

## CREATIVE PSYCHOPHARMACOTHERAPY OF PSYCHOGENIC NON – EPILEPTIC SEIZURES

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### SUMMARY

**Background:** Aim of this review was to evaluate management of PNES from neurological and psychiatric perspective.

**Results:** Management of PNES is interdisciplinary. The first treatment phase in PNES should be engaging patients into treatment, which is often challenging. There are several psychopathological dimensions particularly important vulnerable to develop PNES including endogenous anxiety, avoidance behaviour, dissociation, non-dissociative post-traumatic stress, abuse, interpersonal dynamics, personality structure and society and family factors. Early correct diagnosis can help patients promptly receive the treatment they need and prevent common iatrogenic complications that may occur if the condition continues to be misdiagnosed and mistreated.

**Conclusion:** Although evidence is mixed for the treatment of PNES, psychotherapeutic modalities remain a powerful instrument to help patients and reduce seizures. A multidisciplinary, holistic approach is significant. It is important to aim to improve quality with specific treatment. For patients refractory to all possible treatments further investigation should be performed.

**Key words:** psychogenic non-epileptic seizures, epilepsy, psychotropic medications, psychotherapeutic modalities

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### INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are functional neurological disorders or subtypes of conversive disorders that are neurobehavioral states where are confronted neurology and psychiatry. They may occur at any age from childhood (about 5 years) to the age > 70 years, most commonly between the ages of 20 and 40 years. They are common, accounting for over 10% of seizure emergencies and around 30% of cases in tertiary epilepsy units, but the diagnosis is often missed or delayed (Petelin Gadze et al. 2019). PNES are thought to affect approximately 5% of patients who have a diagnosis of epilepsy (Sigurdardottir KR, Olafsson E. 1998). Video - EEG monitoring (V-EEG) is the gold standard method for differentiating epileptic seizures (ES) from PNES. Laboratory tests may provide a more accessible way in differentiating ES from PNES (Petelin Gadze et al. 2019). Management of PNES is interdisciplinary, often refractory and requires involvement of general practitioners, neurologists and mental health professionals. It has been discussed in the literature so far that all mental health professionals are constantly in urge to offer to their patients the optimal treatment, but in everyday clinical practice commonly do not achieve their desired level of success. Despite the significant progress in understanding etiology and pathogenesis of mental disorders and development of a number of new mental health medications (MHMs), treatment outcomes of many mental illnesses including functional neurological

disorders such as PNES remain poor in both short term and long-term course of the treatment. The concept of transdisciplinary integrative psychiatry, particularly when applied in the art and practice of clinical psychopharmacology as both a science and a therapeutic learning organization, has already been discussed in the literature. It is believed that this approach could help bridge the gap between academic and clinical psychiatry, significantly improving treatment success as well in patients with PNES (Jakovljević 2021).

Aim of this review was to evaluate management of PNES from neurological and psychiatric perspective.

### PNES THROUGHOUT HISTORY

The first description in the medical literature of functional neurological symptoms dates to Jean-Martin Charcot (1825–1893), a re-known neurologist from the 19th century who practiced at the Hospital de la Salpêtrière in Paris. Charcot devoted last years of his life to the study of “hysteria”, a condition that he observed and that could present with similar, not identical, impairment as seen in lesions of central nervous system. In his original descriptions, he used the term “*hystero-epilepsy*” to describe the paroxysmal episodes that were similar, but not identical, to epileptic seizures. Charcot originally described a different evolution of hysterical symptoms compared to epilepsy including a response to hypnotic suggestion and an association to certain personality profiles in patients with hysteria. He

embraced the idea that there was a lesion in the central nervous system, although not structurally identifiable, that was responsible for these symptoms (Goetz, CG et al. 2006). This thesis is still embraced by some authors. PNES were also researched of Sigmund Freud (1856–1939) who described that psychological distress, which could be unconscious to the patient, was the root of the hysterical symptoms. He investigated role of trauma, caused by external events or by inner experiences, and suggested that hysterical patients suffered from “incompletely abreacted psychical traumas” that were “converted” into the symptom. This opened doors for hypnosis and eventually psychoanalysis to be proposed as treatment modalities (Tomlinson, WC. Freud et al.2006).

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) PNES are classified as a form of Conversion Disorder or Functional Neurological Symptom Disorder (FNSD) (American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edition. 2013).

## ETIOLOGY OF PNES

Etiological model of PNES that is universally accepted does not yet exist. In the literature there are described different psychophysiological mechanisms that could be responsible or contribute to the aetiology of PNES (Brown & Reuber, 2016; LaFrance & Bjønæs, 2019). It is also described dualistic categorization “psychological” or “physical” factors (e.g. childhood abuse affects both brain maturation and social functioning) and in some articles PNES are described as “comorbidities” and not as primary disorders. There are several psychopathological dimensions particularly important vulnerable to develop PNES including endogenous anxiety, avoidance behaviour, dissociation, non-dissociative post-traumatic stress, abuse, interpersonal dynamics, personality structure and society and family factors (LaFrance W et al. 2006). Stoyann Popkirov et al. in their article “The aetiology of psychogenic non-epileptic seizures: risk factors and comorbidities” described demographic profile, factors such as trauma or acute stress and comorbid disorders (such as other dissociative and functional disorders, post-traumatic stress disorder, depressive and anxiety disorders, personality disorders, comorbid epilepsy, head injury, cognitive and sleep problems, migraine, pain, and asthma) and their role in PNES (Stoyann Popkirov et al. 2019).

In literature is described importance of emotional regulation (ability to control one’s behaviours when experiencing intense emotions). Under-regulation refers to states of intense emotions where the emotions direct behaviour in an impulsive manner, and over-regulation refers to a distancing and disconnection from emotional states in an attempt to manage them. These conditions were found connected to PNES (Uliaszek AA et al. 2012).

## MANAGEMENT OF PNES

Management of PNES is interdisciplinary. The first treatment phase in PNES should be engaging patients into treatment, which is often challenging. Gaston Baslet, Barbara Dworetzky et al. in their article “Treatment of Psychogenic Nonepileptic Seizures: Updated Review and Findings From a Mindfulness-Based Intervention Case Series” from 2015 described steps of treating PNES from acute interventions, short-term evidence-based interventions to cognitive-behavioral therapy (Gaston Baslet et al. 2015).

General practitioners or neurologists are often the first-line health professionals involved in the evaluation of PNES. The role of the neurologist is extremely important in establishing an accurate diagnosis which when is early diagnosed helps patients to receive treatment and prevent misdiagnosis and mistreatment. Often patients are treated with antiepileptic drugs (AEDs), with an estimated 75% of PNES patients receiving AEDs prior to correct diagnosis.

Early correct diagnosis can help patients promptly receive the treatment they need and prevent common iatrogenic complications that may occur if the condition continues to be misdiagnosed and mistreated. Iatrogenic complications typically involve inappropriate treatment with antiepileptic drugs (AEDs), with an estimated 75% of PNES patients receiving AEDs prior to correct diagnosis (Jakovljevic, 2016). It is often seen in emergency rooms misdiagnosed patients that get severe medications, often intubated and sedated which all can lead to severe complications and sometimes even to death. That is why early diagnosis is important and gives best outcome (Reuber M et al. 2004). The International League Against Epilepsy (ILAE) defines drug-resistant epilepsy (DRE) when seizure control fails with at least two AED schemes (either in monotherapy or in combination). Patients with PNES are usually diagnosed as DRE, and they also tend to suffer the imposition of stigma and restrictions on the lifestyle of patients with DRE (Lanzillotti AI et al. 2021). A small randomized controlled trial (RCT) of withdrawal of AEDs in patients with PNES suggested some possible beneficial effects of withdrawal on seizure frequency, and use of rescue medication, and showed no suggestion of any adverse effect (Oto M et al. 2010).

After diagnosis is established, it is important transition from neurologist/general practice to mental health professionals. Some authors believe that continued involvement of the neurologist who established the diagnosis is needed to allow a safe taper of AEDs, prevent inappropriate treatment, evaluate the development of any new neurological symptoms, including change in semiology, and treat any co-morbid neurological condition (Kanner AM et al. 2008).

Some authors propose ‘functional’ model of the symptoms that is useful both in thinking about the problem and when explaining the symptoms to the patient

with many useful steps in management that do not require a detailed understanding of etiology in an individual patient (Osmanovic 2022). With involvement of mental health professionals there is no determined time period how long should this treatment last. Baslet et al. suggested treatment of PNES conceptualized in phases: engagement, acute treatment, and long-term follow-up. While many patients may move smoothly through these different stages, other patients may be retained at some of these phases. Acute treatment comprises short-term interventions, both psychotherapeutic and psychopharmacological, that require a patient's ongoing participation. Most of the research done in PNES treatment focuses on these active treatments.

In literature it is emphasized the importance of finding a transdisciplinary integrative soul and increasing treatment effectiveness by creation and fostering hope, meaning, personal responsibility, spirit of optimism and commitment that can significantly contribute to overall positive response to pharmacotherapy (Jakovljević 2021). It is also suggested that connection of emotional contamination with creative psychopharmacotherapy is determined in different ways either through narrative psychopharmacotherapy, through assertive and positive communication, creating a favorable and positive therapeutic relationship whereby a partnership is created, which together leads to the main goal, which is the successful treatment of the patient to the mutual satisfaction (Hamidovic J et al. 2021).

## **ROLE OF PSYCHOTROPIC MEDICATIONS AND COGNITIVE BEHAVIOURAL THERAPY IN THE TREATMENT OF PNES**

It is important to understand importance of psychotropic medications in the treatment of PNES and to notice that the evidence-based literature on PNES treatment is limited, especially for psychotropic medications. Studies have been made to evaluate importance of sertraline in treatment of PNES. La France and colleagues conducted a randomized, placebo-controlled trial evaluating the efficacy of flexible-dose sertraline over 12 weeks aimed at reducing event frequency and improving psychiatric co-morbidities and psychosocial domains (LaFrance W, 2010).

Recently cognitive behavioural therapy is considered the "second wave" of behavioural therapies and has wide-range acceptance and evidence as an effective treatment for many psychiatric disorders.

Patients with PNES often develop new medically unexplained symptoms, aside from the PNES, even after diagnosis is established. Clinicians need to be attentive to these varied somatoform presentations and refocus patient's attention on their recovery through mental health treatment (McKenzie PS et al. 2011).

## **CONCLUSION**

Psychogenic non-epileptic seizures (PNES) are functional neurological disorders or subtypes of conversive disorders that are neurobehavioral states where are confronted neurology and psychiatry. They are common, accounting for over 10% of seizure emergencies and around 30% of cases in tertiary epilepsy units, but the diagnosis is often missed or delayed. After diagnosis is established, it is important transition from neurologist/general practice to mental health professionals. Some authors believe that continued involvement of the neurologist who established the diagnosis is needed to allow a safe taper of AEDs, prevent inappropriate treatment, evaluate the development of any new neurological symptoms, including change in semiology, and treat any co-morbid neurological condition. Acute treatment comprises short-term interventions, both psychotherapeutic and psychopharmacological, that require a patient's ongoing participation. Most of the research done in PNES treatment focuses on these active treatments. It is also important to understand importance of psychotropic medications in the treatment of PNES but also to notice that the evidence-based literature on PNES treatment is limited, especially for psychotropic medications. Recently cognitive behavioural therapy is considered the "second wave" of behavioural therapies and has wide-range acceptance and evidence as an effective treatment for many psychiatric disorders. Psychotherapeutic modalities remain a powerful instrument to help patients and reduce seizures. A multidisciplinary, holistic approach is significant. It is important to aim to improve quality with specific treatment. For patients refractory to all possible treatments further investigation should be performed.

To conclude, creative psychopharmacotherapy offers a unique opportunity to assist patients in discovering and exploring a deeper sense of meaning in their lives. This approach can guide individuals toward creating a fulfilled, meaningful existence and realizing their full potential. Mental health challenges may, in this context, serve as a catalyst for breaking away from misguided life goals and values. By embracing new ways of thinking, experiencing, behaving, and creating, patients can turn towards more authentic values, ultimately paving the way for a successful and meaningful life (Mulahalilovic Aron 2021).

## **REFERENCES**

1. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. 5th edition.* Arlington VA: American Psychiatric Publishing; 2013.
2. Baslet G. *Psychogenic non-epileptic seizures: A model of their pathogenic mechanism.* *Seizure.* 2011; 20:1–13.

3. Brown RJ, Reuber M. *Psychological and psychiatric aspects of psychogenic non-epileptic seizures (PNES): a systematic review. Clin Psychol Rev* 2016a; 45: 157-82.
4. Brown RJ, Reuber M. *Towards an integrative theory of psychogenic non-epileptic seizures (PNES). Clin Psychol Rev* 2016b; 47: 55-70.
5. Goetz, CG. *Charcot and Psychogenic Movement Disorders. In: Hallett, M.; Fahn, S.; Jankovic, J.; Lang, AE.; Cloninger, CR.; Yudofsky, SC., editors. Psychogenic Movement Disorders: Neurology and Psychiatry. Philadelphia, PA: Lippincott Williams and Wilkins; 2006. p. 3-13.*
6. Hamidović J, Hasanović M, Pajević I, Dostović Hamidović L, Jakovljević M. *Emotional Contamination in the Context of Creative Psychopharmacotherapy. Psychiatria Danubina. 2021;33(suppl 4):1058-1064.*
7. Jakovljevic M. *Creative, Person Centered Narrative Psychopharmacotherapy (Cp-Cnp): From Theory To Clinical Practice. Psychiatria Danubina, 2021; Vol. 33, Suppl. 2, pp 149-231*
8. Jakovljevic M. *Kreativna psihofarmakoterapija: priručnik za liječnike obiteljske medicine i primarne zdravstvene zaštite. Zagreb : Pro Mente, 2016.*
9. Kanner AM. *Is the neurologist's role over once the diagnosis of psychogenic nonepileptic seizures is made? No! Epilepsy Behav. 2008; 12:1–2.*
10. LaFrance WC, Bjønæs H. *Designing treatment plans based on etiology of psychogenic nonepileptic seizures. In: Schachter SC, LaFrance JWC. Gates and Rowan's nonepileptic seizures. 4th Ed. Cambridge: Cambridge University Press; 2019: 283-99.*
11. LaFrance W, Keitner G, Papandonatos G, Blum A, Machan J, Ryan C, Miller I. *Pilot pharmacologic randomized controlled trial for psychogenic nonepileptic seizures. Neurology. 2010; 75:1166–1173.*
12. Lanzillotti AI, Sarudiansky M, Lombardi NR, Korman GP, D'Alessio L. *Updated Review on the Diagnosis and Primary Management of Psychogenic Nonepileptic Seizure Disorders. 2021;1825—1838.*
13. McKenzie PS, Oto M, Graham CD, Duncan R. *Do patients whose psychogenic non-epileptic seizures resolve, 'replace' them with other medically unexplained symptoms? Medically unexplained symptoms arising after a diagnosis of psychogenic non-epileptic seizures. J Neurol Neurosurg Psychiatry. 2011 Sep; 82(9):967–969.*
14. Mulahalilovic A, Hasanovic M, Pajevic I, Jakovljević M. *Meaning and the Sense Of Meaning In Life From A Health Perspective. Psychiatria Danubina, 2021; Vol. 33, Suppl. 4 (part III), pp 1025-1031*
15. Oto M, Espie C, Duncan R. *An exploratory randomized controlled trial of immediate versus delayed withdrawal of antiepileptic drugs in patients with psychogenic nonepileptic seizures. Epilepsia 51, 1994–1999 (2010)*
16. Petelin Gadže Ž, Poljaković Z, Nanković S, Šulentić V. *Epilepsija – dijagnostički i terapijski pristup. Zagreb: Medicinska naklada, 2019.*
17. Reuber M, Baker G, Gill R, Smith D, Chadwick D. *Failure to recognise psychogenic nonepileptic seizures may cause death. Neurology. 2004; 62:834–835.*
18. Sigurdardottir KR, Olafsson E. *Incidence of psychogenic seizures in adults: a population based study in Iceland. Epilepsia 39, 749–752 (1998).*
19. Sinanović O. *The Creative Pharmacotherapy of Functional Neurological Disorders in the Context of ICD-11. Psychiatria Danubina, 2022; Vol. 34, Suppl. 9, pp 5-23.*
20. Stoyan Popkirov, Ali A. Asadi-Pooya, Roderick Duncan, David Gigineishvili, Coraline Hingray, Andres Miguel Kanner, W. Curt LaFrance Jr, Chrisma Pretorius, Markus Reuber on behalf of the ILAE PNES Task Force. *The aetiology of psychogenic non-epileptic seizures: risk factors and comorbidities. Epileptic Disord 2019; 21 (6): 529-47*
21. Tomlinson, WC. *Freud and Psychogenic Movement Disorders. In: Hallett, M.; Fahn, S.; Jankovic, J.; Lang, AE.; Cloninger, CR.; Yudofsky, SC., editors. Psychogenic Movement Disorders: Neurology and Psychiatry. Philadelphia, PA: Lippincott Williams and Wilkins; 2006. p. 14-19.*
22. Uliaszek AA, Prensky E, Baslet G. *Emotion regulation profiles in psychogenic non-epileptic seizures. Epilepsy Behav. 2012; 23(3):364–369.*

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