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Review

New insights into psychogenic nonepileptic seizures 2011–2014☆

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ABSTRACT

Purpose: There has been a rapid increase in the rate of publications about psychogenic nonepileptic seizures (PNES). This review summarises insights from the 50 most important original articles about PNES published since 2011 and describes the advances made in the understanding of PNES over the last 3 years.
Method: We carried out a systematic literature search of all English language publications about PNES published between October 2011 and October 2014 on Scopus, Ovid Medline and Web of Knowledge, and inspected all abstracts. Having excluded all review articles, case reports, conference abstracts, articles exploring PNES in children, and articles not actually focussing on PNES, we considered 150 papers for inclusion in this review. We assessed the quality of the identified studies and used expert judgement to identify the 50 most important publications from the review period and composed a narrative review based on these original papers.
Results: Almost one half of the studies initially identified only provided Class 4 evidence. Recent work has provided more support for a biopsychosocial account of PNES. It has illustrated the heterogeneity of PNES, identifying varying and distinct psychological profiles of individuals with this disorder. These findings suggest that intervention needs to be flexible or adaptive if it is appropriately to target the different mechanisms which may give rise to PNES. Several educational and psychotherapeutic interventions for PNES have been described, but sufficiently powered randomised controlled trials are yet to be undertaken. Recent research using social, economic and quality of life indicators has provided further evidence of the societal and individual burden of PNES.
Conclusion: The research into PNES published over the last 3 years has deepened our understanding of the condition as a biopsychosocial disorder which is neither a "physical" nor a "psychological" condition. A number of small studies have demonstrated the potential of educational and psychotherapeutic treatments, but rigorous and sufficiently large trials still need to be conducted to determine the effectiveness of these interventions.

1. Introduction

Psychogenic nonepileptic seizures (PNES) superficially resemble epileptic seizures (ES) but are not caused by the abnormal electrical discharges in the brain which are associated with epileptic seizures. PNES are considered an experiential and behavioural manifestation of distress. PNES are one of the three most common diagnoses made when patients present to clinicians with transient loss of consciousness, and explain about 20% of presentations to seizure clinics [1].

Whilst PNES may be under-researched compared to epilepsy, the number of publications about this disorder has increased rapidly over the last three decades. Whereas 10 years ago, it still seemed possible to give a reasonably comprehensive overview of the whole literature about the disorder [2], it has since become necessary to summarise recent developments in the field more frequently. We have previously provided a summary of research about PNES published between 2008 and 2011 [3]. For this current review we have carried out a systematic literature search of publications about PNES from the last 3 years. We then used subjective expert judgement to select the 50 publications from the 3-year review period, which we deemed most important and discuss these publications in greater detail. However we provide the full list of publications identified as additional online content and invite interested readers to look at all papers published between October 2011 and October 2014 (see additional web content). Notably

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this review focuses entirely on primary research studies – important review articles or policy statements (such as the publications of the Commission on Neuropsychobiology or the Psychogenic Nonepileptic Seizure Task Force of the International League against Epilepsy [4,5]) are not covered.

In addition to providing a summary of the key research findings of the last 3 years and to discussing the likely direction of future research, we aimed to assess the quality of research about PNES during this period using the criteria for evaluating research methodologies proposed by the American Academy of Neurology [6]. Given that the particular expertise of the authors is in the assessment and treatment of adults with PNES, and that there are important differences between PNES in adults and children, this review focuses entirely on the adult literature.

2. Method

The most recent publications covered in our previous update about progress in the understanding and treatment of PNES was from October 2011 [3]. Our systematic literature search for this review therefore covered work published between October 2011 and October 2014. We conducted the search using three comprehensive databases (Web of Knowledge, Ovid Medline and Scopus). The following search parameters were used in the topic, title, abstract and keywords fields: ((nonepileptic NEAR attack$) OR (non-epileptic NEAR attack$) OR (nonepileptic NEAR seizure$) OR (non-epileptic NEAR seizure$) OR (pseudoseizure$) OR (dissociative NEAR seizure$) OR (dissociative NEAR convulsion$) OR (pseudoepilep$) OR (hysterical NEAR seizure$) OR (hysterical NEAR convulsion$) OR (hysteroepilepsy$) OR (conversion NEAR seizure$) OR (psychogenic NEAR seizure$) OR (functional NEAR seizure$) OR (nonepileptic NEAR event$) OR (non-epileptic NEAR event$)). These search terms were considered to include the various terms associated with PNES. The systematic search was complemented by hand searches of publications not picked up but referenced in the identified papers. We examined the abstracts of all identified publications and excluded all original articles published in languages other than English, review articles, conference abstracts, case studies, book reviews, journal letters, journal notes, studies on functional disorders generally rather than PNES specifically, studies focussing entirely on PNES in children (below 16 years of age), and studies which focused predominantly on epilepsy.

In order to assess the quality of recent PNES research, we graded all publications identified using the criteria published by the American Academy of Neurology [6]. The criteria which are considered when grading the quality of evidence of a study vary depending on the nature of the research question, but elements such as generalisability, objectivity of assessment, randomisation, and blinding are generally considered. Class 1 evidence is obtained when the study design is prospective, randomised and controlled, and when the sample includes a broad spectrum of individuals, using a reference standard for case definition. Researchers must be blinded during the outcome assessment. Class 2 studies can include well-designed retrospective studies as long as they include a broad spectrum of individuals diagnosed with the condition under investigation. Retrospective research which only includes a narrow selection of the target population is graded as Class 3 evidence. If the outcome is not objective then it must be measured in an independent evaluation. Studies considered to be the lowest grade of evidence, Class 4 evidence, is provided by uncontrolled studies in which assessments are not applied independently. Expert opinions and case studies are also included at this level of evidence.

To identify recent research trends in PNES, expert judgement was used to select the 50 most important publications from the review period. We summarise and discuss the main findings of these papers. The expert judgement was made by MR and was necessarily subjective. Whilst taking account of the quality of the methodologies employed, our selection was mostly influenced by our impression of which publications would be most relevant to future progress in the field.

3. Overview of identified PNES research papers

The systematic search of the literature described above yielded a total of 819 English language publications. Once duplicates were removed, the application of the listed exclusion criteria identified 145 relevant papers. A further five papers were identified by checking reference lists. Only one of the recent research studies met the requirements for a Class I study. The majority of studies had a lack of control and randomisation, utilised small sample sizes, and had insufficient levels of blinding and objective assessment, leading to 28 studies being graded as Class 2 evidence, 48 as Class 3 evidence, and 73 as Class 4 evidence.

The 50 most important publications are summarised and discussed below under the thematic headings Diagnosis, Psychological Factors, Neurobiology, Burden, Treatment and Prognosis.

4. Diagnosis

The accurate and timely diagnosis of PNES continues to present a clinical challenge, and recent research confirms that the accurate diagnosis of PNES still tends to be made several years after the manifestation of seizures. The publications discussed in this section could, potentially, contribute to improvements in the speed and accuracy of the diagnostic process.

4.1. Ictal observations

Various diagnostic methods have been considered for aiding the differential diagnosis of seizures, and research has focused on evaluating the sensitivity and specificity of these techniques. Bayly et al. [7] used data from wristband movement monitors to analyse movement patterns associated with epileptic seizures and PNES. Accelerometer traces from 56 convulsive seizure events from 35 patients were analysed. Twenty-six of these participants had a diagnosis of PNES, eight had a diagnosis of epilepsy, and one participant presented with mixed seizures. An epileptologist blinded to other clinical information, was able to use wristband data alone accurately to classify 92.7% of seizures as nonepileptic and 75% as epileptic. Additionally, he was able to differentiate between the epileptic and nonepileptic events exhibited by the participant with both seizure types. This study suggests that frequency analysis of wristband movement data might be a useful diagnostic tool in patients whose PNES involve motor activity.

Rosemergy et al. [8] explored whether postictal respiration patterns could be an additional method to assist in differentiating between ES and PNES. Video recordings of 72 convulsive seizure episodes from 56 patients were examined by blinded readers, who counted the rate of respiration for one full minute at 2-min intervals. They determined significant differences in the postictal respiration rates between the two patient groups, and concluded that patients with PNES breathe more rapidly immediately after a seizure event although their respiratory rate then normalises quickly, whereas patients with epilepsy may exhibit a more prolonged period of stertorous respiration. The time it took for respiration to return to normal, was twice as short in individuals with PNES as in those with ES. Whilst this method alone is not suitable for determining seizure classification, it could be useful for clinicians as an initial indicator of seizure type at a patients' bedside.

A recent meta-analysis has suggested that monitoring ictal eye closure might be a useful method for identifying seizure type. Six