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Semiology and Classifications of Paediatric Psychogenic Nonepileptic Seizures – a Systematic Review

Degree Project in Medicine

Jesper Esbjörnsson

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Supervisor: Tove Hallböök, Associate Professor, PhD
The Institution for Clinical Sciences, Department of Paediatric Neurology,
Queen Silvias Childrens Hospital
Co-supervisor: Colin Reilly, Neuropsychologist, PhD
The Institution for Clinical Sciences, Department of Paediatric Neurology,
Queen Silvias Childrens Hospital

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Abstract

Introduction: One of the main differential diagnoses of epilepsy is psychogenic nonepileptic seizures(PNES). The presentation of symptoms are paroxysmal events of motor, non-motor, behavioural and subjective characteristics. They are viewed as a subtype of conversion disorder and being of psychogenic nature. One of the main methods of diagnosing PNES is through a professional assessment of the semiology of an event directly or via video, preferably video EEG monitoring. Although there is evidence in this approach concerning adults, research into the semiology of paediatric PNES is lacking.

Aim/Objectives: To search the literature systematically and present current knowledge pertaining to semiology and classification of such in paediatric PNES. **Methods:** The databases PubMed, Scopus and PsychINFO were searched with a search string consisting of three blocks. The blocks corresponded to PNES, children and investigation/assessment. All papers were screened and matched against inclusion/exclusion criteria and the relevant data from remaining papers were tabulated and presented in a narrative form. The quality of papers were assessed using assessment tools from the national heart, lung and blood institute(NHLBI). PRISMA guidelines for systematic reviews were used.

Results: 1099 papers were found out of which 233 full text were screened and 23 papers included in the qualitative synthesis. No quantitative synthesis was performed. The data were limited and the quality of included papers low. Certain trends could be seen such as lesser female to male ratio in younger children, younger children having less motor symptoms and more negative ones and that semiological signs of PNES seen in adults were less common in children. Classifications were reported on, but no study validated the classification systems against any form of control.

Conclusion: This paper concludes that data on paediatric PNES is insufficient to allow parallels to be drawn with research undertaken with adult populations. Furthermore, differentiating PNES from other paroxysmal disorders such as epilepsy in children through assessing semiology remains relatively untested and caution is advised.

Introduction

Paroxysmal events and seizures

Seizures have been described for thousands of years and were initially thought to be caused by evil spirits[1]. This spiritual view of seizures, and especially epileptic ones, was over time replaced by the modern physiological view of the disorders. Seizures are usually defined as epileptic in nature but as terms such as “non-epileptic seizures” are commonly used, these events are also partially covered by the term. The events are paroxysmal, more or less sudden in nature and symptoms regress after the event. They can either affect consciousness, function or both and may cause convulsions.

Seizures in paediatric patients

Seizures in paediatric patients are a common occurrence in the emergency room. The pathogenesis and expression of these seizures are heterogenous in nature. One common way of subdividing these events are into epileptic and non-epileptic events. Both groups containing various subgroups with different pathology and treatments. Severity of these subgroups vary from potentially life-threatening to completely benign.

The initial investigation is focused on the clinical expression of the seizure, circumstances surrounding it, physical examination and medical history[2]. For ongoing seizures, this examination is usually sufficient, however EEG would confirm or reject the diagnosis of epilepsy with potential epileptiform activity. If the seizure is the patients first one and is uncomplicated, further investigation is usually not pursued. Examples of complicating factors would be unprovoked status epilepticus, unprovoked generalized epileptic seizures in patients with heredity for epileptic disorders or radiological and/or EEG abnormalities in the vicinity the seizure is thought to originate from.

If a patient presents with repeated seizures clinically interpreted as epileptic, diagnosis is made and treatment is usually initiated.

Differential diagnoses

Epileptic seizures can be either unprovoked or provoked[2]. That is, in close temporal proximity with factors such as fever, sleep deprivation or intoxication. They can also symptomatically be motor or non-motor, aware or unconscious, partial or generalized. They show typical, epileptiform patterns on an EEG if viewed during said event and many patients have abnormalities on their EEG in-between seizures. Epileptic seizures have typical semiology during the event that clinicians identify to support the diagnosis such as tonic-clonic movement and stereotypy. Some epileptic events are preceded by certain symptoms such as “epigastric rising”, a feeling of “something” rising up the stomach. There are also symptoms after the event called post-ictal symptoms. These come from a fatigue in neurons after the seizure that can cause muscle weakness, sensory loss, general fatigue, concentration difficulties, migraine and more for several hours after the event.

Non-epileptic seizure is a term covering all other forms of paroxysmal events that mimic epilepsy[2]. It covers, but is not limited to, syncope, psychogenic non-epileptic seizures, breath-holding spells, hypoglycaemia, migraine and sleep-disorders. These events have more or less specific symptoms that differ from epilepsy and also occur more frequently in different age groups. Syncope being the most frequent in adolescents and symptomatically being very distinct. The event is usually preceded by a swift but gradual blackout, atonia with subsequent fall to the ground and speedy recovery without a post-ictal state. Shaking is not uncommon and may delay a correct diagnosis. Breath-holding spells on the other hand occurs in toddlers who after an unpleasant stimulus hold their breath, sometimes to the point of cyanosis, and turn limp. They may cry and follow the event by sleeping.

Psychogenic non epileptic seizures(PNES)

PNES are events resembling those of epileptic seizures but without ictal EEG patterns. They are of psychological origin[3] and are one of the main differential diagnoses of epilepsy[4]. The events can be both motor, characterised by shaking of upper and lower limbs and tonic postures as well as negative, that is loss of function, with limpness and unresponsiveness as main symptoms. Other frequently mentioned symptoms include subjective ones such as visual and sensory sensations as well as a characteristic “aura”[3]. The similarities to epileptic

seizures result in a long diagnostic delay[5]. This can result in receiving anti-epileptic medication for a long period before PNES is diagnosed and medication can be phased out[5]. This exposes the patients to potential iatrogenic side-effects as well as the stress that accompanies the constant hospital visits.

Certain semiological signs have been prescribed to PNES such as ictal eye closure and resistance to opening the eyes[6,7], not being alone at the onset of an attack and absence of ictal injury, especially significant ones[8]. The condition is more prevalent in the adult population with mean age of onset in the late twenties[9] and rare but existing in the paediatric population[10,11] in ages as low as 4-5 years of age[12–14]. Through the years the condition has been referred to by many names such as hysteria, pseudoseizure, nonepileptic attack disorder(NEAD) and functional seizures[15–17]. The diagnostic means and criteria have varied and changed substantially over time, reflecting the difficulty of diagnosing and specifying the disorder. In DSM-V the disorder is part of the broader condition of conversion disorder[6] where attacks or seizures are one of several possible symptoms. In ICD-10 it falls under the code “F44.5, Conversion Disorder with attacks or seizures”[18] and in the previous edition of ICD-9 no subcategory specifying the presence of seizures existed, prompting the use of “300.11, Conversion disorder”[19]. No specific diagnostic means have been found to date, the most common way being usage of clinical assessment of health history and semiological characteristics in combination with various investigations such as video EEG monitoring(VEEG). A recent review proposed by the International League against Epilepsy(ILAE) found some support for the use of VEEG[7], video recordings of motor events and some semiological signs. This evidence is however not specifically concerning PNES in children.

PNES in children

PNES is less frequent in paediatric populations, with prevalence showing trends of rising with age[4,11]. Incidence in paediatric patients in one recent study from Denmark was shown to be 2.4 per 100,000 person/years[11]. In one study from Sudan PNES was found in 15 patients out of 74,949 children[20]. Paediatric patients with PNES have significantly more psychiatric co-morbidities than healthy controls as one study found, showing the need for these patients

to be assessed by a psychiatrist/psychologist[21]. A previous review by Reilly et al. on paediatric PNES found most research to have small sample sizes, lacking robust methods and comprehensive descriptions[4]. Research has shown health care staff to be lacking knowledge about the condition in children, with diagnostic codes and naming of the condition varying greatly as well as clinicians employing different diagnostic strategies[22,23]. Feelings of confusion, guilt, being less than epilepsy and fear are some of the emotions displayed by paediatric patients and their families during and after a PNES diagnosis[24]. Patients and their families can show reluctance towards the diagnosis, further increasing the necessity of robust diagnostic tools[25].

The condition has nonetheless been found to show dissimilarities to adult PNES concerning the proportions of motor symptoms compared to more negative symptoms[4]. As the diagnosis in part relies on the clinical assessment of ictal characteristics and the evidence used in practice largely revolves on research done on adults, these dissimilarities may cause further diagnostic delay in children.

Research objectives

A review by Asadi-Pooya et al.[26] recently summarised the data on PNES classifications covering both adult and paediatric PNES. A similar study focusing on exclusively paediatric PNES has not been done in recent years. The semiological presentation and classification of such in paediatric PNES as presented in the literature and quality of the evidence was therefore investigated in this systematic literature review study. Furthermore, the level of confidence that clinicians can have when using semiology to assess the pathology of suspected PNES in paediatric patients will be investigated.

Method

Study information

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses(PRISMA) checklist for systematic reviews were used to help structure the research[27].

Search blocks and keywords

To find the most relevant papers three search blocks were used corresponding to “psychogenic non epileptic seizures”, “children” and “investigation/assessment” ([See Appendix - Keywords](#)). A basic set of words representing each block was synthesised. Reasonable synonyms for these were found through various online synonym databases and chosen at the authors discretion. A scoping search was performed on the 10/02/2020 with the keywords found so far. Papers with relevant focus were examined and relevant keywords were extracted and added to the search string. The term “functional neurological symptoms” was added later as a relevant study was missing from the search results.

Choosing databases and filters

Three databases were used in undertaking the literature search: PubMed, Scopus and PsychINFO. PubMed has a broad coverage and is used widely in the medical field[28]. Scopus has a wider reach but less tools to specify the search string[29]. PsychINFO is dedicated to the field of psychology and provides excellent tools to specify the search and allow for a wider set of keywords if in combination with limiting tools[30].

The purpose of using these three databases was to ensure wide coverage and that no relevant articles were missed.

The filters chosen for the different databases depend on the nature of the filters available for each of the databases. For PubMed the only filter applied was language with the search limited to papers in English since this filter should be relatively safe to use without affecting sensitivity, that is the reach of the search. Other filters were not used because of the lack of an “exclude” function on the site.

In Scopus the filters applied were exclusion of reviews, books, conference papers, chapters and editorials. The search was also limited to papers in English. These exclusion filters were deemed to be less likely to effect the sensitivity of the search as it only excludes papers that have been actively tagged as one of the previously mentioned types of papers.

The PsychINFO search was filtered with the exclusion criteria: literature reviews, systematic reviews, books and papers in languages other than English.

Building the search string

Support

Contact was taken with the staff at the biomedical library of Gothenburg University to verify the acceptability of planned search method and search string. Construction of the search string was undertaken with their advice and before using the finalised search string it was deemed to be of acceptable quality and without errors.

Pubmed

To widen the search further a scoping search was performed on PubMed to find relevant papers. From these studies MeSH-terms were extracted and added to the search. The MeSH-trees were also browsed at the authors discretion for additional terms. Terms with relevant grammatical variants were truncated to shorten the search string while allowing for greater width. Certain MeSH-terms were too broad and were therefore limited with an “AND” operator. The MeSH-term “Conversion disorder” for example was combined with “seizure” or “event” through an “AND” operator. All non MeSH-terms were set to search title and abstract for a reasonable balance between specificity and sensitivity, i.e. covering as many relevant papers as possible without including too many irrelevant ones.

The MeSH-term “Seizure/psychology” added 217 results to the search and these additional results were examined. The studies mainly discussed patients with epilepsy and psychiatric co-morbidities and were deemed to be unlikely to cover PNES. Thus the term was excluded from the search. The term “somatization” resulted in too many irrelevant results and was changed in the PubMed string to “somatization with seizure”.

SCOPUS

Search terms were tagged to cover ‘title’ and ‘abstract’. In the case of more specific term they also covered ‘keywords’ in order to broaden the search. To find both plural and singular forms truncation was used in the PubMed string, but this is unnecessary in Scopus. However,

in some terms other forms of variants exists where truncation was used in order to be covered such as “child” and “children”.

As “somatization” was deemed to be too broad of a term the proximity operator “W/10” was used in combination with “seizure” to limit the results to more relevant topics. A proximity operator controls that the two terms are within ten words of each other in order to fall out as a ‘hit’.

PsychINFO

The search terms were tagged to cover ‘title’ and ‘abstract’. A scoping search was performed to find relevant papers from which subject-terms were extracted and added to the string. To cover both singular and plural forms wildcards were used when necessary. As with the Scopus string certain terms were instead truncated to cover greater variation. As in the Scopus string, “somatization” was combined with “seizure” through the proximity operator “N/10”. The subject terms were found to be too broad and were combined with the term “seizure” in the ‘abstract’ or ‘title’. Certain terms were tagged as identifier (keyword) because of the nature of the words.

Screening

Screening for duplicates

After downloading Research Information Systems(RIS)-files containing all the articles from the used databases, and applying described filters, the references were imported to Endnote. This resulted in 1099 references. Using Endnote’s “find duplicates” function, 334 duplicates could be removed (see Figure 1). Duplicates were inspected manually and the title, publishing date, authors and abstract compared. If found to be true duplicates the reference with a longer abstract and full names of the authors were chosen to simplify further inspection down the line. The remaining 761 references were then inspected manually to find remaining duplicates. Ordering the articles after authors, references with the same first author were compared by title, authors and publishing date. When a duplicate was found and these attributes matched the same method of to publishing date in which case the article was searched on PubMed or PsychINFO and the choosing reference as earlier was used. In some cases, the references did not match according additional 71 duplicates. The references were

then ordered by title and inspected again to reveal additional duplicates, and no further duplicates were found.

Reviews and other documents

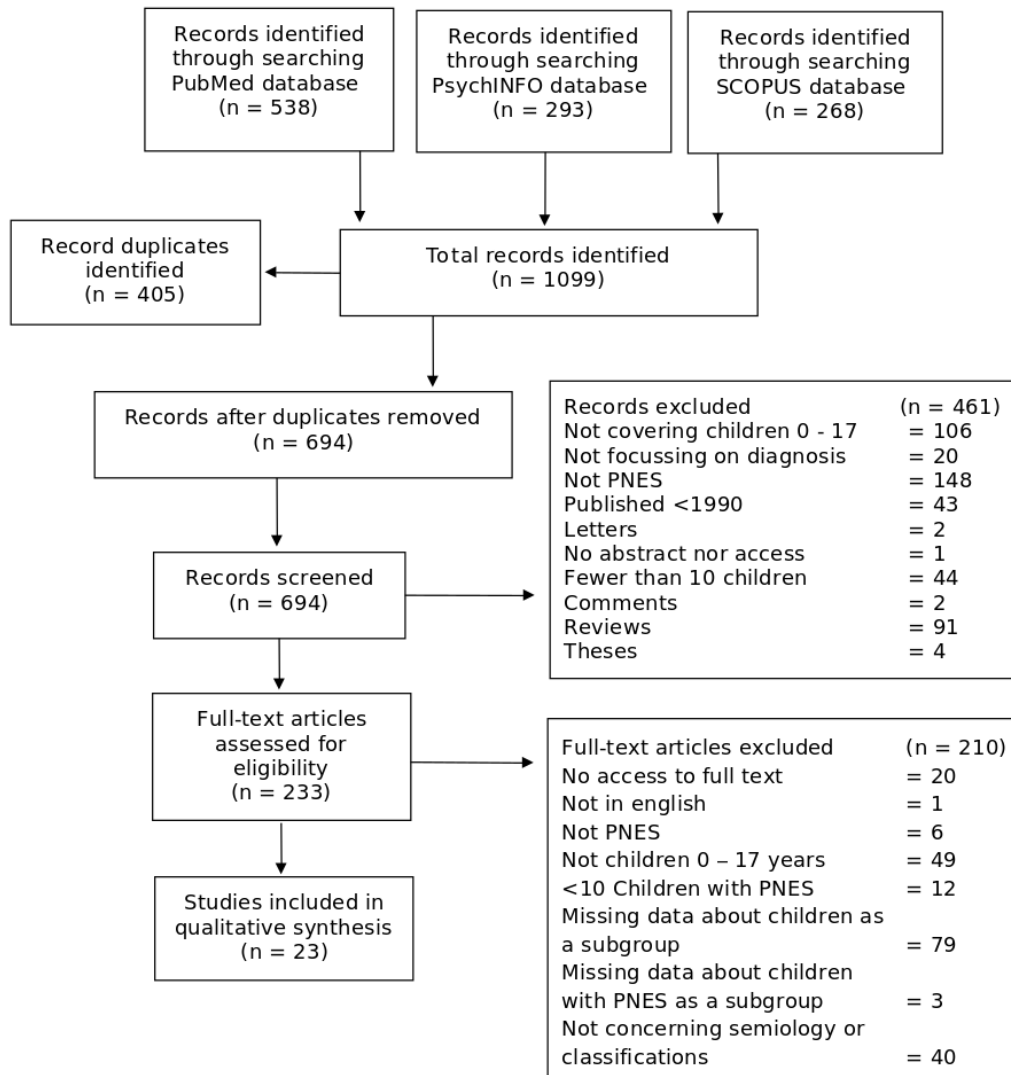
To remove any reviews the Endnote search-function was used to find any articles containing the word “review(s)” in the ‘title’ or ‘abstract’. Out of the 694 articles the search found 127 matches. The matching articles ‘title’ and ‘abstract’ were manually inspected and systematic reviews, literature reviews and meta-analyses were removed. The original PubMed search was performed with the applied filters review/systematic review/meta-analysis turning up 54 results which were inspected and removed from the reference list if they had not been found earlier. Six studies under the flag “review” did not fall under this category and were not removed. In the more thorough screening additional reviews were identified and in total 91 reviews were removed from the reference list. Four thesis papers were also found and removed.

It was also decided that only papers released after 1990 would be included as it quickly became apparent that older papers were using diagnoses such as ‘hysteria’ and it was difficult to determine if the patients described could be seen as analogous to PNES patients as currently understood. The techniques used for examination/investigation of patients with suspected PNES in these pre 1990 papers is also not applicable to recent studies as Video-EEG usage became common in the 1990s. This excluded 43 papers in total.

Figure 1 - Flowchart



PRISMA 2009 Flow Diagram



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(7): e1000097. doi:10.1371/journal.pmed1000097

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

Thorough screening

All remaining papers were ordered by author name and placed in a folder for non-categorised papers and the abstracts and keywords of the papers were read. When found to match inclusion and not the exclusion criteria it was moved to an “included” folder. If not matching a criterion the paper was placed in a folder based on which of the criteria it was excluded for.

Table 1 - Inclusion/exclusion criteria

If excluded because of several criteria, not meeting the inclusion criteria was deemed prioritised. If not meeting several inclusion/exclusion criteria the best matching criteria was chosen. (see Table 1)

This screening process was performed by one of the authors and when uncertainty arose the papers were saved and gone through together with a more experienced colleague on a weekly basis.

Papers were determined to be meeting the inclusion criteria if the study population included at least 10 children who were <18 years of age. Papers whose study population and sample size were not specified in the abstract or in keywords, were determined to be included/excluded depending on the total population size and mean age e.g., in a paper including 20 patients and is tagged adult, elderly and adolescent the chances of the paper having >10 children is probably low and the paper was excluded. A paper including 20 patients with a mean age of 20.0 was for the same reasons included. Any paper not mentioning children, adolescents or comparable was excluded.

Papers met the inclusion criteria “about PNES” if any synonymous word to PNES was used to describe the condition affecting the study group. More broad diagnoses such as conversion disorder were accepted if in combination with what could be interpreted as a ‘seizure’ or ‘event’ of some form. Papers focussing on clinicians working with PNES patients were also excluded.

Papers with fewer than 10 participants were excluded. Letters, editorials, reviews, thesis or comments were also excluded.

| <i>Inclusion/exclusion criteria</i> | |
|-------------------------------------|------------------------------------|
| <i>Inclusion criteria</i> | About PNES |
| | About children 0-17 years |
| | About investigation/diagnosis |
| <i>Exclusion criteria</i> | Published <1990 |
| | Letters |
| | No access to abstract or full text |
| | Less than 10 children with PNES |
| | Comments |
| | Reviews |
| | Thesis |

One exclusion criterion was added later in the process due to the effects of the Coronavirus disease 2019 (COVID-19) crisis on the schedule of the study. It was decided that the focus of the study would be limited to clinical semiology and classification of PNES in children and thus any study not covering this aspect was therefore excluded. In the thorough screening process only studies not covering investigation or diagnosis of PNES were excluded e.g. a study about cognitive behavioural therapy and its effect on PNES would be excluded according to criterion.

To evaluate the effects of this change, a search was performed on PubMed including only the results excluded by block III. A short screen of these articles found none of interest to this study.

Full text screening

Acquiring full text

The screened papers were divided in two groups and organised in folders in the reference program Zotero[31]. Two researchers then downloaded and screened the full papers of their respective half. The automatic full text retrieval function of Zotero was first used to acquire a sub portion of the texts. Access to the remaining papers were first and foremost through Gothenburg University but other proxies were also used such as Umeå University.

Screening

Each paper was compared to a list of exclusion/inclusion criteria which were ordered in a hierarchical way (see Table 2). If excluded, a paper would fall under the criteria highest on the list. Where uncertainty arose, the papers were discussed between the two researchers and consensus was reached.

Papers of which full text were unavailable or only available through ordering paper copies were excluded due to time constraints. Most papers excluded in this stage were due to not including children between the age 0 – 17 (n= 49), not including >10 children with PNES (n= 12) or not providing any separate data about children in the study (n= 79). There were many studies including both children and adults without analysing these as separate subgroups. Studies not considering semiology were also a large portion of excluded papers. In the end all included papers were available in the PubMed database.

Table 2 - Detailed list of exclusion criteria

| Detailed exclusion criteria organised hierarchically |
|---|
| <i>No access/unavailable text</i> |
| <i>Not in English</i> |
| <i>Review</i> |
| <i>Letter/comment</i> |
| <i>Not a clinical study</i> |
| <i>Not about pnes</i> |
| <i>Not about children 0 – 17 years</i> |
| <i>Not about investigation, diagnosis or demography</i> |
| <i>About other functional symptoms</i> |
| <i>Less than 10 children with pnes</i> |
| <i>Missing pure data about children</i> |
| <i>Missing pure data about children with pnes</i> |
| <i>Not about semiology</i> |
| <i>Missing pure data about children with pnes</i> |

Tabulation

Twenty-three papers remained after full text screening (see **Fel! Hittar inte referenskölla.**). All data in the individual papers concerning semiology or classification of PNES in children were extracted in a LibreOffice spreadsheet. The words used to describe semiological signs by the individual authors were used to first extract the information. Data on semiological classifications as reported by the authors were tabulated in a separate spreadsheet.

After tabulating the data, semiological descriptions similar to one another were incorporated into an overarching term in order to reduce the list of terms. As methodology and description of these terms were almost universally lacking, any lost detail that would have been provided by the removed terms were deemed insignificant. Any term containing a mix of semiology was added to all blanket terms that fit the description. A term called “mixed syncope-like and tonic-clonic-like” would therefore be added to both “generalised motor movements” and “atonic event”. Due care was taken to ensure that in case several terms from one paper were

placed under one blanket term, the terms did not represent the same events. If this could not be determined the term with the largest number was kept and the other term was removed.

Classifications were tabulated in a different spreadsheet. In most cases the classification systems used were either developed by the author of the study or a paper describing the system was referred to. In the cases of the studies by Patel et al. and Yılmaz et al. the methodology and used terms largely overlapped and were therefore, judged to be closer to a classification system than a pure description of occurring events. Demographic data, seizure frequency and seizure duration were gathered in different spreadsheets to reduce the table sizes. The findings of statistical significance according to the statistical methods used in the study were extracted and tabulated together with study quality rating and notes about study limitations.

Study quality assessment

To grade the quality of included studies the National Health Institutes(NIH) study quality assessment tools from NHLBI were used, assessing all the points of relevant checklist to the individual study[32]. The tools were used as they can be used to appraise the quality of cohort, cross-sectional and case-control studies, covering the expected study types[33]. Most of the included papers were of the “chart review study” type and were assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. One study[34] was of the case-control type and was assessed using the Quality Assessment of Case-Control Studies. Two studies by Kozłowska et al. were of a qualitative nature, one of which had also employed quantitative methodology. The one with mixed methodology was included with findings based on this method and assessed using the quality assessment tool for observational studies. The other study could not be assessed with NIH’s assessment tools and the findings were excluded. The description of semiology was included as the data by large is of quantitative nature.

Quality was assessed with respect to the study type, i.e. assessing whether the study was a ‘good’, ‘fair’ or ‘poor’ quality example of that study type. Most of the papers were chart review studies which by nature provides weaker results. Factors such as population size, statistical methods and the extent to which data is reported was considered.

Synthesis of results

Due to the heterogeneous nature of the semiological descriptions and the fact that the classifications were tested in only a few studies, any statistical analysis of the data would only provide a biased view and was therefore not performed. Results are presented in a narrative form in order to provide direction for future studies concerning semiology of PNES in children. Findings are presented in plain text together with reported p-values. Calculations of percentages and medians were done in LibreOffice Calc.

Results

Included studies

23 studies were included out of the 694 unique papers screened. Most papers were of the chart review study type (n= 14, 61%), reviewing VEEG and patient chart data. Some papers were of the cross-sectional observational study type (n= 6, 26%), including patients “prospectively” and study demographics and patient history, sometimes compared with control groups, sometimes within the PNES group. Two (9%) studies were qualitative in nature, including patients prospectively and researching the psychological environment of the patient or researching PNES classifications [35,36]. One (4%) case-control study was included researching the clinical and psychosocial characteristics of children with PNES and short-term outcome compared with healthy and “seizure” control groups [34].

Demographics

Population size varied between 17 and 229 [34,37] patients with 42 participants being the median. The studies included patients from the countries Australia (n= 2, 8.7%), Brazil (n= 4, 17.4%), Canada (n= 2, 8.7%), Hungary (n= 1, 4.3%), India (n= 4, 17.4%), Iran (n= 2, 8.7%), Saudi-Arabia (n= 1, 4.3%), South Korea (n= 1, 4.3%), Turkey (n= 2, 8.7%), United Kingdom (n= 2, 8.7%), USA (n= 6, 26.1%) and Venezuela (n= 1, 4.3%) (See Table 8 in the appendix). In two studies [37,38] differences in semiology between different cultures were compared and thus patients from several countries were included.

Age varied between the studies and total age range was 2 – 19 [39,40] and mean age varied between 8.9 – 14.8 [12,39]. Two studies did not report a mean age [40,41] but one of these did

provide full data on each included individual allowing for mean age calculation[42,43]. One paper studied semiological differences between pre-pubertal and pubertal patients[44].

Gender ratio differed greatly between studies however, in most(78%) cases the majority were female. The percentage of female patients varied between 43% – 86% [42,45] with 65% being the median. In two studies the proportion of female/male patients could not be determined[35,43]. Yilmaz et al.[46] compared Psychogenic to organic/physiologic paroxysmal events and found PNES to have a significantly higher female to male ratio ($p=0.027$). Kotagal et al.[47] found PNES patients below the age of 12 more likely to be male($p<0.03$) compared to patients above 12 years of age. Co-existing epilepsy was present to a varying degree ranging from 0% to 92% [43,44,48], 23% being the median.

Semiology

Semiology was described in varying detail, some studies using broad terms such as “predominantly motor events”[47] while other studies used more detailed descriptions such as “unilateral clonic movement” referring to upper limb movement[34]. Initially there were 153 unique items concerning semiological descriptions. As previously mentioned, similar items were grouped together under broad terms to provide a more comprehensive and useful data table. After combining similar terms, 55 unique terms remained(see , Table 13, Table 14 and Table 15).

Motor events

As the different papers report movements differently, comparing the frequency of motor movement prove difficult. The range of generalised motor movement was 20% – 73% [38,40]. The 20% found by Dhiman et al. is due to reporting 11 cases of “Out of phase asynchronous body movements” and further reported 29% lower limb movement, 27% upper limb movement and 21% side to side body movement. Furthermore, Asadi-Pooya et al.[38] report 16 cases of “Generalised motor activity” but no further events of motor type are described. Asadi-Pooya et al.[37] found statistically significant differences in the likelihood of generalised motor seizures with percentages varying between 30%(Venezuela) and 84%(Iran). Say et al.[49] compared semiology between male and female adolescents and found “tonic-clonic limb movement” to be more likely in male patients($p=0.036$). Madaan et

al.[48] also compared male and female patients finding motor events to be more likely in male children($p= 0.01$). Kramer et al.[12] compared children <10 years of age to those >10 and found the older children more likely to have “mainly motor” type semiology ($p= 0.029$). Pubertal patients were found more likely($p= 0.018$) to have motor events compared to pre-pubertal ones in one study by Verrotti et al. [44].

Three studies report on upper and/or lower limb movement[34,40,42]. One of the studies however reported only 1 case of “Bizarre arm movement” [42]. The other two papers report 27% – 71%[34,40] upper limb movement and 29% – 47%[34,40] lower limb movement. Chinta et al. reports 53% of participants having no limb movement during seizures. Head movement such as “Side to side head shaking”[37,49,50], “Flexion/extension movements of the head”[40] and “Prolonged head deviation to either side”[42] were reported in 2% – 17%[37,49] of cases.

Negative events

Events reported as “dialeptic”[51], “Unresponsive events”/“Unresponsiveness”[34,36–38,44,45,47,49,52] or “Trancelike state”[42] were categorised as dialeptic/unresponsive events and ranged 5% – 86%[42,52]. “Staring spell”/“Blank spell”[36,52,53], “Absence”[41] and “Staring with upward gaze and blinking”[42] were deemed comparable and represented by the term “Staring event” ranging 2% – 29%[36,52,53].

Atonic events were described by many papers using a wide variety of terms such as “Syncope-like fall”[35,36,42], “Swoons”[53], “Atonic fall”[49] and “Generalised limpness”[52] and were found ranging 4% – 50%[36,39]. Say et al. found atonic events to be more likely in female patients($p= 0.02$). In the paper by Verrotti et al. pre-pubertal patients were found significantly more likely to have “unresponsive events” ($p= 0.001$).

Aura

Aura or other subjective sensations preceding or co-occurring with recorded seizures was also described in a wide variety of terms, most prevalent being “Aura” or “Visual/auditory aura” used by 5 out of 9 papers[37,38,49,51,52]. Other papers used descriptions such as “Sensory sign”, “Sensory experiences” and “Subjective sensations”[14,36,46]. These auras were present in 7% – 77%[38,46]. Asadi-Pooya et al. found statistically significant differences in

likelihood of aura before seizure($p= 0.005$) varying between 54%(in Brazilian patients) – 90%(in Canadian patients).

Specific signs

Specific signs often present in adult PNES[3] or signs often seen as strong indicators of true epileptic seizures are described by some of the studies[3,7]. Ictal eye closure, often seen as an indicator of PNES[7] was reported by 4 studies and varied between 14.3% – 68.8% [7,37,48–50]. Alessi et al. also compared likelihood of ictal eye closure in PNES in children to PNES in adults, finding adults to be significantly more likely to have this sign($p= 0.006$). Asadi-Pooya et al. also found statistically significant differences in ictal eye closure between PNES in children from different cultures($p= 0.0001$), where patients from Iran had the sign in 84% of cases and patients in USA had as little as 30%. In the paper by Alessi et al. postictal speech change was found significantly more likely in adults compared to children with PNES($p= 0.021$). Four papers[14,40,48,49] report cases with abrupt onset and/or offset, with percentages between 39% – 80% [14,49]. Tongue biting was reported by two papers with one patient having this sign in each paper[40,48]. Urine incontinence was present and reported on in 3 papers and present in 2% – 9% [38,40] of seizures. Ahmed et al. compared the presence of Chvostek’s sign in epilepsy compared to among others, PNES, and found a lower likelihood in PNES. Vincentiis et al. found that out of 19 patients with concomitant epilepsy, 10(53%) had PNES mimicking their epileptic seizures. Eight papers report presence of hyperventilation prior to or during seizures, being present in 3% – 58% [36,49] of cases[14,36,39–41,48–50]. Pelvic thrusting, considered in 6 studies[14,34,40,48–50], was present in 3% - 24% [14,34] participants. Alessi et al. found pelvic thrust movement to be more likely in adults than in children with PNES ($p= 0.035$).

Seizure duration

Seizure duration is reported in some form in nine papers[14,38,41,44,46,48–50,52]. Three papers report the number of patients having seizures below or above two minutes[46,49,50]. 26% - 77% of patients had up to two minutes duration while 22% - 74% had a longer than two minutes duration[49,50]. Asadi-Pooya et al.[38] reports 25% of patients as having seizure duration longer than 10 minutes and 75% as having less than 10 minutes. Five papers report duration range out of which two reports median (see Table 3)[14,41,44,48,52]. Yilmaz et al. found PNES to have a significantly longer duration than organic/physiological paroxysmal events ($p= 0.001$). Say et al. found female patients significantly($p= 0.04$) more likely to have events longer than 2 minutes[49]. Alessi et al. saw a higher likelihood($p<0.001$) of motor phenomenon lasting more than 2 minutes in adults compared to in children[50].

Table 3 - Duration of PNES in children

| | Duration of event (median) | Duration of event (range) |
|-------------------------|----------------------------|---------------------------|
| (Madaan et al., 2018) | 180s | 11-1500s |
| (Szabó et al., 2012) | 269s | 1-3417s |
| (Bhatia & Sapra, 2005) | | 10-35 min |
| (Verrotti et al., 2009) | | 10-35 min |
| (Wyllie et al., 1990) | | 0,5-17 min |

Table 4 - Duration of PNES in children

| | Duration >2 mins | | Duration <2 mins | | Duration <10 mins | | Duration >10 mins | |
|----------------------------|------------------|------|------------------|------|-------------------|------|-------------------|------|
| (Say et al., 2015) | 48 | 77 % | 14 | 23 % | | | | |
| (Yilmaz et al., 2013) | 35 | 65 % | 17 | 31% | | | | |
| (Alessi et al., 2013) | 11 | 26 % | 31 | 74 % | | | | |
| (Asadi-Pooya et al., 2019) | | | | | 38 | 75 % | 13 | 25 % |

Frequency

Three studies mention seizure frequency[38,46,51]. Valente et al.[51] report 34% of patients having daily events, 19% having weekly, 19% having monthly, 15% having less than monthly and 11% of patients only having attacks while stressed. Yilmaz et al.[46] report 35% of patients having daily attacks and 61% having attacks less than daily. Furthermore, they also found PNES to have a significantly lower frequency than organic/physiological paroxysmal events ($p<0.001$). Asadi-Pooya et al.[26] report a mean of 109 attacks per month with variation between included subgroups from Iran, Saudi Arabia and Canada. The difference was not statistically significant.

Classifications

Four types of classifications were used in included studies namely, classification methods according to Seneviratne et al.[3], Szabó et al.[14], Dhiman et al.[40] and Griffith et al.[54]. One method was used by Patel et al.[55] and later a similar method was used by Yilmaz et al.[46]. These methods were not described as standardised classification methods but were considered to have features of classification systems and will therefore be included in the classification portion of this paper.

Classification according to Seneviratne et al.

The most commonly used classification method in the included papers was the one from Seneviratne et al.[3]. It classifies PNESs into one of six categories namely rhythmic motor, hyper motor, complex motor, dialeptic, aura and mixed (see Table 5) [3]. The original paper creates this classification out of the data from a population with age ranging 16 – 83 years. Madaan et al.[48] uses this in pediatric PNES, finding some differences between female and male semiology. They also saw less back arching and pelvic thrusting in their population than reported in the adult patients of Seneviratne et al.[3]. They also note that dialeptic PNES is the largest group in their study compared to rhythmic motor being the largest in adults. Say et al.[49] compare semiology and clinical characteristics in male and female adolescent PNES patients. Using this classification, no statistically significant difference could be found comparing semiology in male and female patients. Dhiman et al.[40] studied the different semiological patterns in children with PNES and found classifying the patients according to this classification difficult. They report 26 (46%) patients remained unclassifiable after using the method described previously[3]. They developed a new classification system enabling classification of all their patients. Szabó et al.[14] also found classifying their population according to Seneviratne et al.[3] difficult and go on to propose their own classification method. They too found the dialeptic group to be larger than reported in adult patients when compared to previous work[3]. It is also noted that the dialeptic group had the lowest mean age compared to the other categories, however no statistical analysis was performed to confirm this association. Comparing the data from the four studies is difficult since the data from Dhiman et al. is split into classified and unclassified s. Comparisons will thus be done on the remaining three papers. Rhythmic motor was seen in 10% - 24% [14,48], hyper motor in

0% - 13%[14,49], complex motor in 4% - 19%[48,49], dialeptic in 29% - 43%[14,48], aura in 10% - 28%[14,49] and mixed in 4% - 29%[14,48].

Table 5 - Classification methods according to Seneviratne et al. and Szabó et al.

| | | (Madaan et al., 2018) | (Say et al., 2015) | (Dhiman et al., 2014) | (Szabó et al., 2012) | (Valente et al., 2017) |
|--|---|-----------------------|--------------------|-----------------------|----------------------|------------------------|
| | Patients | 80 | 62 | 56 | 27 | 53 |
| | Number of events | | | | 75 | |
| | Female | 35 44 % | 44 71 % | 30 54 % | 21 78 % | 32 60 % |
| Categories according to Seneviratne et al. | Rhythmic motor | 8 10 % | 13 21 % | 3 5 % | 18 24 % | |
| | Hyper motor | 1 1 % | 8 13 % | 2 4 % | 0 0 % | |
| | Complex motor | 3 4 % | 12 19 % | 5 9 % | 10 13 % | |
| | Dialeptic | 34 43 % | 19 31 % | 8 14 % | 22 29 % | |
| | 'Aura' | 11 14 % | 6 10 % | 3 5 % | 21 28 % | |
| | mixed | 23 29 % | 4 7 % | 9 16 % | 3 4 % | |
| | Unclassifiable according to this classification | | | 26 46 % | | |
| Categories according to (Szabó et al., 2012) | Dialeptic | | | | 22 29 % | 15 28 % |
| | 'Aura' | | | | 21 28 % | 6 11 % |
| | Minor motor | | | | 19 25 % | 11 21 % |
| | Major motor | | | | 10 13 % | 21 40 % |
| | Major motor synchronous | | | | 8 11 % | |
| | Major motor asynchronous | | | | 2 3 % | |
| | mixed | | | | 3 4 % | |

Classification according to Szabó et al.

The classification proposed by Szabó et al.[14] categorises PNES into minor motor, major motor, dialeptic, nonepileptic aura and mixed PNES(see Table 5). The categories of dialeptic and nonepileptic aura is described to be unchanged compared to categorisation according to Seneviratne et al. however minor motor and major motor replaces the rhythmic, complex and hyper motor ones. Major motor described as having motor symptoms combined with low responsiveness and minor motor having motor symptoms together with a higher level of responsiveness. The motor symptoms described in the minor motor group are characterised as synchronous and homogeneous, varying in intensity from tremor to tonic-like movement. The major motor symptoms are described as more complex movements involving more limbs. A difference noted by Szabó et al. in their paediatric population compared to the adult one were the level of responsiveness(86% compared to 16%[3,14]) in the rhythmic motor group as well as finding no patient matching the hyper motor group of the classification from Seneviratne et al..

Valente et al.[51] use the classification method proposed by Szabó et al. when researching different factors associated with diagnostic delay in PNES in children. They found no statistically significant difference in diagnostic delay when comparing different semiological classifications. Their data did not follow the pattern seen in the study by Szabó et al. as major motor was the biggest category(40% compared to 13%) with dialeptic being the second largest(28% compared to 29%).

Classification according to Dhiman et al.

Dhiman et al. analyzed the PNES of children and found classification according to Seneviratne et al. to be difficult to apply. They then proceeded to develop a different classification system. Their new method divides the PNES into five main categories and further detail subgroups within these(see Table 6). The main groups consist of abnormal motor, affective/emotional behaviour phenomenon, dialeptic, aura and mixed. Abnormal motor is subdivided into hyper motor and partial motor and mixed is subdivided into combinations of the other groups and subgroups.

Table 6 - Classification methods according to Dhiman et al.

(Dhiman et al., 2014)

| | | Patients | |
|--|-----------------------------------|------------------|------|
| | | Number of events | |
| | | Female | |
| <i>Classification according to (Dhiman et al., 2014)</i> | I. Abnormal motor | | 56 |
| | A. Hyper motor | 13 | 23 % |
| | B. Partial | 8 | 14 % |
| | II. Affective/emotional behaviour | 2 | 4 % |
| | III. Dialeptic | 8 | 14 % |
| | IV. Aura | 3 | 5 % |
| | V. Mixed | 22 | 39 % |
| | A. hyper motor + affective | 10 | 18 % |
| | B. Hyper motor + dialeptic | 3 | 5 % |
| | C. Hyper motor + aura | 1 | 2 % |
| | D. Partial motor + affective | 5 | 9 % |
| | E. Partial motor + dialeptic | 0 | 0 % |
| | F. Partial motor + Aura | 0 | 0 % |
| G. Affective + Dialeptic | 3 | 5 % | |
| H. Affective + aura | 0 | 0 % | |
| I. Dialeptic + aura | 0 | 0 % | |

Classification according to Griffith et al.

Alessi et al.[50] is the sole paper in this review using this classification system that categorises PNES into catatonic, subjective, minor motor and major motor[54](see **Fel! Hittar inte referenskölla.**). The original paper by Griffith et al. unfortunately being unavailable to this papers author, thus not allowing for detailed descriptions of the classification system. Alessi et al. compares the distribution of PNES according to classification by Griffith et al.[54] between adult and paediatric patients finding adult more likely to have the major motor type($p<0.001$).

Unnamed classifications

The classifications used by Patel et al. and Yilmaz et al. had many similarities as they both grouped the seizures into either “prominent motor activity” or “subtle motor activity”(see **Fel! Hittar inte referenskölla.**). The two categories was then subdivided into smaller groups. Prominent motor activity had the subgroups generalised jerking/flailing, focal motor activity, complex motor activity and generalised tremor. Subtle motor activity had the subgroups

Table 7 - Classification methods according to Dhiman et al.

| | | (Patel et al., 2007) | (Yilmaz et al., 2013) | (Alessi et al., 2013) |
|---|----------------------------------|----------------------|-----------------------|-----------------------|
| | Patients | 59 | 54 | 42 |
| | Number of events | 73 | | |
| | Female | 37 63 % | 36 67 % | 20 48 % |
| Classification according to (Griffith et al., 2007) | catatonic | | | 10 24 % |
| | subjective | | | 9 21 % |
| | Minor motor | | | 16 38 % |
| | Major motor | | | 7 17 % |
| Prominent motor activity | | 43 59 % | 27 50 % | |
| | Generalised jerking/flailing | 19 26 % | 23 43 % | |
| | Focal motor activity | 12 16 % | 1 2 % | |
| | Complex motor activity | 9 12 % | 2 4 % | |
| | Generalised tremor | 3 4 % | 1 2 % | |
| Subtle motor activity | | 30 41 % | 27 50 % | |
| | Staring | 11 15 % | 8 15 % | |
| | Head shaking | 6 8 % | | |
| | Generalised limpness | 5 7 % | 9 17 % | |
| | Stereotypic movement | | 6 11 % | |
| | Behavioral changes/combativeness | 5 7 % | | |
| | Eye fluttering/visual blurring | 2 3 % | 0 0 % | |
| | Oromotor activity | 1 1 % | | |
| | Subjective sensation | | 4 7 % | |

staring, generalised limbness and eyefluttering/visual blurring. The two papers also had their own respective subgroups for subtle motor activity, Patel et al. had head shaking, behavioural changes/combateness and oromotor activity while Yilmaz et al. had stereotypic movement and subjective sensation. Both studies found similar levels of prominent motor activity(50% - 59%[46,55]) although the distribution within the subgroups was less consistent. The two papers saw similar numbers for subtle motor activity as well.

Quality and strength of evidence

The quality of included studies was assessed and divided into ‘poor’ (n= 10, 43.5%), ‘fair’ (n= 10, 43.5%) and ‘good’ (n= 2, 8.7%). One (4.3%) study was wholly qualitative in nature and thus not assessable with NIH’s quality assessment tools[36]. The other qualitative study used quantitative methodology for a substantial part of the research and this part of the study and findings thereof was assessed and included[35].

Overall, the quality was low mostly due to lacking or limited statistical analysis(see , and), small study population and not adequately describing methodology. In many cases it was difficult to determine whether children were included through retrospective review of chart data or by direct recruitment at the clinic. When comparing groups, 11/17(65%) studies had performed some form of statistical analysis. No apparent conflicts of interest were found in the studies, reflecting the fact that no paper discuss factors with commercial consequences.

Tabell 1 - Quality assessment part I

| | How is PNES diagnosed? | Study type | What is researched | Findings | Quality Rating (Good, Fair, or Poor) | Limitations |
|------------------------------|---|--|---|--|---|--|
| (Madaan et al., 2018) | Through observed event in VEEG assessed for presence or absence of clinical characteristics through pre-designated standardised means | Cross-sectional observational study | demographics and semiology in pediatric PNES | Motor events more common in boys (P=0.01). Could see semiological differences (more dialeptic events than motor) comparing with earlier studies on adults however statistical analysis was not performed. | Fair | The amount of statistical analysis that was performed is not mentioned. Bonferroni adjustment was not reported to be used. |
| (Pakalnis & Paolicchi, 2003) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Prospective observational cohort study | Conversion symptoms in children with PNES and outcome after treatment. | Patients with poor outcome in their PNES also had epilepsy. | Poor | No statistical analysis was performed. Methodology when classifying semiology was not reported. |
| (Patel et al., 2007) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | Clinical features and differences in these between children and adolescents. | "Subtle motor activity" only was more prevalent in the group <13 years compared to those >13 (p < 0.01) but rising above significant threshold set at P<0.003 after bonferroni adjustment. Prominent motor activity was more prevalent in the group >13 years (p < 0.001). | Good | bonferroni adjustment were made, no other statistical adjustments were mentioned. |
| (Say et al., 2015) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | The difference in clinical characteristics such as semiology, psychopathology and precipitating stress factors between male and female adolescents with PNES. | Semiologically, statistical significance was found in "Atonic fall" where females were more likely (p = 0.020). In "ictal duration >2mins" females were more likely (p=0.040) and in "tonic-clonic limb movements" males were more likely (p=0.036). | Fair | Many tests were performed and there are no mentions of using bonferroni corrections or similar. |
| (Szabó et al., 2012) | Through observed event in VEEG assessed for presence or absence of clinical characteristics through pre-designated standardised means | Chart review study | The semiological characteristics of PNES in children. | Found it difficult to categorise PNES according to (Seneviratne et al., 2010) and proposes a modified model. The prevalence of abrupt start of episodes were high compared to earlier studies on adult PNES, no statistical comparisons are made in the study however. They also found dialeptic forms to be more frequent than in adult populations described by seneviratne and the mean age of their dialeptic patients were the lowest (not statistically tested). | Fair | Data concerning rhythmic movement, symmetric movement, intensity change, UL involvement, LL involvement, trunk, head movement and axial arching were excluded as the percentages provided did not correspond with whole numbers of the presented total. |
| (Valente et al., 2017) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Cross-sectional observational study. | Time until diagnosis and factors associated with diagnostic delays. | They found no statistical significance in amount of diagnostic delay when comparing semiology (motor/non-motor), presence of "PNES status" or attack frequency. | Fair | They research the potential factors contributing to diagnostic delays but exclude patients and parents having trouble to understand "the protocol and to give precise and accurate information". It is not specified how many were excluded and why. No adjustment for gender, age or Bonferroni correction was applied even though the measured factors were numerous. Power estimates were either not performed or not reported. |
| (Verrotti et al., 2009) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | The clinical features of PNES in children with epilepsy, comparing pre-pubertal and pubertal patients. | Pre-pubertal patients were statistically more likely to have "unresponsive events" compared to pubertal patients (P=0,001). Likewise Pubertal patients were statistically more likely to have "motor events" compared to pre-pubertal patients (P=0,018). Pubertal patients also had a longer mean duration of symptoms prior to PNES diagnosis (P=0,019). | Poor | It isn't reported how they make the diagnosis PNES, if the same criteria/process were applied to all participants. Measurements were not predetermined nor applied consistently over all patients. It's not clear how many patients were considered for inclusion, and later excluded. No statistical adjustments were performed when it comes to gender, epilepsy type nor bonferroni or similar. |
| (Vincentiis et al., 2006) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Cross-sectional observational study | Possible risk-factors for PNES in children with epilepsy. | 47,6% of patients had PNES mimicking their epileptic seizures. | Poor | No statistical analysis was performed to evaluate their findings. The specifics on How PNES is diagnosed and defined is not reported. The semiology of the patients with PNES mimicking their epilepsy isn't reported. |

Tabell 2 - Quality assessment part II

| | How is PNES diagnosed? | Study type | What is researched | Findings | Quality Rating (Good, Fair, or Poor) | Limitations |
|----------------------------|---|-------------------------------------|--|---|---|--|
| (Wyllie et al., 1990) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | Long-term(6-66 months) outcome after diagnosis. | They found a large part of the patients had stopped having seizures (14 out of 18 in the followup). | Poor | Follow-up time was vastly different between patients. Not reported on what basis the PNES diagnosis was made except for the use of VEEG and clinical judgement. No statistical analysis was performed. |
| (Yi et al., 2014) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | the characteristics and clinical outcomes of PNES in children | They found most patients were seizure-free(80%) or had reduced frequency(12%) of events. Motor events such as "generalised tonic-clonic movements"(8) and "focal tremor"(5) were more frequent than unresponsive/atonic events. | Fair | The time to follow-up was vastly different between patients making comparisons difficult. Patients received different treatments. |
| (Yilmaz et al., 2013) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | Demography, frequency and clinical manifestations of PNES(paryoxsomal non-epileptic events) in children. Differences between psychogenic and organic events. | When comparing psychogenic to organic events, psychogenic events had longer durations(P=0.001) but lower frequencies(P<0.001). Patients with psychogenic seizures were older(P<0.001) both at onset and at VEEG. They had symptoms for a shorter duration prior to diagnosis(P=0.024) and had a higher female to male ratio(P=0.027). They were less likely to have had perinatal asphyxia(P=0.041). No statistically significant difference in semiology could be established. | Fair | No statistical adjustment were made either through bonferroni adjustment or by factors such as gender or age. |
| (Ahmed et al., 2004) | Presented as "pseudoseizures" but definitions are not reported. | Cross-sectional observational study | Presence of Chvostek's sign in patients with different seizures and paroxysmal events. | Positive Chvostek's sign was more likely in patients with epilepsy than in pseudo-seizures. | Poor | The amount of eligible patients are not reported. From which clinics and how many, respectively, that were included was not reported. No statistical analysis was performed. |
| (Alessi et al., 2013) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | Semiological differences between children and adults with PNES. | They found certain signs/events to be more likely in adults than in children, namely ictal eye closure(P=0.006), "motor phenomenon lasting >2 min"(P<0.001), "postictal speech change"(P=0.021) and "pelvic thrust movement"(P=0.035). | Fair | No statistical adjustment due to factors in the participants nor bonferroni or similar was performed. |
| (Asadi-Pooya et al., 2019) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Multi-center chart review study | Clinical characteristics and differences of PNES in pediatric patients from different countries and cultures (Iran, Saudi arabia & Canada) | No differences between countries were found after bonferroni adjustment. Without adjustment, significant differences were seen in age at onset, likelihood of "aura before seizure" and history of physical abuse. | Fair | Although bonferroni adjustments were made, no adjustments for patient factors were. The diagnosis of PNES was not standardised and performed in various countries. |
| (Asadi-Pooya et al., 2019) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Multi-center chart review study | Clinical characteristics and differences of PNES in pediatric patients from different countries and cultures (Iran, Brazil, USA, Canada and Venezuela) | Statistically significant difference between children from different countries after bonferroni adjustment was seen in "aura before seizures"(P=0.005), "closed eyes during the seizures"(P=0.0001) and "generalised motor seizures"(P=0.0001). There was also a statistically significant difference in age of onset between the countries. | good | Although bonferroni adjustments were made, no adjustments for patient factors were. The diagnosis of PNES was not standardised and performed in various countries. |
| (Bhatia & Sapra, 2005) | Conversion disorder were diagnosed according to ICD- 10 (by WHO,1992). Clinical characteristics were partly procured from secondary sources, partly through direct observation. | Chart review study | The psychosocial and clinical characteristics of children with PNES(pseudoseizures). | They found generalised motor PNES to be most common, followed by focal motor and "akinetik" events. Most likely frequency of attacks were 5-6 per week. | Poor | No statistical analysis was performed. Specifics of how pseudoseizure was diagnosed and how the data was collected was not reported on. |

Tabell 3 - Quality assessment part III

| | How is PNES diagnosed? | Study type | What is researched | Findings | Quality Rating (Good, Fair, or Poor) | Limitations |
|--------------------------|--|-------------------------------------|--|---|---|---|
| (Chinta et al., 2008) | Through clinical assessment using history and observation of common characteristics. In some cases by VEEG monitoring. | Case-control study | Clinical and psychosocial characteristics of children with PNES and short-term outcome compared with "seizure control" and healthy control groups. | They found the NES group to have significantly more "life events" and higher "stress scores" than the two control groups. | poor | P-values are not reported. No statistical adjustments were reported as being used. It is not reported on how the data about semiology is collected. Only 12 out of 17 had the diagnosis confirmed by VEEG. Data about life events and stress scores are tabulated without specifying which data belongs to which group. |
| (Dhiman et al., 2014) | Through observed event in VEEG assessed for presence of common clinical characteristics and absence of epileptic activity on EEG | Chart review study | Different semiological patterns in PNES in children, categorising these into a new classification system. | They found it hard to classify their patients into the classification according to Seneviratne et. al. And 26/56 patients were unclassifiable. A new classification was introduced with more detailed subdivisions were all patients could be classified. | Fair | They propose a new classification system but no comparison between their system and the mentioned one by Seneviratne et. al. is made in a systematic way. |
| (Irwin et al., 2000) | Through clinical assessment using history and observation of common characteristics. In some cases by VEEG monitoring. | Chart review study | Causes, management and outcome of PNES in children. | They found patients with concurrent epilepsy to have a good outcome to a larger extent than to those without. "blank spells or swoons" were more likely in patients without epilepsy(17/24) compared to those with epilepsy(3/11). 7/11 patients with epilepsy had PNES mimicking their epileptic seizures. | Poor | No statistical analysis was performed. Seizure semiology was reported differently between the whole group and the group without epilepsy. Semiology for patients with concurrent epilepsy was not reported on in detail. |
| (Kotagal et al., 2002) | Through clinical assessment using history and observation of common characteristics. In many cases by VEEG monitoring. | Chart review study | Frequency of different paroxysmal non-epileptic events in a epilepsy monitoring unit. | They found PNES patients below 12 years old to be more likely to be male compared to patients above 12 years (P<0.03). Out of 883 patients monitored, 134 had paroxysmal non-epileptic events out of which 62 were due to conversion disorder(=PNES). | Poor | They compare the gender distribution between patients with paroxysmal non-epileptic events due to conversion disorder below and above 12 years of age. This was not announced in their objectives. No statistical adjustments were performed. Statistical methods are not reported in "MATERIALS AND METHODS". |
| (Kozłowska et al., 2018) | Patients referred from neurological clinic. Details on diagnostic means were not reported. | Qualitative observational study | Diagnostic formulations to identify different subgroups of PNES. | Not included | NA | As the study uses a qualitative research method comparisons to other studies in this paper is not possible. Use of NIH's Study Quality Assessment Tools are also not possible. Any findings are therefore not included. Numbers representing semiology are included as they are not affected significantly by the qualitative nature of the study. |
| (Kozłowska et al., 2011) | As symptom of conversion disorder according to DSM-IV-TR after referral to the authors clinic. | Observational study | How children and adolescents with PNES process their emotions compared to healthy controls. | More patients had predominantly motor(tonic-clonic-like) episodes than syncope-like. | Fair | Other conversion symptoms such as "whole body floppy weakness", "conversion tics and tremors", "blindness or visual loss" etc. was categorised under other specific conversion symptoms and not PNES. The study use both qualitative and quantitative methods. The data provided by use of qualitative methods are excluded from this paper due to difficulties comparing results and quality to the other papers. No statistical analysis was performed on the quantitatively gathered data. |
| (Kramer et al., 1995) | Using Volow's definition for PS as "episodic behavioral spells that mimic or imitate true epileptic seizures". | cross-sectional observational study | Comparing clinical features in young children with adolescents. | No statistically significant difference between patients <10 and those >10 years comparing "staring as a single phenomenon". "mainly motor" symptomatology was more frequent in the adolescent group (P=0.029). | Poor | Sample size was very low in the group <10 years(5 patients), making statistical analyses hard to interpret. No statistical adjustments were performed. |

Discussion

This systematic literature review attempts to find and present current knowledge pertaining to semiological presentation of PNES in children. The majority of studies were of low quality overall, the methodology mostly retrospective in nature and few studies present their methods adequately. Some papers present a more detailed methodology however as the used methods differ, a comparison of data collected in the different studies proved difficult. Few studies compare semiology between different groups such as between genders, over different age groups or across medical conditions, providing little evidence to presenting a comprehensive overview of the semiological presentation in paediatric PNES.

Classification and semiological descriptions

Differences between semiological descriptions and classifications

In this paper it was decided that classifications and semiological descriptions were to be addressed separately as they are two different entities. Classifications try to separate patients into one of several pre-designated categories while descriptions are a list of signs that may or may not be present in a specific event. Most of classifications employed follow the methodology of work previously published by other authors mostly with adult patients whilst some describe a new classification method.

Semiology in paediatric PNES

In this review an attempt to compare the different semiological signs presented by the literature was made. The extensive variety of descriptions used made such a comparison difficult. But certain conclusions could be drawn.

As noted in several papers, the proportion of events with negative symptoms compared to motor symptoms seems to be higher in paediatric PNES[14,48,50]. Signs that in the adult population are often seen as strong indications that an event is psychogenic such as pelvic thrusting are seen less often in children and need to be systematically researched and compared to paediatric epileptic patients[50,56]. None of the included articles compared semiology between PNES and epilepsy in children except for one study from Ahmed et al.[43] that investigated Chvostek's sign without any statistical analysis done. No conclusion

on the importance of semiology when differentiating PNES from epilepsy in children can thus be drawn. Only one article compares semiology between adults and children in a systematic way[50], making comparisons between children and adults difficult as well. A few studies compare younger children with older ones with PNES but use different descriptions, age groups and methodology and cannot be directly compared[12,44,47,48,55]. This review has shown the wide variety of terms used to describe semiology in these patients and point towards a need for a more structured way of describing ictal presentation. Formal definitions of signs during events need to be established for future research to be able to compare the work from different researchers.

PNES classification in paediatric patients

As shown the most used classification method in the included articles were the one from Seneviratne et al.[3]. Even with common methodology the three studies show considerable variations in the proportions of the different categories suggesting a lack of agreement between rates across studies. The other classifications were only used by at most two papers making it difficult to draw any conclusions. None of the classification methods compared PNES with epilepsy nor compared results of different clinicians using the same method on the same patients. Both are important to establish reliability if one is to rely on these classifications during research. The reliability of research results is therefore lacking. Further research is required to establish a reliable classification that clinicians can use to provide usable data in the future.

Reasons for variance in results between studies

As noted, in the paper by Kozłowska et al.[35] certain symptoms that in other papers were assessed as PNES were instead seen as other conversion symptoms rather than PNES. The large variation seen in the different studies could be associated with a different definition of PNES. Another possibility is that the events themselves are assessed differently by different assessors, that is they have a low inter-rater reliability. A combination of these two factors could be the most likely but further research is clearly necessary.

Study quality

As PNES in children is relatively rare[10], gathering a sufficient sample size is difficult and is reflected in the study types as well as the study population (median sample size of 42) of included papers. The chart review study type used by most researchers allows for a larger sample sizes without needing several years of ongoing data collection. This study type however, does not allow for systematic testing of pre-designated signs that require some form of agreement at the time of inclusion.

Only two studies were rated as of ‘good’ quality, these were retrospective in nature and used pre-designated statistical methods[37,55]. Both used Bonferroni adjustment as the tested factors were numerous, however no other statistical adjustments were performed. Sample-sizes were fair, especially in the case of Asadi-Pooya et al.[37] with 229 patients. However, as none of the included articles performed sample size calculations, acceptable sample size estimates are difficult. The rating however does not consider the weaknesses of chart reviews in general and findings must thus still be viewed with caution. No study using prospective methods reached “fair” rating (see , and). Studies rated as “fair” were of either chart review type or cross-sectional observational type. This further shows the difficulty researching PNES in children.

Asadi-Pooya et al. showed some differences in PNES semiology comparing patients from different countries[37]. In two studies differences between male and female PNES could be found[48,49]. Furthermore, several studies[12,44,50,55] show differences in clinical presentation of PNES depending on age. Kotagal et al.[47] found younger patients to be more likely to be male. This suggests that there is some form of difference in PNES semiology depending on age and gender. Considering that none of included articles statistically adjusted their results for control variables such as age and male/female ratio, the results could be biased. Adding to this are the findings of Alessi et al.[50] showing significant differences in PNES semiology when comparing adults to children. Future research into these differences are required to confirm the findings.

Clinical implications

This review has shown the lack of scientific research supporting the use of assessing semiological presentation when diagnosing PNES in children. The evidence that does exist is from research of adult or adult and paediatric populations and some studies reviewed in this article suggests certain differences in semiological presentation between adults and children. The duration of events seems to be longer, motor activity seems less likely and less prominent, specific semiological signs of PNES such as ictal eye closure, pelvic thrusting and slow seizure onset less likely in children compared to what is seen in adult populations. Comparisons to epileptic seizures in children have not been investigated. Caution must therefore be used when assessing paediatric PNES based on ictal presentation.

There are several semiological classifications that have been used to describe PNES in children. Their usefulness in the clinical setting is limited as these classifications to date have shown no association with treatment outcome, no increased diagnostic accuracy or suggesting of different underlying medical conditions. Furthermore, inter-rater reliability is untested and comparing results from different studies suggests such reliability to be poor.

Directions for future research

Semiology

The wide variety of terms used to describe ictal phenomenon by included articles presents difficulties when attempting to apply results in the clinical setting. Different researchers use different terms to describe seemingly equivalent semiological presentations. The terms used to describe paroxysmal events including epilepsy and PNES need to be standardised in order to enable clinical applications of research done. Using standardised means of classifying and observing, the difference in semiology comparing epileptic, psychogenic and other paroxysmal events needs to be investigated. Furthermore, the clinical presentation of PNES needs to be compared between children and adults in order to enable or discard parallels between the populations. Before such research is performed the usage of results from research with adult populations on paediatric patients are dubious.

Classifications

Agreed classifications of the semiological presentation in PNES could allow for a more standardised means of reporting data and enable comparisons between research groups. However, the reliability of these classification systems is yet to be confirmed. Research into inter-rater reliability is necessary before any conclusions can be drawn from the results showing differences between different groups.

Limitations

Changing research goal

Because of time constraints and practical reasons, the goal of this paper had an interim change. Instead of covering all aspects concerning assessment and diagnosis, this papers author decided to pursue semiology and classification methods.

Switching to Zotero

Due to multiple incidents during the screening process where Endnote crashed and many hours of work was lost, a decision to move all references to the open source program Zotero was taken. This was also affected by the COVID-19 crisis as working from home became more prioritised and Zotero had a more streamlined interface for collaborative work. Due care was taken to ensure the integrity of the reference list and that all papers were successfully transferred to the correct folders. The work was then continued as with Endnote and did not affect the study to any larger extent.

Methodology

The method used to grade the quality of included papers was not designed for chart review studies and a more appropriate method should have been considered. As this papers author is inexperienced with PNES, the grouping of semiological terms might have been sub-optimal but expert advice was sought.

Bias and funding

The author of this study reports no bias and no funding was provided for the research done in this paper.

Conclusion

Drawing conclusions about semiology in paediatric PNES is difficult due to low study quality. Certain demographical trends could be seen such as lesser female to male ratio in younger children, younger children having less motor symptoms and more negative ones and that semiological signs of PNES seen in adults were less common in children. Children would appear to have a more abrupt onset of symptoms, lower likelihood of showing ‘pelvic thrusting movement’ or ‘ictal eye closure’ and shorter duration of events compared to adults. Furthermore, differences were found in the proportion of motor symptoms presented between different cultures. Classifications were reported on but no study validated used classification against any form of control. This paper concludes that data pertaining to semiology in paediatric PNES is insufficient to allow parallels to be drawn with research undertaken with adult populations. Furthermore, differentiating PNES from other paroxysmal events such as epileptic seizures through assessing semiology remains relatively untested.

Semiologi och klassifikationer av psykogena icke epileptiska anfall hos barn – en systematisk litteraturöversikt

Psykogena icke epileptiska anfall(PNES) är anfall som liknar epileptiska anfall. Man tror att anfällen har en psykisk orsak men det är fortfarande inte helt klarlagt. Patienterna har ofta mer psykiska trauma, framför allt hos vuxna, i sin bakgrund som då tyder på detta. En patient med PNES kan börja skaka i armar och ben, rycka med huvudet ifrån sida till sida och till synes tappa medvetandet. Ibland är anfällen mer lugna och patienter blir okontaktbar och lealös. Dessa anfall undersöks av erfarna läkare inom fältet med hjälp av bland annat video EEG övervakning. Detta går ut på att patienternas elektriska aktivitet i hjärnan läses av med elektroder fästa på skalpen samtidigt som de filmas under en längre tid. När de får ett anfall kan man då se på den avlästa elektriska aktiviteten om det ser ut som epilepsi. Om det inte gör det tittar man ofta på hur anfällen ser ut för att kunna lista ut vad som ligger bakom anfällen.

Utseendet på anfällen är alltså en viktig pusselbit för att kunna urskilja PNES från andra sjukdomar. Hittills har forskningen om anfällens utseende framför allt utförts på vuxna och

syftet med min studie var att gå igenom den forskning som gjorts hittills för att se vad denna säger om anfallens utseende hos just barn. Genom att använda tre olika vetenskapliga databaser hittade jag 1099 artiklar. Jag sållade dessa med hjälp av olika kriterier och fick till slut fram 23 artiklar som handlade om det ämnet jag utforskar. Jag tog ut den data som fanns i dessa artiklar och försökte dra slutsatser utifrån detta.

Det jag kom fram till var att vissa specifika tecken under anfallen hade berörts men som helhet var det ett väldigt utforskat område. Man kunde till exempel se att yngre barn hade lugnare anfall än äldre, att barn hade kortare och mindre motoriska anfall än vuxna och att flickor möjligen hade lite lugnare anfall än pojkar. Jag kunde inte hitta något stöd för att urskilja PNES ifrån epilepsi hos barn, inte heller för skillnader mellan barn och vuxna. Det viktigaste fyndet var att forskning behövs på ämnet och att läkare som står inför dessa patienter idag bör vara försiktiga när de gör bedömningar med hjälp av anfallens utseende.

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Appendix

Keywords

Block 1: PNES, pseudo-seizure, pseudoseizure, non-epileptic seizure, nonepileptic seizure, non-epileptic convulsion, nonepileptic convulsion, psychogenic seizure, functional seizure, conversion disorder with seizure, functional somatic symptom disorder with seizure, functional neurological disorder, functional neurological symptom, dissociative seizure, somatization W/10 seizure, somatization with seizure, somatoform seizure, non-epileptic attack disorder, nonepileptic attack disorder, stress seizure, non epileptic seizure, “seizure, nonepileptic”, “seizure, non-epileptic”, “seizure, non epileptic”

Block 2: child, pediatric*, paediatric*, young people, adolescen*, teen*, youth, youngster, juvenil*, toddler, kid, preadolescent

Block 3: Assessment, Investigation, screening, examination, diagnosis, diagnose, interview, EEG, video-EEG, electroencephalography, evaluation, checkup*, examen, serum prolactin

Search string for PubMed:

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(((((((((((((((((((((((((((((((((PNES[Title/Abstract])) OR (pseudo-seizure*[Title/Abstract])) OR (pseudoseizure*[Title/Abstract])) OR ("non-epileptic seizure*[Title/Abstract])) OR ("nonepileptic seizure*[Title/Abstract])) OR ("psychogenic seizure*[Title/Abstract])) OR ("functional seizure*[Title/Abstract])) OR ("conversion disorder with seizure*[Title/Abstract])) OR ("functional somatic symptom disorder with seizure*[Title/Abstract])) OR ("functional neurological disorder"[Title/Abstract])) OR ("functional neurological symptom*[Title/Abstract])) OR ("dissociative seizure*[Title/Abstract])) OR ("somatization with seizure*[Title/Abstract])) OR ("somatoform seizure*[Title/Abstract])) OR ("non-epileptic attack disorder"[Title/Abstract])) OR ("nonepileptic attack disorder"[Title/Abstract])) OR ("stress seizure*[Title/Abstract])) OR ("non-epileptic convulsion*[Title/Abstract])) OR ("nonepileptic convulsion*[Title/Abstract])) OR ("non epileptic seizure*[Title/Abstract])) OR ("seizure, nonepileptic"[Title/Abstract])) OR ("seizures, nonepileptic"[Title/Abstract])) OR ("seizure, non-epileptic"[Title/Abstract])) OR ("seizures, non-epileptic"[Title/Abstract]))
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OR ("seizure, non epileptic"[Title/Abstract])) OR ("seizures, non epileptic"[Title/Abstract]))
OR (("Conversion Disorder"[Mesh]) AND ((seizure*[Title/Abstract]) OR
(event*[Title/Abstract]))) AND (((((((((((((((Child*[Title/Abstract])) OR
(pediatric*[Title/Abstract])) OR (paediatric*[Title/Abstract])) OR ("young
people"[Title/Abstract])) OR (adolescen*[Title/Abstract])) OR (teen*[Title/Abstract])) OR
(youth[Title/Abstract])) OR (youngster[Title/Abstract])) OR (juvenil*[Title/Abstract])) OR
(toddler[Title/Abstract])) OR (kid[Title/Abstract])) OR (preadolescent[Title/Abstract])) OR
("Adolescent"[MeSH])) OR ("Child"[Mesh])) OR ("Infant"[Mesh]))) AND
((((((((((((((((((((Assessment[Title/Abstract])) OR (Investigation[Title/Abstract])) OR
(screening[Title/Abstract])) OR (examination[Title/Abstract])) OR
(diagnosis[Title/Abstract])) OR (diagnose[Title/Abstract])) OR (interview[Title/Abstract]))
OR (EEG[Title/Abstract])) OR (video-EEG[Title/Abstract])) OR
(electroencephalography[Title/Abstract])) OR (evaluation[Title/Abstract])) OR
(checkup[Title/Abstract])) OR (examen*[Title/Abstract])) OR ("serum
prolactin"[Title/Abstract])) OR ("Symptom Assessment"[Mesh])) OR ("Neurologic
Examination"[Mesh])) OR ("Diagnostic Tests, Routine"[Mesh])) OR
("Electroencephalography"[Mesh])) OR ("Neurophysiological Monitoring"[Mesh])) OR
("Pituitary Function Tests"[Mesh])) OR ("Psychiatry/diagnosis"[Mesh])) OR
("Psychiatry/instrumentation"[Mesh])) OR ("Psychiatry/methods"[Mesh]))

Search string for PsychINFO:

(TI,AB(PNES OR pseudo-seizure? OR pseudoseizure? OR "non-epileptic seizure?" OR
"nonepileptic seizure?" OR "non-epileptic convulsion?" OR "nonepileptic convulsion?" OR
"psychogenic seizure?" OR "functional seizure?" OR "conversion disorder with seizure?" OR
"functional somatic symptom disorder with seizure?" OR "dissociative seizure?" OR
"somatization with seizure?" OR "somatoform seizure?" OR "non-epileptic attack disorder"
OR "nonepileptic attack disorder" OR "stress seizure?" OR "non epileptic seizure*" OR
TI,AB"functional neurological disorder" OR TI,AB"functional neurological symptom?") OR
TI,AB,IF("seizure?, nonepileptic" OR "seizure?, non-epileptic" OR "seizure?, non epileptic")
OR (SU("somatoform disorders" or "conversion disorder" or "dissociative disorders" or
"psychophysiologic disorders" or "somatization disorder") AND TI,AB(seizure?)) OR

TI,AB(somatization N/10 seizure?)) AND (TI,AB(Child* OR p?ediatric* OR "young people" OR adolescen* OR teen* OR youth OR youngster OR juvenil* OR toddler OR kid OR preadolescent) OR SU(pediatrics or adolescent or child or "child, preschool")) AND (TI,AB(Assessment OR Investigation OR screening OR examination OR diagnosis OR diagnose OR interview OR EEG OR video-EEG OR electroencephalography OR evaluation OR checkup? OR examen OR "serum prolactin") OR SU(electroencephalography or "surveys and questionnaires" or "video recording" or "diagnostic and statistical manual of mental disorders" or psychodiagnosis))

Search string for Scopus:

(TITLE-ABS-KEY(PNES) OR TITLE-ABS-KEY(pseudo-seizure) OR TITLE-ABS-KEY(pseudoseizure) OR TITLE-ABS-KEY("non-epileptic seizure") OR TITLE-ABS-KEY("nonepileptic seizure") OR TITLE-ABS-KEY("non-epileptic convulsion") OR TITLE-ABS-KEY("nonepileptic convulsion") OR TITLE-ABS-KEY("psychogenic seizure") OR TITLE-ABS-KEY("functional seizure") OR TITLE-ABS-KEY("conversion disorder with seizure") OR TITLE-ABS-KEY("functional somatic symptom disorder with seizure") OR TITLE-ABS("functional neurological disorder") OR TITLE-ABS("functional neurological symptom") OR TITLE-ABS-KEY("dissociative seizure") OR TITLE-ABS(somatization W/10 seizure) OR TITLE-ABS-KEY("somatization with seizure") OR TITLE-ABS-KEY("somatoform seizure") OR TITLE-ABS-KEY("non-epileptic attack disorder") OR TITLE-ABS-KEY("nonepileptic attack disorder") OR TITLE-ABS-KEY("stress seizure") OR TITLE-ABS-KEY("non epileptic seizure") OR TITLE-ABS-KEY("seizure, nonepileptic") OR TITLE-ABS-KEY("seizure, non-epileptic") OR TITLE-ABS-KEY("seizure, non epileptic")) AND (TITLE-ABS(child*) OR TITLE-ABS(pediatric*) OR TITLE-ABS(paediatric*) OR TITLE-ABS("young people") OR TITLE-ABS(adolescen*) OR TITLE-ABS(teen*) OR TITLE-ABS(youth) OR TITLE-ABS(youngster) OR TITLE-ABS("juvenil*") OR TITLE-ABS(toddler) OR TITLE-ABS(kid) OR TITLE-ABS(preadolescent)) AND (TITLE-ABS(Assessment) OR TITLE-ABS(Investigation) OR TITLE-ABS(screening) OR TITLE-ABS(examination) OR TITLE-ABS(diagnosis) OR TITLE-ABS(diagnose) OR TITLE-ABS(interview) OR TITLE-ABS(EEG) OR TITLE-

ABS(video-EEG) OR TITLE-ABS(electroencephalography) OR TITLE-ABS(evaluation) OR TITLE-ABS(checkup*) OR TITLE-ABS(examen) OR TITLE-ABS("serum prolactin"))

Tables and figures

Demographics

Table 8 - Details about study demography

| | Parti- pants | Land | Age (mean) (SD) | Age (range) | Pre-pu- bertal | Pu- ber- tal | Girls | PNES with epilepsy dia- gnosis |
|------------------------------|-----------------|------------------|-----------------------|----------------|-------------------|--------------------|-------------|--------------------------------------|
| (Madaan et al., 2018) | 80 | India | 10.5 (SD 1.6) | 6-16 | | | 35 (43,75%) | 0 |
| | 61 | | | 6-11 | | | 24 (39,3%) | |
| | 19 | | | 12-16 | | | 11 (57,9%) | |
| (Pakalnis & Paolicchi, 2003) | 22 | USA | 13,5 | 7-17 | | | 19 (86,4%) | 5 |
| (Patel et al., 2007) | 41 | USA | | | | | 37 (62,7%) | 26,00 |
| | 22,00 | | 10.2 (SD 2.1) | <13 | | | 11 (50,0%) | 15 |
| | 37,00 | | 15.3 (SD 1.8) | >13 | | | 26 (70,2%) | 11 |
| (Say et al., 2015) | 62 | Turkey | 14.2 (SD2.0) | 11-18 | | | 44 (71,0%) | 25 |
| | 44 | | | | | | 44 (100%) | |
| | 18 | | | | | | 0 (0,0%) | |
| (Szabó et al., 2012) | 27 | Hungary | 14.8 (SD 2.8) | 8-18 | | | 21 (77,8%) | 9 |
| (Valente et al., 2017) | 53 | Brazil | 12,81 (SD 3,15) | 7-17 | | | 32 (60,4%) | 21 |
| (Verrotti et al., 2009) | 36 | Italy | 12,3 | 6-17 | 14 | 22 | 26 (72,2%) | 33 |
| | 14 | | 9,25 | | 14 | 0 | 9 (64,3%) | 11 |
| | 22 | | 14,25 | | 0 | 22 | 17 (77,3%) | 22 |
| (Vincentiis et al., 2006) | 21 | Brazil | | 5-18 | | | 9 (42,9%) | 19 |
| (Wyllie et al., 1990) | 21 | USA | 14,5 | 8-18 | | | 15 (71,4%) | 0 |
| (Yi et al., 2014) | 25 | South Ko- rea | 13,71 (SD 2,69) | 8,77- 19,93 | | | 14 (56,0%) | 8 |

| | | | | | | |
|-------------------------------------|-------|----------------|--------------------|---------|----------------|----|
| (<i>Yılmaz et al., 2013</i>) | 54 | Turkey | 13,79 (SD 2,81) | 5-18 | 36 (66,7%) | 6 |
| (<i>Ahmed et al., 2004</i>) | 27,00 | United Kingdom | | | | 0 |
| (<i>Alessi et al., 2013</i>) | 42 | Brazil | 12 | 6-17 | 20 (47,6%) | 17 |
| (<i>Asadi-Pooya et al., 2019</i>) | 51 | Mixed | 13,4(SD2,2) | 8-16 | 32 (62,7%) | 13 |
| | 22 | Iran | 14,2(SD 1,9) | | 13 (59,1%) | 6 |
| | 14 | Saudi-arabia | 12,1(SD 1,8) | | 10 (71,4%) | 1 |
| | 15 | Canada | 14,1(SD2,2) | | 9 (60,0%) | 6 |
| (<i>Asadi-Pooya et al., 2019</i>) | 229 | Mixed | 12,1(SD3,2) | 4-16 | 148 (64,6%) | 43 |
| | 83 | Iran | | | 52 (62,7%) | 27 |
| | 50 | Brazil | | | 31 (62,0%) | 20 |
| | 39 | canada | | | 25 (64,1%) | 10 |
| | 30 | USA | | | 20 (66,7%) | 15 |
| | 27 | Venezuela | | | 20 (74,1%) | 9 |
| (<i>Bhatia & Sagra, 2005</i>) | 50 | India | 8,9 | 6,8-12 | 28 (56,0%) | |
| (<i>Chinta et al., 2008</i>) | 17 | India | 10,7 | 7-13 | 13 (76,5%) | |
| (<i>Dhiman et al., 2014</i>) | 56 | India | 12,3(SD4,0) | 2-17 | 30 (53,6%) | 9 |
| (<i>Irwin et al., 2000</i>) | 35 | United Kingdom | 14,1 | 6-18 | 24 (68,6%) | 11 |
| (<i>Kotagal et al., 2002</i>) | 62 | USA | | 5-18 | 34 (54,8%) | 11 |
| | 22 | | | 5-12 | 8 (36,4%) | |
| | 40 | | | 12-18 | 26 (65,0%) | |
| (<i>Kozłowska et al., 2018</i>) | 60 | Australia | 13,45(SD 2,61) | 8-17,67 | 42 (70,0%) | 7 |
| (<i>Kozłowska et al., 2011</i>) | 36 | Australia | | 6-18 | | |
| (<i>Kramer et al., 1995</i>) | 27 | USA | 12,6(SD3,4) | 6-17 | 18 (66,7%) | 4 |
| | 5 | | | 6-9 | 2 (40,0%) | 0 |
| | 22 | | | 10-17 | 16 (72,7%) | 4 |

Semiology

Tabell 4 – Semiology data part I

| | (Madaan et al., 2018) | (Pakalnis & Paolicchi, 2003) | (Say et al., 2015) | (Szabó et al., 2012) | (Valente et al., 2017) | (Verrotti et al., 2009) | (Vincentis et al., 2006) | (Wyllie et al., 1990) | (Yi et al., 2014) | (Yilmaz et al., 2013) |
|---------------------------------|-----------------------|------------------------------|--------------------|----------------------|------------------------|-------------------------|--------------------------|-----------------------|-------------------|-----------------------|
| Study population | 80 | 22 | 62 | 27 | 53 | 36 | 21 | 21 | 25 | 54 |
| Spontaneous PNES | | | | | | | | 15 | 11 | |
| PNES after provocation | | | | | | | | 6 | 11 | |
| Abrupt onset/offset | 58 72,50 % | | 24 38,70 % | 51 – 60 68,0 – 80,0% | | | | | | |
| Gradual onset/offset | | | | | | | | | | |
| Rapid postictal reorientation | | | | | | | | | | |
| Lament/Negative emotion | 14 17,50 % | | | 32 42,70 % | | | | | | |
| Ictal eye closure | 55 68,80 % | | 32 51,60 % | | | | | | | |
| Eye movement | | | | 28 37,40 % | | | | 3 14,30 % | | |
| Situational onset | | | | | | | | | | |
| Eyewitness | | | | 67 89,30 % | | | | | | |
| Precipitate by stimuli | | | | | | | | | | |
| Mimics epileptic seizures | | | | | | | 10 47,60 % | | | |
| Confusion | | | | | | | 2 9,50 % | | | |
| Ictal reactivity | | | | | | | | | | |
| Ictal injury | | | | | | | | | | |
| Vegetative symptoms | | | | 7 9,30 % | | | | | | |
| Semiological heterogeneity | | | 12 19,40 % | 4 5,30 % | | 10 27,80 % | | | | |
| Dissociative symptom | | | | | | | | | 1 4,00 % | |
| Hyperventilation | 13 16,30 % | | 2 3,20 % | 14 18,70 % | | | | | 1 4,00 % | |
| Clenching of teeth | 11 13,80 % | | | | | | | | | |
| Tongue bite | 1 1,30 % | | | | | | | | | |
| Closed mouth in the tonic phase | | | | | | | | | | |
| Hiccoughs | 3 3,80 % | | | | | | | | | |
| Coughs | | | | | | | | | | |
| Gaspings/hiccups | | | | | | | | | | |
| Frothing | 2 2,50 % | | | | | | | | | |
| Urine incontinence | | | | | | | | | | |
| Chvostek's sign pos | | | | | | | | | | |
| Chvostek's sign neg | | | | | | | | | | |
| Dialectic/ unresponsive events | | 7 31,80 % | 22 35,50 % | | 15 28,30 % | 18 50,00 % | 1 4,80 % | 18 85,70 % | | |
| Staring event | | | | | | | 1 4,80 % | 6 28,60 % | 2 8,00 % | |

Table 9 - Semiology data part II

| | (Madaan et al., 2018) | (Pakalnis & Paolicchi, 2003) | (Say et al., 2015) | (Szabó et al., 2012) | (Valente et al., 2017) | (Verrotti et al., 2009) | (Vincentiis et al., 2006) | (Wyllie et al., 1990) | (Yi et al., 2014) | (Yilmaz et al., 2013) |
|--------------------------------------|-----------------------|------------------------------|--------------------|----------------------|------------------------|-------------------------|---------------------------|-----------------------|-------------------|-----------------------|
| Aura/sensational event | | | 22 35,50 % | 31 41,30 % | 6 11,30 % | | | 3 14,30 % | 4 16,00 % | 4 7,40 % |
| Vocalization/speech | | | 14 22,60 % | 12 16,00 % | | | | 1 4,80 % | | |
| Pseudosleep | | | | | | | | | | |
| Nocturnal seizures | | | | | | | | | | |
| Generalized motor movements | | 8 36,40 % | | | 21 39,60 % | 26 72,20 % | | | 8 32,00 % | |
| Purposeful/semi-purposeful movements | | | | | | | | | | |
| Undulating motor activity | | | | | | | | | | |
| Opisthotonos | | | | | | | | | | |
| Pelvic thrusting | 4 5,00 % | | 3 4,80 % | 2 2,70 % | | | | | | |
| Side to side body movement | | | | | | | | | | |
| Clonus | | | | 7 9,30 % | | | | | 3 12,00 % | |
| Myoclonus | | | | 8 10,70 % | | | | | | |
| Atonic event | | | 16 25,80 % | | | | 2 9,50 % | 1 4,80 % | 1 4,00 % | |
| Tonic events | | | | 12 16,00 % | | | | 1 4,80 % | 2 8,00 % | |
| Focal motor events | | 7 31,80 % | | | | | | | | |
| Minor motor | | | | | 11 20,80 % | | | | | |
| Generalized limb movement | | | 13 21,00 % | | | | 1 4,80 % | 10 47,60 % | | |
| Tremor | | | 17 27,40 % | 19 25,30 % | | | | 1 4,80 % | 5 20,00 % | |
| No limb movement | | | | | | | | | | |
| Violent movements | | | 8 12,90 % | | | | 1 4,80 % | | | |
| Head movement | | | | | | | 1 4,80 % | | | |
| Facial contractures | | | | | | | | | | |
| Upper limb movement | | | | | | | 1 4,80 % | | | |

Table 10 - Semiology data part III

| | (Ahmed et al., 2004) | (Alessi et al., 2013) | (Asadi-Pooya et al., 2019) | (Asadi-Pooya et al., 2019) | (Bhatia & Sapro, 2005) | (Chinta et al., 2008) | (Dhiman et al., 2014) | (Irwin et al., 2000) | (Kotagal et al., 2002) | (Kozłowska et al., 2018) | (Kozłowska et al., 2011) |
|---------------------------------|----------------------|-----------------------|----------------------------|----------------------------|------------------------|-----------------------|-----------------------|----------------------|------------------------|--------------------------|--------------------------|
| Study population | 27 | 42 | 22 | 229 | 50 | 17 | 56 | 35 | 62 | 60 | 36 |
| Spontaneous PNES | | | | | | | | | | | |
| PNES after provocation | | | | | | 4 23,50 % | | | | | |
| Abrupt onset/offset | | | | | | | 43 76,80 % | | | | |
| Gradual onset/offset | | 18 42,90% | | | | | | | | | |
| Rapid postictal reorientation | | 17 40,50 % | | | | | | | | | |
| Lament/Negative emotion | | | | | | | 17 30,40 % | | | | |
| Ictal eye closure | | 6 14,30 % | | 140 61,10 % | | | | | | | |
| Eye movement | | 2 4,80 % | | | | | | | | | |
| Situational onset | | 17 40,50 % | | | | | | | | | |
| Eyewitness | | | | | | | | | | | |
| Precipitate by stimuli | | 11 26,20 % | | | | | | | | | |
| Mimics epileptic seizures | | | | | | | | | | | |
| Confusion | | | | | | | | | | | |
| Ictal reactivity | | 9 21,40 % | | | | | | | | | |
| Ictal injury | | | 3 13,60 % | 35 15,30 % | | | | | | | |
| Vegetative symptoms | | | | | | | | | | | |
| Semiological heterogeneity | | | | | 3 6,00 % | | | 4 11,40 % | 3 4,80 % | 19 31,70 % | 8 13,30 % |
| Dissociative symptom | | | | | | | | | | | |
| Hyperventilation | | 8 19,00 % | | | 5 10,00 % | | 7 12,50 % | | | 35 58,30 % | |
| Clenching of teeth | | | | | | | | | | | |
| Tongue bite | | | | | | | 1 1,80 % | | | | |
| Closed mouth in the tonic phase | | 1 2,40 % | | | | | | | | | |
| Hiccoughs | | | | | | | | | | | |
| Coughs | | | | | | | 1 1,80 % | | | | |
| Gasping/hiccups | | | | | | | 4 7,10 % | | | | |
| Frothing | | | | | | | | | | | |
| Urine incontinence | | | 2 9,10 % | 15 6,60 % | | | 1 1,80 % | | | | |
| Chvostek's sign pos | 3 11,10 % | | | | | | | | | | |
| Chvostek's sign neg | 24 88,90 % | | | | | | | | | | |
| Dialeptic/ unresponsive events | | | 17 77,30 % | 167 72,90 % | | 12 70,60 % | | | 43 69,40 % | 6 10,00 % | |

Table 11 - Semiology data part IV

| | (Ahmed et al., 2004) | (Alessi et al., 2013) | (Asadi-Pooya et al., 2019) | (Asadi-Pooya et al., 2019) | (Bhatia & Sapra, 2005) | (Chinta et al., 2008) | (Dhiman et al., 2014) | (Irwin et al., 2000) | (Kotagal et al., 2002) | (Kozłowska et al., 2018) | (Kozłowska et al., 2011) |
|--------------------------------------|----------------------|-----------------------|----------------------------|----------------------------|------------------------|-----------------------|-----------------------|----------------------|------------------------|--------------------------|--------------------------|
| Staring event | | | | | 4 8,00 % | | | 10 28,60 % | | 1 1,70 % | |
| Aura/sensational event | | | 17 77,30 % | 151 65,90 % | | | | | | 10 16,70 % | |
| Vocalization/speech | 4 9,60 % | | | 31 13,50 % | | 4 23,50 % | 21 37,50 % | | | | |
| Pseudosleep | 2 4,80 % | | | | | | 9 16,10 % | | | | |
| Nocturnal seizures | | | 3 13,60 % | | | | | | | | |
| Generalized motor movements | | | 16 72,70 % | 149 65,10 % | 30 60,00 % | | 11 19,60 % | 11 31,40 % | 28 45,20 % | 19 31,70 % | 21 35,00 % |
| Purposeful/semi-purposeful movements | 2 4,80 % | | | | | | | | | | |
| Undulating motor activity | 9 21,40 % | | | | | | | | | | |
| Opisthotonos | | | | | | | | | | | |
| Pelvic thrusting | 7 16,70 % | | | | | 4 23,50 % | 5 8,90 % | | | | |
| Side to side body movement | | | | | | | 12 21,40 % | | | | |
| Clonus | | | | | | | | | | | |
| Myoclonus | | | | | 3 6,00 % | | | | | | |
| Atonic event | 7 16,70 % | 4 18,20 % | | | 5 10,00 % | 2 11,80 % | 12 21,40 % | 10 28,60 % | | 30 50,00 % | 13 21,70 % |
| Tonic events | | | | | | 6 35,30 % | | | | | |
| Focal motor events | | | 1 4,50 % | | | | | | | | |
| Minor motor | | | | | | | | | | | |
| Generalized limb movement | 16 38,10 % | | | | 5 10,00 % | | | | | 15 25,00 % | |
| Tremor | | | | | | | 14 25,00 % | | | | |
| No limb movement | | | | | | 9 52,90 % | | | | | |
| Violent movements | | | | | | | 6 10,70 % | | | | |
| Head movement | 5 11,90 % | | | 39 17,00 % | | | 9 16,10 % | | | | |
| Facial contractures | | | | | | | | | | | |
| Upper limb movement | | | | | | 12 70,60 % | 15 26,80 % | | | | |
| Lower limb movement | | | | | | 8 47,10 % | 16 28,60 % | | | | |