

* This English manuscript is a translation of a paper originally published in the *Psychiatria et Neurologia Japonica*, Vol. 122, No. 2, p. 87-104, which was translated by the Japanese Society of Psychiatry and Neurology and published with the author's confirmation and permission. If you wish to cite this paper, please use the original paper as the reference.

Review Article

Psychogenic Nonepileptic Seizures Revisited: Toward the Comprehensive Treatment of PNES in Japan

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Psychiatria et Neurologia Japonica 122: 87-104, 2020

Abstract

Certain symptoms that appear in psychogenic nonepileptic seizures (PNES) are similar to those in epileptic seizures, such as loss of normal function or loss of self-control in sensory, motor, and cognitive functions. The name PNES originated from a viewpoint intending to differentiate PNES from epileptic seizures; however, it is not an officially defined psychiatric diagnosis. It involves various pathological conditions that are central to the diagnosis of dissociative disorder or conversion disorder in general psychiatric diagnoses. It is difficult to attribute the cause of PNES to a single psychological factor as derived from the terminology of "psychogenic," and PNES are rather believed to develop and become chronic because of complexed multiple factors that affect each other, including biopsychosocial vulnerabilities and trauma. The quality of life of patients with PNES decreases owing to the high doses of antiepileptic drugs and repetitive examinations without appropriate psychiatric treatment over a long period of time from the first attack until a definite diagnosis is achieved. It is not rare that a patient continues to suffer from PNES without visiting a psychiatrist for various reasons even after the diagnosis is confirmed. Neurological considerations, such as seizure symptomatology and electroencephalography (EEG), and psychiatric considerations are necessary for the diagnosis and treatment of PNES, respectively. The development of long-term video EEG monitoring has revealed that some of the signs of seizure previously considered to

be characteristic of PNES are not necessarily distinctive features. Notifying the patient regarding the diagnosis plays a significant part in treatment, and PNES sometimes disappear even without intervention or further treatment. The aim of standard psychiatric treatment and environmental adjustment through multi-professional collaboration include the acquisition of stress-coping skills, proper expression of unpleasant emotions, self-affirmation, and increasing levels of activity. Various methods are used in full-scale psychotherapy for PNES, and cognitive behavioral therapy has been attracting attention as a treatment method, supported by high-quality studies that have demonstrated its effectiveness. Psychiatrists are expected to play a central role in the comprehensive treatment of PNES that requires seamless linkage from diagnosis to treatment. To this end, psychiatrists should have up-to-date knowledge about PNES and epilepsy to eliminate their prejudice and misunderstandings about PNES.

Keywords : psychogenic nonepileptic seizures, epilepsy, conversion disorder, communication of the diagnosis, comprehensive treatment

Introduction.

Psychogenic nonepileptic seizures (PNES) are paroxysmal manifestations of loss of normal function or self-control in motor, sensory, cognitive, and other domains.²⁵⁾ PNES are similar to epileptic seizures (ES). PNES is so called because it shows symptoms similar to those of ES but is unrelated to overexcitation of cerebral neurons (non-epileptic seizures), and some psychological background is inferred (psychogenic) without other physical or physiological conditions.

PNES, which has been known since the time of Charcot, J.-M. in the 19th century, was sometimes referred to as

"hysterical seizures" or "pseudo-seizures", or "pseudo-epileptic seizures". However, the current global standard is that the use of these names should be discouraged, considering that the term "hysteria" is still highly prejudicial to the general public and that the words "pseudo" and "pseudo-epileptic" contain negative value judgments by medical professionals.

While some argue that the name PNES has therapeutic implications, suggesting that a broad psychotherapeutic approach is useful,⁸⁷⁾ others are critical of the "psychogenic" nature of PNES and argue that NES (non-epileptic seizures)

should be used. In the early stages of PNES, the relationship with psychogenic factors is often unclear, but this may lead to an endless series of exclusionary diagnoses and delay in appropriate treatment. Other terms that have been used include NEAD (non-epileptic attack disorder), because "seizure" is reminiscent of ES, dissociative seizures, which is taken from dissociative convulsions in ICD-10, and seizures. In addition, the term "psychological non-epileptic event" is sometimes used because it more accurately describes the condition and is less humiliating to the patient⁵⁷).

Thus, PNES is a name that arose from the viewpoint of differentiating it from ES and is not an officially defined psychiatric diagnosis⁴¹⁸⁶). However, in the case of PNES complicated by intellectual disability, symptoms often appear in the form of erroneous behavioral patterns (a kind of disease gain) rather than psychological conflicts, and these behaviors are reinforced by the responses of supporters, and it is said that patients unconsciously control their surroundings⁵³). In addition, there are cases of PNES that meet the diagnostic criteria for panic disorder⁸⁵). In addition to symptoms similar to ES, PNES often has various problems that can be considered unique to PNES, including background psychosocial problems and medical structural

problems such as the division between diagnosis and treatment. It is necessary to know about these problems before treatment.

I. Epidemiological and Clinical Overview

It is estimated that 5-10% of patients visiting outpatient epilepsy clinics and 20-40% of patients hospitalized for long-term video-EEG recording are diagnosed with PNES⁶), making it a disorder that is routinely encountered in epilepsy clinics. Although there are no large-scale epidemiological studies in Japan, the incidence of PNES is thought to be 3 to 5 per 100,000 population according to overseas studies³⁰⁷⁷). The prevalence of PNES is estimated to be 2-33 per 100,000 population, which is almost the same as multiple sclerosis and trigeminal neuralgia, so it is not a rare disorder¹⁹).

PNES can occur at any age, from children⁷⁶) to the elderly²⁸), but it is most common in adolescents and young adults⁷⁴³⁵⁰). In a study comparing adolescent-onset PNES (<18 years old) with PNES (18-55 years old), there was no difference in seizure symptoms, but the former had more history of abuse, academic problems, epilepsy, and family history of epilepsy, while the latter had more medically problematic physical complications⁵). In another study, patients who developed PNES after the

age of 55 years reported more health-related traumas, such as males and serious physical complications, and less history of abuse than patients who developed PNES before that age²⁸).

It has long been known that patients with PNES are predominantly female⁷). A review of 21 studies estimated a male to female ratio of 1:2.94, with approximately 75% of patients with PNES being female, although this ratio varies depending on the patient (whether or not the disease is complicated by intellectual disability or epilepsy, and whether or not the disease has childhood or elderly onset) and the country or region (it tends to be lower in Asia and higher in Europe and the United States)⁵²).

PNES can be associated with epilepsy⁷)⁴⁶). The percentage of patients with PNES and epilepsy varies widely, ranging from 5 to 50% in previous studies, depending on how epilepsy is defined. A recent meta-analysis showed that 22% of patients with PNES have epilepsy and 12% of patients with epilepsy have PNES⁴⁶).

Factors associated with the development of PNES include psychological trauma (sexual and physical abuse), head trauma, and physical complications (health-related trauma).³⁵) In a review by Beghi, M. et al, psychological trauma was reported to be involved in 21-100% of patients with

PNES.¹⁷)

Among psychological traumas, the relationship between PNES and history of sexual and physical abuse has been studied intensively, especially in Europe and the United States. Patients with PNES had significantly higher rates of sexual abuse (24% vs. 7.1%) and physical abuse (16% vs. 3%) than patients with epilepsy⁴). The odds ratio of previous sexual and physical abuse was 3.35 when PNES patients without epilepsy were compared with epilepsy patients³²).

The rates of sexual abuse and physical abuse among PNES patients vary widely among reports, ranging from 8 to 67% and 16 to 67% of PNES patients, respectively⁷). This may be due to the difficulty in assessing traumatic experiences such as abuse and differences in regional and cultural backgrounds. It has been reported that there is less history of abuse among PNES patients in Asia than in Europe and the United States. Kanie A, reported that psychological trauma was present in 38% of PNES patients, but the details were not described and the frequency of abuse is unknown⁴⁵). Kanemoto, K., reported that a history of sexual abuse was not found in PNES patients with intellectual disability, but in 4% of PNES patients without intellectual disability.⁴⁴) Therefore, there is no consensus on the history of

abuse in PNES patients in Japan.

In Western studies, where history of abuse is often discussed, there is less history of abuse in childhood-onset PNES than in adolescent-onset PNES, with a greater proportion of school-related problems such as bullying and academic problems, family problems such as parental disagreement and overprotection, and personal problems such as anxiety and lack of self-confidence.⁶⁴⁾ There are many opinions⁶⁴⁾.

In a study comparing PNES patients with and without intellectual disability, the former were significantly more likely to have a history of epilepsy, to have extremely long seizure durations, to be treated with multiple antiepileptic drugs, to have a low history of sexual abuse, and to be triggered by psychological environmental stress²⁹⁾. However, most PNES studies exclude patients with intellectual disability, and there is limited evidence on PNES complicated by intellectual disability⁸²⁾.

A number of studies have pointed out the problems of excessive testing and treatment for PNES.

27-78% of patients with PNES have a history of "PNES status epilepticus," a condition in which seizures last longer than 30 minutes⁶⁷⁾. Patients with PNES often present to the emergency room for a variety of other reasons. Frequent visits to the emergency room

can be a burden not only on the patient, but also on family members, caregivers, and the health care system²⁾. An Australian study reported that the medical costs of repeated tests, ICU visits, and emergency visits averaged A\$26,500 (approximately ¥2 million) to establish a PNES diagnosis⁷³⁾. Another study reported that total per capita medical costs decreased from an average of US\$4,567 in the 12 months before PNES diagnosis to an average of US\$2,783 in the 12 months after diagnosis²⁾. Martin, R. C., et al. reported that total medical costs at 6 months after PNES diagnosis were 84% lower than before diagnosis, with a 76% decrease in laboratory tests, 69% decrease in pharmacotherapy, 80% decrease in outpatient care, and 97% decrease in emergency visits⁵⁴⁾. A recent study comparing medical costs before and 6 months after PNES diagnosis also found a 94% reduction in emergency visits, 100% reduction in hospital admissions, 94% reduction in emergency telephone calls, and 100% reduction in EEG after PNES diagnosis⁶³⁾.

Thus, early and appropriate diagnosis of PNES has proven to be of great benefit not only to the patient but also to the medical economy.

However, there are many patients who continue to have PNES without seeing a mental health specialist such

as a psychiatrist or clinical psychologist after the PNES diagnosis is confirmed⁴³). This problem is thought to be due to the opposition to PNES diagnosis by the patients and their families, who have been treated for years as having "intractable epilepsy," and the lack of active treatment providers⁴¹).

In addition, after the diagnosis of PNES is confirmed, it tends to be treated as a fraudulent disease by physical medicine departments, and psychiatrists tend to avoid treating it, making it a "no man's land" where there is no one willing to treat it⁴¹). The problem is the lack of a seamless transition from diagnosis to treatment, which paradoxically makes it difficult to receive medical care once the diagnosis is confirmed.

II. Pathological model of PNES

PNES is not a single disease, but a disorder that develops and persists due to heterogeneous biological and psychosocial factors, and there is no single PNES etiological model that can explain the pathogenesis of all PNES patients. However, the diagnosis and treatment of PNES require cooperation among various departments and professions, and a broad pathological model that can serve as a common language and be easily understood by patients is necessary³⁹⁸⁰). Although

various PNES pathological models have been proposed, such as the psychokinetic model and the learning theory model,⁷⁹) in recent years, PNES experts have come to support the BPS-3Ps model (bio-psychosocial and P, the first letter of the three factors): (1) predisposing factors, (2) precipitating factors, and (3) perpetuating factors are involved in the development and chronicity of PNES, and each factor is defined by the influence of biological, psychological, and social factors (Fig. 1)²⁶³⁹⁴⁸⁴⁹⁶⁹⁷⁰).

Predisposing factors are those that may be preparatory or predisposing factors for PNES, and include vulnerabilities such as a history of epilepsy or head trauma, intellectual disability, psychological characteristics such as psychological trauma, alexithymia, and dissociative tendencies, and social and environmental problems such as a history of childhood abuse, poor upbringing, and bullying. (Table 1).

PNES develops when a precipitating factor is added to an individual who has a predisposing factor (Fig. 1). The precipitating factor does not necessarily have to be a large load, but can be a trivial load in itself, such as the "last straw" (there is an English proverb, "the last straw breaks the camel's back". If you pile up as many straws as you can on the camel's back, even if they are

light straws, the last straw will eventually break the camel's back). It includes psychological problems such as depression, anxiety, and psychological stress; life events at work, home, and school; and physical invasions such as head trauma and craniotomy²⁶) (Table 1). Although it is sometimes difficult to strictly distinguish between predisposing factors and precipitating factors, many studies define the former as factors that occurred more than 1 year before the onset of PNES and the latter as factors that occurred within 1 year before the onset of PNES⁶⁹).

The perpetuating factor is the factor that causes repeated fixation of PNES caused by the onset of PNES (Fig. 1). PNES patients have decreased physical functions due to excessive treatment with antiepileptic drugs, and they are also sensitive to side effects, sensitive to physical sensations, and complain of various complaints. In addition, they are sensitive to the side effects of antiepileptic drugs²⁶). The onset of PNES can isolate patients and complicate depression, and these internal problems themselves can lead to PNES. In addition, sometimes there is a so-called disease gain. These factors are included in the perpetuating factors (Table 1).

In order to elucidate the biological basis of PNES, various functional brain imaging studies have been actively

conducted in recent years⁷⁸). To elucidate the biological basis of PNES, various functional brain imaging studies have been actively conducted in recent years⁷⁸). In addition, it has been hypothesized that there is a dysfunction or abnormalities in the network between these regions, such as (1) the insular cortex, anterior cingulate gyrus, dorsolateral frontal cortex, amygdala, etc., (2) the posterior parietal cortex, etc., (3) regions involved in body consciousness and perception, and (4) regions controlling cognition, movement, and behavior, such as the temporoparietal junction, motor cortex, and anterior cingulate gyrus⁶¹).

However, these functional brain imaging studies are limited by the small number of cases and the fact that they are not necessarily specific to PNES, as many cases are associated with neuropsychiatric symptoms such as depression, anxiety, and other conversion disorders.

III. Diagnosis of PNES

The diagnosis of PNES can range from easy for non-epileptologists to difficult for epilepsy specialists.

A history of frequent emergency room visits due to uncontrolled seizures despite years of treatment with multiple antiepileptic drugs and seizure symptoms that are not typical for ES, with unclear diagnostic evidence of

epilepsy, may trigger consideration of the possibility of PNES⁵⁰).

The gold standard for diagnosis of PNES is confirmation of the non-epileptic nature of the seizures by long-term video-EEG recording. If the recorded seizure video-EEG is analyzed by a physician with experience in epilepsy, the accuracy of the diagnosis can be significantly increased. This level of diagnosis would be Documented PNES according to the 2013 criteria⁵⁰) by the PNES Task Force of the International League Against Epilepsy (ILAE) (Table 2). In the case of no seizure recording during video-EEG, the diagnosis is Clinically Established or Probable, depending on the epilepsy experience of the physician who witnesses the PNES symptoms or confirms them by video. Experienced epileptologists have been shown to be able to accurately differentiate between PNES and ES, especially those with motor symptoms, based on video information alone²⁷)³³). It is also known that the witness of patients and family members about seizure symptoms are not always accurate⁷⁵). Therefore, it is important to inform family members and supporters to record seizure symptoms on video whenever possible.

If the physician is unable to witness or video-record the seizure symptoms, the diagnosis of Possible PNES is made

with the lowest probability.

The diagnosis of PNES requires knowledge of seizure symptomatology and EEG, and this article will focus on the former. For more information on seizure symptomatology related to PNES diagnosis, please refer to Kanemoto's review⁴²), which will help you acquire the basic concepts.

In seizure syndromes, it is important to understand that there is no single symptom that can diagnose or rule out PNES, and to avoid short-sighted diagnosis. Furthermore, even if a certain type of seizure is confirmed as PNES, it should not be assumed that all other seizures in the same individual are PNES⁴¹).

1. Points to differentiate between PNES and epileptic seizures (Table 3)

Various clinical signs are thought to be useful in differentiating PNES from ES. Among these, the following are most useful: head shaking during seizures, asynchronous motor symptoms, eye closure during seizures, prolonged seizures, agitation of seizure symptoms, and biting tongue¹⁰)⁴¹)⁴²)⁵⁰). However, even with these clinical signs, it would be a mistake to immediately diagnose PNES based on the symptoms alone, and they should be treated as one of the reference findings for suspicion of PNES⁴¹)⁴²)⁵⁰).

A side-to-side shaking of the head

during convulsive or motor seizure symptoms is most likely PNES,¹⁰) but may also be observed in complex partial seizure with automatisms.

In the case of convulsive seizures, asynchronous motor symptoms (especially arm and leg out of phase) are suspicious for PNES.¹⁰) However, severe motor symptoms may also appear asynchronously in hypermotor seizures of frontal lobe epilepsy. A systematic review by Brigo, F. et al. showed that eye closure during seizures in PNES patients had a sensitivity of 58%, a specificity of 90%, a positive likelihood ratio of 5.5, and a negative likelihood ratio of 0.47). In a study comparing 441 patients with PNES and 341 patients with epilepsy, the mean seizure duration was 148.7 seconds for PNES and 47.7 seconds for epileptic seizures, and the sensitivity and specificity for PNES diagnosis were 65% and 93%, respectively, with a threshold of 123.5 seconds, and the odds ratio for PNES was 24 when the seizure duration exceeded 5 minutes⁷²). In contrast to ES, which have a regular onset and conclusion, such as "tonic," "fast clonic," and "slow clonic," the rhythm of convulsive PNES is monotonous and unchanging, or rhythm changes are irregular, as confirmed by measurements using surface electromyography and wearable accelerometers¹⁵). In the case of

convulsive PNES, the seizure symptoms are characterized by fluctuation, such as stopping in the middle of the seizure and resuming after a while⁸⁴). In the case of convulsive seizures, evaluation of tongue biting after the seizure is useful to differentiate between ES and PNES; PNES also causes tongue biting, but it is often at the tip of the tongue, whereas ES often cause biting on the outside of the tongue.

A review by Brigo et al. showed that bite wounds on the outside of the tongue had a sensitivity of 22%, specificity of 100%, positive likelihood ratio of 21, and negative likelihood ratio of 0.79 in ES²²). It is known that repeated biting of one side of the tongue in seizures is suggestive of ipsilateral epileptogenesis¹⁸).

In the case of convulsive seizures such as generalized tonic-clonic seizures, the respiratory rhythm after the seizure can also be a point of differentiation. ES are often accompanied by snoring⁷¹) and deep, slow breathing with a constant rhythm, whereas PNES is characterized by shallow, fast breathing with a variable rhythm¹¹).

2. Signs that may be misdiagnosed as PNES if misjudged

There is a lack of reports verifying its diagnostic value, and it is currently considered an insufficient sign for the diagnosis of PNES.) It is important to

note that Opisthotonus “arc en cercle” is sometimes observed in anti-NMDA receptor antibody encephalitis, which may be the first manifestation of dissociation-like psychiatric symptoms¹³⁾¹⁶⁾.

In a prospective study by Asadi-Pooya, A. A. et al. of 211 patients with PNES, approximately 31% (65 patients) had some kind of seizure-related injury. ⁶⁾ The most common injury was biting tongue (13%), followed by lacerations and bruises of the face, head, and extremities, and some serious injuries such as fractures, broken teeth, and burns⁶⁾. In addition, there was a significant difference in the mean time required to confirm the diagnosis of PNES between patients with and without PNES-related injuries: 7 years for the former and 4.8 years for the latter. The odds ratio of seizure-related injury was 3.6 in a study comparing patients who took more than 10 years to be diagnosed with PNES with those who were diagnosed within 1 year¹²⁾.

In the past, it was thought that seizure-related urinary incontinence was specific to ES and not observed in PNES, but it has been shown that seizure-related urinary incontinence is also observed in patients with PNES, although less frequently⁸⁾²⁴⁾⁶⁰⁾, and its presence alone is not sufficient to differentiate it as a sign⁵⁰⁾. The presence or absence of urinary

incontinence is not sufficient to differentiate between the two groups.)

Alessi, R. et al. reported that 47% of patients with PNES had their PNES reduced by less than half with antiepileptic drugs, and 11% of patients had seizure resolution for a period of time. ³⁾ Oto, M., et al. reported that 43% of patients experienced improvement in seizures after starting antiepileptic drugs, and that the placebo effect was higher than in other diseases. Oto, M. et al. reported that 43% of patients experienced improvement in seizures after starting antiepileptic drugs, and the placebo effect was higher than in other diseases⁵⁹⁾.

There was once a view that patients with conversion disorder, the core of PNES, were characterized by an indifferent attitude toward the severity of their own symptoms (*la belle indifférence*). However, a systematic review by Stone, J. et al. concluded that *la belle indifférence* is present in 29% of patients with conversion disorder, but also in 29% of patients with organic disease, and has little diagnostic value⁷⁴⁾.

3. "Psychogenic factors" in PNES diagnosis

In the past, the diagnosis of conversion disorder, which is the core of PNES, required "the absence of

neurological abnormalities that could explain the functional impairment" and "the involvement of psychogenic factors in the development of symptoms. This was intended as a warning against the easy diagnosis of conversion disorder⁵⁸). However, as a result, psychiatric treatment was postponed for many patients with conversion disorder, and excessive testing was repeated. In addition, due to criticism that the diagnostic criterion of psychogenic factors was diagnostically unreliable, "presence of psychogenic factors" in the diagnosis of conversion disorder was excluded from the diagnostic criteria in DSM-5⁵⁸).

Similarly, the review on PNES diagnosis published by the PNES Task Force of the ILAE in 2013⁵⁰) and the Guidelines for the Diagnosis and Treatment of PNES published by the Japanese Epilepsy Society in 2009⁴¹) do not mention the necessity of the "presence of a psychogenic factor" in PNES diagnosis. Rather, the latter rejects the easy theory of psychogenesis, saying, "PNES should not be diagnosed simply because psychogenesis is present.

As mentioned above, PNES develops and becomes chronic due to the complex influence of multiple factors, and it is difficult to attribute the cause to a single psychogenic factor. In addition, PNES patients tend to be less aware of their own emotions and tend to

associate anxiety-related physical changes with "external" seizures⁴⁹). Therefore, it is not uncommon for a psychogenesis to be uncovered in a short examination.

In other words, the presence or absence of psychogenic factors alone does not confirm or deny the diagnosis of PNES.

4. Importance of follow-up in PNES diagnosis

As mentioned above, long-term video EEG recording is the gold standard for PNES diagnosis⁴³)⁵⁰), but it is not practical to perform it in all cases. In addition, even if a seizure is recorded during a long-term video EEG, it may be difficult to differentiate between PNES and ES based on EEG findings alone in cases of seizure symptoms without impairment awareness, because simple partial seizures do not show significant scalp EEG changes. When PNES is suspected, therapeutic intervention should be initiated as described below, depending on the circumstances of each case and medical institution. Some patients may have atypical epileptic seizures, or may have unremarkable epileptic seizures in between highly visible PNES.⁴¹) Therefore, it is practical to monitor for changes with therapeutic intervention and reconsider the diagnosis each time.⁴¹)⁵⁰)

IV. Treatment of PNES

The author's idea of PNES treatment that can be performed in Japan is described based on a flowchart (Figure 2).

1. Step 1: Presenting the diagnosis (explanation of medical condition) 1.

In the treatment of PNES, Communicating the diagnosis of PNES is an important element of treatment in itself, and PNES disappears with this step alone in some patients, while in others, emergency visits are stopped (30)55). On the other hand, this step may end up being unsuccessful and PNES may become rather aggravated, or it may lead to anti-treatment results such as seeking a diagnosis of "epilepsy" and visiting other medical institutions (49)57). Reuber, M. et al. found that 40% of patients who discontinued antiepileptic drugs after diagnosis of PNES were still taking them 4 years later.

There are several studies that have examined the specific explanatory procedures for this important step, which is to communicate well with the patient, promote acceptance of the diagnosis, and bridge the gap to psychiatric treatment (49). While referring to the points of explanation of medical conditions common to these studies (Table 4) and the BPS-3Ps model described above, try to explain

carefully in a positive manner, based on the level of diagnostic evidence and taking into account the psychological agitation and comprehension of each patient. If PNES is associated with epilepsy, inform the patient, family, and supporters of the distinction between ES and PNES.

It is important to continue to see an epileptologist for a period of time after the diagnosis is made, even if the patient has PNES without epilepsy. It has been reported that many epileptologists consider their role to be that of a consultant until the unnecessary antiepileptic drugs are tapered off.

However, for many patients with PNES, especially those who have been treated for years as having intractable epilepsy, this step should be taken by an epilepsy specialist. Ideally, a psychiatrist should also be present at the presentation of the diagnosis to help the patient and family understand the condition.

2. Step 2: Standard psychiatric treatment and environmental adjustment

If the patient and family are somewhat receptive to the diagnosis, proceed to Step 2. This is because PNES may recur in the long term without continued treatment, even in patients whose PNES has been controlled in Step

1. As mentioned above, a psychiatrist working in the same general hospital as the epileptologist should be the mainstay of this step in order to facilitate concurrent consultations with the epileptologist (needless to say, it does not matter whether it is a clinic or a psychiatric hospital if there is already a system of collaboration between the epileptologist and the psychiatrist). This step is an important framework for long-term support of the patient, and psychiatric considerations are necessary for its implementation. The details of the practical approach of the psychiatrist in this step are described in a separate article⁸⁰), and only the main points are described here.

Many patients with PNES do not voluntarily seek psychiatric care. Therefore, in the early stages of treatment, we aim to establish a therapeutic relationship by actively interviewing the patient and family about their problems⁸⁰).

The Japanese Epilepsy Society guidelines state that psychotherapy should be the mainstay of treatment for PNES without intellectual disability, and environmental adjustment should be the mainstay of treatment for PNES with intellectual disability.⁴¹) In this step, both standard psychiatric treatment and environmental adjustment should be tried in all patients with PNES, with the intensity

of the treatment depending on the patient background. Needless to say, standard psychiatric treatment begins with a psychiatric examination, and since PNES is often complicated by depression and anxiety⁴⁹), and there are many cases with a history of or complications from other conversion disorders, as well as cases that meet the diagnostic criteria for panic disorder⁸⁵) and PTSD⁵⁶), evaluation of complications from these psychiatric disorders is necessary.

LaFrance, W. C. Jr. et al. conducted an RCT and found that the sertraline group had a 45% reduction in seizures, but no statistically significant difference from the placebo group (8% increase in seizures) was detected⁴⁷).

Psychotherapy is the mainstay of PNES treatment, and it is recommended that 1) deepening understanding of how PNES occurs and changes in emotions and physical sensations before seizures, and learning how to avoid seizures through coping such as abdominal breathing, 2) appropriate expression of unpleasant emotions such as anxiety and anger, and 3) increasing self-esteem and activity be done according to the needs of each patient⁵⁷) . It is best to tailor the treatment to the needs of each patient⁵⁷).

The other keystone of PNES treatment is environmental adjustment,

which begins with support targeting the perpetuating factor in a multidisciplinary team³⁹⁾⁸⁰). It is recommended that the BPS-3Ps model be used in conferences to organize and share information about the patient's distress and problems. The multidisciplinary team approach is therapeutic in itself for PNES patients who are isolated and tend to drop out of psychiatric treatment in the early stages of treatment¹⁴), and the presence of multiple supporters can help maintain adherence to treatment. Furthermore, it reduces the burden on general hospital psychiatrists and enables long-term management. Support that does not provide a fundamental solution through easy environmental adjustment may reinforce the so-called disease gain, and PNES may become a means to solve the patient's problems, leading to chronic PNES⁸⁶). Therefore, it is advisable for the multidisciplinary team to meet at regular intervals to discuss whether the environmental adjustments are working to achieve the goals of reducing PNES and promoting appropriate social participation.

Although it is not exact evidence, some experts say that "the majority of PNES is relatively easy to approach and has a high therapeutic efficacy "⁵⁷⁾⁷⁷), and many patients may respond well to Step 2 treatment.

3. Step 3: Specialized psychotherapy

For PNES patients with presumed traumatic experiences, it is rather important to have an individual therapeutic relationship between the patient and the therapist⁵⁶⁾⁵⁷). If the impact of the traumatic experience becomes apparent during the examination, it may be helpful to consult a physician or clinical psychologist who can provide specialized treatment for the traumatic experience.

If there is a need for other specialized psychotherapy, the patient should be moved to Step 3.

Among the various methods of psychotherapy for PNES, cognitive behavior therapy (CBT) has been gaining attention in recent years.

In 2010, an RCT reported that 4 months of CBT in patients with PNES without epilepsy significantly reduced seizure frequency with a moderate or greater effect size and an odds ratio of 3.125 for seizure suppression over 3 months³⁶). In addition, LaFrance et al. demonstrated in a multicenter RCT that PNES was reduced in patients who received a total of 12 sessions of CBT (51% reduction in PNES with CBT alone and 59% reduction with CBT plus antidepressants), and associated depression was also improved⁵¹). However, these studies exclude PNES

with intellectual disability, and there are problems such as short duration of efficacy evaluation. Furthermore, it has been shown that a small group of patients drop out of psychiatric treatment at the end of CBT⁸¹).

In order to avoid this situation, it is desirable to create a system that allows patients to move smoothly back and forth between the doctor in charge of Step 2 and the therapist in charge of Step 3 (e.g., return to Step 2 when treatment has settled down, and continue treatment for a certain period of time in Step 3 when full-scale treatment is needed).

4. Establishing a system to receive and respond to PNES emergencies

In addition to seizures, patients with PNES tend to seek emergency care for a variety of reasons. This is especially true in the early stages of psychiatric treatment, so it is necessary to establish a system for emergency admissions. It is recommended that treatment be provided within a sustainable framework that suits the treatment style of each therapist and the circumstances of the hospital : Kanemoto et al. have established a framework for treatment of PNES patients with intellectual disabilities, such as recommending a psychiatric consultation instead of an emergency department visit if an emergency

consultation is necessary, or within 15 minutes if the consultation is not scheduled⁴⁴).

What I would like to convey here so that there is no misunderstanding is that patients with PNES are indeed more likely to visit the emergency room, but unlike so-called borderline cases, they are less likely to approach their physicians without a framework, such as special visits outside of office hours or requests that the attending physician treat the patient "in the flesh."⁴⁰

In the case of PNES emergencies, such as "PNES status," the basic response of medical personnel and observers is to maintain a supportive, unperturbed attitude, ensure safety, and monitor the patient's progress. In patients with PNES, oxygen should be administered as needed. Anxiolytics should be avoided, as injection pain and disinhibition may aggravate PNES.

It is important to discuss the seizure response in advance so that patients and their families can practice it.

V. Prognosis of PNES

Although epidemiological data on the prognosis of PNES are still scarce, existing reports from Europe and the United States indicate that PNES completely resolves in a small number of patients (25-38%), and even if seizures resolve, nearly half of these patients are unable to work and

continue to require support from the national and local governments³⁴⁾⁶⁶⁾⁶⁸⁾.

However, to date, there are no studies with high evidence of prognosis in Japan, where the patient background and healthcare system are different from those in the West.

Conclusion: Toward a Comprehensive PNES Practice

In the past 20 years, much has been learned about the diagnosis of PNES, and in the past 10 years, much has been learned about its treatment⁴³⁾. However, many patients continue to be inadequately diagnosed and treated worldwide, and there are many challenges to be overcome⁴³⁾. One of them is the difficulty of seamless transition from diagnosis to treatment⁴³⁾. In the past, the main reasons for this were thought to be patients' difficulty in accepting the diagnosis and inappropriate explanations by epilepsy specialists, but more recently, the effects of insufficient knowledge and misunderstanding by mental health professionals who undertake treatment have also been discussed³¹⁾.

For example, when a questionnaire was sent to French psychiatrists to confirm their knowledge of PNES, 45% of them responded that PNES occurs to attract the attention of others,

indicating that there is still a high tendency to emphasize the association between PNES and "hysterical personality" ¹⁾. Furthermore, a systematic review by Rawlings, G. H. et al. found that mental health professionals tend to treat PNES patients with (1) a lack of confidence in diagnosis and treatment, (2) a "mental versus physical" dualism of etiology and the belief that PNES is solely a mental problem, and (3) a belief that PNES patients are troublesome and difficult to deal with. (3) patients with PNES are troublesome and difficult to treat, (4) they have mixed feelings about continuing to treat patients, and (5) PNES is not a serious disorder compared to epilepsy.⁶²⁾

Sometimes there is a dualistic view of whether epilepsy specialists (neurologists) or psychiatrists should be the primary providers of PNES care.³⁷⁾ However, this is a misconception. As mentioned above, neurological considerations such as seizure symptomatology and electroencephalography (sometimes requiring sophisticated testing equipment such as long-term video EEG recording) are necessary for the diagnosis of PNES, and psychiatric considerations are necessary for treatment. It is difficult for a single physician to handle all aspects of PNES from diagnosis to treatment.

Psychiatrists (many of whom do not specialize in epilepsy) are expected to play a central role in the treatment of PNES, and they need to update their knowledge of PNES and epilepsy and resolve their own misconceptions and prejudices about PNES in order to provide effective treatment. It is necessary to update our knowledge of PNES and epilepsy and to eliminate our own misconceptions and prejudices.

Patients with PNES experience a lot of trauma before they reach a psychiatrist, and having a positive attitude that the psychiatrist will take care of them first can be a great psychotherapy in itself.

It is hoped that as many psychiatrists as possible will become involved in the treatment of PNES instead of treating it as a fire on the shore.

Note: This is a review paper requested by the editorial board.

There are no conflicts of interest to be disclosed in relation to this paper.

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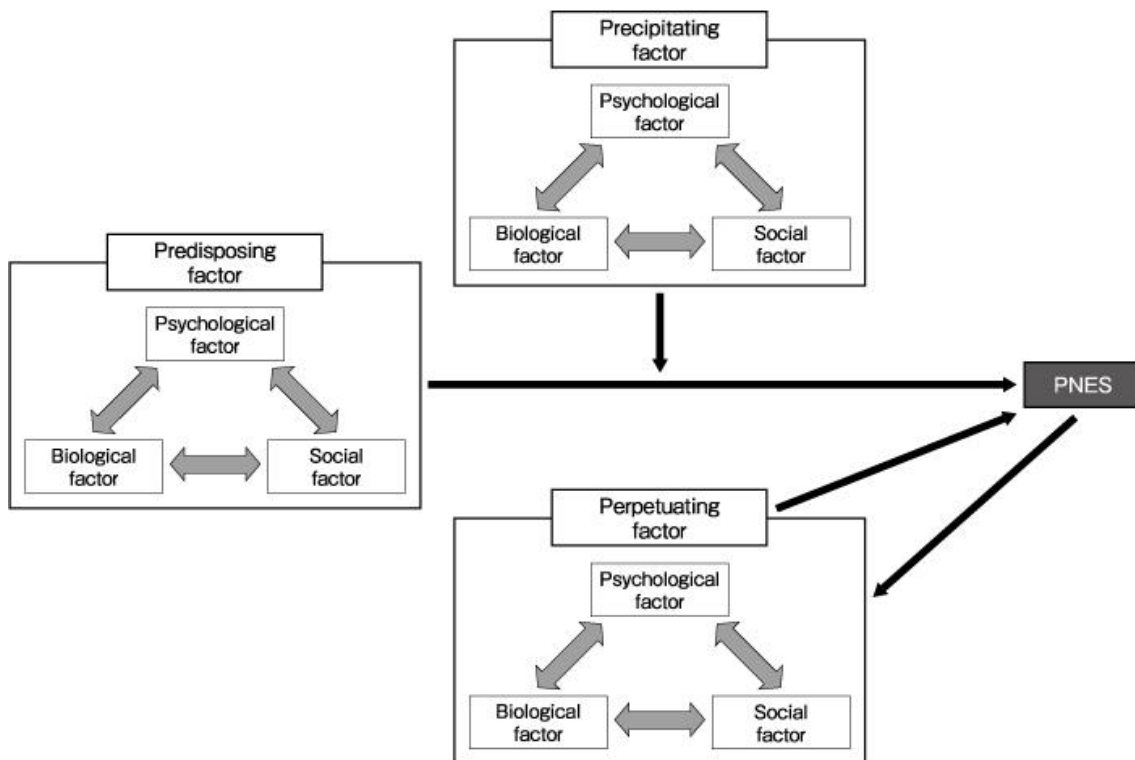


Fig. 1 Conceptual diagram of predisposing, precipitating, and perpetuating factors associated with the development and chronicity of PNES (BPS-3Ps model)

PNES is caused by predisposing factors and precipitating factors, and becomes chronic with the addition of persistent factors. Each factor is further defined by the influence of biological, psychological, and social factors. (Prepared by the author based on references 26 and 46)

	Biological factor (生物的要因)	Psychological factor (心理的要因)	Social factor (社会的要因)
Predisposing factor (素因)	てんかん 頭部外傷 精神疾患の家族歴 知的障害	トラウマ体験 抑うつ アレキシサイミア 心理的葛藤	幼少時の虐待 劣悪な生育環境 いじめ 不登校
Precipitating factor (誘発因子)	頭部外傷 手術 自律神経系の不調	不安 抑うつ 回避的行動 心理的ストレス	職場, 学校や家庭で のライフイベント
Perpetuating factor (持続因子)	抗てんかん薬 自律神経系の不調 不眠 身体感覚増幅	不安 抑うつ 誤った疾病理解 自尊心低下	過剰な医療行為 (頻回の救急受診) 孤立 依存 疾病利得

Table 1: Biological, psychological, and social factors associated with PNES

Biological factor

(Biological factor) Psychological factor

(Psychological factor) Social factor

Social factor

Predisposing factor

(Predisposing factor) Epilepsy

Head trauma

Family history of mental illness

Intellectual disability Traumatic experience

Depression

Alexithymia

Psychological conflicts Childhood abuse

Poor upbringing

Bullying

Truancy

Precipitating factor

(Precipitating factor) Head trauma

Surgery

Autonomic Nervous System Disorders Anxiety

Depression

Avoidant behavior
 Psychological stress Life events at work, school or home
 Perpetuating factor
 (Persisting factor) Antiepileptic drugs
 Autonomic nervous system disorders
 Insomnia
 Somatosensory amplification Anxiety
 Depression
 False understanding of disease
 Low self-esteem Excessive medical treatment
 (Frequent emergency visits)
 Isolation
 Dependence
 Gains from disease
 (Prepared by the author based on literature²⁶)

	病歴	発作の目撃または動画			発作時 ビデオ 脳波
		患者・家族	主治医 (専門外)	てんかん診療 経験を積んだ 医師	
Possible	○	○			
Probable	○		○		
Clinically established	○			○	
Documented	○			○	○

Table 2: Levels of certainty for PNES diagnosis

Medical history
 Witness or video of seizure At time of seizure
 Patient/family Primary care physician/(non-specialist) Epilepsy care/Experienced
 physician
 Video-EEG
 Possible PNES
 Probable PNES
 Clinically established PNES
 Documented PNES

(Prepared by the author based on reference 50)

PNESが 疑われる徴候	長時間の発作持続	発作後もうろう状態の鑑別が難しい
	発作症状の動揺	発作症状が途中で止まったり再開したりする
	非同期性の運動症状	前頭葉てんかんでも観察される
	発作中の閉眼	強制開眼に抵抗することがある
	発作中の首の横振り	複雑部分発作時の自動症でも観察される
てんかん発作が 疑われる徴候	舌の外側の咬創	PNESの場合は、舌先の咬創がありうる
	発作後のいびき呼吸	強直間代発作の後に観察されることがある

Table 3 Signs of suspected PNES and epileptic seizures, respectively

Signs of PNES

Long-lasting seizures Difficult to distinguish from post-ictal daze

Fluctuation of seizure symptoms Stopping and restarting of seizure symptoms

Asynchronous motor symptoms Also observed in frontal lobe epilepsy

Eye closure during seizures May resist forced eye opening

Head swiveling during seizure Also observed in complex partial seizure automatism

Signs of Epileptic Seizures

Signs of epileptic seizures Outward bite of the tongue In PNES, bite of the tip of the tongue may be present

Snoring and breathing after seizures May be observed after tonic-clonic seizures

Posterior arch retraction, seizure injury, and urinary incontinence are insufficient signs to differentiate PNES from epileptic seizures.

(Prepared by the author based on references 10, 42, and 50)

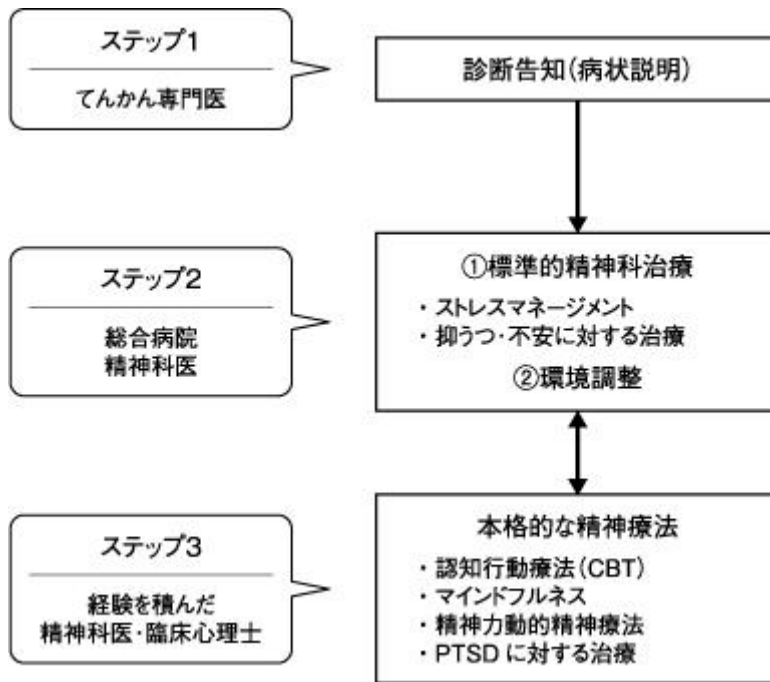


Figure 2 PNES treatment flowchart

The main content of each treatment step and the occupation that will play a central role in that step are listed. In Step 1, the epilepsy specialist (neurologist) explains the patient's condition and provides a bridge to psychiatric consultation. In Step 2, psychiatric treatment is initiated with standard psychiatric treatment and environmental adjustment. Patients with PNES without intellectual disability should focus on the former, while those with intellectual disability should focus on the latter. Most patients settle down after Step 2, but sometimes full psychotherapy (Step 3) is necessary.

-
- ・てんかん発作ではないので、抗てんかん薬は有効ではないことを説明する
 - ・わざとやっているわけではないこと、生活に支障を与えている深刻な発作症状であり専門的な治療が必要であることを説明する
 - ・PNESの病態に関して説明する
例) てんかんとは異なる原因だが、脳に負荷がかかりすぎて体の機能をコントロールできなくなっている状態
 - ・原因(心因)はすぐにはわからないこと、特定できないことが多いことを説明する
 - ・精神科的治療によって症状が改善する可能性が高いので一度精神科を受診したほうがよいと思われることを伝える
 - ・精神科通院が安定するまで、てんかん専門医のフォローアップも継続することを伝える
-

Table 4: Key points for explaining PNES condition

Explain that it is not an epileptic seizure and that antiepileptic drugs are not effective.

Explain that the seizures are not deliberate, that they are serious symptoms that interfere with daily life, and that specialized treatment is necessary.

Explain the pathogenesis of PNES.

Explain the pathology of PNES, e.g., a condition that is different from epilepsy but in which the brain is overloaded and the body's functions are uncontrollable.

Explain that the cause (psychological cause) is not immediately known and often cannot be identified.

Explain that the cause (psychological cause) is not immediately apparent and often cannot be identified. ・ Tell the patient that it would be better to see a psychiatrist

because the symptoms are likely to improve with psychiatric treatment.

Tell the patient that it is recommended to see a psychiatrist because psychiatric treatment is likely to improve symptoms.

(Prepared by the author based on Reference 49)