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# Management of psychogenic nonepileptic seizures (PNES): a multidisciplinary approach

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**Key Words:** conversion disorder, EEG, epilepsy.

**Abstract**

**Background.** The International League Against Epilepsy (ILAE) proposed a diagnostic scheme for psychogenic nonepileptic seizures (PNES). The debate on ethical aspects of the diagnostic procedures is ongoing, the treatment is not standardized, and management might differ according to the age groups.

**Objective.** To reach an expert and stakeholder consensus on PNES management.

**Methods**. A board comprising adult and child neurologists, neuropsychologists, psychiatrists, pharmacologists, experts in forensic medicine and bioethics as well as patients' representatives was formed. The board chose five main topics regarding PNES: "diagnosis"; "ethical issues"; "psychiatric comorbidities"; "psychological treatment"; "pharmacological treatment". After a systematic review of the literature, the board met in a Consensus Conference in Catanzaro (Italy). Further consultations using the model of Delphi panel were held.

**Results.** The global level of evidence for all topics was low. Even though most questions were formulated separately for children/adolescents and adults, no major age-related differences emerged. The board established that the approach to PNES diagnosis should comply with ILAE recommendations. Seizures' induction was considered ethical, preferring the least invasive techniques. The board recommended: to carefully look for mood disturbances, personality disorders

and psychic trauma in persons with PNES; to consider cognitive-behavioural therapy as first line psychological approach and pharmacological treatment to manage comorbid conditions, namely anxiety and depression.

**Conclusions.** PNES management should be multidisciplinary. High-quality, long-term studies are needed to standardize PNES management.

## INTRODUCTION

Psychogenic nonepileptic seizures (PNES) are paroxysmal, time-limited alterations in motor, sensory, autonomic, and/or cognitive signs and symptoms that are not accompanied by ictal epileptiform activity [1]. Recently, the International League against Epilepsy (ILAE) has proposed a stepwise approach for the diagnosis of PNES.[2] ILAE recommendations provide a scientific basis for the diagnosis of PNES, but their application in clinical practice is also influenced by ethical considerations, particularly when induction procedures are considered. Moreover, numerous studies explored the occurrence of psychiatric diseases in people with PNES, the ethical issues linked to the diagnosis and treatment, and the optimal treatment strategy, including psychological approaches and pharmacologic treatment. No high-quality studies are currently available. Recognizing that there is insufficient high-level evidence for the majority of issues to draw a guideline, the Epilepsy Study Group of the Italian Neurological Society (SIN) promoted the formation of a national expert panel to review the existing literature and to formulate consensus recommendations for PNES management. This panel comprised clinicians treating all age groups (from children to elderly) as well as pharmacologists, experts in forensic medicine and bioethics, and representatives of patients' associations. The inclusion of these different profiles has allowed to produce a comprehensive document that deals with clinical, ethical, and social aspects inherent to the diagnosis and management of PNES.

## METHODS

### Panel composition

Members of the multidisciplinary board were identified among adult epileptologists, child neurologists, neuropsychologists, psychiatrists, pharmacologists, nurses with experience in the field of neuroscience, and experts in forensic medicine and bioethics with an undisputable knowledge in the field of PNES diagnosis and management, as documented by their scientific production. All board members were representative of the Italian scientific societies involved in PNES management. The board also comprised representatives of patients' associations. Patients' representatives were included among jury members and actively took part to the debate during the Conference. Moreover, they were part of the Delphi panel and formulated specific observations on the manuscript. Details about Consensus Conference methodology, event, panel members and role are given in Supporting Information 1 (online only).

The panel chose five main topics: "Diagnosis of PNES"; "Ethical issues in the diagnosis and treatment of PNES"; "Psychiatric comorbidities of PNES"; "Psychological treatment of PNES"; "Pharmacological treatment of PNES". Each topic comprised different questions that are listed in tables 1 to 5.

### Study search, selection, and quality evaluation.

A thorough literature search was performed using the National Library of Medicine's MEDLINE (PubMed interface) and EMBASE database with the terms "Psychogenic seizure/seizures" in different combinations. Search strategies are detailed in Supporting Information 2 (online only). The reference lists of identified papers were reviewed for additional studies.

Studies were selected and evaluated by the Scientific Committee. Duplicates and non-pertinent studies were excluded on the basis of the title and/or abstract. Potentially relevant studies were retrieved in full and examined. Six authors (Aguglia U, Beghi E, Belcastro V, De Masi S, Ferlazzo E, Labate A) evaluated a subset of papers. Each of these six authors independently assigned a rating to the papers and decided whether each paper was suitable to be included among the core literature for the consensus. Rating was assigned on the basis of the Classification of Evidence Scheme of the Clinical Practice Guideline Process Manual of the American Academy of Neurology. [3] Briefly, each study was rated from Class I (highest) to Class IV (lowest) evidence according to study design, blinding, representativeness of population, bias assessment and management. Levels of recommendations (from A to U) are detailed in Supporting Information 1 (online only).

**RESULTS**

Literature search was performed in February-March 2017 and retrieved a total of 4089 unique records which were screened in title/abstract or full text for inclusion, and 394 were included. The flowchart of included and excluded papers is reported in Figure 1. The majority of included studies were of low quality: in particular, 3 were rated as Class I, 17 as Class II, 254 as class III and 116 as class IV. Three papers were not rated, as they expressed personal opinions on ethical topics. The complete list of rated papers is reported in Supporting Information 3 (online only). Two hundred and ninety-one studies, all rated as Class III and IV, were excluded because of small sample size (110), study sample overlapping with other included studies (38), research question not strictly pertinent with the Consensus aims (143). Thus, 103 studies constituted the core literature for the consensus. All these papers are cited in the answers to specific questions and are listed in the Supporting Information 3 (online only). For each question, the tables report the related references with rating, one or more synthetic answers representing the summary of existing literature on the specific topic, and the consequent level of evidence. When no study is available, the tables do not report any answer to the specific question.

Hereafter, we report a summary of the panel's recommendations for each of the five topics.

## 1. Diagnosis of PNES

The diagnostic approach to the person with suspected PNES has been outlined by the ILAE Nonepileptic Seizures Task Force. [2] The ILAE Task Force foresees a stepwise approach for growing levels of certainty, ranging from possible PNES (history of a possible nonepileptic event and normal interictal EEG) to documented PNES (absence of epileptiform activity immediately before, during or after an event captured on ictal video EEG with typical PNES semiology). The Consensus panel reviewed the literature on PNES diagnosis (Table 1; Supplementary file 3) and agreed with the ILAE recommendations. In summary, the panel recommends to perform video-EEG aimed at the recording of an episode, either spontaneously (during ambulatory or prolonged video-EEG monitoring) or by means of induction techniques (preferring the least invasive manoeuvre) whenever possible. In case of motor PNES, a video recording alone can, in selected cases, be sufficient for the diagnosis. The panel underlines that a number of ictal signs and symptoms may help in confirming or discarding the diagnosis of PNES (Table 1) although no symptom/sign has diagnostic value. Diagnostic biomarkers, especially prolactin, may also be useful in the differential diagnosis between motor PNES and bilateral tonic-clonic seizures (Table 1).

## 2. Ethical and legal aspects concerning PNES diagnosis.

Given the particular nature of ethical questions, levels of recommendation are not applicable. The panel highlights that the answer to each question in this section is uniquely based on expert opinion (Table 2), taking into account the debate occurring in the literature on these topics. In recent years, some debate around the ethicality of PNES induction has risen. Concerns about undermining the patient-physician relationship caused by an intentionally misleading procedure are counterbalanced by advantages of obtaining a fast and reliable diagnosis. A debate on the more ethical induction

manoeuvres also exists (Table 2). It is unquestionable that some induction techniques (e.g., intravenous saline injection) are invasive and potentially harmful. Moreover, there is a risk for provoking episodes that are different in semiology from habitual episodes, but changes in clinical manifestations may also occur in spontaneously recorded attacks. The panel considers that PNES induction is ethical, provided that: a) other diagnostic procedures, according to clinical practice and scientific evidence, have been ineffective or are not feasible in that particular person; b) the procedure is fully explained and is approved by the person with PNES (or legal guardian). In case of minors with sufficient judgment, their opinion must be sought. It is recommended to proceed according to increasing degrees of direct damage, preferring the use of procedures routinely performed during standard EEG (hyperventilation or intermittent photic stimulation) and, subsequently, by non-invasive suggestion manoeuvres. When the diagnosis is documented, physicians must clearly and completely inform persons with PNES regarding their health status. The panel recommends to adapt the communication to the person's age and ability to understand the information, aiming to the acceptance of diagnosis. The family members or others may be informed only if the affected person agrees, provided that he or she is of legal age and able to express valid consent. The legal guardian must be always informed. As regards the right to obtain the status of disability, Italian law does not include PNES among disabling diseases. The panel underlines that the presence of disability should be individually assessed considering the comorbid conditions, following a bio-psycho-social approach [4].

## 3. Psychiatric comorbidities in persons with PNES

Details about the prevalence and the diagnostic utility of psychiatric comorbidities in persons with PNES are reported in Table 3. In summary, the presence of a psychiatric comorbidity is very common in persons with PNES. However, in adults and elderly, prevalence of psychiatric disorders is similar to those reported in persons with epilepsy, while data for children and adolescents are scarce. Thus, the panel highlights that the presence or absence of such comorbidities is not helpful for PNES

diagnosis; nevertheless they should be carefully searched, due to the high frequency of such disorders and the necessity to treat them. Conversely, a previous psychic trauma or sexual abuse is more frequent in adults and elderly with PNES as compared to persons with epilepsy (Table 3). Lastly, the panel affirms that there is no robust evidence on the role of psychiatric consultation to confirm or exclude PNES diagnosis. Nonetheless, evaluation by a psychiatrist or psychologist may be necessary to define the psychopathologic profile of persons with PNES.

## 4. Psychologic treatment of PNES

Details about psychological treatments for PNES are reported in Table 4. In summary, the panel states that, although the communication of diagnosis is undoubtedly necessary, it is unclear whether this communication influences the prognosis of PNES or PNES-related psychopathology. There is no robust evidence on efficacy of psychological interventions in children and adolescents with PNES; however the panel recommends that this approach should be encouraged. Cognitive-behavioral therapy (CBT) may be a first line psychological treatment in adults and elderly with PNES. There is no robust evidence on efficacy of other psychological interventions. The panel states that the management of persons with PNES should rely on a multidisciplinary team including a psychiatrist and a psychologist.

## 5. Pharmacological treatment of PNES

Details about pharmacological treatment of PNES are reported in Table 5. In summary, the panel recommends not to use any pharmacological treatment in children and adolescents with PNES, since no study is available. There is no robust evidence on efficacy of pharmacological treatment in adults and elderly with PNES. Antidepressants may be useful in adults and elderly with PNES and concomitant anxiety or depression. The panel suggests that antiepileptic drugs might be slowly withdrawn in persons with PNES without concomitant epilepsy.

**CONCLUSIONS AND FUTURE DIRECTIONS.**

This Consensus statement represents a synthesis of the best available evidence on PNES management. The panel reached complete agreement for each of the discussion points, thus this document fully expresses the opinion of Italian experts in this field. The contribution of different professional roles and of patients' representatives has allowed to formulate recommendations that cover problems related to common clinical practice as well as ethical and legal issues.

The absence of high-quality scientific evidence limits the strength of recommendation for many of the topics. Another limitation of this study is the regional nature of the panel's composition; thus some issues may reflect local peculiarities and may not be generalizable (e.g., regulatory aspects). Yet, many recommendations may be extended to other audiences, since diagnostic tools and therapeutic approaches do not differ across the world.

Even though most questions were formulated separately for children/adolescents and adults, no major differences in evidence and recommendations exist. As regards diagnosis, in agreement with the ILAE recommendations [2], video-EEG recording of an episode can still be considered the gold standard, even though more cost-effective alternatives are needed. Seizure induction is ethically justified, provided that other diagnostic procedures have failed or are not easily feasible. Less invasive techniques, like routine EEG activation manoeuvres, should be preferred over placebo administration. A history of psychic trauma, the presence of suggestive ictal signs and symptoms and the normality of serum prolactin levels may favor the diagnosis of PNES versus epileptic seizures. Special attention should be paid to the communication of PNES diagnosis, considering the person's age and cognitive status. Many psychiatric comorbidities are common in people with PNES, including depression, anxiety, post-traumatic stress disorders, personality disorders, but none is pathognomonic, since the prevalence in persons with PNES is similar to the prevalence in persons with epilepsy. The presence of psychiatric comorbidities should be assessed to allow the achievement of disability benefits, since PNES are not considered a disabling condition according to Italian law. Data regarding treatment are globally of low quality. All these studies report short-term efficacy data and most carry a high drop-

out rate. Many psychological approaches, including psychotherapy and other interventions, are anecdotally reported. Data from a single controlled study indicate that CBT should be a first line psychological treatment for adults and elderly with PNES. To date, most interventions still rely on clinicians' experience. In the light of existing evidence, antidepressant treatment should be recommended in adults or elderly with PNES and concomitant anxiety or depression. The work of this multidisciplinary panel has highlighted a critical need for studies with robust design in the field of PNES management, which would be crucial to standardize clinical practice and to respect the needs of persons with PNES.

**Legend to figures**

**Figure 1.** Flowchart of included and excluded studies.

**Legend to Supplementary Files**

**Supporting Information 1:** details about Consensus Conference methodology, event, panel members and role.

**Supporting Information 2:** literature search strategy.

**Supporting Information 3:** Table containing the complete list of rated papers. References included in the recommendations are listed in progressive order from e1 to e59. All other papers are listed in alphabetical order by first author.

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**Table 1. Diagnosis of Psychogenic Non Epileptic Seizures (PNES).**

| Questions | References | Ratings[a] | Answers | Levels of evidence[a] |
|---|---|---|---|---|
| Is video-EEG recording of an episode the gold standard for confirmation of PNES diagnosis? | Benbadis SR et al., 2009 (e1) | III | The diagnostic yield of video-EEG is good, with moderate-high interrater agreement for PNES diagnosis | C |
| | Syed TU et al., 2011 (e2) | III | | |
| Should prolonged video-EEG monitoring aimed to record spontaneous PNES always be used to confirm diagnosis? | Woollacott IO et al., 2010 (e3) | III | The probability to record spontaneous PNES is 50-70%, almost always during the first 2 days of monitoring, but this procedure is not cost-effective | C |
| | Lobello K et al., 2006 (e4) | III | | |
| | Lawley A et al., 2006 (e5) | III | | |
| | Jin B et al., 2014 (e6) | III | | |
| | McGonigal et al., 2002 (e7) | III | | |
| Is ictal video recording alone, when observed by expert epileptologists, a valid instrument for the diagnosis of motor PNES? | Erba G et al., 2016 (e8) | I | Video recording alone, if observed by experts, is sufficient for accurate diagnosis of motor PNES | B |
| Is ictal video recording alone, when observed by expert epileptologists, a valid instrument for the diagnosis of nonmotor PNES? | Erba G et al., 2016 (e8) | I | Video recording alone, even though observed by experts, is not sufficient for the diagnosis of non-motor PNES | B |
| Should PNES induction be used during video alone or video-EEG recording for diagnosis confirmation? | Lancman ME et al., 1994 (e9) | III | No data support induction during video recording alone. Induction may be useful during video-EEG | C |
| | Walczack TS et al., 1994 (e10) | III | | |
| Is there a PNES induction technique better than others? | Goyal G et al., 2014 (e11) | III | All induction manoeuvres have 100% specificity and positive predictive value, but different diagnostic yields | U |
| Are there single signs or symptoms that, if present, allow the confirmation of PNES diagnosis? | Benbadis SR et al., 2009 (e1) | III | Duration (longer than epileptic seizures, often > 120 seconds) (e2,e12-e19) | C |
| | Syed TU et al., 2011 (e2) | III | Fluctuating course of ictal sign and symptoms: sensitivity 42-69%, specificity 96% (e2,e19) | C |
| | Brown MC et al., 1991 (e12) | IV | | |
| | Azar NJ et al., 2008 (e13) | III | Asynchronous movements: variable sensitivity (17-95%), high specificity (78-100%) (e2,e13,e16,e19) | C |
| | Henry TR et al., 1998 (e14) | III | Pelvic thrusting: sensitivity 9-31%, specificity (96-100%) (e2,e13,e16,e19) | C |
| | Jedrzejczak J et al., 1999 (e15) | III | Side-to-side movements: | |

| | | | | |
|---|---|---|---|---|
| | Gates J et al., 1985 (e16) | IV | sensitivity 25-95%, specificity 87-100% (e2,e13,e16,e19) | C |
| | Pierelli F et al., 1989 (e17) | IV | Eye closure/flickering: sensitivity 33-96%, specificity 95-100% (e1,e13,e19,e21,e22) | C |
| | Saygi S et al., 1992 (e18) | III | Ictal crying: sensitivity 5-32%, specificity 91-100% (e2,e10,e19,e23,e24]) | C |
| | Chen DK et al., 2008 (e19) | III | | |
| | Geyer JD et al., 2000 (e20) | II | Seizure awareness/recall: sensitivity 56-77%, specificity 75-93% (e2,e24,e25) | C |
| | Chung SS et al., 2006 (e21) | III | Susceptibility to interference by other people: sensitivity 55%, specificity 94% (e2) | U |
| | DeToledo JC et al., 1996 (e22) | III | Specific linguistic features during seizure description, as detected by means of conversation analysis: able to discriminate PNES from epileptic seizures (85% correct classifications) (e26,e27) | |
| | Slater JD et al., 1995 (e23) | III | | |
| | Devinsky O et al., 1996 (e24) | III | | U |
| | Bell WL et al., 1998 (e25) | III | | |
| | Reuber M et al., 2009 (e26) | III | | |
| | Schwabe M et al., 2008 (e27) | IV | | |
| Are there single signs or symptoms that, if present, allow the exclusion of PNES diagnosis? | Syed TU et al., 2011 (e2) | III | | |
| | Azar NJ et al., 2008 (e13) | III | Occurrence during sleep: sensitivity 20-59%, specificity if sleep is EEG-verified 86-100% (e16,e18,e28-e30) | C |
| | Gates J et al., 1985 (e16) | IV | | |
| | Saygi S et al., 1992 (e18) | III | Post-ictal confusion: sensitivity 67-100%, specificity 70-88% (e2,e13,e23) | C |
| | Chen DK et al., 2008 (e19) | III | | |
| | Bazil CW et al., 1994 (e28) | III | Stertorous breathing: sensitivity 22-93%, specificity 50-100% (e2,e13,e19,e31) | C |
| | Orbach D et al., 2003 (e29) | IV | | |
| | Seneviratne U et al., 2017 (e30) | III | Abrupt onset: sensitivity 94%, specificity 55% (e2) | U |
| | Sen A et al., 2007 (e31) | IV | | |
| Are there biomarkers that | Pritchard PB 3rd, 1985 (e32) | III | If prolactin level is in range a | B |

| | | | | |
|---|---|---|---|---|
| can confirm or exclude PNES diagnosis? | Laxer KD et al., 1985 (e33) | I | few minutes after a seizure, this supports PNES diagnosis *versus* bilateral tonic-clonic epileptic seizure: 47-100%, specificity 74-100% (e32-e39) | |
| | Wroe SJ et al., 1989 (e34) | III | | |
| | Fisher RS et al., 1991 (e35) | II | | |
| | Ehsan T et al., 1996 (e36) | II | Elevated creatinkinase levels support the diagnosis of epileptic seizure: sensitivity 15-87%, specificity 85-100% (e39-e42) | C |
| | Alving J, 1998 (e37) | II | | |
| | Shah AK et al., 2001 (e38) | III | | |
| | Rao M et al., 1989 (e39) | II | | |
| | Willert C et al., 2004 (e40) | III | Increase in nesfatin-1 and reduction in ghrelin levels may be useful as markers of an epileptic seizure (e43) | U |
| | Petramfar P et al., 2009 (e41) | IV | | |
| | Wyllie E et al., 1985 (e42) | III | Heart rate before, during and after PNES and seizure may vary, but data are conflicting (e44-e46) | U |
| | Aydin S et al., 2001 (e43) | III | | |
| | Opherk C et al., 2002 (e44) | III | | |
| | Silva VAP et al., 2007 (e45) | III | | |
| | Reinsberger C et al., 2012 (e46) | III | | |

Legend to Table 1: [a]According to the American Academy of Neurology Guidelines [3]; e1 to e46: references in supplementary file 3

**Table 2. Ethical and legal aspects concerning Psychogenic Non Epileptic Seizures (PNES) diagnosis.**

| Question | References | Rating[a] | Answer | Level of evidence[a] |
|---|---|---|---|---|
| Is it ethical to induce PNES in order to make a diagnosis? | Benbadis SR, 2001 (e47) | NA | PNES induction is ethical, provided that other diagnostic procedures have proven ineffective or are unfeasible | NA |
| | Leeman BA, 2009 (e48) | NA | | NA |
| | Kanner MA et al., 2009 (e49) | NA | | NA |
| Should diagnosis be always communicated to persons with PNES and to family members? | No data available | NA | - | NA |
| Is the person with PNES in right to obtain the status of disability? | No data available | NA | - | NA |

Legend to Table 2: [a]According to the American Academy of Neurology Guidelines [3]; e47 to e49 references in supplementary file 3; NA not applicable.

**Table 3. Psychiatric comorbidities in persons with Psychogenic Non Epileptic Seizures (PNES).**

| Question | References | Rating[a] | Answer | Level of evidence[a] |
|---|---|---|---|---|
| Does the concomitant presence of any psychiatric or cognitive condition or the history of psychic trauma support PNES vs epilepsy diagnosis in children and adolescents ? | Plioplys S et al., 2014 (e51) | IV | Children and adolescents with PNES show a high prevalence of depression (43%), anxiety (40-85%), sexual or physical abuse (6% and 32%, respectively) | U |
| | Plioplys S et al., 2016 (e52) | III | | |
| | Salpekar J et al., 2010 (e53) | III | | |
| | Wyllie E et al., (e54) | III | | |
| Does the concomitant presence of any psychiatric or cognitive condition or the history of psychic trauma support PNES vs epilepsy diagnosis in adults and elderly ? | Direk N et al., 2012 (e55) | III | Variable proportions (55-100%) of psychic disorders on Axes I and II according to DSM-IV in persons with PNES, not significantly higher than in people with epilepsy (e55-e61) | B |
| | Krishnamoorty ES et al., 2001 (e56) | II | | |
| | Scévola L et al., 2013 (e57) | III | | |
| | Strutt Am et al., 2011 (e58) | III | | |
| | Arnold LM et al., 1996 (e59) | II | No significant differences in prevalence of depression between persons with PNES and persons with epilepsy (e53,e54,e56-e59) | |
| | Binder LM et al., 1994 (e60) | III | | |
| | Akyuz G et al., 2004 (e61) | II | | |
| | Salinsky M et al., 2012 (e62) | III | | |
| | Galimberti CA et al., 2003 (e63) | III | | |
| | Dikel TN et al., 2003 (e64) | III | No robust data on prevalence of anxiety disorders (e55-e58,e60-e62) | B |
| | Harden CL et al., 2009 (e65) | III | | |
| | Kaplan MJ et al., 2013 (e66) | III | | |
| | Koby DG et al., 2010 (e67) | III | No significant differences in prevalence of post-traumatic stress disorder between persons with PNES and persons with epilepsy (e55,e57,e59,e61,e63) | U |
| | Rosenberg HJ et al., 2000 (e68) | III | | |
| | Alper K et al., 1993 (e69) | III | | |
| | Tojek TM et al., 2000 (e70) | III | | |
| | Dixit R et al., 2013 (e71) | III | No significant differences in prevalence of personality disorders between persons with PNES and persons with epilepsy (e57,e59- | |
| | Proenca IC et al., 2011 (e72) | III | | |
| | Lally N et al., 2010 (e73) | III | | |
| | Holman N et al., 2008 (e74) | III | | |

| | | | | |
|---|---|---|---|---|
| | | | e61,e64,e65)<br><br>Higher prevalence of psychic trauma in persons with PNES as compared to those with epilepsy (e57,e59,e61,e67-e75) | C<br><br>C<br><br>B |
| | Bodde NM et al., 2007 (e75) | IV | | |
| Is psychiatric consultation mandatory for the confirmation of PNES diagnosis? | No data available | — | — | U |

Legend to Table 1: [a]According to the American Academy of Neurology Guidelines [3]; e51 to e75: references in supplementary file 3

**Table 4. Psychologic treatment of Psychogenic Non Epileptic Seizures (PNES).**

| | References | Rating[a] | Answer | Level of evidence[a] |
|---|---|---|---|---|
| Does the sole communication of the diagnosis to the person with PNES and to the family influence the prognosis of PNES or of PNES-related psychopathology in children and adolescents? | No data available | ___ | ___ | U |
| Does the sole communication of the diagnosis to the person with PNES and to the family influence the prognosis of PNES or of PNES-related psychopathology in adults and elderly? | Bodde NM et al., 2007 (e75) | IV | The role of the communication of PNES diagnosis on prognosis is unclear | U |
| | Salinsky M et al., 2016 (e76) | IV | | |
| | Mayor R et al., 2012 (e77) | IV | | |
| | Thompson N et al., 2013 (e78) | III | | |
| | Gambini O et al., 2014 (e79) | IV | | |
| | Razvi S et al., 2012 (e80) | IV | | |
| | Farias ST et al., 2003 (e81) | IV | | |
| | Duncan R et al., 2016 (e82) | IV | | |
| | Duncan R et al., 2014 (e83) | IV | | |
| | Arain AM et al., 2007 (e84) | IV | | |
| | Drane DL et al., 2006 (e85) | III | | |
| Can children and adolescents with PNES benefit from psychological interventions? | LaFrance WC Jr et al., 2009 (e86) | IV | There is no robust evidence of efficacy | U |
| | Yi YY et al., 2014 (e87) | III | | |
| Can adults and elderly with PNES benefit from psychological interventions? | Mayor R et al., 2012 (e77) | IV | Cognitive behavioural therapy is effective in the treatment of PNES | B |
| | LaFrance WC Jr et al., 2009 (e86) | IV | | |
| | Kuyk J et al., 2008 (e88) | IV | | |
| | LaFrance WC Jr et al., 2014 (e89) | II | | |
| | Myers L et al., 2004 (e90) | IV | | |
| | Myers L, Zaroff C, 2004 (e91) | IV | | |
| | Conwill M et al., 2014 (e92) | IV | | |
| | Goldstein LH et al., 2010 (e93) | III | | |
| | Dade G, Brown SW, 1992 (e94) | IV | There are no data for other psychological interventions | U |
| | Meierkord H et al., 1991 (e95) | IV | | |
| | Mayor R et al., 2010 (e96) | IV | | |
| | Metin SZ et al., 2013 (e97) | IV | | |
| | Santos Nde O et al., 1992 (e98) | IV | | |
| | Zaroff CM et al., 2004 (e99) | IV | | |
| | Rusch MD et al., 2001 (e100) | IV | | |
| Is a single psychological treatment superior to others? | No data available | ___ | ___ | U |
| Should the management of persons with PNES be in charge of psychiatrists or psychologists? | No data available | ___ | ___ | U |

Legend to Table 4: [a]According to the American Academy of Neurology Guidelines [3]; e75 to e100: references in supplementary file 3.

**Table 5. Psychologic treatment of Psychogenic Non Epileptic Seizures (PNES).**

| Question | References | Rating[a] | Answer | Level of evidence[a] |
|---|---|---|---|---|
| Are there drugs of proven efficacy for the treatment of PNES in children and adolescents? | No data available | Not applicable | — | U |
| Are there drugs of proven efficacy for the treatment of PNES in adults and elderly? | LaFrance WC Jr et al., 2014 (e89) | II | The efficacy of sertraline and venlafaxine is unclear | U |
| | LaFrance WC Jr et al., 2010 (e101) | II | | |
| | Pintor L et al., 2010 (e102) | III | | |
| Is withdrawal of antiepileptic drugs safe in persons with PNES without epilepsy? | Oto M., 2005 (e103) | IV | Slow AED withdrawal might be safe | C |
| | Oto M et al., 2010 (e104) | II | | |

Legend to Table 5: [a]According to the American Academy of Neurology Guidelines [3]; e89 and e101 to e104: references in supplementary file 3

**Figure 1.** Flowchart of included and excluded papers.