizure frequency as the primary outcome measure [17,18,54].

As earlier described, one study did not differentiate between participants with NEAD and participants with co-morbid NEAD and epilepsy, in terms of the post-diagnosis outcome [34]. By not reporting on the outcomes for these groups separately no conclusions can be made about the impact of diagnosis on non-epileptic attack frequency in this study.

4.2. Future research

Future research should endeavour to employ more statistically rigorous designs including larger sample sizes, and calculations of power and effect size. It is possible that research could utilise data already collected as in one of the studies in this review [34]. Twenty years on, data collected during inpatient assessment and diagnosis may be standardised and more comprehensive. This would enable direct comparisons of pre and post diagnosis measures without the complication of follow-up after discharge increasing the risk of attrition.

It is advised that future research standardises the collection of attack/seizure frequency data using V-EEG monitoring, as in one study included in this review [26]. If due to cost and prioritising equipment for clinical purposes this is not feasible, alternatives such as recording frequency in diaries could be considered. Research

should also prioritise measuring psychosocial, psychological, and medical outcomes to further explore their relationship to attack frequency and cessation [37,51,52]. Qualitative research is also indicated in order to explore what patients with NEAD consider a positive outcome.

It would also be favourable for future research to standardise the communication of the diagnosis. Although two studies included in this review [26,37] adhered to a developed communication strategy [20], this has been succeeded by more recently developed protocols [21,22]. With confusion about NEAD associated with poorer prognoses [19], more up to date protocols with more educational information may improve outcomes. It may be useful to compare outcomes after using various communication strategies. A study in this review compared standard diagnostic communication with a brief educational intervention, but found no significant differences in HRQoL or seizure frequency between groups [35].

As noted earlier, the reported levels of cessation in this study were wide ranging (20-82%). If future studies with more rigorous designs continue to find such variability, it would be appropriate to explore what may moderate response. Patient, clinician, or process characteristics (including the communication strategy) may account for variability in the outcomes of diagnosis. Existing research has identified predictors of outcome, typically patient characteristics, but this has focused on responses to active treatment or longer-term follow up rather than diagnosis [10,19,24,36,55-57].

Research, including one study in this review, found that epileptic seizures can also reduce post-diagnosis [37,58]. The topographical similarities led to NEAD being commonly misdiagnosed as epilepsy [10]. NEAD once being a diagnosis based on the exclusion of epilepsy [13,14] has left a legacy of epilepsy patients continuing to be utilised as a control group in NEAD research. With the theory that non-epileptic attacks are underpinned by psychological processes being widely accepted [4], why are patients with epilepsy, underpinned by neurological processes, considered a suitable control group? It may be more appropriate to compare NEAD with other psychological phenomena - further investigation of this is recommended.

5. Conclusions

Clinicians have reported their observations that receiving a diagnosis of NEAD has a positive impact, particularly by reducing/ceasing seizures. The results of this review have found that a limited evidence base of six studies including 153 participants was not consistent or of sufficient quality to draw definitive conclusions regarding this. More rigorous research is required to understand the impact receiving a NEAD diagnosis has on various outcome measures.

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