Personality Traits, Illness Behaviours and Psychiatric Comorbidity in Individuals with

Psychogenic Non-Epileptic Seizures (PNES), Epilepsy and Other Non-Epileptic Seizures

(oNES):

Differentiating Between the Conditions

by

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SUMMARY

One of the most pressing issues in psychogenic non-epileptic seizure (PNES) diagnosis is to ensure that the condition is successfully differentiated from epileptic seizures (ES) and other non-epileptic seizures (oNES). Video electroencephalography (vEEG), which is considered to be the gold standard for PNES diagnosis, is largely inaccessible to most in this country. Hence, more often than not, individuals suffering from this psychiatric condition are assumed to have epilepsy and are erroneously treated with anti-epileptic drugs, which creates individual and societal financial strain, poses numerous health risks and complications, and delays access to appropriate treatment. Very little is still known about the South African PNES population and as of yet, there have been no attempts at developing any cheaper, quicker and easier to administer alternative diagnostic measures for PNES in South Africa. The study aimed to investigate if South African individuals with PNES differ from individuals with ES and oNES in terms of demographic and seizure characteristics, personality traits, illness behaviours, and depression, anxiety and post-traumatic stress disorder (PTSD) in statistically significant ways; and if so, to test if these differences can be utilised in raising suspicion of PNES as the differential diagnosis to epilepsy and oNES. Twenty-nine adults with seizure complaints were recruited using convenience sampling from two private and government hospitals with vEEG technology. A quantitative double-blind convenient sampling comparative design was used. A demographic and seizure questionnaire, the NEO Five Factor Inventory-3 (NEO-FFI-3), Illness Behaviour Questionnaire (IBQ), the Beck Anxiety Inventory – Primary Care (BAI-PC) were administered. Only data from twenty-four people from the private hospital was made available for data analysis. Cronbach's alphas, ANOVA, Cross-tabulation, Fisher exact test, and ROC analyses results are reported. The final sample consisted of 5 PNES (21%), 16 ES (67%) and 3 oNES (13%) patients. The PNES group was found to be significantly more male and to experience significantly more monthly seizures, when comparing PNES and ES, and PNES and the combined ES and oNES group. No significant differences between groups were found in terms of age, population group, language, education, and age at first seizure. No significant differences were found between the groups on any of the NEO-FFI-3 subscales. Only item "Do you experience a lot of pain with your illness?" on the IBQ exhibited a significant difference, with PNES tending to answer "Yes" more often when compared to the other two groups. All three groups scored above the cut-off point of 5 exhibiting depression, anxiety and PTSD symptoms on the BAI-PC. However, the PNES group tended to score significantly

higher than the ES and the combined group. A cut-off point of 12 was found to be optimal in predicting PNES in this seizure population using the BAI-PC. Descriptive statistics or tendencies are reported for all used measures. This study provided a greater understanding of personality domains, abnormal illness behaviours, psychiatric comorbidity and demographic and seizure factors in the PNES population and discussed the potential for these factors to be used in the future for PNES screening.

Keywords: psychogenic non-epileptic seizures, epilepsy, other non-epileptic seizures, personality, illness behaviours, psychiatric comorbidity, diagnosis, South Africa

OPSOMMING

Een van die belangrikste aspekte in die diagnose van psigogene nie-epileptiese toevalle (PNES) is om te verseker dat die toestand behoorlik onderskei word van epileptiese toevalle (ES) en ander nie-epileptiese toevalle (oNES). Video-elektroënsefalografie (vEEG) wat as dié maatstaf vir die diagnose van PNES beskou word, is meestal ontoeganklik vir die meeste mense in Suid-Afrika. Individue wat aan hierdie psigiatriese toestand ly, word dus baie dikwels verkeerdelik met anti-epileptiese middels behandel omdat aangeneem word dat hulle epilepsie het. Dit plaas finansiële druk op die individu en gemeenskap, dit lei tot verskeie gesondheidsrisiko's en -komplikasies en vertraag toegang tot gepaste behandeling. Tans is baie min bekend oor die Suid-Afrikaanse PNES-populasie. Geen poging is ook nog aangewend om alternatiewe diagnostiese maatstawwe vir PNES in Suid-Afrika te ontwikkel wat goedkoper, vinniger en makliker is om te gebruik nie. Die studie het gepoog om vas te stel of Suid-Afrikaanse individue met PNES beduidend verskil van individue met ES en oNES wat betref kenmerke van demografie en toevalle, persoonlikheidstrekke, siektegedrag, en depressie, angs en post-traumatiese stresversteuring (PTSV); en indien wel, om te bepaal of sodanige verskille gebruik word om 'n vermoede van PNES as die differensiële diagnose vir epilepsie en oNES te versterk. Nege en twintig volwassenes met klagtes van toevalle is met behulp van geriefsteekproefneming van twee privaat en publieke hospitale wat vEEG-tegnologie gebruik verkry. 'n Kwantitatiewe, dubbelblinde gerieflikheids-steekproef en vergelykende ontwerp is gebruik. 'n Vraelys oor demografie en toevalle, die *NEO Five Factor Inventory-3* (NEO-FFI-3), *Illness Behaviour Questionnaire* (IBQ), die *Beck-Anxiety Inventory – Primary Care* (BAI-PC) is toegepas. Slegs data van vier en twintig mense van die privaat hospitaal is gebruik vir die data-ontleding. Cronbach se alphas, ANOVA, kruistabellering, die Fisher eksakte toets, en ROC-ontledings se resultate is gerapporteer. Die finale steekproef het uit 5 PNES- (21%), 16 ES- (67%) en 3 (13%) oNES- pasiënte bestaan. Die PNES-groep het uit beduidend meer mans bestaan en het beduidend meer maandelikse toevalle ervaar in vergelyking met die ES-groep, asook in vergelyking met die gekombineerde ES- en oNES-groep. Geen beduidende verskille wat betref ouderdom, bevolkingsgroep, taal, opleiding, en ouderdom met eerste toeval is gevind nie. Ook is geen beduidende verskille tussen die groepe gevind op enige van die subskale van die NEO-FFI-3 nie. Slegs een item van die IBQ, "*Do you experience a lot of pain with your illness?*" het 'n beduidende verskil getoon, met PNES-pasiënte wat meer dikwels "Ja" geantwoord het in vergelyking met die ander twee groepe. Op die BAI-PC was al drie groepe se tellings bo die

afsnypunt van 5, wat simptome van depressie, angs en PTSV aandui. Die PNES-groep het egter beduidend hoër tellings gehad as die ES-groep en die gekombineerde groep. 'n Afsnypunt van 12 op die BAI-PC was optimaal vir die voorspelling van PNES in hierdie populasie pasiënte met toevalle. Beskrywende statistiek of tendense word vir al die maatstawwe wat gebruik is gerapporteer. Die studie het 'n groter begrip van persoonlikheidskenmerke, abnormale siektegedrag, psigiatriese komorbiditeit en faktore van demografie en toevalle in die PNES-populasie verskaf. Die potensiaal om hierdie faktore in die toekoms vir PNES-sifting te gebruik, is ook bespreek.

Sleutelwoorde: psigogene nie-epileptiese toevalle, epilepsie, ander nie-epileptiese toevalle, persoonlikheid, siekte gedrag, psigiatriese komorbiditeit, diagnose, Suid-Afrika

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ABBREVIATIONS

AED	Anti-epileptic drug
BAI	Beck Anxiety Inventory
BAI-PC	Beck Anxiety Inventory - Primary Care
BDI	Beck Depression Inventory
BDI-PC	Beck Depression Inventory – Primary Care
BRIQ	Behavioral Reaction to Illness
CASE–Epilepsy	Communication and Attitudinal Self-
CBT	Efficacy - Epilepsy measure
CBT-ip	Cognitive-behavioural therapy
	CBT-informed psychotherapy
DAPP-BQ	Dimensional Assessment of Personality
	Pathology – Basic Questionnaire
DSM-5	Diagnostic and Statistical Manual of
	Mental Disorders, Fifth Edition
EEG	Electroencephalography
ES	Epileptic seizures
FFM	Five Factor Model
FFT	Five Factor Theory
HPLP	Health-Promoting Lifestyle Profile
HRQOL	Health-related quality of life
IBQ	Illness Behavior Questionnaire
ICD-10	International Classification of Diseases,
	10th Edition
IPQ	Illness Perception Questionnaire
MHLC	Multidimensional Locus of Control
MMPI	Minnesota Multiphasic Personality
	Inventory
NEO-FFI-3	NEO Five Factor Inventory-3
NEO-PI-R	NEO Personality Inventory - Revised
oNES	Other non-epileptic seizures
PAI	Personality Assessment Inventory
PIT	Psychodynamic interpersonal therapy

PNES	Psychogenic non-epileptic seizures
PTSD	Post-traumatic stress disorder
RCT	Randomised controlled trial
SMC	Standard medical care
QOL	Quality of life
vEEG	Video electroencephalography

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Chapter 1 Introduction

1.1 Introduction, Research Problem and Rationale

Psychogenic non-epileptic seizures (PNES) are seizure-like events that mimic epileptic seizures (ES), but are caused by psychological distress rather than abnormal electrical discharges in the brain (Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al., 2009). PNES research is still in its early stages in South Africa (Anderson, Damianova, Hanekom, & Lucas, 2017; Cronje & Pretorius, 2013; Pretorius, 2016; Pretorius & Cronje, 2015; Pretorius & Sparrow, 2015) and awareness of the condition is still considered to be low among healthcare professionals in this country (Pretorius, 2016). Furthermore, video electroencephalography (vEEG), which is considered to be the gold standard for PNES diagnosis, is expensive and thus largely inaccessible to most in this country (Pretorius & Cronje, 2015). Hence, more often than not, individuals suffering from this psychiatric condition are assumed to have epilepsy and are erroneously treated with anti-epileptic drugs (AEDs; Pretorius, 2016), which not only creates financial strain (LaFrance, 2008) but also poses numerous health risks and complications that may even result in death (Reuber, Baker, Gill, Smith, & Chadwick, 2004). In addition, late correct diagnosis means a delayed access to appropriate treatment (Reuber & Elger, 2003) and a higher burden on the economy in the form of medical care and lost labour (LaFrance, 2008; Reuber, Fernandez, Bauer, Helmstaedter, & Elger, 2002). Currently, the most pressing issue for PNES in South Africa is to ensure that the condition is successfully differentiated from ES in healthcare settings that are resource-challenged. This can be done by using measures that have been shown to be reliable, cheap, quick and easy to use. In light of the heterogeneity of the PNES population in terms of aetiology and symptomatology, multifaceted approaches addressing multiple PNES aspects have shown to be most successful at differentiating between PNES and ES patients (Syed et al., 2009). Personality factors, prevalence of abnormal illness behaviour and psychiatric comorbidity have been shown to distinguish PNES from ES populations in significant ways, but their utility is yet to be tested in South Africa.

1.2 Research Aims

In light of the research problem outlined above, this study aims to examine if South African individuals with PNES differ from individuals with ES and oNES in terms of demographic and seizure characteristics, personality traits, illness behaviours as well as depression, anxiety and PTSD symptoms in statistically significant ways; and if so, to test if these differences may be utilised in raising suspicion of PNES as the differential diagnosis to epilepsy and oNES.

1.3 Research Questions

With the research aims outlined above in mind, the present study seeks to answer the following questions:

- What NEO personality domains prevail among the South African patients of PNES;
- What illness behaviours South African patients of PNES demonstrate;
- If the NEO-FFI-3, IBQ, or BAI-PC questionnaires can differentiate between patients with PNES and those with ES or oNES.

1.4 Definition of Key Terms

1.4.1 Psychogenic Non-Epileptic Seizures (PNES).

PNES can best be defined as paroxysms that resemble epileptic seizures, but stem from psychogenic rather than neurobiological factors that are not accompanied by electrophysiological changes in the brain, which are characteristic of epilepsy (Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al., 2009). Aetiologically PNES is largely considered to be a physical expression of psychological distress (Alsaadi & Marquez, 2005), however, other aetiological theories exist (discussed in detail in Chapter 2).

1.4.2 Electroencephalography (EEG) and Video Electroencephalogram (vEEG).

Electroencephalography can be defined as the recording of the brain's electrical activity over time through electrodes attached to the scalp (Fallon & Cataldo, 2009). EEG provides gross anatomical correlates of brain activity and is the primary tool for the diagnosis of epilepsy (Fallon & Cataldo, 2009). Video EEG, in turn, adds the ability to observe patient behaviour while following their electrical brain activity patterns on the EEG at the same time

and is considered to be the current gold standard in diagnosing PNES (Benbadis & LaFrance Jr, 2010).

1.4.4 Abnormal Illness Behaviour.

Pilowsky (1986) defines abnormal illness behaviour as a way of persistently "experiencing, perceiving, evaluating and responding to one's own health status" (p. 76) that could be considered an inappropriate or maladaptive response considering the objective level of pathology present in an individual. To measure such behaviour Pilowsky and Spence (1976) created the Illness Behaviour Questionnaire, which was used in the present study.

1.4.5 NEO/Big Five Personality Domains/ the Five Factor Model.

The Five Factor Model or the Big Five Personality facets evolved in the 1980s when many psychologists realised that there were certain major themes that kept recurring when describing personality both in the natural language and scientific theories (McCrae & Costa, 2010). While at first many competing theories existed when it came to specifying just what exactly the five factors were, over years of research McCrae and Costa (2010) came to the conclusion that the following five factors represented the personality structure the best: Neuroticism, Extraversion, Openness to Experience, Agreeableness and Conscientiousness. Since the present study will be using the NEO Five Factor Inventory-3 (NEO-FFI-3), which was developed by McCrae and Costa (2010), to measure these broad personality domains, it is useful to look at how these authors describe each of them.

1.4.5.1 Neuroticism (N).

The personality domain scale of Neuroticism is considered to contrast adjustment or emotional stability with maladjustment or emotional instability, i.e. Neuroticism (McCrae & Costa, 2010). Those scoring highly on the domain are considered to experience more emotional distress and negative affect such as fear, sadness, embarrassment, guilt and disgust (McCrae & Costa, 2010). Low scorers, on the other hand, tend to be emotionally well-adjusted, calm, even-tempered, relaxed and more resilient when faced with stressful situations (McCrae & Costa, 2010).

1.4.5.2 Extraversion (E).

Extraversion can be understood largely as a dimension of interpersonal tendencies (McCrae & Costa, 2010). According to McCrae and Costa (2010) those scoring high on the domain scale of Extraversion tend to be more sociable, assertive, active, talkative, energetic, and optimistic as well as prefer large groups, excitement and stimulation. The authors suggest that those scoring low on Extraversion, in other words – introverts – are most often reserved, independent, even-paced, and prefer to be alone.

1.4.5.3 Openness to Experience (O).

McCrae and Costa (2010) suggest that those scoring high on the Openness to Experience domain scale tend to have an active imagination, intellectual curiosity, aesthetic sensitivity, attentiveness to inner feelings, independence of judgement and a preference for variety. They also tend to have richer experiential lives and experience both positive and negative emotions more keenly. Those who score low on the O scale tend to be conventional in their behaviour and outlook, prefer the familiar, have a narrower scope and lower intensity of interests, and somewhat muted emotional responses.

1.4.5.4 Agreeableness (A).

Similarly to Extraversion, Agreeableness denotes interpersonal tendencies (McCrae & Costa, 2010). Those scoring highly on the Agreeableness domain tend to be altruistic, sympathetic, and eager to help, holding the belief that others will help them in return. Those scoring low tend to be antagonistic, egocentric, sceptical of other people's intentions and competitive.

1.4.5.5 Conscientiousness (C).

McCrae and Costa (2010) suggest that the personality domain of Conscientiousness measures the active process of self-control, denoted by planning, organising and carrying out tasks. Individuals who score high on this domain tend to be purposeful, strong-willed, determined and high achievers, however, they may also exhibit fastidious, compulsively neat or workaholic behaviour. Those scoring low tend to be less exacting when applying their moral principles, more easy-going when it comes to working toward their goals and often more hedonistic.

1.5 Chapter Overview

Chapter 2 provides an overview of relevant literature in terms of PNES nosology, history, signs and symptoms, epidemiology, classification, aetiology, diagnostic methods, level of burden, treatment approaches and course and outcome. A special emphasis is put on the role of personality, abnormal behaviours and psychiatric comorbidity in the abovementioned areas of PNES research.

Chapter 3 elaborates on the Five Factor Theory (FFT) of the person (Costa & McCrae, 1994) as a framework for explaining the factors contributing to the development, maintenance and aetiologically-focused approaches to PNES diagnosis. Again, the focus will be put on the aetiological and disease-maintaining aspects targeted by the present study - personality, abnormal illness behaviour and psychiatric comorbidity.

Chapter 4 goes into detail on the methodological approach taken in this study and describes the research design, the study sample characteristics and size, and the sampling strategy. Measures used in the study, the approach to data collection and analysis are described further, and lastly, the ethical considerations pertaining to this study are discussed.

Chapter 5 presents the results and key findings of the study. The descriptive and comparative statistics for each of the used measures as well as the reliability analyses for the NEO-FFI-3 and BAI-PC are presented.

Chapter 6 discusses the key findings in the current study. The chapter follows with the discussion of the limitations and significance of current study, as well as some recommendations for future research. The chapter finishes with concluding remarks on the study.

Chapter 2 Literature Review

2.1 Introduction

In the last few decades PNES research has experienced a considerable proliferation. While the literature is still saturated with studies conducted in the Global North, PNES studies from countries like Iran (Asadi-Pooya, Emami, & Emami, 2013, 2014), India (Dhiman et al., 2013), Brazil (Alessi & Valente, 2013), as well as South Africa (Anderson et al., 2017; Cronje & Pretorius, 2013; Pretorius, 2016; Pretorius & Cronje, 2015; Pretorius & Sparrow, 2015) have begun to emerge offering a more global look at the disorder. The following chapter will give an overview of both international and local research (where available) on the topics of nosology, history, signs and symptoms, epidemiology, classification, aetiology, diagnosis, role of personality and abnormal behaviours, treatment and the level of burden in terms of individuals with PNES.

2.2 PNES Nosology

Currently, PNES still raises numerous questions with regard to its nature and that is well reflected in the fact that it is classified differently in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and the International Classification of Diseases, 10th Edition ([ICD-10]; Beghi et al., 2015). DSM-5 classifies PNES as a conversion disorder "with attacks or seizures" type and locates it within the family of somatic symptom and related disorders (American Psychiatric Association [APA], 2013), while International Statistical Classification of Diseases and Related Health Problems (ICD-10) places it within dissociative [conversion] disorders as dissociative convulsions (World Health Organization [WHO], 1990).

The biggest difficulty in classifying PNES within the existing psychiatric taxonomies is the fact that PNES patients do not fall into a single distinct psychopathological category (Griffith & Szaflarski, 2010). In fact, as will be discussed further in this chapter, PNES has been suggested not to be a unitary disorder but often has multiple aetiologies and manifestations (Reuber, Howlett, & Kemp, 2005). Hence, in the following sections I wish to shed some light on the current state of knowledge in the area of PNES.

2.2 Historical Overview

While the name "psychogenic non-epileptic seizures" might not suggest this, the condition is largely the modern reincarnation of the well-known hysteria, at the time of its inception proposed by the Egyptians and later the Greeks to be caused by a wandering womb frustrated by a lack of use. Already then the typical symptoms of this condition were considered to be globus hystericus (now known as "globus sensation" or "globus pharyngeus" [Harding, 2015]), as well as paralyses and convulsions (Trimble, 2010).

Later, at the time of the Middle Ages and the concurrent stifling of scientific thought the disorder was seen to be associated with witchcraft and thus a punishable crime (Institoris, Sprenger, & Sommers, 1948). Despite this, an English physician Edward Jorden was the first to link the aforementioned symptoms to "perturbations of the mind", suggest their connection to the female sex, as well as their multifaceted nature in his treatise of 1603 (Jorden, 1603). The focus on the mind became more central as instances of hysteria began to be noted in men and senile women, thus challenging the uterine theories (Trimble, 2010).

In turn, the eighteenth and nineteenth centuries saw the question of hysteria and epilepsy differentiation arise more clearly with some suggesting that epileptic seizures could degenerate into hysteric ones and others suggesting few differences between the disorders (Trimble, 2010). While the theories of the wandering uterus have dwindled, sexual inhibitions began surfacing as potential causative mechanisms (Trimble, 2010). Furthermore, certain personality types were considered to be more susceptible and external experiences, such as accidents, began to be considered relevant (Trimble, 2010). While the sexual origin theme became revived by some of the thinkers of the French school of the mid- to late-nineteenth century (Trimble, 2010), theories of cerebral origins of hysteria found their support more famously in neurologists Pierre Briquet and Jean-Martin Charcot, and psychologist Pierre Janet. In fact, Briquet ([1989]; originally published in 1859) ridiculed uterine theories and proposed that hysteria was a neurosis originating in the portion of the brain responsible for receiving sensations and affective impressions. However, he recognised many possible interacting causative factors, such as heredity, emotional predisposition as well as accidents or physical abuse (Briquet, 1989). Similarly, Charcot (1877) rejected uterine theories and argued that hysteria should be treated as any other neurological disorder. Via clinical observation, Charcot identified the physical stigmata of hysteria and suggested that certain nervous constitutions were more susceptible to the condition than others

(Charcot, 1877). Another important French School thinker, Pierre Janet (1901) was the first to suggest dissociation as an important mechanism in hysteria, which later morphed into the Freudian idea of repression (Trimble, 2010). Furthermore, a concept of a posttraumatic hysteria emerged during the period, as well as a conceptualisation of two variations of hysteria - one where a clear differential diagnosis between hysteria and epilepsy was possible, and one where epileptic and hysterical symptoms were intertwined thus considered to make such a differentiation impossible (Trimble, 2010).

With the dawn of the nineteenth century, Freud's hypnosis work with Joseph Breuer saw the development of psychoanalysis (Trimble, 2010). Breuer and Freud ([1955]; originally published in 1893-1895) conceptualised hysterical symptoms as relating to traumatic ideas and stemming from the unconscious. The unconscious mind in turn ridden with conflicts converted this energy into physical symptoms as a way to resolve psychic tension (Breuer & Freud, 1955). Famously the trauma in Freudian thought was related to real or imagined childhood sexual seduction leading him to notions of the Oedipus and Elektra complexes (Trimble, 2010). Hence, to Freud the causes of hysteria were epigenetic - based in the postnatal and developmental processes (Breuer & Freud, 1955). Furthermore, Freud considered epilepsy to be closely related to hysteria suggesting that no pathological disorder could be identified to explain it, hence mostly equating the two as far as aetiology was concerned (Breuer & Freud, 1955).

The ideas about aetiological similarity between epilepsy and PNES survived into the twentieth century. This marked the emergence of concepts such as 'epileptic personality', suggesting that the personality change sometimes seen in individuals with epilepsy was a causal factor rather than a result of the condition, as it is considered now (Trimble, 2010). Furthermore, the twentieth century saw the emergence of the EEG which became the golden standard for epilepsy diagnosis (Benbadis & LaFrance Jr, 2010). However, cases of hysteria continued to be recorded widely in the aftermath of the First World War among soldiers who were shown to exhibit a variety of "textbook" hysteria symptoms, hence, negating the idea that all neuroses stemmed from sexual traumas (Trimble, 2010). Later wars, such as the Second World War, and then wars in Korea, Vietnam, and the Falklands saw further cases of hysteria being recorded and marked the recognition of the psychological nature of the disorder and the introduction of psychological interventions (Trimble, 2010). Lastly, the introduction of vEEG monitoring in the latter part of the twentieth century led to the

realisation that many PNES patients were misdiagnosed with epilepsy (Griffith & Szaflarski, 2010).

While the condition has gone through a number of name iterations including hysteria, hystero-epilepsy, neurosis, or, more recently, pseudoseizures (Bhatia & Sapra, 2005; Derry & McLachlan, 1996; Stone, Sharpe, & Binzer, 2004; Trimble, 2010); psychogenic non-epileptic seizures (PNES), psychogenic non-epileptic spells, non-epileptic seizures or non-epileptic attacks tend to be the preferred terms nowadays (Ekanayake et al., 2017; Smith, 2014). Hysteria and neurosis have been replaced due to the general moving away of psychiatric systems such as the DSM from psychodynamically-centered terminology and the term "pseudoseizures" tends to be less used due to the implication that the seizures in PNES are somehow feigned, disregarding the uncontrollable nature of the seizures for the patient. While psychogenic non-epileptic seizures is perhaps the most used term nowadays, some choose to replace the term 'seizures' with 'attacks' (Oto, Espie, & Duncan, 2010) or spells (Hendrickson, Popescu, Ghearing, & Bagic, 2015) in order to further distance epilepsy from PNES. The current study will use the term PNES to refer to the condition, which is in accordance with most current literature on the subject internationally and in South Africa.

2.3 Signs and Symptoms

Signs in a medical context can be defined as any objective evidence of disease (Shiel Jr., 2017). A plethora of signs has been reported to be present in the PNES population, however, some are considered to be more specific to PNES than others, such as: occurrence from sleep; fluctuating course; closed eyes; eye fluttering; closed mouth; asynchronous (limb) movements; side-to-side head movements; pelvic thrusting; opisthotonus (spasm of the muscles causing backward arching of the head, neck, and spine); rotation in bed; responsiveness during attack; ictal crying/weeping; persistent rigidity; persistent clenched fist; persistent ictal hyperventilation; urinary incontinence; convulsion duration of above two minutes; and memory of the period when patient appears unconscious (Avbersek & Sisodiya, 2010; De Paola et al., 2016; Seneviratne, Rajendran, Brusco, & Phan, 2012; Syed et al., 2011).

While signs are understood as objectively verifiable, symptoms can be understood as subjective experiences of the disease (Shiel Jr., 2017). There are still very few studies that have addressed the subjective experience of PNES patients. Only one study so far by Plug,

Sharrack, and Reuber (2009) has investigated seizure metaphors used by PNES and epilepsy patients. Their research suggests that while individuals with epilepsy tended to describe the experience of seizures as an external event or situation or a self-directed agent or force, individuals with PNES tended to see it as a space or place that they 'get into' and 'out of'. Hence, PNES patients actually seemed to attribute more agency to themselves than epilepsy patients in the onset of their attacks. While the attacks in PNES are never considered to be deliberate, this is an interesting finding in light of the delicate line that needs to be walked by healthcare providers in terms of helping PNES patients realise their agency in managing the attacks and yet understanding that they are not being blamed for the onset of their PNES.

2.4 Epidemiology

2.4.1 Incidence and prevalence internationally and in South Africa.

On the whole, general population-based studies on the incidence of PNES are scarce and tend to come from developed countries (Asadi-Pooya & Sperling, 2015). Two studies, one from Scotland (Duncan, Razvi, & Mulhern, 2011), another from Iceland (Sigurdardottir & Olafsson, 1998) reported an incidence of 4.9/100,000/year and 1.4/100,000/year, respectively. However, studies concentrating on populations in epilepsy clinics report higher numbers. Five to 10% of outpatients and 20-40% of inpatients in epilepsy clinics have been reported to have PNES (Alsaadi & Marquez, 2005; Asadi-Pooya et al., 2014; Martin et al., 2003). Only very recently an epidemiological study was conducted in South Africa. The researchers carried it out at a private clinic in Johannesburg and found that 50% of seizure patients in the clinic had epilepsy and a staggering further 50% suffered from PNES (Anderson et al., 2017). This suggests a rate of PNES that is 10-30% higher than reported international averages at epilepsy monitoring units (Alsaadi & Marquez, 2005; Asadi-Pooya et al., 2014; Martin et al., 2003). Nonetheless, true prevalence of PNES in the general population remains unknown. Using current knowledge about PNES incidence, Benbadis and Hauser (2000) calculated PNES prevalence to be somewhere between 2-33/100,000, however, the accuracy of the figure presently remains unclear.

2.4.2 Age.

PNES can affect individuals of various ages, including children and the elderly (Asadi-Pooya & Sperling, 2015). However, it tends to manifest most in adolescence or young adulthood (Asadi-Pooya & Sperling, 2015). Nonetheless, when discussing any estimation of

incidence or prevalence in terms of age, it has to be kept in mind that PNES is considered to be largely underdiagnosed as well as associated with an average of 7-10-year delay in correct diagnosis (Benbadis, 2009). A small study carried out in South Africa found that in their sample of 22 participants with PNES, seven were between 14-18 (31,8%), three belonged to the 20-30 age range (13,6%), three to the 30-40 age range (13,6%), six to the 40-50 age range (27,3%), and three to the 50-60 age range (13,6%; Cronje, 2013), while the epidemiological study by Anderson et al. (2017) reported that the age of patients with PNES in their sample of 123 ranged from 12 to 69 years of age (M=34.88, SD=13.5).

2.4.3 Gender.

International research consistently finds a higher prevalence of PNES among women. A number of studies report the ratio between females and males to be 3:1, with women predominating the condition (Lesser, 1996; Noe, Grade, Stonnington, Driver-Dunckley, & Locke, 2012; Sigurdardottir & Olafsson, 1998; Szaflarski, Ficker, Cahill, & Privitera, 2000). An exception is China where a ratio of 1:1 has been found (An, Wu, Yan, Mu, & Zhou, 2010). Similarly, in the aforementioned South African studies 73% (Anderson et al., 2017) and 77% (Cronje, 2013) of the samples were female, and 27% (Anderson et al. 2017) and 23% (Cronje, 2013) were male, approximating international epidemiological research.

2.5 Classification

PNES population is a highly heterogeneous one in terms of aetiology and semiology. Hence, some research suggests that PNES instances can be divided into subtypes, which tend to differ in terms of outcomes and treatment needs. The lack of a classification system that could account for variation within PNES is considered to be to the detriment of the wider recognition and management of the condition (Seneviratne, Reutens, & D'Souza, 2010). Hence, the research efforts dedicated to aid the possibility of such PNES subtype classification are presented below. Depending on their chosen basis for classification these studies can be broadly divided into three groups, based on: (1) semiology; (2) aetiology or suspected psychological mechanism; and (3) multidimensional efforts, which include studies that have tried combining the two abovementioned groups.

2.5.1 Semiology.

Perhaps the greatest number of attempts at isolating PNES subtypes have been made using seizure semiology. Early attempts at classification often focused on a dichotomy of hypermotor vs. atonic spells (Griffith & Szaflarski, 2010) also termed by some "attacks of collapse" vs. "attacks of prominent motor activity" (Meierkord, Will, Fish, & Shorvon, 1991) or simply, those who have motor manifestations and those who present with limpness and unresponsiveness (Abubakr, Kablinger, & Caldito, 2003). Griffith and Szaflarski (2010) suggest this bipolar view stems from the initial understanding of PNES as a 'hysterical' reaction or expression of basic human needs or drives, especially evident in earlier subtype suggestions, such as "swoons", "tantrums" and "abreactive attacks" by Betts and Boden (1992). While later efforts started identifying more possible PNES subtypes, this dichotomy can be seen to underlie not only the earlier but also even more recent attempts at classification. For example, Groppel, Kapitany, and Baumgartner (2000) identified three symptom clusters: (1) "psychogenic motor seizures", characterised by clonic and hypermotor movements of the extremities, pelvic thrusting, head movements, and tonic posturing of the head; (2) "psychogenic minor motor or trembling seizures", comprising trembling of the upper and lower extremities; and (3) "psychogenic atonic seizures", which consisted of falling to the floor as the only symptom. Interestingly, while using different terminology, An, et al. (2010) found similar results in a Chinese PNES sample; and Reuber et al. (2003) found similar results in theirs with the addition of a purely sensory subtype PNES.

Some early (e.g., Silva et al., 2001; van Merode, De Krom, & Knottnerus, 1997), as well as more recent (e.g., Seneviratne et al., 2010) attempts would also use terminology reminiscent of epileptic seizure types. For example, Hubsch, Baumann, Maillard, Maillard, and Vignal (2011) retrospectively analysed 22 clinical signs of 145 PNES occurrences recorded by vEEG in 52 patients and then conducted a multiple correspondence analysis and hierarchical cluster analysis. The authors came up with five PNES clusters, namely: (1) "dystonic attacks" with primitive gestural activity (31.6% of patients), characterised by tonic movements of the four limbs, primitive gestural activity (e.g., hiding the face, punching) and an altered responsiveness; (2) "pauci-kinetic" attacks with preserved responsiveness (23.4%), characterised by a sudden onset and end, no movement of the trunk, a fine tremor usually in a limb or the head as well as preserved responsiveness in most cases and wailing in 37.9% of the seizures; (3) "pseudosyncopes" (16.9%) characterised by short and sudden loss of

responsiveness without any vocalisation or movement of the trunk apart from bilateral myoclonus (in 57% of cases) or bilateral tremor (42% of cases); (4) "hyperkinetic prolonged attacks" (11.7%) characterised by a progressive onset and end preceded by warning symptoms, hyperventilation, partial loss of responsiveness, as well as abnormal movements (mainly tremor and tonic posturing) involving the limbs and head but sparing the trunk; and (5) "axial dystonic prolonged attacks" (16.4%) characterised by prolonged, violent and tonic axial manifestations, such as opisthotonos as well as vocalisation and hyperventilation.

Interestingly, Wadwekar, Pankajakshan, and Murgai (2014) tried replicating Hubsch et al. (2011) study on a South Indian sample and found that using their method they could classify 42 (77.77%) PNES patients without modifying the defining criteria proposed in the original study and 62 (94.96%) patients having slightly modified the criteria, thus leaving 3 (5.6%) PNES cases unclassified, suggesting a potential usefulness of the Hubsch et al. (2011) classification method.

An international study by Asadi-Pooya and colleagues had even more success when they compared the semiology of PNES between patients from the USA and Brazil and were able to successfully classify all instances of PNES from both countries by dividing them into generalized motor, akinetic, focal motor, and subjective symptom subtypes (Asadi-Pooya, Valente, Alessi, & Tinker, 2017).

However, many efforts have also tried to move away from a dichotomous view and epilepsy-reminiscent terminology and better capture the subtleties of PNES semiology, resulting in a greater number of PNES clusters than before (e.g., Selwa et al., 2000). For example, Dhiman et al. (2013) reviewed the classification systems proposed by Meierkord et al. (1991); Groppel et al. (2000); and Seneviratne et al. (2010) and found unable to classify 40.2-65.9% of the patients in their sample. Hence, in turn, they proposed their own subgroups created by modifying the abovementioned ones: (1) "Abnormal motor response" group, which was subdivided into (a) "hypermotor" seizures, characterised by out-of-phase limb movemements, violent and jerky movements, and whole body rigidity, and (b) "partial motor" seizures, characterised by head and neck side-to-side, flexion/extension movements, flexion/extension abduction/adduction movements of the limbs, jerking and coughing, gagging, and hyperventilation; and (2) "Affective/emotional behaviour phenomena", characterised by weeping, grimacing, screaming, moaning, and grunting; (3) "dialeptic type", typified by a coma-like state, falling, and flaccidity; (4) "nonepileptic aura", characterised by

subjective feeling during the attack without any external manifestations and patient pressing the 'alarm button' used to announce a seizure; and (5) mixed pattern, comprising of nine abovementioned subtype combinations.

Interestingly, a study by Asadi-Pooya, Tinker, and Fletman (2017) studied 49 patients and reviewed 220 seizures in an attempt to classify them. The authors found that merely 28 (57%) patients had only one seizure class, while 19 (39%) patients had two different seizure classes and two (4%) patients had three seizure classes. Furthermore, among 28 patients with one seizure class, 14 (50%) patients had variable semiologies from one seizure to the other, highlighting a difficulty in dividing PNES into subtypes.

Overall, there have been many attempts at categorising PNES into subtypes based on semiology with what often seem to be similar results but different terminology - such as the almost universal presence of both a hypermotor and an unresponsive seizure subtypes in most studies. However, the variability of seizure semiology within patients and seemingly similar yet still different results across studies, which can often be explained by different methods used to reach conclusions, complicate the efforts of semiological classification and begs for some centralised endeavour or at least a greater number of replication studies for specific classifications. While the largest benefit of semiological classification may be improving PNES diagnosis and standardization across future studies (Asadi-Pooya, Tinker, & Fletman, 2016), such attempts are complicated by the fact that many PNES patients tend to experience multiple types of seizures (Asadi-Pooya, Tinker, et al., 2017).

2.5.2 Aetiology or Suspected Psychological Mechanism.

Classification grounded in aetiology groups patients with PNES based on factors that are considered to precede the condition. The research so far has focused on aspects such as personality and its facets, psychiatric comorbidity, and combinations of aetiological factors. The present paragraph will give an overview of attempts at isolating different types of PNES based on aetiology and suspected psychological mechanisms so far.

2.5.2.1 Personality.

As will be discussed further, personality factors play an important role in the development, treatment and outcomes of PNES. Hence, personality and personality pathology measures such as the NEO Personality Inventory - Revised (NEO-PI-R),

Minnesota Multiphasic Personality Inventory (MMPI), MMPI-2 and the Dimensional Assessment of Personality Pathology – Basic Questionnaire (DAPP-BQ) have been used in more than one attempt to categorise different types of PNES.

For example, a study by (Reuber, Pukrop, Bauer, Derfuss, & Elger, 2004) administered the DAPP-BQ to 85 participants and three PNES clusters emerged: (1) largest cluster (n=43) resembled borderline personality disorder, (2) second largest cluster (n=37) was characterised by an overly controlled personality, and (3) third smallest cluster (n=4) was similar to the profile in avoidant personality disorder. Furthermore, the authors found that treatment outcomes differed between the identified clusters with more cluster 1 patients undergoing psychiatric inpatient treatment and fewer cluster 1 patients being seizure-free at follow up when compared to cluster 2.

A slightly different approach was taken by Cragar, Berry, Schmitt, and Fakhoury (2005), who performed a cluster analysis of normal personality traits, rather than personality pathology, using the NEO-PI-R on a sample of 74 PNES patients. The authors found the following three personality clusters prevail: (1) very high neuroticism, low extraversion, low openness, high agreeableness, low conscientiousness; (2) average on all domains; and (3) very high neuroticism, average extraversion, low openness, low agreeableness, average conscientiousness (Cragar et al., 2005). Subsequenly, the individuals in these three clusters were given the MMPI-2 in order to assess how each cluster would perform in terms of a measure of psychopathology. Having combined the results from the two questionnaires the authors termed the clusters that emerged as: (1) "depressed neurotics" - individuals low in energy and sociability and experiencing negative affect (as per NEO-PI-R results) and experiencing clinically significant symptoms of depression (as per MMPI-2 results); (2) "somatic defenders" - a group similar to the general population on all personality traits, except for exhibiting a significant somatic profile on the MMPI-2; and (3) "activated neurotics" - a group experiencing negative affect, however, more active and sociable than cluster 1.

2.5.2.1.1 Emotion regulation.

Emotion regulation may be considered to be a part of personality (McCrae & Costa, 2010) and can be understood as the ability to understand and accept negative emotions as well as act in a situation-appropriate manner when experiencing them (Uliaszek, Prensky, &

Baslet, 2012). Related to this is the fact that research suggests that aetiologically PNES may be linked to difficulties in processing psychological distress and alexithymia (Urbanek, Harvey, McGowan, & Agrawal, 2014), which can be defined as a condition that makes it difficult for individuals to express affect and recognise it in others (Reuber, 2009). Hence, Uliaszek et al. (2012) administered Difficulties in Emotion Regulation Scale to 70 PNES patients and found that two clusters emerged: (1) a highly emotion dysregulated group when compared to normative data; and (2) a low emotion dysregulated group when compared to normative data. Furthermore, the authors found that cluster 1 tended to get higher scores on psychological distress measures in terms of depression, anxiety, stress, dissociation, health concerns and overall quality of life; and got higher rates of comorbid diagnoses.

2.5.2.2 Psychiatric comorbidity.

Comorbid conditions within the PNES population are a frequent occurrence (Hovorka, Nezadal, Herman, Nemcova, & Bajacek, 2007; Mökleby et al., 2002). While it is not entirely clear what role psychiatric comorbidity plays in PNES, most suggest that it is likely a precipitating (Reuber, 2005) or at least a moderating factor for the condition (Bodde, Brooks, Baker, Boon, Hendriksen, & Aldenkamp, 2009). Hence, some argue that focusing on PNES subtypes based on psychiatric comorbidity is especially important since knowledge of such comorbidities often guides treatment, moderates outcomes and may sometimes hold the key to PNES remission (Reuber & House, 2002).

As a result, there have been a few efforts to classify PNES based on psychiatric comorbidity. For example, Reuber and House (2002) came up with the following groups: (1) disorders of mood - depression, anxiety, panic and post-traumatic stress disorder; (2) somatisation and abnormal illness behaviour; and (3) problems of emotional and behavioural regulation, often referred to as borderline personality. A similar approach was taken by Rusch, Morris, Allen, and Lathrop (2001), who divided PNES patients into groups based on six psychiatric symptom patterns and psychotherapeutic interventions that were found to be useful in PNES treatment. The authors came up with the following categories: (a) acute anxiety/panic, (b) impaired affect regulation and interpersonal skills, (c) somatization/conversion, (d) depression, (e) posttraumatic stress disorder, and (f) reinforced behaviour pattern (where PNES was a behaviour reinforced by family or others).

2.5.2.3 Combined psychological factors.

Some authors have incorporated multiple psychological factors in an attempt to classify PNES (e.g., Barrash, Gates, Heck, & Beniak, 1989; Gumnit & Gates, 1986). For example, Alsaadi and Marquez (2005) subdivided PNES into types based on suspected psychogenic pathways into: (1) misinterpretation of physical symptoms; (2) psychopathologic processes (such as anxiety disorders, including posttraumatic stress disorder, conversion disorder, dissociative disorders, hypochondriasis, psychoses, somatization disorders); (3) reinforced behaviour patterns in cognitively impaired patients; (4) response to acute stress without evidence of psychopathology.

In a more recent attempt, Bodde et al. (2013) used a test battery measuring trauma, global cognitive level, mental flexibility, speed of information processing, personality factors, dissociation, daily hassles and stress, and coping factors across 40 PNES patients. The authors came up with the following three PNES subtypes: (1) 'psychotrauma subgroup', (2) 'high vulnerability somatizing subgroup'; and (3) 'high vulnerability sensitive personality problem subgroup'.

Following a different approach and using a small review of literature, Lesser (2003) divided PNES based on the following groups of aetiological factors: (1) interpersonal; (2) intrinsic emotional problems or internalised conflicts (e.g., anxiety, posttraumatic stress disorder, conversion/somatization); (3) psychosis; (4) personality disorders; (5) cognitive difficulties or a history of head trauma; and (6) difficult to classify aetiologies (e.g., attention deficit disorder and tic), and admitted that multiple aetiologies are possible in one patient.

Overall, it is evident that many detailed attempts have been made at classifying PNES based on aetiology. Some argue that due to the intrinsically psychological nature of the condition, an aetiologically-based classification, when compared to a semiologically-based one, may be particularly useful for the development and communication of evidence-based treatment practices among treatment providers (Griffith et al., 2007), which is still fairly lacking. However, the difficulty of such an effort lies in the multidimensionality of PNES aetiology, which is clearly reflected in the wide variety of approaches and results in aetiological classification attempts. This issue may be partly resolved by adopting meta-analytic aetiology literature review approaches, however, no such attempt has been made yet.

2.5.3 Multidimensional efforts.

Some efforts at combining multiple aspects of PNES in classifying the condition have also been made. For example, in an early study by Wilkus and Dodrill (1989) semiology and MMPI profile data was combined and the authors came up with the following two PNES subtypes: (1) mostly motor and limited/none affectual; and (2) limited motor/ prominently affectual; somewhat reflecting the previously dualistic thinking of PNES mentioned earlier.

In a later study Magaudda et al. (2011) divided their sample of mixed PNES (PNES with epilepsy) patients into three groups based on epilepsy type, mental level, comorbid psychiatric disorders, and history of traumatic experiences. The authors identified the following groups: (1) patients with pharmaco-resistant epilepsy, normal cognition, and comorbid anxiety and/or depressive disorders, PNES aetiology being epilepsy-related problems; (2) patients where the epilepsy is associated with mental impediment and dependent personality traits and the aetiology is represented by the reduction or cessation of epileptic seizures, where the PNES allows patients to continue receiving attention from caregivers; and (3) patients who have epilepsy, normal cognition, comorbid cluster B personality disorders and anxiety disorders, and psychic trauma, the latter representing the PNES aetiology.

Following a different approach, Brown et al. (2013) compared PNES patients to those with epilepsy on emotional dysregulation, alexithymia, attachment, and psychopathology and the following two groups emerged: (1) 11 patients fell into a group characterised by higher levels of psychopathology, somatization, alexithymia, and difficulties with most aspects of emotional regulation (including identifying, accepting, and describing feelings, accessing adaptive regulatory strategies, performing goal-directed behaviours, and controlling feelings and actions) compared to the epilepsy group; (2) 32 patients fell into the group characterized by high somatization and depression scores but normal levels of alexithymia and emotional regulation compared to the epilepsy group.

While it is evident that studies adopting a multidimensional approach to PNES classification exhibit similar lack of agreement as those focusing solely on semiology or aetiology, such an approach may offer the best of both worlds. Research shows that the heterogeneity of the PNES population poses a challenge for PNES treatment, as evidenced by the highly differing outcomes within this patient population (Reuber et al., 2003).

Furthermore, treating PNES as one group tends to overlook the presence of different PNES subgroups and thus the heterogeneity of PNES patients and their differing treatment needs (Bodde et al., 2013; Reuber et al., 2003). Hence, classification systems that bring us closer to diagnosing, understanding and, importantly, treating the condition better are extremely important.

2.6 Aetiology and Risk factors

2.6.1 Trauma.

Trauma is an often cited aetiological factor of PNES. In a recent extensive review of literature published 2004-2014 in Italian, French or English, Beghi, Cornaggia, et al. (2015) found that sexual or physical abuse was reported in 3.5% to 74% of PNES patients. A recent study on PNES has found that individuals with PNES or PNES and comorbid epilepsy have a significantly higher prevalence of physical and sexual abuse when compared to those with epilepsy only (Elliott & Charyton, 2014). While sexual and physical trauma are perhaps most prominently linked to PNES, other types of trauma are also reported to be associated with the condition are divorce, bereavement, migration (Bora et al., 2011) or serious illness (Tojek, Lumley, Barkley, Mahr, & Thomas, 2000).

The significantly higher rates of trauma and often PTSD (Fiszman, Alves-Leon, Nunes, D'Andrea, & Figueira, 2004) in PNES patients have led some researchers to even suggest that PNES may be a particular form of PTSD, theorising that non-epileptic seizures become a way of acting out flashbacks or a defence mechanism preventing intrusion of painful memories (Betts & Boden, 1992). Varying levels of trauma exposure observed among cultures and societies have been considered to account at least partly for the variance of PNES incidence between different areas of the world (Martínez-Taboas, Lewis-Fernández, Sar, & Agarwal, 2010). Thus the role that traumatic experiences play in the development of PNES makes it especially important to investigate further in countries where trauma is prevalent, such as South Africa. For example, recent South African Police Service (SAPS) statistics indicate that there was a total of 53 617 sexual offences reported between April 2014 - March 2015 (SAPS, 2015) and 182 556 incidences of assault with the intent to inflict grievous bodily harm in the same period (SAPS, 2015). While not all individuals with PNES have had trauma, nor all who have gone through a traumatic experience develop seizures, environments with heightened levels of violence certainly pose a risk for PNES development.

2.6.2 Gender and sex.

The proportion of women as opposed to men being diagnosed with PNES is 3:1 (Noe et al., 2012), making it substantially more common among women. The approach to the factor of gender with regards to PNES could broadly be divided into two camps of social and neurobiological explanations.

Researchers advocating a social explanation for greater female prevalence of PNES point to the fact that sexual, physical and emotional trauma often coincide with the female gender in PNES patients (Reuber, Howlett, Khan, & Grünewald, 2007). Additionally, recently, some hypothesising on neurobiological explanations for female prevalence among PNES sufferers has emerged. Most notably, Asadi-Pooya (2016) argues that there exist inherent functional connectivity differences between the sexes in the brain regions responsible for emotional and cognitive processing and these result in women and men being affected differently by physical and emotional trauma thus making women more prone to psychopathology, such as PNES.

2.6.3 Personality.

2.6.3.1 Personality disorders.

Research into personality disorders among the PNES population has largely been concentrated within high income countries with any such research lacking in middle to low income countries, including South Africa. Based on the current state of research, there is no specific personality disorder that can be called indicative of PNES. However, cluster B personality disorders (Borderline, Histrionic, Narcissistic, and Antisocial) have emerged more often than others in relation to PNES patients (Galimberti et al., 2003; LaFrance, Deluca, MacHan, & Fava, 2013; LaFrance & Devinsky, 2002), with Borderline Personality predominating (Direk, Kulaksizoglu, Alpay, & Gurses, 2012; Lacey, Cook, & Salzberg, 2007). This suggests a population that often appears dramatic, emotional, or erratic and in the case of those with borderline personality, may often exhibit a pattern of instability in interpersonal relationships, self-image, affects, as well as self-damaging impulsive behaviours (American Psychiatric Association, 2013). Additionally, cluster A personality disorders (Paranoid, Schizoid, and Schizotypal) may sometimes be associated with PNES mostly comorbid with those in cluster B (D'Alessio et al., 2006; Kuyk, Swinkels, &

Spinhoven, 2003; Reuber & Mayor, 2012) and seldom Cluster C disorders (Avoidant, Dependent, and Obsessive-Compulsive) predominate (Galimberti et al., 2003).

2.6.3.2 Personality traits and factors.

While personality research into PNES in the West has been relatively extensive, it is still currently considered that there is no one personality profile that is associated with PNES. However, when specifically compared to epilepsy patients, those with PNES tend to show consistent differences on personality measures. The most widely researched personality measures so far have been the MMPI and MMPI-2 (Dodrill, 2010). However, other measures, such as the Personality Assessment Inventory (PAI; Hill & Gale, 2011; Thompson, Hantke, Phatak, & Chaytor, 2010), the DAPP-BQ (Reuber, Pukrop, et al., 2004), and NEO-PI-R (Cragar et al., 2005) have also been used. When compared to ES patients, individuals with PNES have been shown to score higher on the various personality subscales of anxiety (Cragar et al., 2005; Hill & Gale, 2011; Owczarek, 2003a; Thompson et al., 2010), depression (Cragar et al., 2005; Hill & Gale, 2011; Thompson et al., 2010), angry hostility (Cragar et al., 2005; Mökleby et al., 2002), modesty (Cragar et al., 2005) and lower on the NEO-PI-R personality facets of trust (in others) and gregariousness (Cragar et al., 2005; Kranick et al., 2011).

2.6.3.3 Coping mechanisms.

A special element of personality is coping (Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al., 2009). Some studies suggest that PNES patients may have a specific coping pattern. The coping strategies most often associated with PNES are avoidance (Goldstein, Drew, Mellers, Mitchell-O'Malley, & Oakley, 2000) and distancing (Cronje & Pretorius, 2013). This may in part be associated with the fact that many sufferers of PNES often also have alexithymia (Urbanek et al., 2014). Hence, it is hypothesised that due to their lack of ability in adequate expression of feelings, individuals with PNES subconsciously express their psychological distress through dissociative states such as seizures (Goldstein et al., 2000).

2.6.4 Psychiatric comorbidity.

Other than the abovementioned personality disorders, patients with PNES are often found to have more comorbid DSM disorders when compared to ES patients (Hovorka et al.,

2007; Mökleby et al., 2002). Most often PNES patients have comorbid depression and anxiety disorders, as well as post-traumatic stress disorder (PTSD), and less so other dissociative and somatoform disorders (Abubakr et al., 2003; Alsaadi & Shahrour, 2014; Diprose, Sundram, & Menkes, 2016; Griffith & Szaflarski, 2010; LaFrance & Devinsky, 2002; Reuber, 2008a). However, the exact pathway in which psychiatric comorbidity contributes to the development of PNES is still rather unclear. Bodde, Brooks, Baker, Boon, Hendriksen and Aldenkamp (2009) argue that, psychiatric comorbidity may quite possibly be the result of having PNES, especially when having the condition for a prolonged period of time.

2.6.5 Family dysfunction.

Family dysfunction has been indicated by some as a possible precipitating factor in the onset of PNES, however, at the moment its role is still inconclusive. While some suggest that family dysfunction is one of the most significant predisposing features in PNES patients (Reuber, Howlett, et al., 2007) and differentiates PNES patients from those with ES (Krawetz et al., 2001), others have found that family functioning does not indicate a significant difference between the two groups (LaFrance et al., 2011).

2.6.6 Mechanisms of PNES development and maintenance.

Brown and Reuber (2016b) argue that too many PNES theories focus on the predisposing, precipitating and perpetuating factors without discussing the mechanisms at play in the development of PNES. Brown and Reuber (2016b) suggest that currently, there are four competing models of PNES that try to explain the mechanisms behind the development and maintenance of PNES. Model 1 "PNES as the activation of dissociated material" (Brown & Reuber, 2016b, p. 56) emphasises the findings of elevated trauma levels in the PNES population and the dissociation of memory/mental functions from consciousness reported by PNES patients during the attacks (e.g., Bowman, 2006; Harden, 1997; Kuyk, Spinhoven, & van Dyck, 1999). Model 2 "PNES as hard-wired responses, such as "panic without panic" (Brown & Reuber, 2016b, p. 57) considers PNES to be a pre-wired response to stress associated with an acute state of detachment, similar to other defensive reactions, such as 'freezing', such as an altered state of consciousness akin to a panic attacks without the actual 'panic' due to the fear component becoming dissociated from awareness (e.g., Baslet, 2011; Goldstein & Mellers, 2006; Nijenhuis, Vanderlinden, & Spinhoven, 1998).

Model 3 "PNES as physical manifestation of emotional distress" (Brown & Reuber, 2016b, p. 57) views PNES as a defensive response which allows the individual to express their emotional distress physically without acknowledging its emotional origin (e.g., Breuer & Freud, 1955). Lastly, Model 4 "PNES as learned behaviours" (Brown & Reuber, 2016b, p. 57) postulates that PNES is a learnt behaviour which elicits some sort of positive and negative reinforcement and/or because it evokes certain intrinsic and/or extrinsic benefits (e.g., Moore & Baker, 1997). While Brown and Reuber (2016b) suggest that while all the above mentioned models have their strengths, all of them exhibit weaknesses that fail to explain at least a portion of PNES occurrences. In order to address this, the authors propose their own integrative model outlined below.

2.6.6.1 Integrative Theory of PNES.

Brown and Reuber (2016b) argue that there is a lack of a theory explaining the mechanism of PNES development as well as identifying necessary and sufficient features for the pathogenesis of this disorder. Hence, the authors suggest a theory of their own, which they consider to integrate already existing theories and findings concerning PNES aetiology as well as fill the necessary gaps in previous models – the Integrative Theory of PNES (depicted in *Figure 1*). The authors use the Integrative Cognitive Model (ICM) of medically unexplained symptoms as their basis and argue that PNES results from the "seizure scaffold" (Brown & Reuber, 2016b, p. 62) – a rogue mental representation which is automatically activated by relevant internal or external triggers (e.g., traumatic intrusions). These mental representations are argued to consist of cognitive-emotional-behavioural action programs that are in turn made up of a combination of inherent schemata (e.g., how to respond to fear) and the results of experience and learning. The activation of this "seizure scaffold" may or may not be a result of abnormal arousal, or emotional or cognitive processing, which is considered to account for the different manifestations within the PNES population.
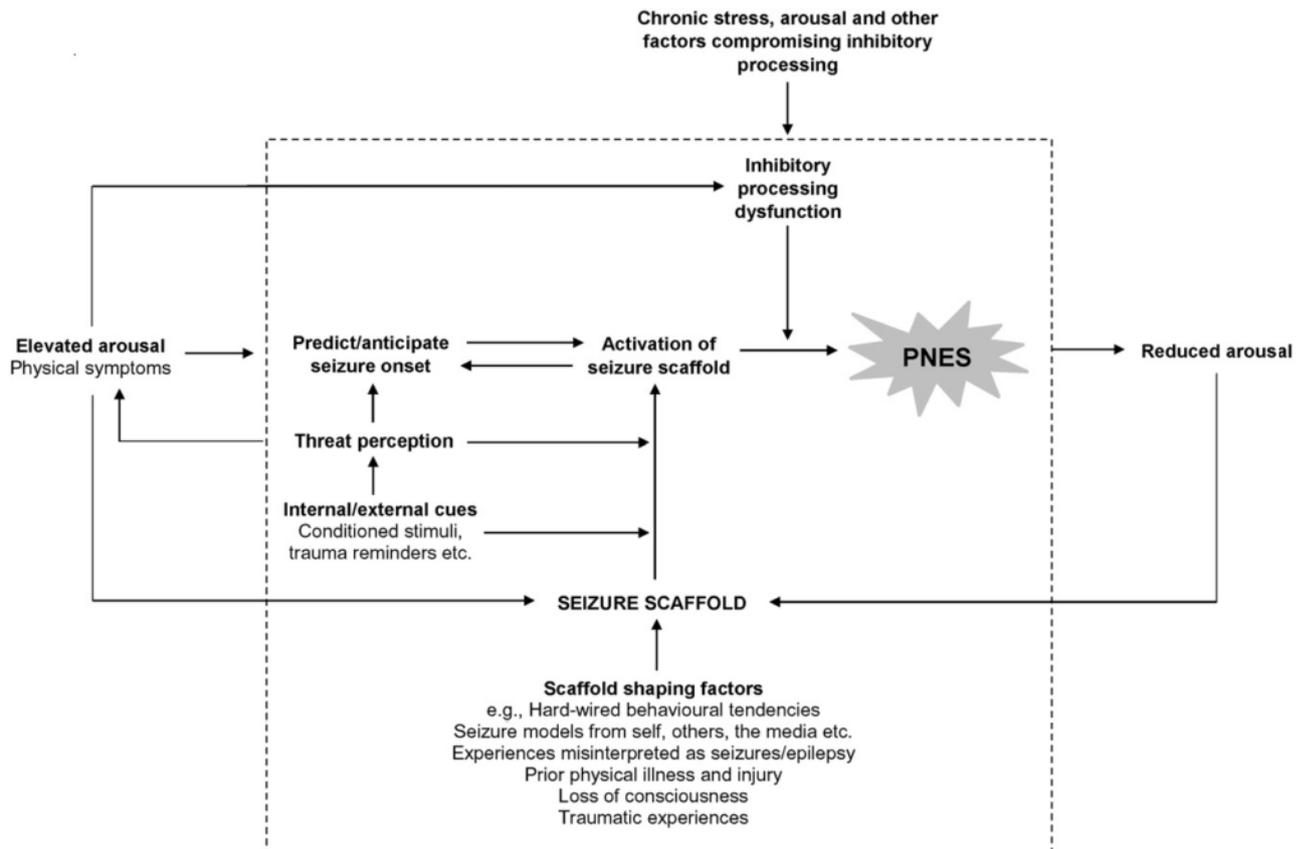
Figure 1. Hypothesized sequence of events in PNES (reproduced with permission [Appendix K] from Brown & Reuber, 2016b).

2.7 Diagnosis

On average a PNES patient will wait 7-10 years for a correct diagnosis (Benbadis, 2009). Most often PNES is misdiagnosed as epilepsy, however PNES may also resemble oNES, which are often physiologic spells manifesting as non-epileptic seizures but arising from physiologic conditions (Alsaadi & Marquez, 2005). However, oNES represent only a small portion of overall non-epileptic seizures compared to PNES (Krumholz, 1999). PNES diagnosis is further complicated by the fact that epilepsy and PNES tend to coexist in around 5-20% of PNES patients (Alsaadi & Marquez, 2005; Benbadis, Agrawal, & Tatum, 2001; Griffith & Szaflarski, 2010; LaFrance Jr & Benbadis, 2011; LaFrance Jr & Devinsky, 2002). Hence, prompt correct diagnosis of PNES is important for several reasons. Perhaps most importantly, correct diagnosis helps to avoid or at least cease the unnecessary use of AEDs, which may often result in a number of side effects and even death (Bodde, Brooks, Baker, Boon, Hendriksen, & Aldenkamp, 2009; Brown, Syed, Benbadis, LaFrance Jr, & Reuber,

2011; Lee, 2010). Related to this is the considerable financial burden that incorrectly diagnosed individuals with PNES put on both themselves and the healthcare system (Gene-cos & Ring, 2005). Thus, correct diagnosis allows for the PNES patient to start appropriate treatment focusing on the psychological nature of the disorder sooner (Alsaadi & Shahrour, 2014; Reuber et al., 2003). Lastly, diagnosis itself in some cases has been shown to be therapeutic (Iriarte, Parra, Urrestarazu, & Kuyk, 2003).

2.7.1 Diagnostic methods.

PNES diagnosis currently can be understood in terms of three stages: 1. suspicion; 2. diagnosis; and 3. confirmation (Brown et al., 2011), which will be explained below.

2.7.1.1 Suspicion stage: semiology.

Before the relatively recent advancements in medical technology, specialists relied heavily on seizure semiology when diagnosing PNES, i.e. the signs and symptoms of the seizures (Jordan, 2007). However, even when sophisticated technology is available, semiology is still relied upon in the initial evaluation of patients presenting to epilepsy clinics (Syed et al., 2011) and is especially important in cases where EEG equipment is lacking (Iriarte et al., 2003). As evidenced earlier, numerous clinical signs have been associated with PNES and sustained efforts have been made to identify the specific clinical factors that would help in differential diagnosis between PNES and epilepsy. While no clinical sign is considered to be pathognomonic of PNES, experienced clinicians may find some to be more useful in differentiating between the two conditions than others. Signs and behaviours most often associated with PNES are considered to be: situational onset; gradual onset and cessation; ability to induce seizure via suggestion; asynchronous limb movements; dystonic posturing; undulating motor activity; closed eyes during seizure; side-to-side head movements; ictal crying; pelvic thrusting; prolonged seizures; memory recall; and absence of postictal confusion (Alsaadi & Shahrour, 2014; Avbersek & Sisodiya, 2010; Brown et al., 2011; LaFrance Jr & Benbadis, 2011). Thus, semiology can be a useful tool in PNES diagnosis, however, it is important that a patient's semiologic characteristics be defined by a professional, rather than family members to ensure accuracy (Syed et al., 2011). While semiology is considered to not be enough in definitively confirming the diagnosis of PNES, it plays an essential part in raising suspicion of PNES as an alternative diagnosis to epilepsy (Brown et al., 2011).

2.7.1.2 Diagnosis stage: EEG.

With the development of electroencephalogram (EEG) came the possibility to record ictal (during a seizure), interictal (between seizures) and postictal (after a seizure) electrical brain activity (R. S. Fisher, Scharfman, & DeCurtis, 2014). Epilepsy is usually diagnosed via interictal epileptiform discharges, which can be understood as abnormal brain waves or spikes present in the EEG (Ko, 2014). Hence, the absence of such activity in the presence of a chronic seizure complaint would normally suggest an alternative cause. Brown, Syed, Benbadis, LaFrance Jr, and Reuber (2011) suggest that one of the reasons why PNES is often not considered when using EEG is due to the 'overinterpretation' of nonspecific EEG patterns which are then erroneously assumed to indicate epilepsy.

2.7.1.3 Confirmation stage: vEEG.

The introduction of the simultaneous video component to the EEG at the end of the twentieth century now allows for the patient behaviour to be observed over a period of time while following their electrical brain activity patterns on the EEG (Benbadis & LaFrance Jr, 2010). If no abnormal findings in the EEG are found while the person is demonstrating seizure-like behaviours and other physiologic aetiological factors have already been ruled out, the PNES diagnosis is confirmed (Benbadis & LaFrance Jr, 2010). Hence, vEEG is considered to be the "gold standard" of PNES diagnosis (Benbadis & LaFrance Jr, 2010).

2.7.2 Alternative methods of diagnosis.

Since confirmed PNES diagnosis currently relies exclusively on the ruling out of epilepsy via a vEEG, a number of efforts have been made in searching for alternative cost and time effective measures that would help the differentiation between epilepsy and PNES. The more successful research efforts have focused on using the following in distinguishing the two: illness behaviours and locus of control (Goldstein et al., 2000; Stone, Binzer, & Sharpe, 2004); neuropsychological and personality testing (Cragar et al., 2005; Dodrill, 2010); seizure semiology and history, such as age at seizure onset and seizure frequency (Reuber & Elger, 2003; Syed et al., 2011); coping style questionnaires (Goldstein et al., 2000); taking of historical and clinical details (Alsaadi & Shahrour, 2014; LaFrance Jr & Benbadis, 2011); post-ictal prolactin level measurement (Alsaadi & Shahrour, 2014; Cragar, Berry, Fakhoury, Cibula, & Schmitt, 2002); single photon emission computed tomography (Neiman, Noe, Drazkowski, Sirven, & Roarke, 2009); heart rate variability (Ponnusamy,

Marques, & Reuber, 2011, 2012); and resting-state connectivity fMRI (van der Kruijs et al., 2012).

2.7.2.1 Multifaceted methods of differential diagnosis.

Perhaps the most successful attempt to date at diagnosis by differentiating PNES from ES is that of Syed and colleagues (2009). This group of researchers created a 209-item questionnaire, which after a variable reduction procedure was reduced to 53 questionnaire items and combined items covering: age at seizure onset; monthly seizure frequency; fibromyalgia; nutrition subscale of Health-Promoting Lifestyle Profile (HPLP) measure; understanding subscale of the Communication and Attitudinal Self-Efficacy (CASE–Epilepsy) measure; limiting behaviour and practical support seeking subscales of the Behavioral Reaction to Illness (BRIQ) measure; chance and other people subscales of the Multidimensional Locus of Control (MHLC) Form C; and Zung Self-Rated Depression Scale (Syed et al., 2009). The questionnaire was able to correctly predict PNES with 94% sensitivity and 83% specificity when implemented at a training centre, and with 85% sensitivity and 85% specificity when implemented at another epilepsy centre. However, perhaps the biggest drawback of the measure is its complex method of scoring which relies on a hybrid neural-bayesian classifier, thus making it largely not viable in both academic and healthcare contexts where such expertise is inaccessible. While the authors in the article refer to online access and scoring of the measure to be available soon, Syed, when approached, said that the measure has not been developed any further due to lack of resources (personal communication, 2016). In spite of this, the study is an indication that efforts concerning alternative diagnostic methods should focus on multifaceted approaches.

2.7.3 Diagnostic issues internationally and in South Africa.

While vEEG is currently considered to be the most accurate way of diagnosing PNES the biggest limitation to using vEEG, especially in developing countries, is still the costliness of the method (Cragar et al., 2002). Misdiagnosis remains a big issue in South Africa, where vEEG equipment is not available to the majority of the population (Pretorius, 2016). This is further complicated by the fact that there is a lack of awareness of PNES on the part of medical professionals in South Africa (Pretorius, 2016).

Some relatively successful international studies investigating cheaper diagnostic alternatives to vEEG do exist. However, they have so far mostly focused on lengthy

questionnaires such as the MMPI or MMPI-2 (60-90 minutes), PAI (60 minutes), DAPP-BQ (50 minutes; Dodrill, 2010); questionnaire batteries requiring sophisticated scoring algorithms (Syed et al., 2009); or post-ictal prolactin level measurement, which requires seizure monitoring (Alsaadi & Shahrour, 2014). This makes these methods difficult to use in healthcare contexts where giving prolonged individual attention is difficult or medical care is not easily accessible, such as in many poorer areas of South Africa (Gaede & Versteeg, 2011). Hence, if PNES diagnosis is to be simplified and brought to under-resourced contexts lacking in PNES awareness, such as South Africa, efforts need to be focused on finding time and cost-efficient measures that have been widely validated and could be easily translated in at least some of the more frequently used of South African languages.

2.8 Role of Personality in PNES

The relationship between personality traits and psychopathology has been widely demonstrated through empirical research (Andersen & Bienvenu, 2011) and PNES is no exception in this regard. The role of personality factors in PNES extends beyond aetiology (discussed in detail earlier) to treatment approach, outcomes and diagnosis.

A number of studies report that comorbid personality disorders, especially borderline personality disorder, tend to be associated with poorer response to treatment in PNES compared to other comorbidities, such as depression or anxiety (Hovorka et al., 2007; Reuber, 2005; Rusch et al., 2001) perhaps owing to relative stability of personality. Similarly, it is considered that PNES patients who have a comorbid personality disorder tend to experience poorer outcomes (Kanner et al., 1999). A 10-year follow-up study by Reuber and colleagues (Reuber et al., 2003; Reuber, Pukrop, et al., 2004) used the dimensional assessment of personality pathology – basic questionnaire (DAPP-BQ), which uses a personality framework in line with that of the Five Factor Model (FFM) by Costa and McCrae (1990), to see if belonging to different personality trait clusters may impact the outcome of PNES patients. They found that 83.7% of PNES patients belonging to a trait cluster resembling borderline personality disorder and 59.5% of those who belonged to a personality cluster termed "overly controlled personality" (high 'compulsivity', normal scores in 'emotional dysregulation,' 'dissocial behaviour,' and 'inhibitedness'; Reuber, Pukrop, et al., 2004, p. 743) were associated with poor outcome (being not seizure-free and dependent).

However, the biggest challenge in managing PNES currently is that of approaching the actual diagnosis due to the low awareness of PNES among primary health care professionals and the condition mimicking ES symptomatically. Evidently an individual with PNES misdiagnosed with epilepsy cannot access appropriate treatment. Hence, the role of personality factors in every area of PNES and the consistent findings of significant personality differences in PNES compared to ES subjects (Cragar et al., 2005; Reuber, Pukrop, et al., 2004), makes it a potentially valuable factor in distinguishing between the two conditions.

Measures such as the MMPI and MMPI-2 (Owczarek, 2003a, 2003b), as well as PAI (Testa, Lesser, Krauss, & Brandt, 2011; Thompson et al., 2010; Wagner, Wymer, Topping, & Pritchard, 2005) have already been used to differentiate between the two conditions with relative success. The MMPI and MMPI-2 subscales measuring Hypochondriasis and Hysteria (Dodrill, 2010), anxiety (Owczarek, 2003a) and somatisation (Owczarek, 2003b) have been shown to be useful. Furthermore, some MMPI and MMPI-2 profile configurations have been shown to be in the 70-75% range of correct classification of ES and PNES group membership (Dodrill, 2010). Additionally, PAI "PNES Indicator" (derived from the somatisation subscale) has shown sensitivity of 58.7-84% and specificity of 56.4-85.3% and the conversion subscale was found to be 58.7-74% sensitive and 67-83.5% specific for the diagnosis of PNES as opposed to ES (Testa et al., 2011; Thompson et al., 2010; Wagner et al., 2005). While some of the results are encouraging, perhaps the biggest limitation to these measures being used in primary healthcare contexts, as evidenced earlier, is their complexity and length.

Perhaps the most acknowledged model of personality at the moment is the FFM (Costa & McCrae, 1990). The latest edition of the DSM - DSM-5 - has acknowledged that by developing its alternative model of personality disorders based on the extreme variants of the five FFM personality domains (APA, 2013), which is considered to overtake the current categorical classification of personality disorders in the future development of the DSM (Mullins-Sweatt, 2013). In spite of this, to date there have been almost no attempts at using the FFM-based personality measures, such as the NEO-PI-3 or the NEO-FFI-3 at differentiating PNES and ES. In order to amend this, the current study used a short version of the NEO Personality Inventory, the NEO-FFI-3, in order to measure the Big Five personality domains within the FFM.

2.9 Role of Psychiatric Comorbidity in PNES

Psychiatric comorbidity has been of much interest to PNES researchers, mainly due to its unclear role in PNES development and maintenance, its ability to differentiate between PNES and ES, and its importance in treatment.

Research suggests that the PNES population overall has a high rate of psychiatric comorbidity (53–100%), with depression, anxiety and PTSD predominating (Diprose et al., 2016). It is suggested that treating any psychiatric comorbidities alongside implementation of a targeted PNES treatment is important in ensuring better outcomes for PNES patients (Genecos & Ring, 2005). However, not only do PNES patients report overall high levels of psychiatric comorbidity, these levels are significantly higher when compared to patients with epilepsy (Diprose et al., 2016). For example, a recent meta-analysis by Diprose et al. (2016) showed that, while personality disorders tended to show significance in differentiating between PNES and epilepsy, so did anxiety and PTSD, while depression did not show a significant difference between the two groups. Hence, studies of alternative diagnostic methods may find it useful to screen for psychiatric comorbidity together with other factors that have been shown to differ significantly between individuals with PNES and individuals with ES.

As discussed earlier, perhaps the most successful multidimensional effort at alternative diagnosis by Syed and colleagues (2009) found that screening for depression together with other factors was useful in differentiating between PNES and other seizure patients. Interestingly, the researchers did not use any anxiety or PTSD measures or items in their final instalment of the questionnaire. The authors report that while in the pilot study both the anxiety and depression measures differentiated between the groups significantly, the anxiety and depression scores in their sample correlated so highly that in order to shorten the questionnaire the researchers decided to only keep depression, since it tended to predict PNES better. This, again, seems to point to the currently pertinent problem in efforts of alternative PNES diagnoses – a need for short questionnaires that can measure the factors that have proven useful in predicting PNES. In order to address this, the current study chose a measure that is short, easily administered and covers all three of the most prevalent psychiatric comorbidities within the PNES population – the Beck Anxiety Inventory – Primary Care (BAI-PC; discussed in detail in Chapter 4), which measures depression, anxiety and PTSD symptoms.

2.10 The Role of Abnormal Illness Behaviours in PNES

The notion of abnormal illness behaviour was introduced by Pilowsky (1994) and can be understood as a way of "experiencing, perceiving, evaluating or responding to one's own health status" (p.567) that could be considered an inappropriate or maladaptive response, considering the objective level of pathology present in an individual. In order to measure unconsciously motivated, somatically focused, and illness affirming type of abnormal behaviour (i.e., somatoform, somatisation, conversion, psychogenic pain, and illness anxiety disorders) Pilowsky and Spence (1975) developed the Illness Behaviour Questionnaire (IBQ). The IBQ was developed with the acknowledgement of the difficulty of diagnosing psychosomatic disorders and measures hypochondriasis, disease conviction, psychological versus somatic illness focus, affective inhibition, affective disturbance, denial and irritability.

Stone et al. (2004) used the IBQ on PNES and ES patients and found that patients with PNES, when compared to those with epilepsy, were significantly more likely to deem psychological factors less imperative to their condition rather than somatic ones and denied non-health life stressors significantly more. A somewhat similar measure with a general illness focus rather than a specifically psychosomatic one - the Illness Perception Questionnaire (IPQ) - has so far presented different and conflicting findings. One study using the IPQ-Revised failed to show any significant differences between the conditions in their sample of 40 PNES and 34 ES patients (Whitehead, Kandler, & Reuber, 2013). However, a more recent study using the Brief IPQ (one item per scale) found that in their sample of 45 PNES and 62 ES patients, the participants with PNES perceived their condition as having more severe consequences on their life, causing a higher number of symptoms, being associated with a higher negative emotional experience, as well as were more concerned, and considered the condition to be more threatening overall (Rawlings, Brown, & Reuber, 2017).

The insignificant results in the Whitehead et al. (2013) study may potentially be explained by the fact that, unlike the IBQ, IPQ measures patients' general views of the symptoms, causes, duration and outcomes of their illness, the efficacy of treatment and their self-efficacy in the face of the illness. Hence, while the view of their illness may not differ between PNES and ES patients (after all, PNES patients have often lived believing they have ES for a number of years), only the PNES group is likely to exhibit grossly misguided beliefs. On the other hand, significant differences found by Rawlings, Brown, and Reuber (2017) suggest a greater disease conviction in the PNES population. This may be a reflection of the

fact that often PNES patients are considered to be "faking" their condition by healthcare providers (Chudleigh et al., 2013; McMillan et al., 2014) and signify the patient's resistance to accept the psychosomatic nature of their disorder (Kanner, 2003). However, overall, it seems that illness behaviours and perceptions have the potential to be a useful factor in differentiating between the two conditions.

2.11 Level of Burden

Shortening the time it takes to reach correct PNES diagnosis is not only important due to often better prognosis (Reuber, 2009), as mentioned earlier. PNES also carries substantial financial and psychosocial burdens, which can be alleviated considerably if proper diagnosis is available sooner.

2.11.1 Financial.

The financial burden of PNES falls both on the PNES patient and the greater societal resources, nevertheless, research investigations in this area are still relatively sparse. In fact, Krawetz et al. (2001) suggest that individuals with PNES are at least as disabled and receive as much family or governmental financial assistance as those with epilepsy. Magee, Burke, Delanty, Pender, and Fortune (2014) calculated that the cost of undiagnosed PNES in Ireland was €20 995.30 per year (R336 504.80, according to XE [2017]), which consisted of costs related to outpatient neurology appointments, use of AEDs, emergency department visits, EEGs, CT and MRI scans, and tilt-table testing (used to rule out vasovagal syncope). The same study also found that the combined annual cost of diagnosis and psychological treatment of PNES decreased to €8 728 (R140 234.20, according to XE [2017]). Ahmedani et al. (2013) calculated that in a US healthcare setting the average PNES patient costs tended to drop from $4 567.01 per year (R62 474.07, according to XE [2017]) prior to diagnosis to $2 783.77 per year (R38 104.41, according to XE [2017]) following PNES diagnosis. The change in costs is considerable when one investigates the change in healthcare demand prior and post PNES diagnosis. An American study conducted by Razvi, Mulhern, and Duncan (2012) suggests that prior to diagnosis the 28 PNES patients investigated were responsible for 14 general practitioner home visits, 31 ambulance calls, 34 emergency department visits, 21 hospital admissions, 8 MRI scans, 24 CT scans, and 35 EEG recordings. However, after diagnosis the numbers were down to no general practitioner visits, 2 ambulance calls, 2 emergency department visits, no hospital admissions, 1 MRI scan, and no CT scans or EEGs.

While, it is of note that a number of PNES patients have comorbid epilepsy (Martin et al., 2003) and the abovementioned figures may differ for this population, it is evident that the PNES population puts high demand on medical resources.

Studies investigating the financial burden of PNES in South Africa still do not exist, however, one study investigated PNES central nervous system (CNS) medication and AED use as part of an epidemiological study (Anderson et al., 2017) and found a significant reduction in both post-diagnosis, which would suggest a potential decrease in financial burden following diagnosis. However, it is of note that most of the studies on the financial burden of PNES have so far been carried out in first world countries, where access to relevant technologies and the support funds needed to use them is much wider when compared to third world countries such as South Africa. This suggests that the financial burden on individuals with PNES and their families may be much greater in low income settings where a family member losing employment due to a disability like PNES may mean considerable financial hardship.

2.11.2 Psychosocial burden.

Some authors argue that people with PNES today face the same kind of stigma that epilepsy did before its neurological origins were discovered (Dekkers & van Domburg, 2000). Hence, it is no surprise that in a qualitative study conducted by Carton, Thompson, and Duncan (2003) to investigate PNES patients' understanding of and reaction to getting a PNES diagnosis the authors found that the participants faced a considerable psychosocial burden. The authors suggested that the participants' lives were marred by social isolation, difficulties obtaining employment and a reduction in self-confidence and self-esteem. Furthermore, many PNES patients face a reduced quality of life, as will be discussed further.

2.11.2.1 Quality of life and related psychiatric comorbidity.

While outcomes in PNES are most often measured via seizure frequency, some authors argue that this is not the best way to gage improvement in this patient group. For example, LaFrance Jr and Syc (2009) found that higher depressive symptom and somatic symptom scores in people with PNES were independently related to worsening quality of life (QOL), while seizure frequency was not. Szaflarski et al. (2003) conducted an extensive study comparing PNES patients' health-related quality of life (HRQOL) to those with epilepsy and found that PNES patients tended to score significantly lower on HRQOL and

higher on mood disorder scales when compared to those with ES. The lower HRQOL in PNES patients was in part explained by their high depression scores and more negative medication side effects, once again highlighting the importance of early correct PNES diagnosis and the discontinuation of AEDs. Similarly, a few other studies found a correlation between lower QOL in PNES and comorbid depression (Karakis et al., 2014; Myers, Lancman, Laban-Grant, Matzner, & Lancman, 2012), as well as elevated anger state, trait and total scores (Myers et al., 2012). To date, there is only one study that has looked into the QOL of people with PNES in South Africa (Cronje & Pretorius, 2013). The researchers compared HRQOL scores of a PNES group with those of a healthy control group and found the former to score significantly lower. Furthermore, the PNES group used escape–avoidance and distancing coping strategies significantly more and this tended to have a significant negative effect on their HRQOL.

The often unemployed status of people with PNES internationally (Duncan, Anderson, Cullen, & Meldrum, 2016) and in South Africa (Cronje & Pretorius, 2013), as well as presence of seizures and the associated risk of injury (Atkinson et al., 2012) may mean that a caregiver is needed. A study by Karakis et al. (2014) found that while QOL of PNES patients was significantly worse when compared to those of epilepsy patients, the caregivers for both groups scored comparably on both the QOL and caregiver burden measures. While there is still a paucity of detailed information concerning PNES patient caregiver experiences, initial results indicate that caregivers of individuals with PNES may need similar support to those of individuals with epilepsy.

2.12 Treatment

Most treatments for PNES are still mostly based on theoretical aetiological models rather than blinded, randomised controlled clinical trials, making it difficult to speak about the effectiveness of different treatment approaches (LaFrance Jr et al., 2006; LaFrance Jr & Devinsky, 2002). Furthermore, developing standard treatments for PNES is difficult due to the multifactorial aetiology of the condition (Reuber, 2008b) and a more individual approach to treatment is currently preferred (Reuber, 2005). However, a recent meta-analysis by Carlson (2017) showed that 82% of individuals with PNES who complete psychotherapy experience a reduction in seizures of $\geq 50\%$, and 47% of individuals with PNES are seizure free upon completion of a psychological intervention.

One of the major obstacles to treatment, as identified by the Nonepileptic Seizures Treatment Workshop group, is the patients' refusal to accept their diagnosis (LaFrance Jr et al., 2006). Most often this is due to the patients feeling that a diagnosis of PNES is equivalent to them being accused of "faking their spells" or being "crazy" (LaFrance Jr et al., 2006). Such denial of the condition occurs a lot more often among PNES patients when compared to those with epilepsy, often hindering psychological treatment that is needed (LaFrance Jr et al., 2006). The denial and non-acceptance of the psychogenic nature of PNES by patients seems to be so intrinsic to their view of their condition that a measure of abnormal illness behaviour could be used in differentiating PNES from Epilepsy (Stone, Binzer, et al., 2004).

Another important treatment factor is the communication of the diagnosis, due to its ability to often lower and even cease seizures (Zaroff, Myers, Barr, Luciano, & Devinsky, 2004), although adverse effects in seizure frequency and seizure return after finding out that the condition is not physiologic, as previously believed by the patient, have also been reported (LaFrance Jr, Reuber, & Goldstein, 2013; Wilder et al., 2004).

Based on their review of current empirical data, LaFrance Jr, Reuber, and Goldstein (2013) suggest a three stage approach to treating PNES. Firstly, a formal psychiatric assessment should be carried out and should inform the treatment plan. The purpose of this assessment should be to exclude any psychiatric disorders that may be confused with PNES (e.g., panic attacks), finding out psychiatric comorbidities, and considering pharmacological treatment of these comorbidities. Secondly, predisposing, precipitating, and perpetuating factors should be listed (Brown & Reuber, 2016a, 2016b). As discussed earlier, often predisposing factors among PNES patients include sexual, physical or emotional abuse, having grown up in a dysfunctional home environment, and developing a perfectionistic and people-pleasing personality style; precipitating factors may include a serious injury or assault as an adult or encountering a reminder of an earlier abuse history; and perpetuating factors are often ongoing family or marital conflict (LaFrance Jr, Reuber, et al., 2013). Lastly, if appropriate, psychotherapy addressing the predisposing, precipitating and perpetuating factors should be initiated, alongside withdrawal of the AEDs where PNES is not accompanied by epilepsy. Therapies that have been used most among specialists treating PNES are: cognitive-behavioural therapy, psychodynamic therapy, group therapy, family therapy, pharmacological treatment and polytherapy (combination therapy).

2.12.1 Different types of treatment.

2.12.1.1 Cognitive-behavioural therapy.

The cognitive-behavioural approach views PNES within the framework of the fear escape-avoidance model, where dissociative responses are triggered by cognitive, emotional, physiological or environmental cues that are associated with the distressing experience that functioned as the predisposing factor for the development of PNES (LaFrance Jr & Devinsky, 2002; LaFrance Jr, Reuber, et al., 2013). Treatments often focus on dealing with these avoidance behaviours, promoting self-efficacy and self-control and teaching relaxation and attention refocusing techniques with the goal of targeting cognitive distortions, as well as the associated emotional, physiologic, and behavioural aspects of PNES (LaFrance Jr, Reuber, et al., 2013).

Cognitive-behavioural therapy (CBT) is the approach that is currently related to the most substantial body of empirical data in relation to PNES treatment (LaFrance Jr, Reuber, et al., 2013). Goldstein et al. (2010) conducted a randomised controlled trial and reported that receiving CBT together with standard medical care (SMC; i.e., explanation of psychological basis of disorder and withdrawal of AEDs) was significantly more likely to result in being seizure-free at three months' follow up when compared to SMC alone. A multicentre randomised clinical trial carried out by LaFrance Jr et al. (2014) compared the efficacy of CBT-informed psychotherapy (CBT-ip), CBT-ip with medication (sertraline), medication only, and SMC. It was reported that the CBT-ip group showed a significant seizure reduction of 51.4% and significant improvement in depression, anxiety, quality of life, and global functioning when compared to baseline; CBT-ip with medication group showed a significant seizure reduction of 59.3% and significant improvements in some secondary measures, including global functioning; while neither medication only nor SMC groups showed any significant reduction in seizures (LaFrance Jr et al., 2014).

2.11.1.2 Psychodynamic therapy.

In general, psychodynamic approaches to treating PNES see it as a condition resulting from unresolved strong and painful emotions resulting from severe trauma, abuse or loss (LaFrance Jr & Devinsky, 2002). Hence, PNES is seen as a defence mechanism allowing these painful emotions to be expressed in a way that still maintains them unconscious (LaFrance Jr & Devinsky, 2002). Therapeutic mechanisms are considered to be: learning

more effective processing of emotions and change of unhelpful patterns of interpersonal relationships in relation to painful memories or areas of life (LaFrance Jr, Reuber, et al., 2013).

While psychodynamic therapy has been the preferred approach to treating PNES historically (LaFrance Jr & Devinsky, 2004), its effectiveness for PNES has yet to be demonstrated in a randomised controlled trial (RCT; LaFrance Jr, Reuber, et al., 2013). Nonetheless, three articles report on using an augmented form of brief psychodynamic interpersonal therapy (PIT; Howlett & Reuber, 2009; Mayor, Howlett, Grünewald, & Reuber, 2010; Reuber, Burness, Howlett, Brazier, & Grünewald, 2007) and one study on using psychoanalytical treatment (De Oliveira Santos, Benute, Santiago, Marchiori, & De Lucia, 2014). Reuber, Burness, Howlett, Brazier, and Grünewald (2007) used service evaluation measures and found the PIT approach to be associated with significant improvements in the number and severity of seizures as well as vitality, social functioning, and mental health. Additionally, it has been found that the treatment is cost-effective (Reuber, Burness, et al., 2007) and its positive effects are maintained over multiple years (Mayor et al., 2010). A study investigating the effectiveness of a 12-month weekly intervention using psychoanalysis found that 29.7% (n=11) of participants reported cessation of seizures, while in 51.4% (n=19) the number of seizures decreased (De Oliveira Santos et al., 2014).

2.11.1.3 Group therapy.

Group therapy may offer a few benefits over individual psychotherapy for PNES patients, namely: it is usually more cost-effective when compared to individual treatment; it is shown to be effective in tackling comorbid conditions often found in the PNES population; the group environment is conducive to the ripple effect of improvement from one patient to another; and being able to receive social support from other group members (Bullock, 2010). So far, three non-RCT studies using a group therapy approach to PNES treatment have been described in literature.

Prigatano, Stonnington, and Fisher (2002) completed a prospective unblinded study using a psychoeducational approach focusing on information about PNES. The researchers reported that out of the 15 patients selected for the study 9 completed at least 58% of the treatment sessions and out of these nine patients six (66%) reported a decrease in the number

of seizures, while one (11%) reported an increase. However, self-reported increase was correlated with paranoid ideation (Prigatano et al., 2002).

Zaroff, Myers, Barr, Luciano, and Devinsky (2004) again using a psychoeducational approach focused on the involuntary nature of somatic and psychological symptoms; the role of anger and trauma in PNES; as well as relaxation and coping techniques. Seven out of the 10 participants completed the majority of the therapy sessions and out of the seven patients three (43%) experienced a cessation of the seizures at treatment initiation, two experienced a decline (29%), one experienced no change (14%) and one reported an increase in paroxysmal events (14%). Additionally, the authors reported significant decreases in posttraumatic and dissociative symptoms as well as emotionally-based coping mechanisms and an improved quality of life (Zaroff et al., 2004).

The third study reported by Barry et al. (2008) used a psychodynamic group therapy approach. Apart from the general conceptualisation of PNES as an expression of unconscious painful emotions and the need to bring them into consciousness, the group therapy additionally focused on understanding PNES, encouraging solving of interpersonal problems through relating to other group members, self-relaxation and self-hypnosis (Barry et al., 2008). The researchers reported that out of the twelve patients who enrolled seven completed at least 78% of the sessions. As a result, six out of seven (86%) experienced a decrease in nonepileptic seizures, including four who reported cessation (57%) with only occasional occurrences triggered by heightened emotional distress (Barry et al., 2008). Additionally, the Beck Depression Inventory and the Global Severity Index of the Symptom Checklist-90 showed statistically significant improvement (Barry et al., 2008). Furthermore, at two-year follow-up five of the seven (71%) participants who completed the trial remained seizure-free apart from infrequent mild exacerbations in the face of stressful periods (Barry et al., 2008). Overall, group therapy shows promise of effectiveness in treating PNES, however, RCTs are needed to make a definitive judgement.

2.11.1.4 Family Therapy.

As discussed earlier, many patients with PNES are part of dysfunctional family systems and family dysfunction is often considered to be an aetiological factor of PNES (Krawetz et al., 2001). Additionally, family functioning seems to be related to PNES outcomes (LaFrance Jr et al., 2011). Hence, some propose that family therapy should be

indicated for PNES patients who are part of dysfunctional families (LaFrance Jr, Reuber, et al., 2013). Currently only four case studies are available describing using family therapy in managing nonepileptic seizures: three of them describe paediatric cases treated with a multimodal approach (Cruz, Chudleigh, Savage, & Kozlowska, 2014; Kozlowska, Chudleigh, Elliott, & Landini, 2016) and one a case of couples therapy using the McMaster Family Functioning Model (Archambault & Ryan, 2010). While all the case studies report success in managing and decreasing seizures, larger controlled studies are needed for a better understanding of family therapy suitability for PNES treatment.

2.11.1.5 Polytherapy.

In many instances an approach combining several disciplines may be needed to treat PNES. Many PNES specialists speak of the important role the neurologist plays in PNES treatment (Jones et al., 2010; LaFrance Jr & Bjørnaes, 2010; Mökleby et al., 2002). While a neurologist can do little to help with the psychological aspects of the condition, follow-ups by the neurologist and good communication with the treating psychology professional are related to better treatment outcomes (LaFrance Jr, Reuber, et al., 2013). Furthermore, a neurologist can be important if any neurological abnormalities coexist with PNES (Jones et al., 2010). Lastly, in the case of comorbid epilepsy, the neurologist's role is even more important as the correct dose of AEDs needs to be worked out (LaFrance Jr, Reuber, et al., 2013).

Similarly, treatment plans combining psychotropic medication and therapy may be needed if the PNES patient suffers from any psychiatric comorbidities, such as depression or anxiety, which is often the case in the PNES population (Goldstein et al., 2010). As noted earlier, in the study conducted by LaFrance Jr et al. (2014) the group where CBT informed psychotherapy was combined with medication, seizure reduction was the largest compared to CBT-informed psychotherapy (CBT-ip) only, medication only, and SMC.

2.13 Course and Outcome/Prognosis

The number of outcome studies in the area of PNES have been relatively few, however, have been increasing in recent years. So far studies have suggested a poor prognosis (continuing seizures or seizure relapse) among 25-80% of PNES sufferers at follow up (Farias, Thieman, & Alsaadi, 2003; O'Sullivan, Sweeney, & McNamara, 2006; Reuber et al., 2003; Reuber & House, 2002). At the same time, seizure cessation has been reported in 16-

58% of patients and seizure reduction in 25-40% at follow-up (Duncan et al., 2016; Ettinger, Dhoon, Weisbrot, & Devinsky, 1999; McKenzie, Oto, Graham, & Duncan, 2016; McKenzie, Oto, Russell, Pelosi, & Duncan, 2010; O'Sullivan et al., 2007; Sadan, Neufeld, Parmet, Rozenberg, & Kipervasser, 2016). However, any discussion of prognosis for PNES is always made problematic by the fact that prognosis is often dependent on the underlying psychological processes and social factors that tend to differ among PNES patients (Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al., 2009).

Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al. (2009) summarise the patient features that are usually associated with better outcomes, namely: early correct diagnosis (Betts & Boden, 1992; Buchanan & Snars, 1993; Reuber, 2009), no abnormal personality characteristics (Reuber et al., 2003), no or mildly severe psychiatric history (Cragar et al., 2005; Gene-cos & Ring, 2005; McKenzie et al., 2010), internal locus of control (Duncan et al., 2016), good communication and coping strategies (Reuber et al., 2003), identifiable acute psychological trauma preceding the onset of PNES, living independently (although this is contested by Reuber et al. [2003]) and absence of concomitant epilepsy (Bodde, Brooks, Baker, Boon, Hendriksen, & Aldenkamp, 2009 [however, this has been recently challenged by Sadan, Neufeld, Parmet, Rozenberg, & Kipervasser, 2016]), being employed (Duncan et al., 2016), a higher IQ and socio-economic status (McKenzie et al., 2010), a higher educational status, less dramatic seizure manifestation and younger age (Aldenkamp & Mulder, 1997; Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al., 2009; Reuber et al., 2003), absence of a past history of violence (Bodde, Brooks, Baker, Boon, Hendriksen, Mulder, et al., 2009), no ongoing use of AED's (Carton et al., 2003), not experiencing seizure clustering (Baird, Harlow, Machan, & LaFrance Jr, 2017) and being female rather than male (Alsaadi & Marquez, 2005; Bowman, 1999; Dworetzky et al., 2005).

2.14 Chapter Summary

This chapter discussed current international and South African knowledge of PNES in terms of nosology, history, signs and symptoms, epidemiology, classification, aetiology, diagnosis, treatment and the level of burden both for the individual and the broader context. The chapter also discussed the important role international research has shown personality factors, abnormal behaviours and psychiatric comorbidity to play in PNES both in terms of differentiating it from epilepsy and the development and maintenance of the disorder.

Chapter 3 Theoretical Framework

3.1 Introduction

In their systematic review of psychological and psychiatric aspects of PNES Brown and Reuber (2016a) suggest that a problem with many theories proposed in PNES research is the lack of empirical evidence behind them when it comes to PNES. In order to address this issue, the well-established Five Factor Theory (FFT) of the person by McCrae and Costa (2003) was chosen. FFT was considered to be the most appropriate theoretical framework for the present study not only due to its extensive empirical backing but also due to its ability to encompass all the variables measured in this study, i.e. PNES, personality traits, illness behaviours and psychiatric comorbidity. Furthermore, as discussed in the literature review, the Big Five personality traits, which are at the centre of the FFT, have already been shown to be useful in describing the PNES population (Reuber et al., 2003) and differentiating it from epilepsy (Cragar et al., 2005) and other conversion-type disorders (Ekanayake et al., 2017). FFT of the person has been adapted to this study in a way that is suggested to explain the process of developing and maintaining PNES.

3.2 Five Factor Theory

The FFT is a theory of the functioning of the person, whose centre is the Five Factor Model of personality traits: Neuroticism (N), Extraversion (E), Openness (O), Agreeableness (O), and Conscientiousness (C). FFT consists of a number of components that interact via numerous dynamic processes as depicted in *Figure 2*. These components are, namely: Biological Bases, Basic Tendencies, Characteristic Adaptations, Self-Concept (which is part of Characteristic Adaptations), Objective Biography, and External Influences (Costa & McCrae, 1994; McCrae & Costa, 2008, 2013). All those factors in turn interact through dynamic processes, which are understood as universal cognitive, affective, and volitional mechanisms, and are differentially affected by an individual's personality traits (McCrae & Costa, 2003).

The person "begins" with the Biological Bases, which can be understood as genetic, developmental, neuroanatomical, or psychophysiological mechanisms. In the case of PNES, these can be understood as any genetic predisposing vulnerability factors.

Biological Bases, even though not yet fully understood by medical sciences, determine personality traits, i.e. the endogenous Basic Tendencies (McCrae & Costa, 2003). Basic Tendencies, in turn can be defined as the abstract psychological potentials, limitations and capacities of the individual as embodied by the five personality dimensions. In this case these would be the broad personality dimensions of Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness, as well as specific personality traits considered to belong to them, in this study measured via the NEO-FFI-3 (measuring only the broad dimensions). While FFT argues that the environment does not have any interaction with personality traits (Basic Tendencies) and hence cannot exhibit direct influence over them, there are instances in which environment, in FFT denoted by the External Influences component, can influence personality traits through the mediation of the Biological Bases, such as head trauma and similar instances (McCrae & Costa, 2008).

External Influences can be understood as social or physical situations or contexts the individual finds themselves in and the demands associated with them (Costa & McCrae, 1994; McCrae & Costa, 2008). Furthermore, individuals are considered to construe, react to, and in turn influence the environment in ways consistent with their personality traits (Basic Tendencies; McCrae & Costa, 2008). In the case of PNES development and maintenance, External Influences may be understood as traumatic events, or dysfunctional family environment.

When External Influences interact with Basic Tendencies they shape Characteristic Adaptations (McCrae & Costa, 2008). Characteristic Adaptations represent the concrete manifestations of personality traits (Basic Tendencies) via patterns, such as, attitudes, beliefs, skills, habits, social roles and typical ways of relating to others (McCrae & Costa, 2013). As McCrae and Costa put it: "They are characteristic because they reflect the enduring psychological core of the individual, and they are adaptations because they help the individual fit into the ever- changing social environment" (2008, pp. 163–164). Within the Characteristic Adaptation component another component is contained, called the Self-Concept. The Self-Concept can simply be defined as the view the individual has of themselves (Costa & McCrae, 1994). This component can be understood in terms of self-schemas, or "cognitive–affective view of themselves that is accessible to consciousness" (McCrae & Costa, 2008, p. 165) and selective perception, which ensures that the information represented in the self-concept is consistent with the person's personality traits and brings a

sense of coherence to the person (McCrae & Costa, 2008). However, while Basic Tendencies are considered to remain constant throughout a person's life, Characteristic Adaptations can undergo considerable change in the face of changing External Influences (McCrae & Costa, 2008). Similarly, while Characteristic Adaptations may vary considerably across different cultures, families and even periods in a lifetime, Basic Tendencies (personality traits) do not (McCrae & Costa, 2008). Hence, in the case of PNES Characteristic Adaptations can be understood as ways of coping, tending to have an external locus of control or abnormal attitudes to one's health. In the case of this particular study, I will be looking at illness beliefs which will be measured via the Illness Behaviour Questionnaire (Pilowsky & Spence, 1983).
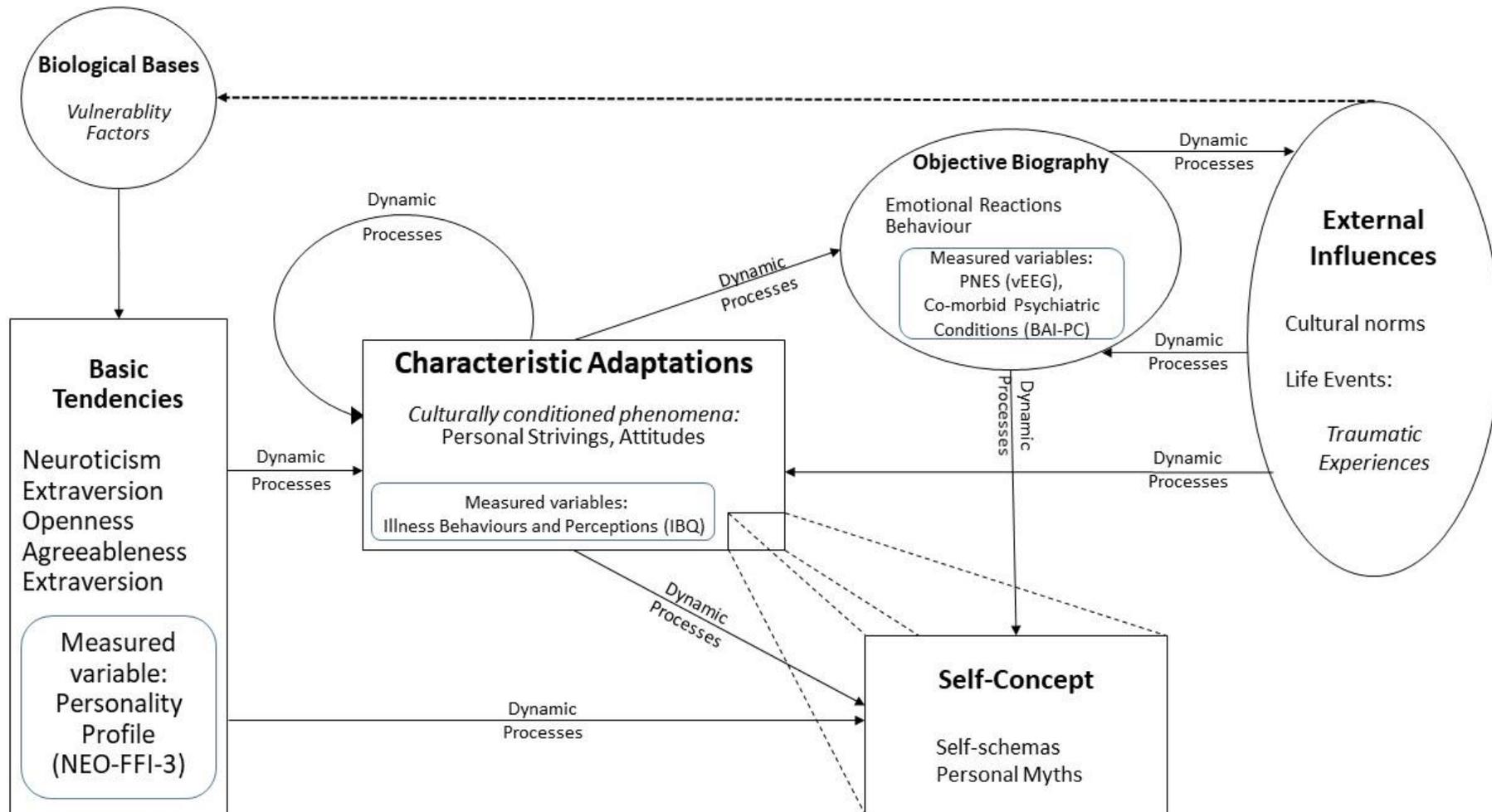
Figure 2. Five Factor Theory model of the person adapted for current study from McCrae and Costa (2008).

When the abovementioned (*Figure 2*) Characteristic Adaptations interact with the External Influences the output of this interaction is considered to be Objective Biography, Objective Biography can be understood as everything the person does, thinks or feels across their lifespan - the output of the person system. Hence, in the case of PNES, while the same event may have no significant effect on one individual, another individual's Characteristic Adaptations (attitudes, beliefs, etc.) may predispose them to experience it as traumatic and in turn predispose someone for PNES. Similarly, certain attitudes, beliefs, and concepts of the self once interacting with the External Influences (environment) can lead to a development of a number of psychiatric disorders. In the case of the present study, these emotional reactions and behaviours that will be measured are PNES (via vEEG) and psychiatric comorbidity of PTSD, depression and anxiety (via BAI-PC).

3.3 Chapter Summary

The chapter presented the FFT of the person as a theoretical framework and a basis for the approach to diagnosis taken in the present study. It is considered that the FFT successfully explains the development and maintenance of PNES by incorporating the aetiological and maintaining factors of PNES shown to be important by previous research and specifically the personality, abnormal illness behaviour and psychiatric comorbidity factors targeted in the present study.

Chapter 4 Methodology

4.1 Introduction

This chapter looks back at the research aims and questions outlined at the beginning of the study and discusses the research methodology and design considered to best target them. The chapter goes into detail into the study sample characteristics and size, the sampling strategy, measures used in the study, the approach to data collection and analysis, as well as the ethical considerations pertaining to this study.

4.2 Research Aims

In light of the research problem outlined earlier, this study aims to examine if South African individuals with PNES differ from individuals with ES and oNES in terms of demographic and seizure characteristics, personality traits, illness behaviours and depression, anxiety and PTSD symptoms in statistically significant ways; and if so, to test if these differences may be utilised in raising suspicion of PNES as the differential diagnosis to epilepsy and oNES.

4.3 Research Questions

With the research aims outlined above in mind, the present study seeks to answer the following questions:

- What NEO personality domains prevail among the South African patients of PNES;
- What illness behaviours South African patients of PNES demonstrate;
- If the NEO-FFI-3, IBQ, or BAI-PC questionnaires can differentiate between patients with PNES and those with ES or oNES.

4.4 Design

The study followed a quantitative double-blind (i.e. neither the researcher nor the participant were aware of the participant's diagnosis during data collection) convenient sampling comparative design.

4.5 Sample Characteristics

The target population group of this study were adults with seizure complaints visiting the Epilepsy Unit in Constantiaberg Medi-Clinic. The focus on adults stemmed from the fact that personality traits have been shown to change as people mature but remain relatively stable in adulthood (McCrae & Costa, 2003). The legal definition of adulthood of 18 years and above was used (Republic of South Africa, 1996). Lastly, the sample only comprised

South African individuals who were comfortable with the English language since the primary investigator is not familiar with other South African languages and this was a self-funded study limiting ability to translate the questionnaires or hiring another individual to help with data collection. All the participants in the study identified themselves as sufficiently proficient in English and any terms that were confusing were explained by the investigator by giving a definition of the word, a synonym and/or an example use, eventually clarifying the term to the participant.

4.6 Sampling Strategy

Convenience sampling was used. Patients staying at the Neuroscience Unit at the Constantiaberg Medi-Clinic and the Department of Neurology at the Tygerberg Hospital in the Western Cape during the data collection period were approached by the principal investigator telling potential participants about the study and inviting them to participate. These two facilities were chosen due to being the only in the Western Cape with vEEG equipment needed to ensure accurate PNES diagnosis (Cronje & Pretorius, 2013). Interested patients communicated their willingness to participate to the researcher on the spot.

4.7 Sample Size

The final sample in the current study consisted of 5 PNES, 16 ES, and 3 oNES patients. Awareness of PNES among healthcare providers in South Africa is still limited (Pretorius, 2016), making it hard to gather large samples of PNES patients. While recently larger studies in high-income countries (Elliott & Charyton, 2014; LaFrance Jr, Deluca, et al., 2013; Myers, Matzner, Lancman, Perrine, & Lancman, 2013) and to some extent in middle- to low-income countries (Asadi-Pooya et al., 2013, 2014) have been published, at the beginning of PNES research studies with approximately 20 participants were the norm (Cragar et al., 2002). Currently, South Africa is very much in its early stage of PNES research and the few studies that have looked into the condition have only managed to gather samples of up to 22 PNES participants when collecting data for up to nine months (Cronje & Pretorius, 2013; Pretorius & Cronje, 2015; Pretorius & Sparrow, 2015). Hence, the prediction is that as awareness of PNES in this country rises with greater research efforts, bigger sample sizes of PNES patients will become more accessible.

4.8 Measures

Members of the Non-epileptic Seizures Treatment Workshop (May 2005) suggested that high numbers of measures used, as well as long and complex measures present a higher likelihood of participants not completing their responses or inaccurate data (LaFrance Jr et

al., 2006). Additionally, the goal of this study is to test an approach to raising suspicion of PNES in a way that is cheap, easy and quick and thus likely to be used in primary care settings. Hence, the measures for this study were chosen based on their adherence to these requirements.

4.8.1 Demographic and seizure-related questionnaire.

Information was gathered about participants' gender, age, educational level, ethnicity, home language as well as age at seizure onset and monthly seizure number (Appendix A), since these variables have been shown to either be associated with different manifestations of PNES aetiology, semiology and outcomes, or be useful in differential diagnosis (as discussed in Chapter 2).

4.8.2 NEO-Five Factor Inventory-3 (NEO-FFI-3).

NEO-FFI-3 (Appendices B and C) is a shortened version of the full NEO-PI-3 measure developed by McCrae and Costa (2010). The NEO-FFI-3 contains five 12-item scales (60 items) measuring each of the "Big Five" trait domains: Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness. The questionnaire measures traits that approximate normal, bell-shaped distributions. Once raw scores for each of the scales are calculated, they are converted into T-scores, which are based on normative samples, with a mean of 50 and a standard deviation of 10. The T-scores indicate a percentile at which a participant scores, hence comparing characteristics across people rather than within an individual. The T-scores are divided into the following ranges: "Very Low", "Low", "Average", "High" and "Very High".

NEO-FFI-3, which is the short version of the NEO-PI-3 was chosen due to the reduced time it takes to administer it. The NEO-FFI-3 takes 5-10 minutes to complete compared to the 30-40 minutes for the NEO-PI-3 (McCrae & Costa, 2010). This is important for a few reasons. Firstly, the measure was administered during a period that the participants spend in the epilepsy unit as part of their observation, meaning that participation in the study was a secondary endeavour for the patients. Hence, taking the minimum amount of time to administer the measure was important to ensure likely participation. Secondly, one of the aims of the study was to see if the NEO-FFI-3 could aid healthcare practitioners in PNES screening, especially in resource-challenged contexts, where the available time and attention per patient is limited. Lastly, while the NEO-FFI-3, unlike the NEO-PI-3, does not provide information on the specific facets within each personality domain, the correlations between the brief NEO-FFI-3 scales and the corresponding full NEO-PI-3 questionnaire range from .87 to .95, making them a good approximation of the full measure (McCrae & Costa, 2010).

The "Big Five" personality domains used in the NEO inventories are considered to be the best validated and reliable model of personality traits (American Psychiatric Association, 2013). The personality factors measured by NEO-FFI-3 were derived via a factor analysis of natural language trait adjectives and through numerous studies the five NEO inventory factors have shown excellent convergent and discriminant validity (McCrae & Cota, 2010). Furthermore, numerous studies have shown these personality dimensions to be predictors of various external criteria, such as psychopathology, coping and defences, needs and motivation, and similar (McCrae & Cota, 2010).

Internal consistency coefficient alpha for the self-report NEO-FFI-3 personality dimensions ranges from 0.78 to 0.86 (McCrae & Cota, 2010). Item factor loadings have been shown to range from 0.87 to 0.99 (McCrae & Cota, 2010). Additionally, item factors have been shown to correspond closely to the domain scores with correlations within the range of 0.94 to 0.97 (McCrae & Cota, 2010). While test-retest reliability for the NEO-FFI-3 has not been established yet, it has been for the NEO-FFI, an earlier and very similar measure (McCrae & Cota, 2010). For the NEO-FFI the test-retest correlations after a 2-week follow-up were reported at .89, .86, .88, .86 and .90 for N, E, O, A, and C dimensions, respectively (Robins, Fraley, Roberts, & Trzesniewski, 2001).

4.8.3 Illness Behaviour Questionnaire (IBQ).

The IBQ (Appendix D) is a questionnaire comprised of 62 yes-no items designed to measure abnormal illness behaviours. It was developed with a specific focus on psychosomatic illnesses, such as somatoform or conversion disorders, which can be understood as expressions of abnormal illness behaviour (Pilowsky, 1975). The questionnaire is comprised of seven subscales, namely: General Hypochondriasis, Disease Conviction, Psychological versus Somatic illness focus, Affective Inhibition, Affective Disturbance, Denial and Irritability. The questionnaire uses a yes/no format and is scored by attributing one point to each answer indicating an abnormal behaviour.

Test-retest reliability correlations for the questionnaire after one to 12-week delay have been shown to range between 0.67 to 0.87, with only three coefficients below 0.84 (Pilowsky & Spence, 1983). While Pilowsky and Spence (1983) do not report on the internal consistency, in a British chronic low back pain sample the Kappa coefficient for individual item reliability has been reported to be significant for all except 10 items (Main & Waddell, 1987). Overall alpha coefficient in a sample of university students, general community members and clinical psychiatric outpatients has been reported to be 0.62 (Boyle & Le Dean, 2000).

The factor structure has been validated on 100 intractable pain patients where eigenvalues of above 1 were rotated according to Kaiser's varimax criterion, as suggested by Kaiser (1960), which yielded 12 factors (Pilowsky, 1975, 1978). Out of the 12 only those with at least two loadings greater than 0.4 were considered (in line with suggestion by Stevens [2009]), which eventually resulted in seven meaningful factors, as described earlier (Pilowsky, 1975, 1978). Perhaps most relevantly to the current study, discriminant validity of the measure has been shown to be good with different subscales efficiently discriminating between PNES and ES patients (Stone, Binzer, et al., 2004); clinical psychiatric outpatients as opposed to general community sample and young healthy university students (Boyle & Le Dean, 2000); and motor conversion patients as opposed to patients with definite organic lesions (Binzer, Eisemann, & Kullgren, 1998).

4.8.4 Beck Anxiety Inventory - Primary Care.

As previously discussed, one of the features that is often different between PNES and ES patients is the higher prevalence of psychiatric comorbidity among the former. Depression, anxiety disorders and post-traumatic stress disorder being the most common comorbidities in the PNES population (Abubakr et al., 2003; Alsaadi & Shahrour, 2014; Griffith & Szaflarski, 2010; LaFrance Jr & Devinsky, 2002; Reuber, 2008a).

In light of the need for short, valid and reliable measures to screen for psychopathology in medical primary care settings, the well-known Beck Anxiety Inventory (BAI; Beck, Steer, & Carbin, 1988) and Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) were shortened to create the Beck Anxiety Inventory – Primary care and Beck Depression Inventory – Primary Care (i.e., BAI–PC and BDI–PC). Unlike the BAI, which consists of 21 items, the BAI-PC (Appendix E) consists of seven and takes around 1 minute to complete (Mori et al., 2003). The measure consists of the following items derived from the full BAI scale, namely: "Incapable of relaxing", "Fear of the worst happening", "Terrified", "Nervous", "Fear of losing control", "Fear of dying", and "Scared". It is rated on a 4-point scale from 0 to 3 just like the full scale measure. Beck and Steer (1997) demonstrated that the measure was 85% sensitive and 81% specific in detecting those who did or did not meet criteria for clinical anxiety (i.e., panic, generalized anxiety, or both). Additionally, Mori et al. (2003) tested the clinical efficacy of BAI-PC in screening for clinical anxiety simultaneously with PTSD and depression. The researchers examined the BAI-PC in comparison to the BAI, BDI and PTSD Checklist (PCL; Weathers, Huska, & Keane, 1991) and with the recommended cut-off score of 5 reported 84.5% sensitivity and 79.5% specificity as a clinical anxiety screen, 91.1% sensitivity and 74.7% specificity in identifying patients with and without depression, 97.2% sensitivity and 72.6% specificity as a

screen for PTSD. When screening for anxiety, depression *or* PTSD, a sensitivity of 82.4% and a specificity of 82.7% was reported (Mori, Lambert, 2003). Furthermore, it is endorsed by the United States Department of Veterans Affairs as a screen for PTSD (U.S. Department of Veteran Affairs, 2016). Hence, using BAI-PC in the current study offers the benefit of minimising the number of measures needed to administer to the sample, while maximising the information available about relevant psychiatric comorbidities. Mori et al. (2003) suggest that BAI-PC should help raising "red flags" in primary healthcare, hence if the measure is helpful in differentiating between PNES and ES patients, it may contribute in raising suspicion of PNES in primary healthcare settings in this country.

4.9 Data Collection

Before data collection could begin buy-in and multiple permissions from key stakeholders had to be obtained. The key contact for this study proved to be a neurologist working both at Constantiaberg Medi-Clinic and Tygerberg Hospital. They are a well-known specialist in epilepsy and PNES and see patients both from South Africa and other African countries. The responsible neurologist was presented with the research proposal for the project and the proposed approach was then discussed together with the project supervisor and primary investigator. As a result, the project received the responsible neurologist's support and some invaluable feedback, which was later incorporated into the final research proposal. Afterward, they put the researcher into contact with the head nurse of the Neuroscience Unit at Constantiaberg Medi-Clinic. In a month's time a meeting with the head nurse was made possible, where they were presented with the updated research proposal. A data collection approach that would work in-line with the usual operation of the ward was discussed and agreed upon. Furthermore, with the responsible neurologist's help, contact was made with the principal technologist at Tygerberg Hospital Neurology Unit to discuss the best way to approach data collection in their unit (outlined below).

Simultaneously, the researcher was going through an ethics approval process at Stellenbosch University, involving submission of the research proposal to the Departmental Ethics Screening Committee and Stellenbosch Research Ethics Committee. Once ethical permission from Stellenbosch University was obtained, the researcher submitted an application for institutional permission to the management of Constantiaberg Medi-Clinic via e-mail and to the Western Cape Government for data collection at Tygerberg Hospital via the electronic portal http://nhrd.hst.org.za/. The institutional permission from Constantiaberg Medi-Clinic was received a month later, in November of 2016. In January of 2017, contact was re-established with the neurologist at Constantiaberg Medi-Clinic and the data collection was given the go-ahead. A meeting with the head nurse was made to finalise the data

collection approach and data collection could commence at Constantiaberg Medi-Clinic Neuroscience Ward at the beginning of February of 2017. The institutional permission for Tygerberg Hospital was received in February 2017. Subsequently contact was made with the principal technician at the Tygerberg Hospital Neurology Unit and a date for the commencement of data collection was agreed upon.

The data collection at both sites proceeded in the way described subsequently. Once new patients have been identified to the researcher by the head nurse (at Constantiaberg Medi-Clinic) or the head technician (at Tygerberg Hospital), she approached them introducing herself as a Master's student from Stellenbosch University running a research project on people with seizures, briefly presenting the aim of the project and asking if they would like to participate. Once potential participants have communicated their interest, the researcher provided participants with an informed consent form (Appendix F) to familiarise potential participants with the project in more detail. Before the form was signed the researcher would ask if the patient had any questions and if they were still happy to participate. Once any questions and concerns have been addressed and the patient indicated their further willingness to participate, the informed consent was signed by both the participant and the investigator. One signed copy was kept by the researcher and another one given to the participant. After the participant had given their informed consent the researcher and participant would discuss a convenient time to administer the measures. All the measures were self-administered, hence the researcher provided participants with the test materials and a pencil and gave them adequate time to answer all the items on the questionnaires. The researcher was also available during the self-administration to explain any items that were unclear. All the participants were able to complete the questionnaires while staying at the clinic. While flyers inviting participants to participate in the study (Appendix G) were prepared and available, all patients when approached preferred to hear about the study from the investigator and thus they ended up not being used.

Once the data was collected from the participants, the researcher presented either the neurologist at Constantiaberg Medi-Clinic or the principal technician at Tygerberg Hospital with a list of participants' names asking for their diagnoses.

4.9.1 Data Collection Challenges

A number of challenges were faced before data collection could commence. Firstly, due to the novelty of the research project and the target group comprising vulnerable individuals at a vulnerable time (during vEEG observation at the hospital), the university ethics approval process proved to be longer than expected, thus delaying the obtainment of institutional permissions. Secondly, due to the considerable amount of time that had elapsed

after discussion with the responsible neurologist and the head nurse in the Neuroscience ward in Constantiaberg Medi-Clinic, contact had to be re-established before data collection could commence. Again, this took longer than expected due to the difficulty in reaching the neurologist and Christmas holidays starting before this could be done, which meant that they were going on leave and no new patients were being admitted. Furthermore, while request for institutional permission from Tygerberg Hospital was submitted right after getting REC approval at the end of September 2016, permission for data collection from Tygerberg Hospital was received only in February 2017, due to the National Health Research Database management forgetting to process the application until further inquiries were made by the researcher. Lastly, While all the diagnoses from Constantiaberg Medi-Clinic with some delay were eventually made available to the researcher, those from Tygerberg were not. When inquiry was made at Tygerberg, the researcher was told that both the Neurology Unit and the patients were still awaiting their diagnoses, some even six months after doing their vEEG monitoring. The reason given for this delay was an apparent lack of expert resources. The main reason for this seems to be the difference between the two clinics in terms of resources and thus approach to vEEG monitoring. While patients in the Constantiaberg Medi-Clinic are being monitored via vEEG there is always at least one staff member nearby who is there to log the time of any seizures that occur. This makes it easy for the expert diagnosing the patient later to go to the logged time of the seizure specifically and view the available simultaneous video and EEG data. However, in the case of Tygerberg Neurology Unit there is no such constant surveillance of those coming in for vEEG monitoring, due to the lack of staff to do so. In the end, this means that the consulting expert who does the diagnosis has to comb through hours of vEEG material looking for relevant data since patients may stay at the unit up to several weeks. In the case of this particular study, the data was collected during a period when the unit experienced a backlog in getting diagnoses from the consulting experts and this resulted in the diagnoses being unobtainable to the researcher. Hence, this meant that the data collected from the Tygerberg Neurology Unit had to be excluded from data analysis.

4.10 Data Analysis

After data was collected the diagnoses of the patients were revealed to the primary researcher by the responsible neurologist. The sample was divided into three groups: PNES, ES, and ES plus other non-epileptic seizure patients. This was done because the group with other diagnoses was too small (N=3) to use for comparative statistical analyses on its own, hence it was combined with the ES group in order to see if any differences in significance could be detected (i.e. some variables becoming insignificant and others significant) when contrasted with just comparing the PNES and ES groups. Since nothing other than the fact that the

"Other" group exhibited seizure-like events was known, while the participants in this group are described to give some context to the comparative statistical analysis, no descriptive statistics were performed on the "Other" group specifically.

Reliability analysis in the form of Cronbach's alphas (Cronbach, 1951) was conducted on data collected from the measurement instruments. ANOVA (Fisher, 1925) was used to compare measured traits between PNES, ES, and the combined ES and oNES groups. Cross-tabulation (Pearson, 1904) and the Fisher exact two-tailed test (Fisher, 1935) was used for categorical variables. ROC curve analyses (Hanley & McNeil, 1982, 1983) were conducted to investigate the ability of measured variables to discriminate between the two groups. Sensitivity and specificity are reported.

4.11 Ethical Considerations

Ethical approval (**SU-HSD-002711**) was obtained from the Research Ethics Committee at Stellenbosch University (Appendix H). Institutional permissions were obtained from the hospital management for Constantiaberg Medi-Clinic (Appendix I) and the Western Cape Government for Tygerberg Hospital (Appendix J).

4.11.1 Informed consent.

The informed consent form (Appendix F) was used to familiarise potential participants of the purpose of the study, issues of anonymity and confidentiality, potential risks and benefits of participating in the study, and their right to refuse to answer any questions or withdraw from the study at any point with no ramifications. Only those individuals who agreed to the informed consent form participated in the study.

4.11.2 Anonymity, confidentiality and privacy.

The informed consent form explained that participants' responses were not going to be anonymous due to healthcare staff and the researcher being able to identify the participants via their medical records. However, participants were assured of confidentiality, which was ensured via means of assigning each participant with a study-specific participant ID linking it to participant identifiers in a separate computer file. Furthermore, the data is currently kept on a password protected computer meaning that only the researchers are able to access it, thus protecting the privacy of the participants. Hard copies will be kept in a locked cabinet in the research supervisor's office for a period of five years and thereafter discarded in an appropriate way.

4.11.3 Potential risks and precautions.

While psychological measures were administered to vulnerable groups (Horn, Graham, Prozesky, & Theron, 2015), the study itself was not considered to pose high risk of physical or psychological harm to the participants. The participants were asked to answer questions with regards to their typical modes of feeling, typical modes of being which tap into their personality traits, as well as the way they experience and perceive their illness. These topics are considered to be a part of normal conversion and hence were not deemed to be triggering. However, if any participants would have experienced discomfort to the point where counselling was needed, provisions were made for them to be referred to psychologists working with seizure patients – Dr. Jacqui Bean (021 761 6332) or Ms. Elspeth Burke (021 7021633) – and have their counselling fees covered by the researcher. Nonetheless, none of the participants needed to be referred for counselling and many reported the process to be a positive experience.

4.12 Chapter Summary

The current study targeted adult seizure patients at the only two clinics in the Western Cape that have vEEG monitoring technology necessary to confirm PNES diagnosis. To an extent, the situation that a patient coming for a vEEG would encounter was recreated, where the patient, the investigator and the doctor were blind to the diagnosis at the time of data collection. Demographic and seizure characteristics were measured, and the NEO Five Factor Inventory – 3 (NEO-FFI-3), Illness Behaviour Questionnaire (IBQ) and the Beck Anxiety Inventory – Primary Care were chosen to measure personality domains, abnormal illness behaviour and anxiety, depression and/or PTSD comorbidity, respectively. Lastly, ethical considerations pertaining to the study sample as well as the approach to handling these considerations were discussed.

Chapter 5 Results

5.1 Introduction

This chapter presents the results and key findings of the data analyses performed on the data set. Section 5.2.1 describes the data set in terms of diagnosis distribution, gender, age, population group, language, level of education, age at first seizure and monthly seizures. Separate statistics on these parameters are made available for the PNES, ES and oNES groups. Section 5.2.2, in turn, presents comparisons on the abovementioned parameters between the PNES and ES groups as well as the PNES and a combined ES and oNES groups and reports any significant differences. Section 5.3.1 presents the results of the reliability analysis performed on the NEO-FFI-3 data and evaluates the reliability of the measure. Section 5.3.2 presents the NEO-FFI-3 scale averages (M) and standard deviations (SD) for the PNES, ES and oNES groups. Section 5.3.3 presents results of ANOVA comparing the PNES and ES, as well as PNES and combined ES and oNES groups on average NEO-FFI-3 scale scores. Section 5.4.1 presents response tendencies of the PNES and ES groups in terms of IBQ subscale items included in the study and section 5.4.2 compares the PNES and ES, as well as PNES and combined ES and oNES groups on these tendencies and reports any significant differences. Section 5.5.1 presents the results of the reliability analysis performed on the BAI-PC data and evaluates the reliability of the measure. Section 5.5.2 reports PNES and ES group averages on the BAI-PC measure and section 5.5.3 compares the averages of PNES and ES, as well as PNES and the combined ES and oNES groups and reports any significant differences. Lastly, the section presents ROC curve results and the optimal BAI-PC cut-off score for PNES screening. Section 5.6 sums up the chapter.

5.2 Demographic and Seizure-Related Questionnaire

5.2.1 Descriptive statistics.

The final sample for which diagnoses were available consisted of 24 patients from Constantiaberg Medi-Clinic. The sample consisted of five (21%) PNES patients, 16 (67%) ES patients and three (13%) patients with oNES (e.g., one of the patients had seizures related to schizophrenia), not including comorbid PNES and ES, of which there were none (Figure 3). While the "Other"/oNES group participants are described below, no descriptive statistics were carried out on this group due to its small size and lack of known common characteristics among the participants in it.
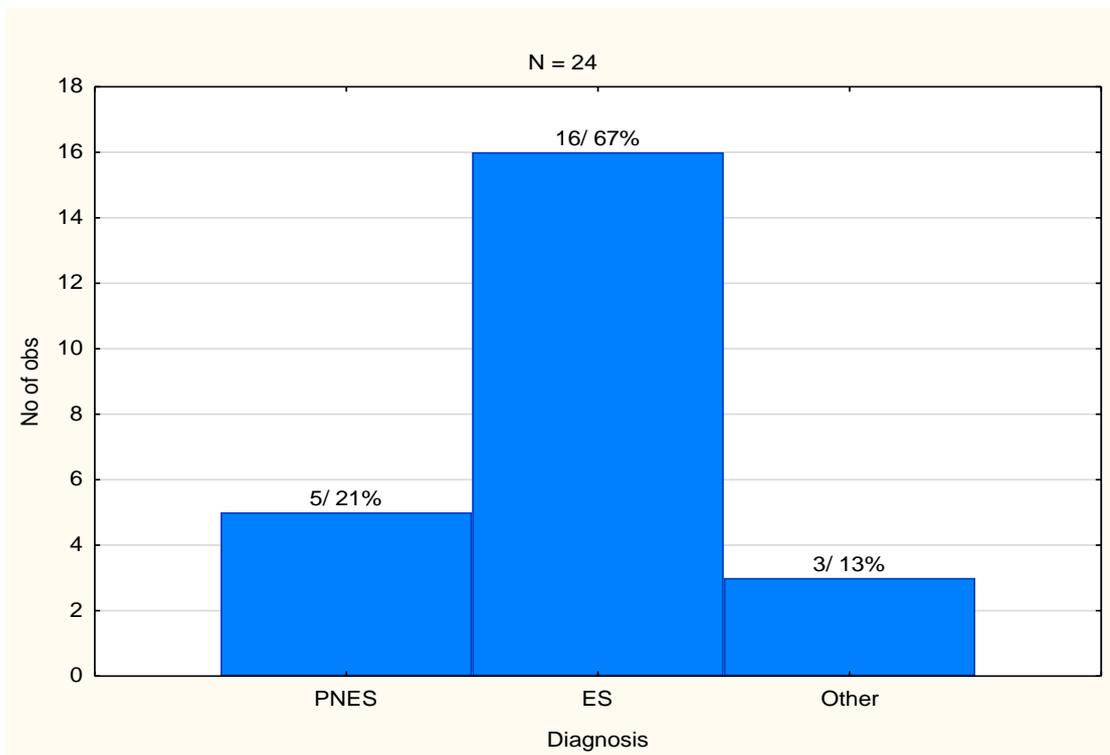
Figure 3. Diagnosis distribution of full study sample.

The PNES sample was comprised of 5 males (100%) and the ES sample comprised of 8 females (50%) and 8 males (50%; *Figure 4*); the "Other" group consisted of 2 males and 1 female.
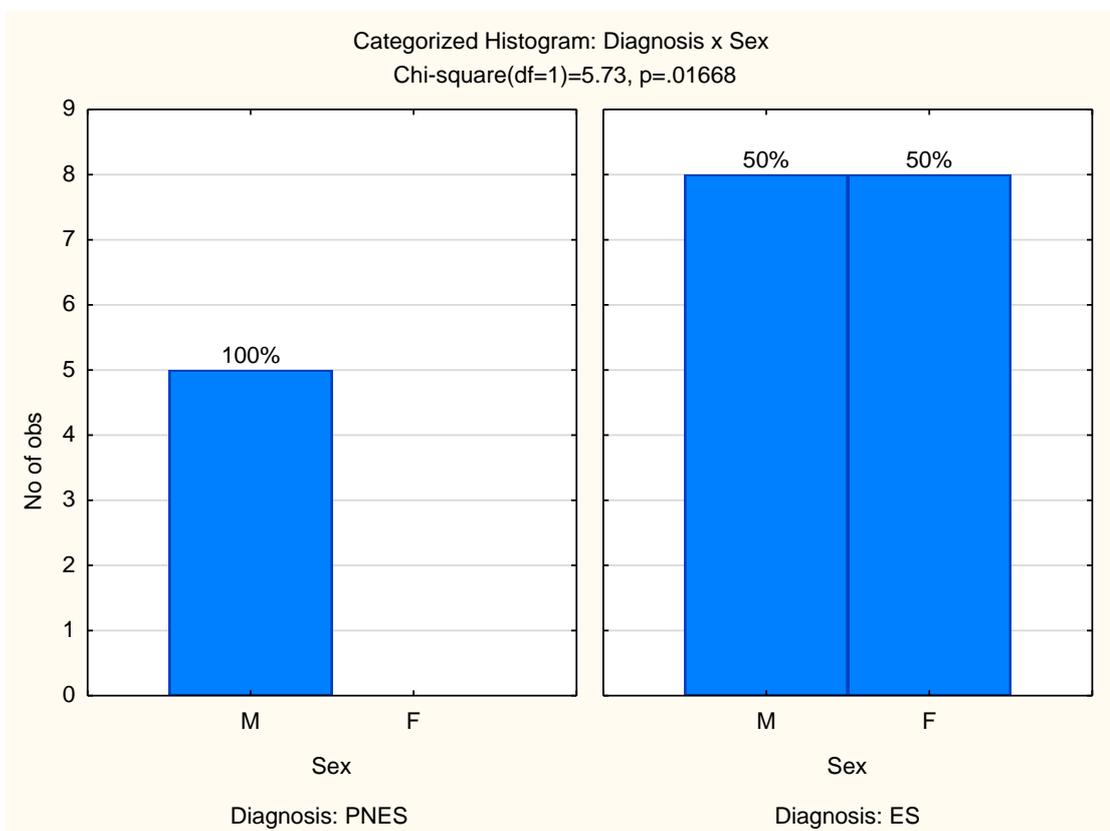
Figure 4. Gender distribution between PNES group (N=5) and ES group (N=16).

The age range of the whole group was 18-78 years (M=35; SD=15). The age range for the PNES group specifically was 20-63 (M=35; SD=17) and for the ES group it was 18-57 (M=33; SD=12); participants in the "Other" group were aged, 22, 37, and 78. The age distributions for the PNES and ES groups are presented in *Figure 5* and *Figure 6*.
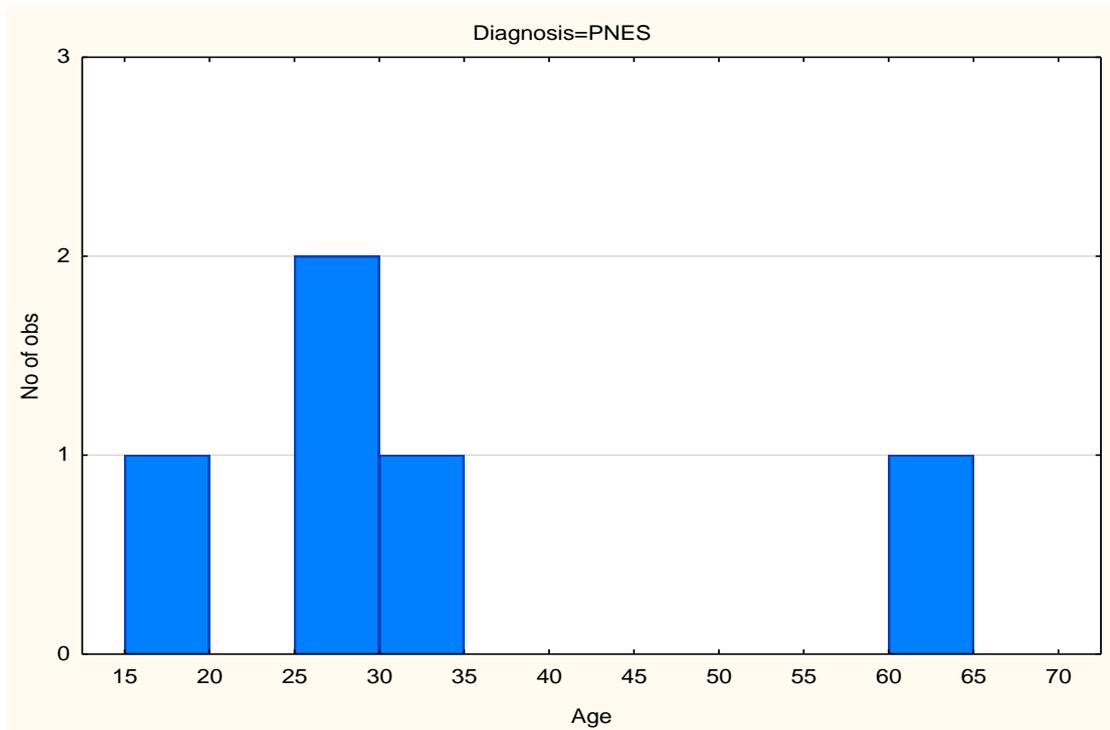
Figure 5. Age distribution in the PNES sample.
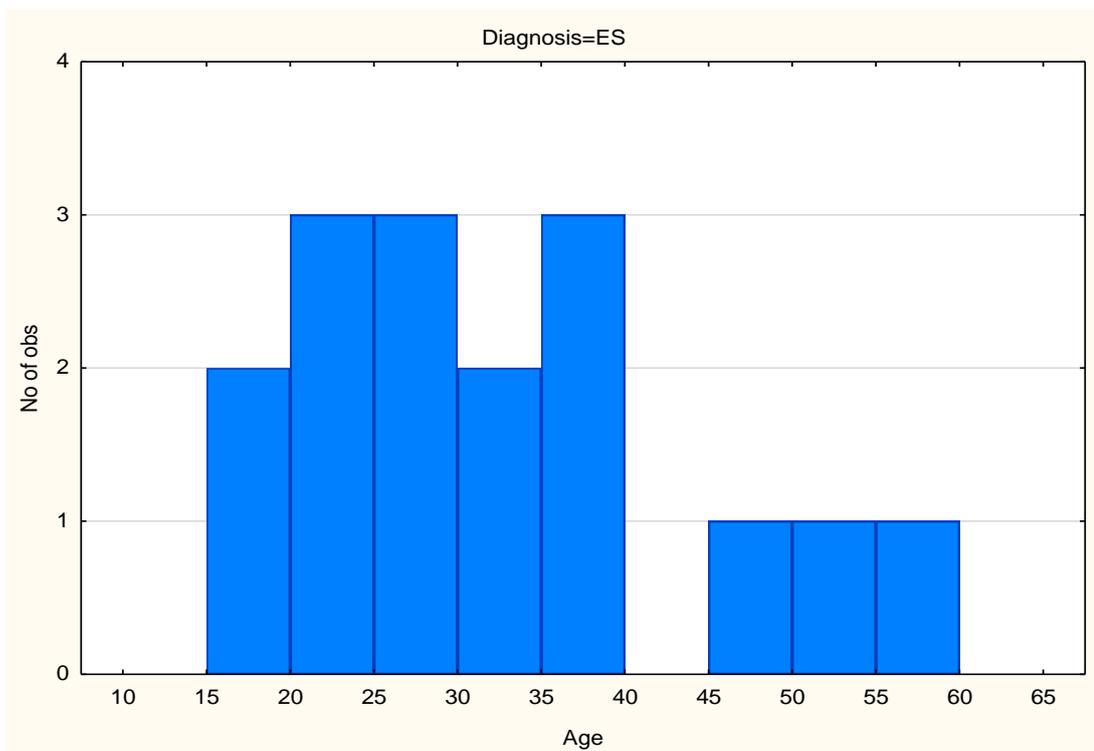
Figure 6. Age distribution in the ES sample.

White[1] participants comprised 75% (18) of the whole sample, 21% (5) of the participants were Brown/Coloured[1] and 4% (1) was Black African[1] (Figure 7). The PNES group consisted of 80% (4) White and 20% (1) Brown/Coloured participants, and the ES group comprised of 75% (12) White, 19% (3) Brown/Coloured and 6% (1) Black African participant (*Figure 8*). The "Other" group consisted of 2 White and 1 Brown/Coloured participant.
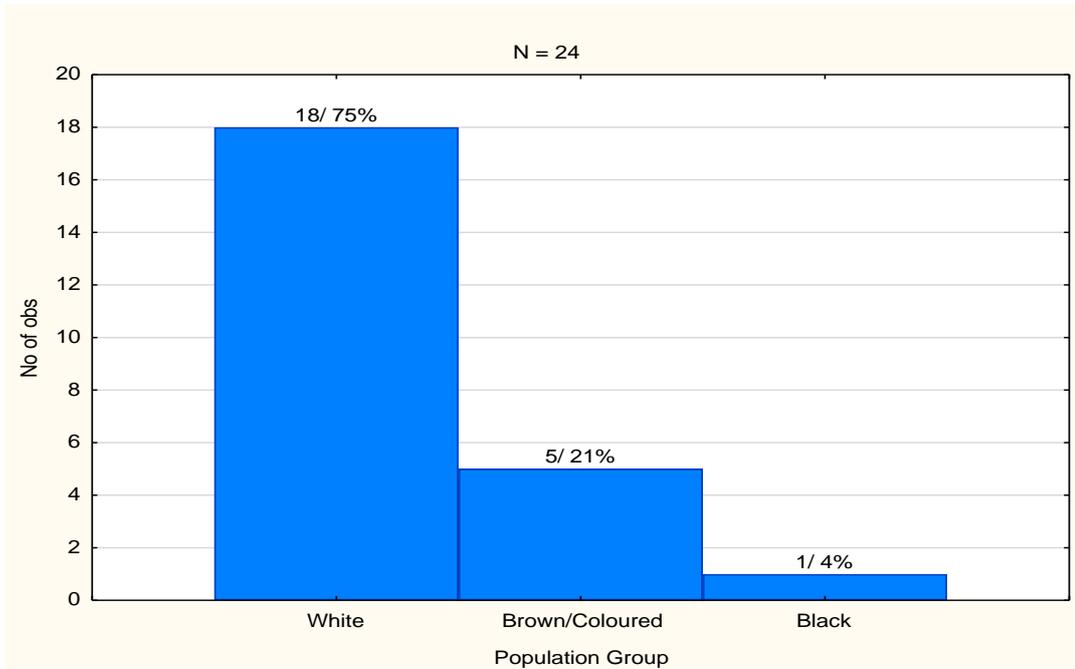
Figure 7. Population group distribution of the sample (N=24).
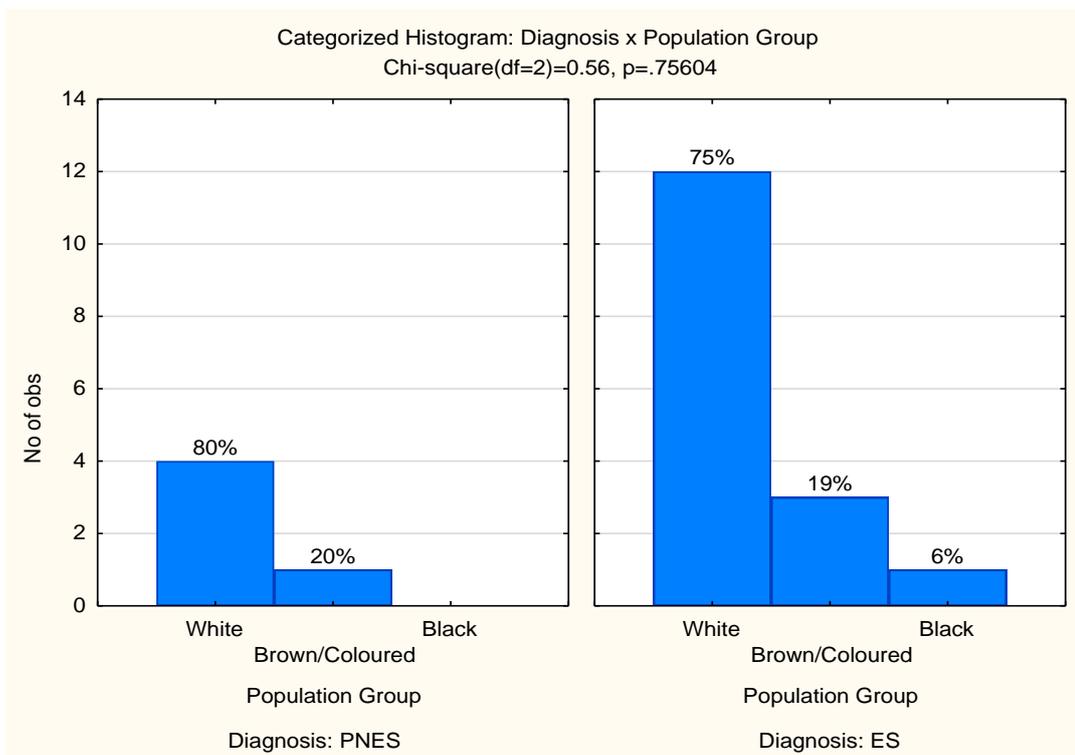
Figure 8. Population group distribution for the PNES group and the ES group.

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[1] "White", "Coloured" and "Black African" are the official terms used to denote racial belonging by Statistics South Africa – the national statistical service in South Africa (Statistics South Africa, 2017).

Afrikaans was reported as a home language by 50% (12) of all the participants, 29% (7) reported English, 17% (4) reported both English and Afrikaans, and 4% (1) of the whole sample reported English and German as their home languages. In the PNES group, 60% (3) chose English, 20% (1) chose Afrikaans, and 20% (1) chose English/Afrikaans as their home language. In the ES group, 19% (3) chose English, 56% (9) chose Afrikaans, 19% (3) chose English/Afrikaans and 6% (1) of the participants chose English/German as their home language (*Figure 9*). In the "Other" group 2 chose Afrikaans as their home language and 1 chose English.
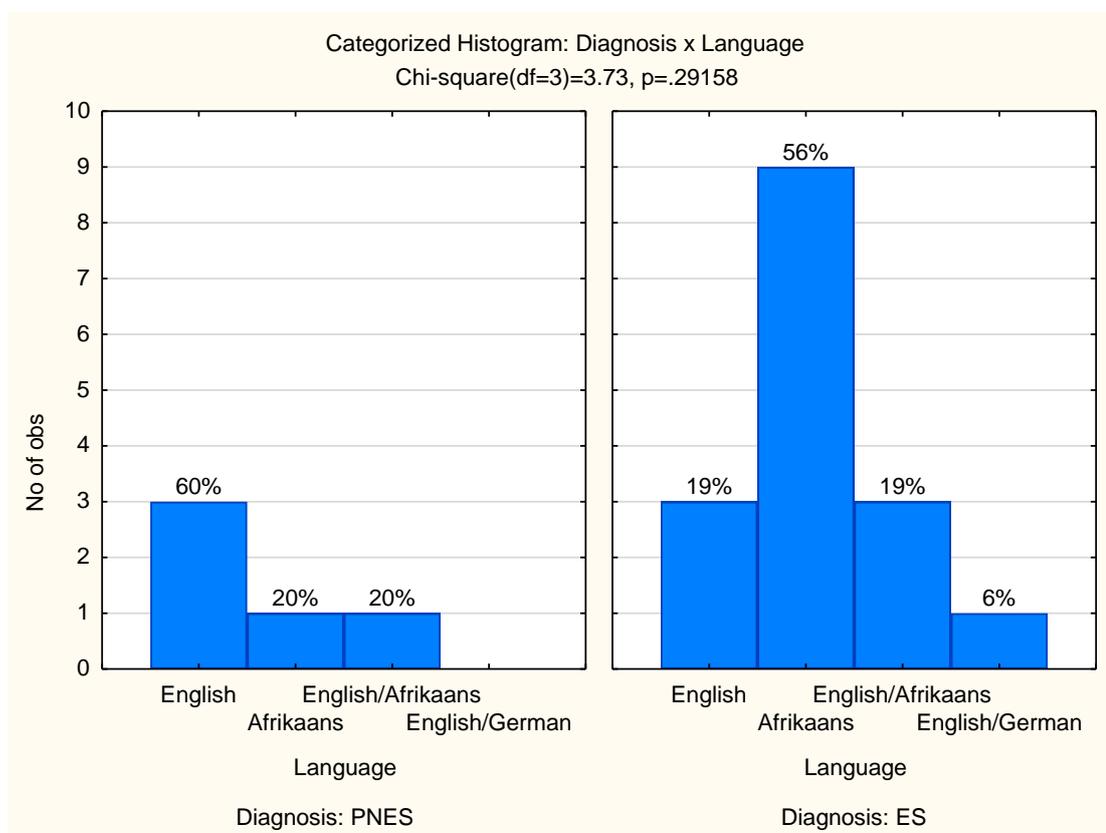
Figure 9. Language distribution for the PNES group and the ES group.

"Before Grade 12" was reported as the highest level of education by 4% (1) of all the participants, 29% (7) of the participants reported that to be "Grade 12", 29% (7) as some tertiary education, 33% (8) as a Bachelor's degree, and 4% (1) as a Master's degree. In the PNES group, 40% (2) reported "Grade 12" to be their highest level of education, 40% (2) reported it as "Bachelor's", and 20% (1) reported it to be "Master's". In the ES group 6% (1) reported their highest education level to be "Before Grade 12", 25% (4) reported "Grade 12", 44% (7) reported some Tertiary education, and 25% (4) reported "Master's" to be their highest level of education (*Figure 10*). In the "Other" group 1 chose "Grade 12" and 2 chose Bachelor's as their highest level of education.
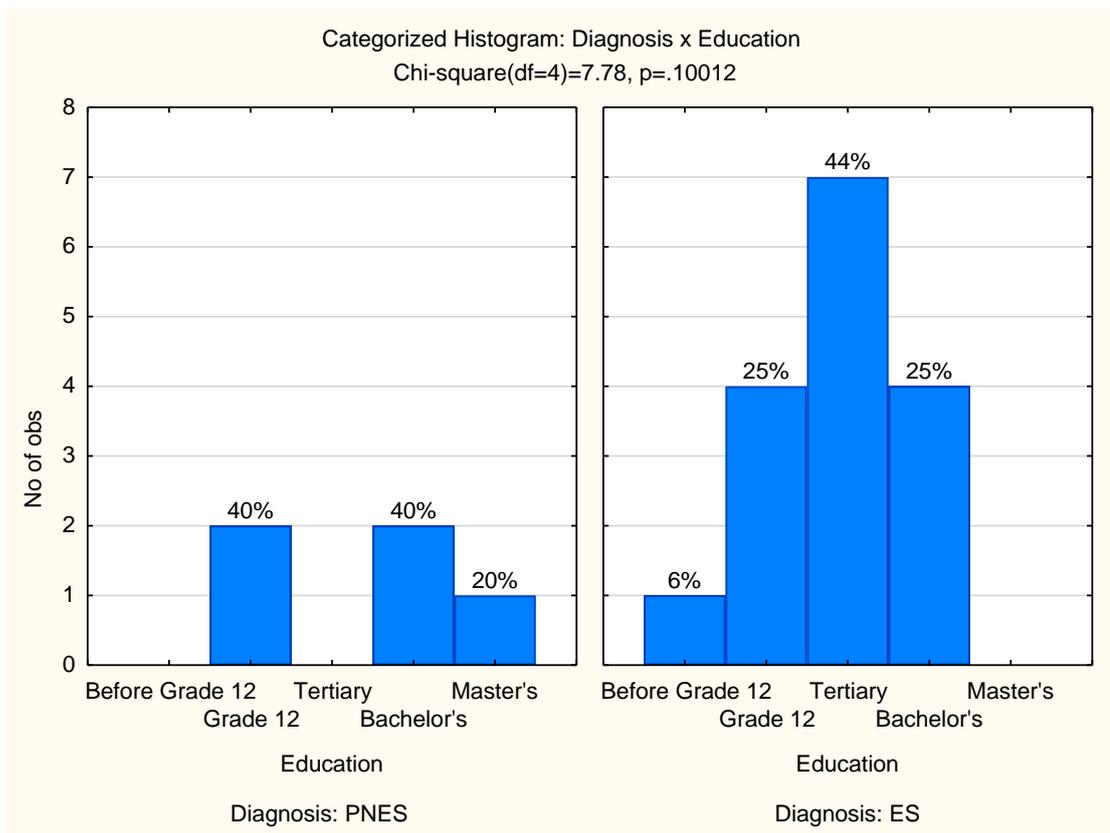
Figure 10. Education level distribution for the PNES group and the ES group.

Average age of seizure commencement for the PNES group was 31 years (SD=13; *Figure 11*), and 17 years (SD=14) for the ES group (*Figure 12*). The participants in the "Other" group reported age of seizure commencement as 19, 78 and "Don't Know".
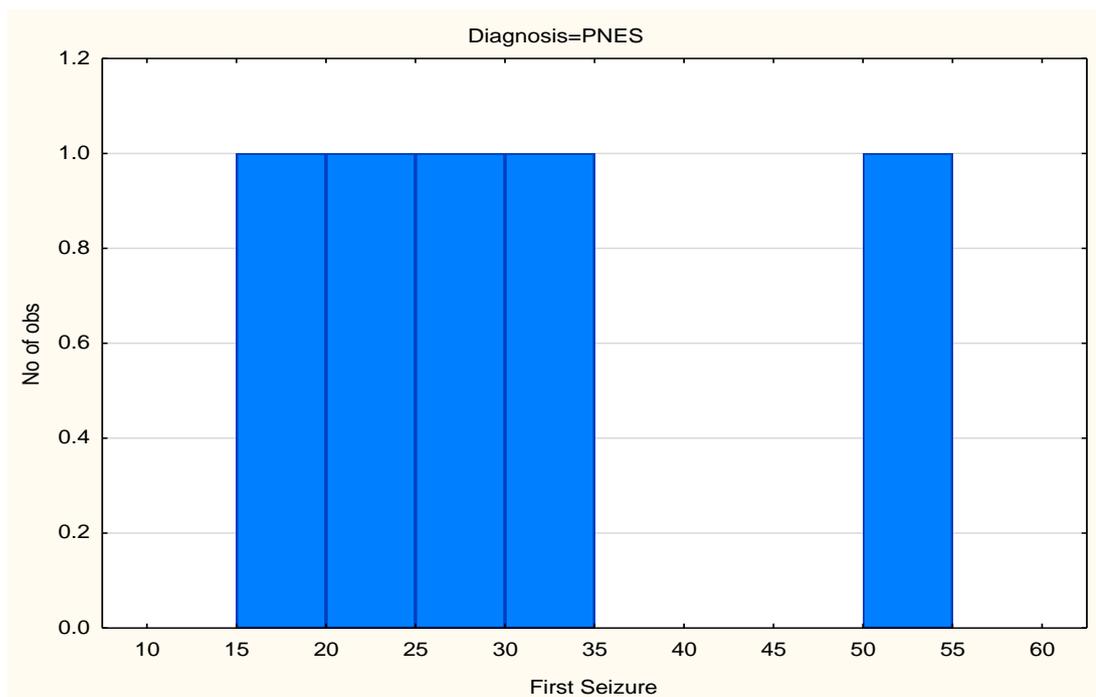
Figure 11. Age at first seizure distribution for PNES group.
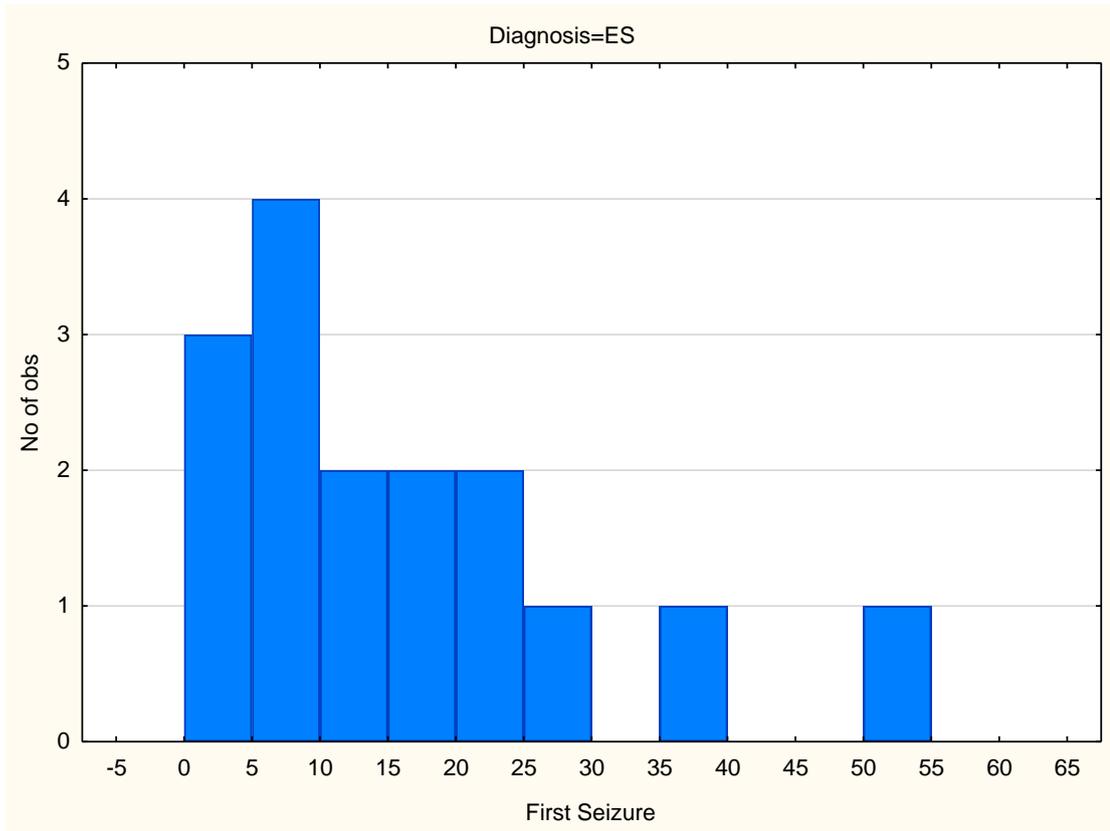
Figure 12. Distribution of age at first seizure in the ES group.

Hence, on average the time elapsed between seizure commencement and coming to the clinic for the vEEG was 3.6 years (SD=3.9) for the PNES group and 16.5 years (SD=13.4) for the ES group. One of the participants in the "Other" group could not tell when their seizures started and the other two had to wait less than a year and 3 years, respectively.

Average monthly seizure number for the PNES group was 18 seizures (SD=24), and 3 seizures (SD=4) for the ES group (*Figure 13* and *Figure 14*). The participants in the "Other" group experienced zero and two seizures with one participant not being able to tell.
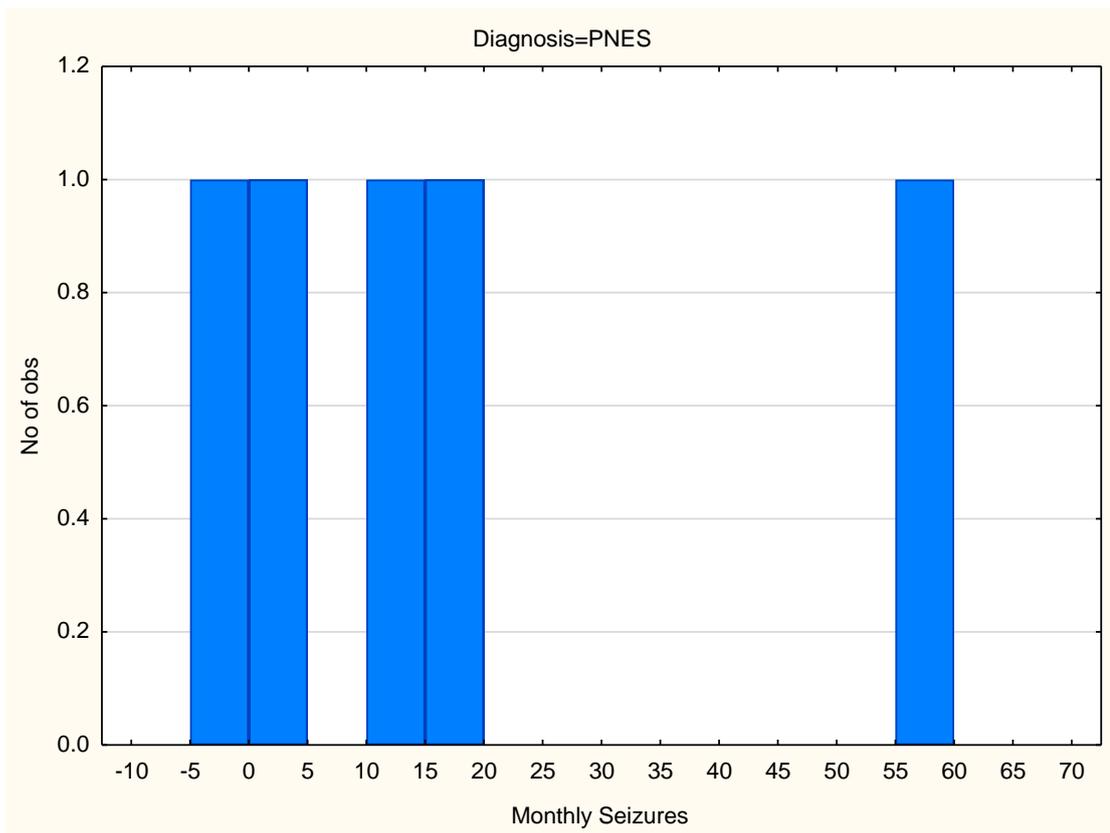
Figure 13. Monthly seizure distribution for the PNES group.
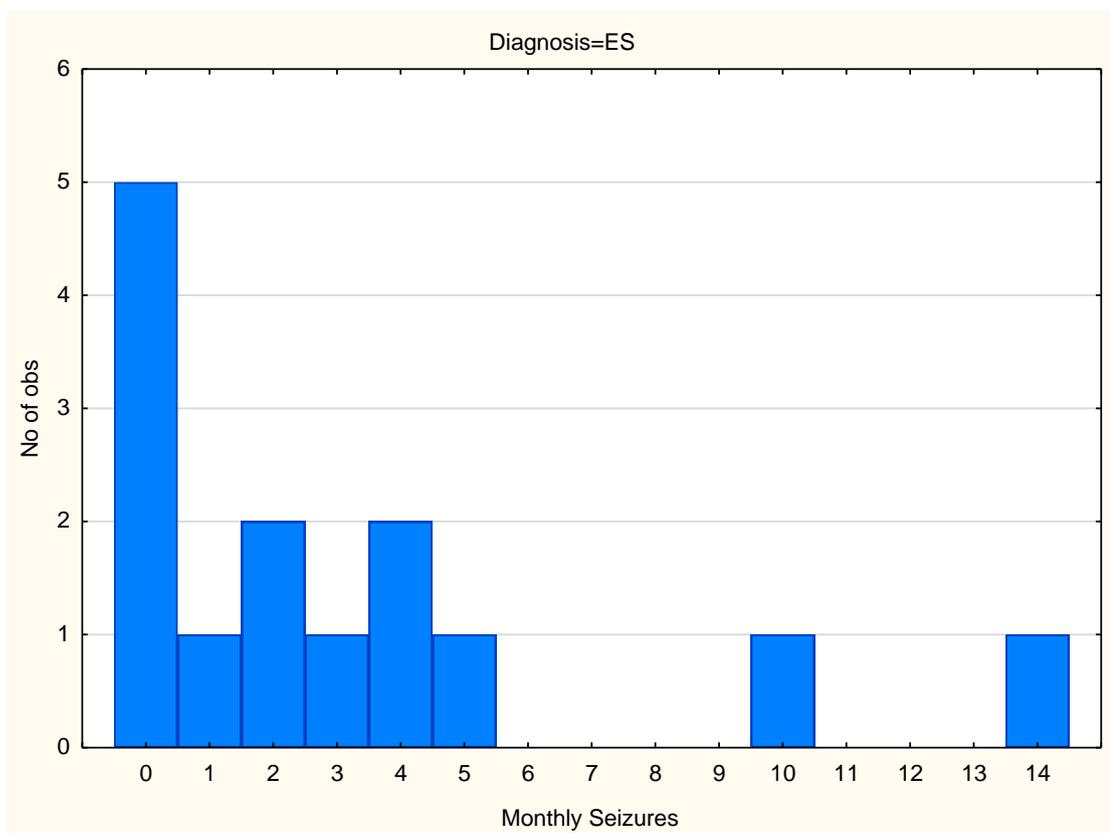
Figure 14. Monthly seizure distribution for the ES group.

5.2.2 Comparative statistics.

The PNES group was significantly more male (p=0.02), and experienced significantly more monthly seizures (p=0.03) when compared to the ES group (Table 1 and Table 2).

Table 1

ANOVA of PNES, ES and ES+Other group age, first seizure and monthly seizure frequencies.

| | Group | | | | | | Group | | | | | |
| | PNES | | ES | | | | PNES | | ES + Other | | | |
	M	SD	M	SD	F	p	M	SD	M	SD	F	p
Age	34.80	16.63	33.44	11.82	0.04	0.84	34.80	16.63	35.37	15.19	0.01	0.94
First Seizure	31.20	13.37	16.91	13.90	4.09	0.06	31.20	13.37	20.42	19.42	1.34	0.26
Monthly Seizures	**18.40**	**24.44**	**3.21**	**4.17**	**5.52**	**0.03**	**18.40**	**24.44**	**2.94**	**3.97**	**6.59**	**0.02**

This was also the case once the Other group was combined with the ES group and compared to the PNES group (Table 1and Table 2). Interestingly, while the significance with regards to sex did not change (p=0.02), significance with regards to average monthly seizures increased more dramatically (p=0.02).

Table 2

Demographic Characteristics of the PNES, ES and ES+Other groups.

| | | | | | | | Group | | | | | |
| | PNES | | ES | | | | PNES | | ES + Other | | | |
	N	%	N	%	χ^2	p	N	%	N	%	χ^2	p
Gender					**5.73**	**0.02**					**5.47**	**0.02**
Male	5	100.00	8	50.00			5	100.00	10	52.63		
Female	0	0.00	8	50.00			0	0.00	9	47.37		
Population Group					0.56	0.76					0.49	0.78
White	4	80.00	12	75.00			4	80.00	14	73.68		
Brown/coloured	1	20.00	3	18.75			1	20.00	4	21.05		
Black African	0	0.00	1	6.25			0	0.00	1	5.26		
Language					3.73	0.29					3.62	0.31
Afrikaans	1	20.00	9	56.25			1	20.00	11	57.89		
English	3	60.00	3	18.75			3	60.00	4	21.05		
English & Afrikaans	1	20.00	3	18.75			1	20.00	3	15.79		
English & German	0	0.00	1	6.25			0	0.00	1	5.26		

No significant differences in terms of age (p=0.84), population group (p=0.76), language (p=0.29), education (p=0.10), and age at first seizure (p=0.06) were found. Once the PNES group was compared to the combined group the following variables still remained non-significant: age (p=0.94), population group (p=0.49), language (p=0.31), education (p=0.13), and age at first seizure (p=0.26).

5.3 NEO-FFI-3

5.3.1 Reliability analysis.

To this researcher's knowledge, NEO-FFI-3 has not yet been used for research purposes with the PNES population, unlike the NEO-PI-R (Cragar et al., 2005; Ekanayake et al., 2017). While the English version of NEO-FFI-3 has been widely validated (McCrae & Costa, 2010), English is only the fourth most spoken language in South Africa (Statistics South Africa, 2012). Hence, a reliability analysis was considered not to be amiss here (Table 3). As is evident in Table 3 the internal consistency Cronbach's alpha (95% CI) for the Neuroticism scale was 0.87, Extraversion scale – 0.77, Openness to Experience scale– 0.73, Agreeableness scale – 0.86, and Conscientiousness scale – 0.86. Bland and Altman (1997) suggest that alpha values of 0.7 to 0.8 are adequate for research purposes, hence, as evident from above, all scales showed good reliability.

Table 3
Reliability analysis for NEO-FFI-3

Instrument	M	SD	α
NEO-FFI-3			
Neuroticism	25.21	10.10	0.87
Extraversion	30.17	7.03	0.77
Openness to Experience	29.46	6.90	0.73
Agreeableness	31.50	8.96	0.86
Conscientiousness	33.00	7.97	0.86

5.3.2 Descriptive statistics.

Average T-scores for the PNES, ES and combined groups on the NEO scales Neuroticism, Extraversion, Openness to Experience, Agreeableness and Conscientiousness are presented in Table 4 (all T-scores were calculated based on gender norms). On the Neuroticism scale on average the PNES group scored in the 60th percentile (SD=14), indicating a high score and the ES group scored in the 55th percentile (SD=13), indicating an average score. The participants in the "Other" group scored in the 75th (very high), 44th (Low), and 51st (Average) percentiles on the Neuroticism scale, respectively. On the Extraversion scale the PNES group on average scored in the 58th percentile (SD=13), indicating a high score and the ES group scored in the 53rd percentile (SD=12), indicating an average score. The participants in the "Other" group scored in the 53rd (Average), 46th (Average), 50th (Average) percentiles on the Extraversion scale, respectively. On the Openness to Experience scale the PNES group on average scored in the 56th percentile (SD=15), indicating a high score, and the ES group scored in the 51st percentile (SD=10), indicating an average score. The participants in the "Other" group scored in the 45th

(Average), 62nd (High), 53rd (Average) percentiles on the Openness to Experience scale, respectively. On the Agreeableness scale the PNES group on average scored in the 54th percentile, indicating an average score, and the ES group scored in the 50th percentile, also indicating an average score. The participants in the "Other" group scored in the 43rd (Low), 57th (High), 38th (Low) percentiles on the Agreeableness scale, respectively. On the Conscientiousness scale, the PNES group on average scored in the 48th percentile, indicating an average score and the ES group scored in the 52nd percentile also indicating an average score. The participants in the "Other" group scored in the 43rd (Low), 51st (Average) and 49th (Average) percentiles on the Conscientiousness scale, respectively.

Table 4

ANOVA of PNES, ES and ES+Other group scores on the NEO-FFI-3

| | Group | | | | | | Group | | | | | |
| | PNES | | ES | | | | PNES | | ES + Other | | | |
Instrument	M	SD	M	SD	F	p	M	SD	M	SD	F	p
NEO-FFI-3												
Neuroticism	60.00	14.40	55.06	13.09	0.52	0.48	60.00	14.40	55.32	13.14	0.49	0.49
Extraversion	58.20	12.72	53.06	11.78	0.70	0.41	58.20	12.72	52.53	10.90	1.01	0.33
Openness To Experience	56.40	15.21	50.69	9.49	1.04	0.32	56.40	15.21	51.11	9.17	1.00	0.33
Agreeableness	53.80	16.75	50.25	14.25	0.22	0.65	53.80	16.75	49.58	13.51	0.35	0.56
Conscientiousness	48.20	11.03	52.31	15.11	0.31	0.58	48.20	11.03	51.58	13.97	0.25	0.62

5.3.2 Comparative statistics.

No significant differences were found neither between the PNES and ES groups nor the PNES and the combined group on any of the NEO-FFI-3 scales (Table 4).

5.4 IBQ

5.4.1 Descriptive statistics.

While the original IBQ consists of 62 items, due to a clerical error only the first 36 items were used for data collection in this study. While this makes it impossible to use the IBQ subscales mentioned earlier, Pilowsky (1993) has suggested that the IBQ is also useful as an item pool. Furthermore, there has been a considerable number of studies who have used various shortened versions of the questionnaire. For example, Prior and Bond (2014) recently validated a 31 item version of IBQ on chronic illness patients, Main and Waddell (1987) a 33 item version on chronic back pain patients, and an early IBQ version of 52 items has been used a number of times on various populations (Pilowsky, Chapman, & Bonica, 1977; Pilowsky & Spence, 1975, 1976). Importantly, in an earlier 52-item version of the IBQ only

30 of them loaded onto a subscale and only 40 out of the 62 items in the newest version load onto one of the seven subscales, other items intended to provide information about the patient (Pilowsky, Spence, Cobb, & Katsikitis, 1984). Hence, this study will use the retained 36 IBQ items as an item pool.

All data for the PNES, ES and ES+Other groups on the IBQ items is presented in Table 5. The descriptive statistics results for the PNES and ES groups are presented in greater detail below.

5.4.1.1 General Hypochondriasis.

Seven out of the total nine items on the General Hypochondriasis subscale were used in the present study. The PNES group tended to say "Yes" more to the items IBQ30 "Do you ever have silly thoughts about your health which you can't get out of your mind, no matter how hard you try?" ("Yes" PNES 60% > 18,8% ES) and IBQ32 "Are you upset by the way people take your illness?" ("Yes" PNES 20% > 12,5% ES) when compared to the ES group. The ES group answered "Yes" to items IBQ20 "Are you more sensitive to pain than other people?" ("Yes" ES 31,3% > 0% PNES), IBQ21 "Are you afraid of illness?" ("Yes" ES 37,5% > 20% PNES); IBQ24 "Do you think that you worry about your health more than most people?" ("Yes" ES 31,3% > 20% PNES) and IBQ29 "Do you find that you get jealous of other people's good health?" ("Yes" ES 18,8% > 0% PNES). Both groups answered "Yes" similarly often to IBQ9 "If you feel ill and someone tells you that you are looking better, do you become annoyed?" ("Yes" PNES 20% > 20% ES).

5.4.1.2 Disease Conviction

Five out of six total items from the Disease Conviction subscale were included in this study. PNES group scored higher in terms of three of these - IBQ2 "Do you think there is something seriously wrong with your body?" ("Yes" PNES 40% > 25% ES), IBQ3 "Does your illness interfere with your life a great deal?" ("Yes" PNES 80% > 56,3% ES) and IBQ35 "Are you sleeping well?" (reverse scored; "No" PNES 80% > 37,5% ES), with the ES group scoring higher in terms of item IBQ10 "Do you find that you are often aware of various things happening in your body?" ("Yes" ES 68,8% > 60% PNES); and both groups scoring similarly in terms of item IBQ7 "If the doctor told you that he could find nothing wrong with you would you believe him?" (reverse scored, "No" PNES 60%=60% ES).

5.4.1.3 Psychological versus Somatic Perceptions of Illness.

Two out of five total items on the Psychological versus Somatic perceptions of illness subscale were included in the present study. The PNES group answered "Yes" to item IBQ11

"Do you ever think of your illness as a punishment for something you have done wrong in the past?" more often than the ES group ("Yes" PNES 40% > 18,8% ES) and the ES group answered "No" more often to item IBQ16 "Are you bothered by many pains and aches?" (reverse scored; "No" ES 62,5% > 20% PNES).

5.4.1.4 Affective Inhibition

Two out of the total five items on the Affective Inhibition scale were used in the current study. The PNES group scored higher on the item IBQ36 "When you are angry do you tend to bottle up your feelings?" ("Yes" PNES 80% > 43,8% ES) and both groups scored similarly on item IBQ22 "Can you express your personal feelings easily to other people?" (reverse scored; "No" ES 25% > 20% PNES).

5.4.1.5 Affective Disturbance

Two out of the total five items on the Affective Disturbance subscale were used in the present study. The ES group scored higher on item IBQ18 "Do you find that you get anxious easily?" ("Yes" ES 68,8% > 60% PNES) and both groups answered "Yes" similarly often to item IBQ12 "Do you have trouble with your nerves?" ("Yes" ES 43,8% > 40% PNES).

5.4.1.6 Denial.

Two out of five total items from the Denial of life stresses was used in the present study – IBQ27 "Except for your illness, do you have any problems in your life?" (reverse scored), with the ES group tending to answer "No" more often than the PNES one ("No" ES 75% > 40% PNES) and IBQ31 "Do you have any financial problems?" (reverse scored) with the ES group answering "No" more often ("No" ES 81,3% > 60% PNES).

5.4.1.7 Irritability.

Two out of four total items from the Irritability subscale were used in the present study. The PNES group scored higher in terms of item IBQ17 "Does your illness affect the way you get along with your family or friends a great deal?" ("Yes" PNES 40% > 25% ES) when compared to ES patients and both groups scored similarly in terms of item IBQ4 "Are you easiest to get along with when you are ill?" (reverse scored; "No" PNES 60% > 56.3% ES).

5.4.1.8 Other items.

The PNES group scored higher on items IBQ5 "Does your family have a history of illness?" ("Yes" PNES 60% > 50% ES); IBQ8 "Is it easy for you to forget about yourself and think about all sorts of other things?" ("Yes" PNES 80% > 62.5% ES); IBQ13 "If you feel ill

or worried, can you be easily cheered up by the doctor?" ("Yes" PNES 100% > 62.5% ES); IBQ19 "Do you know anybody who has had the same illness as you?" ("Yes" PNES 80% > 56.3% ES); IBQ23 "Do people feel sorry for you when you are ill?" ("Yes" PNES 80% > 56.3% ES); IBQ25 "Do you find that your illness affects your sexual relations?" ("Yes" PNES 60% > 25% ES); IBQ26 "Do you experience a lot of pain with your illness?" ("Yes" PNES 100% > 31.3% ES); and IBQ33 "Is it hard for you to believe the doctor when he tells you there is nothing for you to worry about?" ("Yes" PNES 40% > 31.3% ES).

The ES group scored higher on items IBQ6 "Do you think you are more liable to illness than other people?" ("Yes" ES 37.5% > 0%); IBQ14 "Do you think that other people realize what it is like to be sick?" ("Yes" ES 56.3% > 20% PNES); and IBQ34 "Do you often worry about the possibility that you have got a serious illness?" ("Yes" ES 50% > 20% PNES).

Lastly, both groups scored somewhat similarly (within 5%) on items IBQ1 "Do you worry a lot about your health?" ("Yes" PNES - 60%; ES - 62,5%); IBQ15 "Does it upset you to talk to the doctor about your illness?" ("Yes" PNES - 20%; ES - 18,8%); and IBQ28 "Do you care whether or not people realize you are sick?" ("Yes" PNES - 20%; ES - 25%).

5.4.2 Comparative statistics

As evidenced by Table 5 the only item exhibiting a significant difference (p=0.01) between the PNES and ES groups was item IBQ26: "Do you experience a lot of pain with your illness?" All the participants in the PNES group answered "Yes" to this question while only 69% of participants did so in the ES group. For other items, no significant differences between the groups were found. Once the PNES group was compared to the combined group, item IBQ26 remained the only item demonstrating significant difference (p=0.01) between the groups.

Table 5

Answers to IBQ items 1-36 of PNES, ES and ES+Other groups

			Group						Group			
	PNES			ES				PNES			ES + Other	
Item	Yes	No	%	Yes	No	%	p	Yes	No	%	Yes	No	%	p

Item	Yes	No	%	Yes	No	%	p	Yes	No	%	Yes	No	%	p
General Hypochondriasis														
IBQ9. If you feel ill and someone tells you that you are looking better, do you become annoyed?	1		20.00	3		20.0	1.00	1		20.00	4		22.22	1.00
IBQ20. Are you more sensitive to pain than other people?	0		0.00	5		31.3	0.28	0		0.00	5		26.32	0.54
IBQ21. Are you afraid of illness?	1		20.00	6		37.5	0.62	1		20.00	7		36.84	0.63
IBQ24. Do you think that you worry about your health more than most people?	1		20.00	5		31.3	1.00	1		20.00	5		26.32	1.00
IBQ29. Do you find that you get jealous of other people's good health?	0		0.00	3		18.8	0.55	0		0.00	5		26.32	0.54
IBQ30. Do you ever have silly thoughts about your health which you can't get out of your mind, no matter how hard you try?	3		60.00	3		18.8	0.11	3		60.00	4		21.05	0.13
IBQ32. Are you upset by the way people take your illness?	1		20.00	2		12.5	1.00	1		20.00	3		15.79	1.00
Disease Conviction														
IBQ2. Do you think there is something seriously wrong with your body?	2		40.00	4		25.0	0.60	2		40.00	5		26.32	0.61
IBQ3. Does your illness interfere with your life a great deal?	4		80.00	9		56.3	0.61	4		80.00	11		57.89	0.61
IBQ7. If the doctor told you that he could find nothing wrong with you would		3	60.00		9	60.0	1.00		3	60.00		9	50.00	1.00
IBQ10. Do you find that you are often aware of various things happening in your body?	3		60.00	11		68.8	1.00	3		60.00	13		68.42	1.00
IBQ35. Are you sleeping well? (R)		4	80.00		6	37.5	0.15		4	80.00		7	36.84	0.14
Psychological vs Somatic Perception of Illness														
IBQ11. Do you ever think of your illness as a punishment for something you have done wrong in the past?	2		40.00	3		18.8	0.55	2		40.00	3		15.79	0.27
IBQ16. Are you bothered by many pains and aches? (R)		1	20.00		10	62.5	0.15		1	20.00		13	68.42	0.12
Affective Inhibition														
IBQ22. Can you express your personal feelings easily to other people? (R)		1	20.00		4	25.0	1.00		1	20.00		5	26.32	1.00
IBQ36. When you are angry do you tend to bottle up your feelings?	4		80.00	7		43.8	0.31	4		80.00	9		47.37	0.33

Table 5 Continued.

| | Group | | | | | | | Group | | | | | | |
| | PNES | | | ES | | | | PNES | | | ES + Other | | | |
Item	Yes	No	%	Yes	No	%	p	Yes	No	%	Yes	No	%	p
Affective Disturbance														
IBQ12. Do you have trouble with your nerves?	2		40.00	7		43.8	1.00	2		40.00	8		42.11	1.00
IBQ18. Do you find that you get anxious easily?	1		20.00	8		50.0	0.34	1		20.00	10		52.63	0.33
Denial														
IBQ27. Except for your illness, do you have any problems in your life? (R)		2	40.00		12	75.0	0.28		2	40.00		13	68.42	0.33
IBQ31. Do you have any financial problems? (R)		3	60.00		13	81.3	0.55		3	60.00		14	73.68	0.61
Irritability														
IBQ4. Are you easiest to get along with when you are ill? (R)		3	60.00		9	56.3	1.00		3	60.00		10	52.63	1.00
IBQ17. Does your illness affect the way you get along with your family or friends a great deal?	2		40.00	4		25.0	0.60	2		40.00	6		31.58	1.00
Other Items														
IBQ1. Do you worry a lot about your health?	3		60.00	10		62.5	1.00	3		60.00	12		63.16	1.00
IBQ5. Does your family have a history of illness?	3		60.00	8		50.0	1.00	3		60.00	10		52.63	1.00
IBQ6. Do you think you are more liable to illness than other people?	0		0.00	6		37.5	0.26	0		0.00	7		36.84	0.27
IBQ8. Is it easy for you to forget about yourself and think about all sorts of other things?	4		80.00	10		62.5	0.62	4		80.00	13		68.42	1.00
IBQ13. If you feel ill or worried, can you be easily cheered up by the doctor?	4		100.00	10		62.5	0.27	4		100.00	13		68.42	0.54
IBQ14. Do you think that other people realize what it is like to be sick?	1		20.00	9		56.3	0.31	1		20.00	11		57.89	0.32
IBQ15. Does it upset you to talk to the doctor about your illness?	1		20.00	3		18.8	1.00	1		20.00	4		21.05	1.00
IBQ19. Do you know anybody who has had the same illness as you?	4		80.00	9		56.3	0.61	4		80.00	10		52.63	0.36
IBQ23. Do people feel sorry for you when you are ill?	4		80.00	9		56.3	0.61	4		80.00	12		63.16	0.63
IBQ25. Do you find that your illness affects your sexual relations?	3		60.00	4		25.0	0.28	3		60.00	6		31.58	0.33
IBQ26. Do you experience a lot of pain with your illness?	**5**		**100.00**	**5**		**31.3**	**0.01**	**5**		**100.00**	**6**		**31.58**	**0.01**
IBQ28. Do you care whether or not people realize you are sick?	1		20.00	4		25.0	1.00	1		20.00	7		36.84	0.63
IBQ33. Is it hard for you to believe the doctor when he tells you there is nothing for you to worry about?	2		40.00	5		31.3	1.00	2		40.00	6		31.58	1.00
IBQ34. Do you often worry about the possibility that you have got a serious illness?	1		20.00	8		50.0	0.34	1		20.00	10		52.63	0.33

5.5 BAI-PC

5.5.1 Reliability analysis.

Similarly to the NEO-FFI-3, there is no published research of the BAI-PC being used with the PNES or South African populations, hence a reliability analysis was performed (Table 6). As can be seen in Table 6, the Cronbach's alpha was found to be 0.89, indicating excellent internal consistency (Bland & Altman, 1997).

Table 6
Reliability Analysis for BAI-PC

Instrument	M	SD	α
BAI-PC	7.21	5.80	0.89

5.5.2 Descriptive statistics.

The group average of PNES for BAI-PC was 12 points (SD=6.4), and 5.81 points (SD=5.23) for the ES group (Table 7). It is suggested that a BAI-PC cut-off score of 5 and above is used to screen for anxiety, depression and PTSD symptoms (Mori et al., 2003). Thus the results suggest that both groups tend to exhibit symptoms of anxiety, depression and PTSD.

Table 7
ANOVA of PNES, ES and ES+Other group scores on the BAI-PC

| | Group | | | | | | Group | | | | | |
| | PNES | | ES | | | | PNES | | ES + Other | | | |
Instrument	M	SD	M	SD	F	p	M	SD	M	SD	F	p
BAI-PC	12.00	6.40	5.81	5.23	4.82	0.04	12.00	6.40	5.95	5.08	5.07	0.03

5.5.3 Comparative statistics.

ANOVA results for the BAI-PC are presented in Table 7. BAI-PC scores were significantly higher (p=0.04) among the participants with PNES when compared to those with epilepsy. As a result, a ROC curve was plotted in order to determine the optimal cut-off score for BAI-PC in diagnosing PNES (*Figure 15*). This score was determined to be 11 and it could differentiate PNES from ES with 80% sensitivity and 88% specificity.
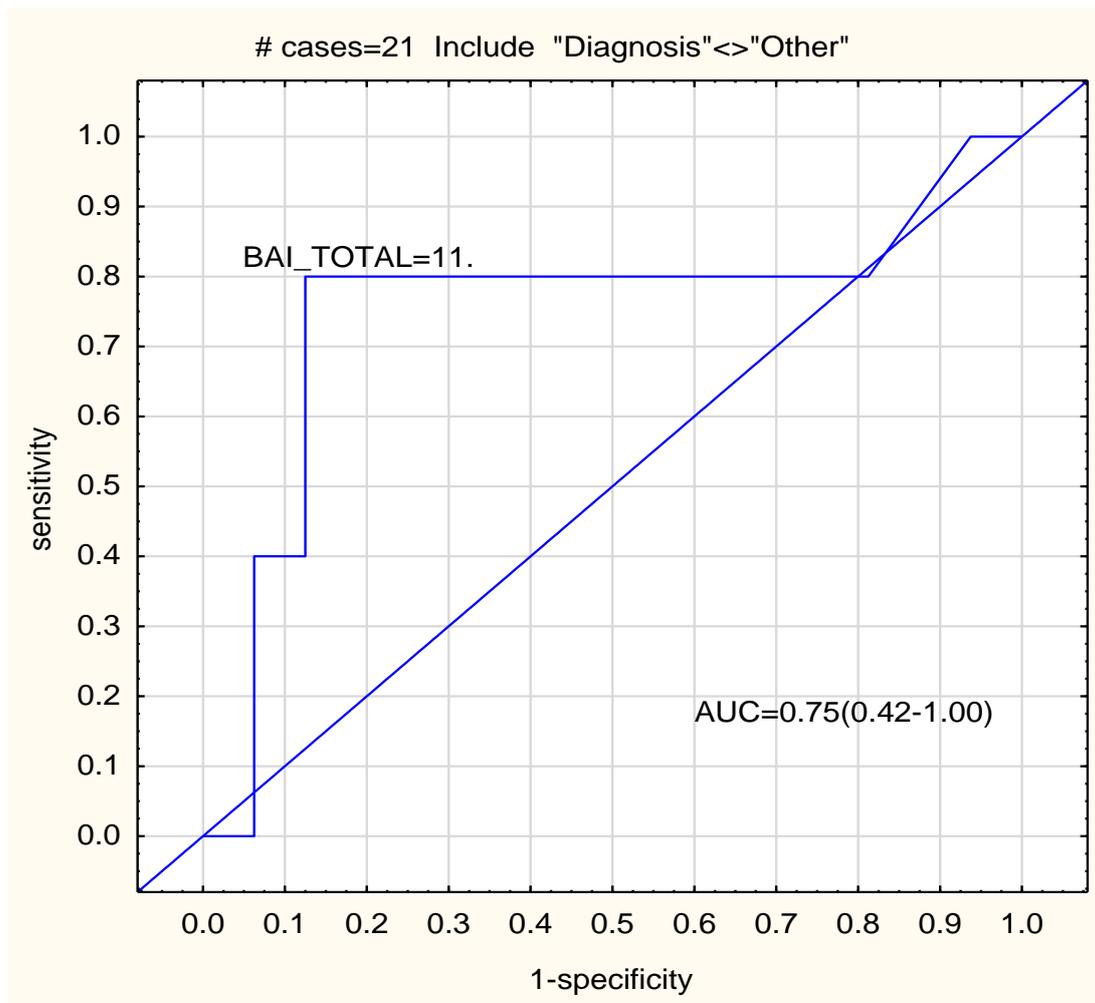
Figure 15. ROC curve and optimal cut-off score for differentiating PNES from ES.

The process was repeated after combining the ES and oNES participants into one group and comparing it to the PNES group. The PNES BAI-PC score remained significantly higher (p=0.03) when compared to the ES and oNES patients combined group. However, when the ROC curve was plotted the optimal cut-off score rose to 12. Nonetheless, it could differentiate between PNES and ES or oNES with 80% sensitivity and 89% specificity (Figure 16).
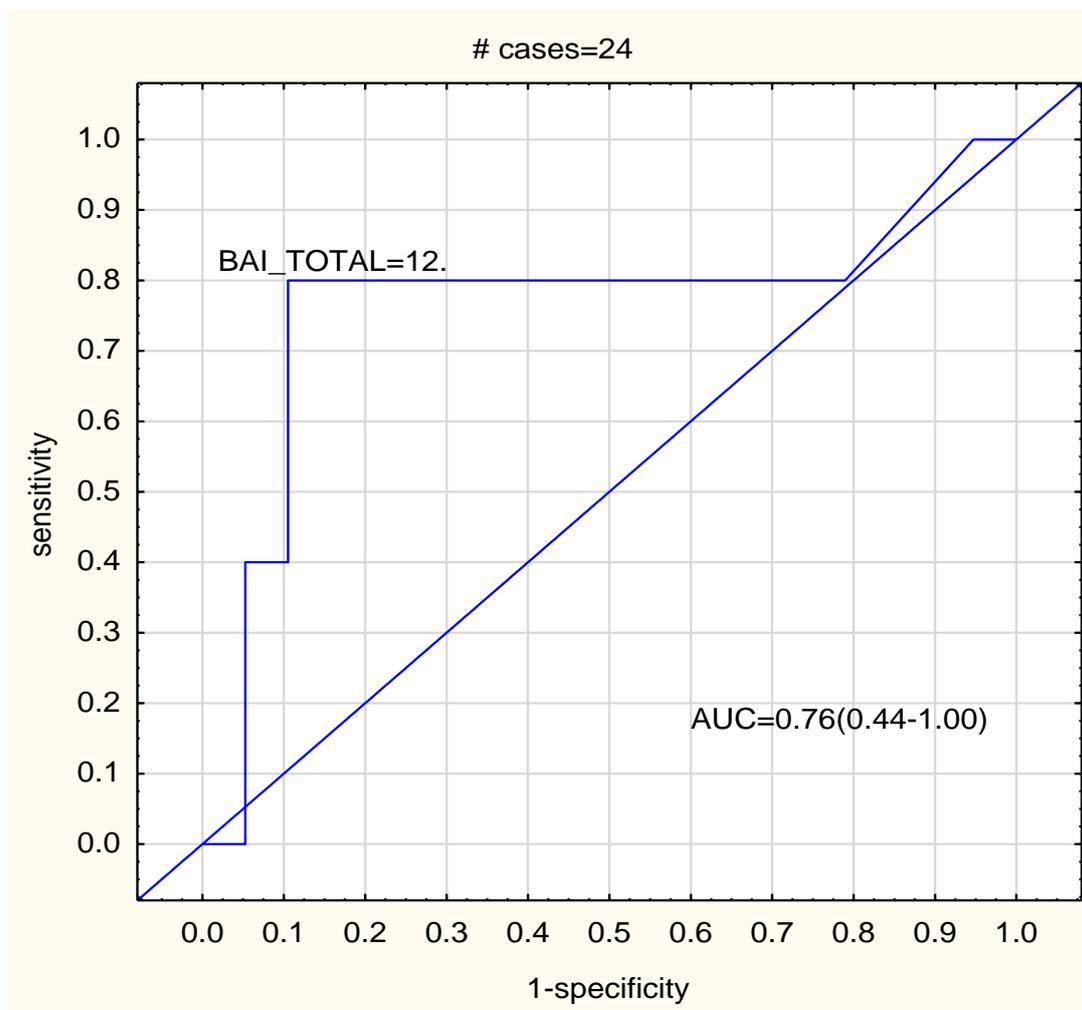
Figure 16. ROC curve and optimal cut-off score for differentiating PNES from ES and oNES.

5.6 Chapter Summary

Both NEO-FFI-3 (see Table 3) and the BAI-PC (see Table 6) showed good reliability. The PNES group was found to be significantly more male (Table 2) and to experience significantly more monthly seizures (Table 1), when comparing PNES and ES, and PNES and the combined ES and oNES group. No significant differences between groups were found in terms of age, population group, language, education, and age at first seizure (Tables 1 and 2). No significant differences were found between the groups on any of the NEO-FFI-3 subscales (Table 4), however, tendencies were reported. In terms of the IBQ, only item IBQ26 exhibited a significant difference, with PNES tending to answer "Yes" more often to the question "Do you experience a lot of pain with your illness?" when compared to the ES and the combined group (Table 5). Full descriptive statistics for group answers were also presented (Table 5). The PNES group tended to score significantly higher on the BAI-PC both than the ES and the combined group (Table 7). A cut-off point of 12 was found to be optimal in predicting PNES using the BAI-PC in our seizure sample (*Figure 16*).

Chapter 6 Discussion and Conclusion

6.1 Introduction

This chapter discusses the results presented in chapter 5 in terms of the broader realm of PNES and ES research and considers how they compare to other similar research. Additionally, the chapter deliberates on the possible limitations of the study as well as its strength and significance of the results. Lastly, concluding remarks on the project are given.

6.2 Measures

6.2.1 Demographic and Seizure-Related Questionnaire Results

International research suggests that in an epilepsy clinic the prevalence of epilepsy is 17-49%, PNES is 20-42% and physiologic events other than epilepsy is 13% (Alsaadi & Marquez, 2005; Asadi-Pooya et al., 2014; Martin et al., 2003; Noe et al., 2012). While oNES usually comprise a small number of cases (Thompson, Osorio, & Hunter, 2005; Vossler, 1995), these cases may nevertheless pose a difficulty when trying to differentiating between them and PNES, and even epilepsy if vEEG is not available. In fact, one study found that oNES were diagnosed correctly without the use of vEEG only between 60-91.7% of the times (Risti et al., 2017). However, compared to studies investigating factors differentiating between PNES and ES, those that include oNES are basically non-existent.

There are no South African studies that present the ratio of PNES, ES and oNES in an epilepsy clinic. Furthermore, as of yet there is only one South African epidemiological study conducted in a private clinic in Johannesburg (Anderson et al., 2017), where a ratio of 1:1 (50%/50%) was found after discounting comorbid PNES and ES and no information was given about individuals with other types of non-epileptic seizures. In the case of the present study, the ratio between the PNES and ES groups in the present study was 5:16 or 24% and 76% respectively if one was to discount patients with other diagnoses, suggesting a lower proportion of PNES than in the abovementioned study.

In the South African epidemiological study mentioned above the sample consisted of 27% males and 73% females in the PNES group (Anderson et al., 2017). Similarly, a South African convenient sampling study, where participants were referred to the researcher by the same two clinics as approached in this study, collected a PNES sample consisting of 23% males and 77% females (Cronje & Pretorius, 2013). The PNES sample in our study consisted solely of males, hence, literature would suggest that while the current ES group approximated previous South African findings, the PNES group constitution was more male than in

previous research. In line with this is the finding that the difference in sex was significant between the two groups, with the PNES group having significantly more males in it and suggesting the possibility that the current sample may not be fully representative of the PNES population. However, the fact that the aforementioned epidemiological study by Anderson et al. (2017) was conducted in a private healthcare setting may also suggest a non-representative sample in a country where the majority of the population does not have access to private healthcare (Pretorius, 2016).

The mean age of 35 in this study's PNES group seems to be right on point when compared to other South African studies suggesting a mean of 33-35 (Anderson et al., 2017; Pretorius & Cronje, 2015). Furthermore, in line with international studies (Cragar et al., 2002), both the abovementioned study by Anderson et al. (2017) and the present study results suggest that no significant age differences are found between the groups, suggesting that age may not be a good differentiating factor for PNES. The reported age of first seizure becomes relevant here. International research indicates that PNES patients tend to have an older age of seizure onset (Cragar et al., 2002) when compared to ES patients and this difference has been shown to be significant (Tojek et al., 2000) as well as has been used successfully in screening for PNES (Syed et al., 2009). While there were no significant differences between the groups in terms of age at first seizure in the present study, $p=0.06$ is close to significance when one considers the small sample of PNES participants and the concomitant higher probability of Type 2 error (Field, 2009) and thus may warrant further investigation where a bigger sample can be obtained. However, it is of interest that once the ES group was combined with the Other group for comparative analysis, the significance of the difference lowered considerably to $p= 0.26$. This suggests that even if a bigger sample is obtained and PNES and ES groups are found to differ significantly on age at first seizure, while being helpful in distinguishing between PNES and ES, presence of oNES may make such distinction from PNES harder.

Anderson et al. (2017) reported that 81% of their PNES sample was White and similarly, in the present sample the PNES group consisted of 80% White participants. Both the present study and the aforementioned South African epidemiological study (Anderson et al., 2017) used data from private clinics, which may explain the prevalence of White participants in a country where they are a minority (Statistics South Africa, 2012). Access to private healthcare in South Africa tends to be reserved for the wealthier and hence remains unaffordable to the majority of the population (Pretorius, 2016). Lastly, no significant difference was found between the study groups in terms of population group in our study. This may suggest that population group is a poor PNES differentiating factor in South Africa,

however, more investigation needs to be made at government hospitals, which are more accessible to the broader South African population (Pretorius, 2016).

While no epidemiological data exists in terms of PNES patients' home languages in South Africa, the Pretorius and Cronje (2015) study may give an indication. Pretorius and Cronje (2015) reported that 50% of their PNES sample was Afrikaans speaking and 50% English speaking. Similarly, in the present study, the Afrikaans language appeared to predominate (50%-Afrikaans, 17% - Afrikaans and English, 29% - English, and 4% - English and German). However, the 2011 Census (Statistics South Africa, 2012) shows that three of the most spoken languages in the Western cape are Afrikaans (49.7%), IsiXhosa (24.7%) and English (20.2%), hence, while Afrikaans and English – two out of the three most spoken languages in the Western Cape were represented in the present study, there were no IsiXhosa participants. Furthermore, no significant difference in group home language distribution was found. However, before suggesting that language may not be a useful differentiating factor for PNES in South Africa, the study should be replicated on a larger sample.

The only South African study that has recorded education level in its sample of PNES participants (Pretorius & Cronje, 2015) reported that "Before Grade 12" was the highest educational level for 50% of their PNES sample, "Grade 12" for 23% , a tertiary diploma for 9% and a degree at university for 14%. In the present study 60% of the PNES participants had a university degree and 40% finished Grade 12, which suggests the current PNES sample to be more educated compared to the aforementioned study. Furthermore, no significant differences between the groups in terms of educational level were found in the present study. On the other hand, international studies paint a contrasting picture. While some suggest that the PNES population tends to be less educated (Bodde et al., 2007; Bodde, Brooks, Baker, Boon, Hendriksen, & Aldenkamp, 2009), others maintain that the two groups are usually of a similar educational level (Cragar et al., 2002). However, since there is no epidemiological data in South Africa on the educational level of individuals with PNES, it is impossible to judge whether the sample is representative on this variable.

Pretorius and Cronje (2015) reported that 54% of their PNES participants had to wait less than a year to get their diagnosis, while 14% waited 1-2 years, 9% waited 2-3 years, 9% waited 3-4 years, and 14% waited more than 7 years. While the present study did not pose such a question, the age of seizure commencement is an indication and suggests that on average patients with PNES had to wait multiple years (M=3.6) until getting the correct diagnosis. However, both studies would suggest that on average individuals with PNES who have easy access to a hospital with vEEG in South Africa have to wait shorter for diagnosis than the internationally suggested average of 7-10 years (Benbadis, 2009). Nonetheless, this

number may change considerably once data from government hospitals in South Africa becomes available.

A number of international research studies report a tendency for higher seizure frequency among PNES patients when compared to those with ES (Alsaadi & Shahrour, 2014; Dimaro et al., 2015). Furthermore, Syed et al. (2009) found that monthly seizure frequency was a useful variable in predicting PNES. Similarly, the present study found that PNES patients had significantly more monthly seizures than those with ES. Pretorius and Cronje (2015) in their study also suggest that PNES patients have a high number of seizures with the majority of their sample (50%) reporting seizures at least once a day. Interestingly, when the PNES group was compared to the ES and Other combined group the significance of the difference only increased (p=0.02), suggesting that knowing a patient's seizure frequency may be a valuable factor in differentiating PNES from ES as well as oNES.

The present study sought to replicate the circumstances in which a patient with seizures would visit a clinic to find out their diagnosis. This meant that at the moment of questionnaire administration both the researcher, the participant and the neurologist were blind to the diagnosis. While such an approach works great to ensure external validity, it inevitably minimises the control the researcher has over their ultimate sample. Hence, the apparent mismatch of the current sample profile in terms of some of the demographic variables with that of the earlier mentioned South African epidemiological study may be explained in a few ways. Firstly, the sample in the present study comprises entirely of adults, which would discount any of those below 18 years of age who have PNES thus possibly resulting in a lower number of total PNES cases as well as thwarting the gender balance. Interestingly, when speaking with one of the head nurses in Constantiaberg Medi-Clinic, she mentioned that a lot of the PNES cases she sees are teenage girls, who would have been excluded in this study (personal communication, 2017). Secondly, the data collection being done by a single person inevitably meant that in a six-month data collection period there will be some days that will be spent away from the clinic, thus potentially missing PNES patients that could have significantly changed the characteristics of the PNES group.

6.2.2 NEO-FFI-3 Results

While there is no published data on South African PNES patients' personality profiles, international research might be an indication. A recent study by Ekanayakea et al. (2017) found that their PNES group tended to score high on Neuroticism, and average on all other scales. Furthermore, the scores for Neuroticism were significantly higher than that of healthy controls. Similarly, Cragar et al. (2005) found that PNES participants in their study on average scored high on Neuroticism, which was significantly higher than the ES group,

and scored average across other domains. The ES participants in the same sample scored average on all domains except for Conscientiousness where they scored low. While generally in the present study the ES group scored average on all the NEO domain scales, PNES group scored high on the Neuroticism, Extraversion and Openness to Experience scales, while scoring average on the Agreeableness and Conscientiousness scales.

According to McCrae and Costa (2010) the tendency PNES patients to score high on the Neuroticism scale in the present study would indicate individuals who are less emotionally stable and less well-adjusted, as well as more prone to experience negative affect such as fear, sadness, and guilt. Interestingly, the tendency to score high on the scale of Extraversion in the PNES group suggests individuals who also enjoy large groups and stimulation and are active and energetic (McCrae & Costa, 2010). Furthermore, scoring high on the Openness to Experience scale would suggest PNES participants having an active imagination, being attentive to inner feelings and experiencing emotion more keenly (McCrae & Costa, 2010). Lastly, the results indicate that participants with PNES exhibited average levels of agreeableness and conscientiousness. Nevertheless, no significant differences were found between the groups in terms of any of the NEO scales, neither when comparing PNES with ES, nor PNES with the combined group.

However, Cragar et al. (2005) went a step further and divided their PNES group into three clusters based on their scores on the NEO-PI-R: (1) very high neuroticism, low extraversion, low openness, high agreeableness, low conscientiousness; (2) average on all domains; and (3) very high neuroticism, average extraversion, low openness, low agreeableness, average conscientiousness. Hence, it is interesting to see the differences within the PNES group which focusing at averages may conceal. Such cluster analyses are considered to be especially useful when it comes to treatment and outcomes (Reuber, Pukrop, et al., 2004). While the present sample (*Figure 3*) is too small to do such cluster analyses, an example of such clustering are the PNES group's Agreeableness scores in the current study - while the mean T-score for the group indicates average Agreeableness, the individual scores are: 31 (very low), 41 (low), 64 (high), 64 (high), 69 (very high), thus even in such a small sample hinting at a clustering tendency.

6.2.3 IBQ Results

So far there has only been one study that has used the IBQ to investigate differences between ES and PNES patients. Stone, Binzer, and Sharpe (2004) found that their PNES group believed psychological factors as less important than somatic ones for their condition and denied life stresses significantly more often than epilepsy patients. While differences between the groups in terms of scales in the present study cannot be reported statistically, one

can investigate the individual items included in this study and their belonging to each of the subscales (refer to Table 5).

As is evident in Table 5, in terms of the Psychologic versus Somatic perceptions of illness scale, the PNES group tended to answer "Yes" to item IBQ11 "Do you ever think of your illness as a punishment for something you have done wrong in the past?" more often than the ES group, and the ES group tended to answer "No" more often to item IBQ16 "Are you bothered by many pains and aches?" (reverse scored – "No"), suggesting that both groups viewed psychological factors and somatic factors as similarly important in the case of the discussed two items. In terms of the Denial of life stresses bscale items, the ES group tended to answer "No" more often than the PNES group on items IBQ27 "Except for your illness, do you have any problems in your life?" (reverse scored – "No") and IBQ31 "Do you have any financial problems?" (reverse scored – "No"), suggesting a somewhat greater tendency for Denial of life stresses in the ES group when compared to PNES patients in the case of these items.

The General Hypochondriasis subscale (Table 5) found the PNES group saying "Yes" more to items IBQ30 "Do you ever have silly thoughts about your health which you can't get out of your mind, no matter how hard you try?" and IBQ32 "Are you upset by the way people take your illness?" when compared to the ES group. The ES group tended to answer "Yes" to items IBQ20 "Are you more sensitive to pain than other people?", IBQ21 "Are you afraid of illness?"; IBQ24 "Do you think that you worry about your health more than most people?" and IBQ29 "Do you find that you get jealous of other people's good health?". Lastly, both groups answered "Yes" similarly often to IBQ9 "If you feel ill and someone tells you that you are looking better, do you become annoyed?". Hence, the abovementioned results suggest a possibly greater tendency for General Hypochondriasis in ES patients when compared to those with PNES. The General Hypochondriasis scale measures a phobic preoccupation with one's health and the possibility of illness (Pilowsky, 1975), which, nonetheless involves some insight into the inappropriateness of these attitudes on the side of the patient (Pilowsky & Spence, 1983). Somewhat similarly to the present study, a few earlier studies found that ES patients tended to score higher on this subscale when compared to those with PNES, however, this difference did not prove to be significant. However, while also being a non-significant finding, another study (Tojek et al., 2000) measuring illness worry found that PNES patients actually tended to score higher than those with ES. Hence, further investigation into the significance of this difference needs to be made for more conclusive results on the South African PNES population.

With regards to the Disease Conviction subscale (Table 5), the PNES group scored higher in terms of items IBQ2 "Do you think there is something seriously wrong with your body?", IBQ3 "Does your illness interfere with your life a great deal?" and IBQ35 "Are you sleeping well?" (reverse scored – "No"), with the ES group scoring higher in terms of item IBQ10 "Do you find that you are often aware of various things happening in your body?", and both groups scoring similarly in terms of item IBQ7 "If the doctor told you that he could find nothing wrong with you would you believe him?" (reverse scored – "No"), appearing to suggest a greater Disease Conviction in the PNES group in terms of the described items. This would in turn indicate a greater tendency in the PNES group to be preoccupied with bodily symptoms to the point of rejecting medical reassurance of their health (Pilowsky, 1978) and a tendency for illness affirming behaviour (Waddell, Pilowsky, & Bond, 1989). Similarly, while, Stone, Binzer, and Sharpe (2004) did not find the difference to be significant, they reported that their PNES group exhibited greater Disease Conviction than the ES patients.

Interestingly, only one out of all the investigated IBQ items showed a significant difference between the groups – item IBQ26 "Do you experience a lot of pain with your illness?" (Table 5). While this item does not belong to any subscale on Pilowsky's IBQ, Prior and Bond (2010) performed exploratory factor analysis on the questionnaire using data from 675 participants, comprising 344 people from the community, 80 individuals with asthma, 95 with diabetes, 79 with chronic pain and 77 with chronic fatigue syndrome, and found item IBQ26 to load on a factor they called Affirmation of Illness. According to the authors, the Affirmation of Illness is a scale measuring patient endorsement of them having an illness and correlates highly (0.82 – 0.88) with the original Disease Conviction scale (Prior & Bond, 2010). Such a result is not surprising in the light of research consistently showing that individuals with PNES are often faced with the perception from healthcare providers that they are 'faking it' (Chudleigh et al., 2013; McMillan et al., 2014), which can raise the resistance to accept their diagnosis (Kanner, 2003). In line with these findings are the results from a recent study by Rawlings, Brown and Reuber (2017) on illness perceptions. Using the Brief IPQ the authors found that participants with PNES perceived their condition as having more severe consequences on their life, causing a higher number of symptoms, being associated with a higher negative emotional experience, as well as were more concerned, and considered the condition to be more threatening overall (Rawlings et al., 2017).

In the case of the Affective Inhibition scale (Table 5), the PNES group scored higher on the item IBQ36 "When you are angry do you tend to bottle up your feelings?" and both groups scored similarly on item IBQ22 "Can you express your personal feelings easily to other people?" (reverse scored – "No"), suggesting a possibly higher affective inhibition in

the PNES group when compared to those with ES. This would in turn suggest a greater tendency to struggle in expressing personal feelings to others, especially when they are negative (Pilowsky & Spence, 1983), which bears resemblance to alexithymia . While in another study (Stone, Binzer, et al., 2004) the finding was not significant, the authors reported that their PNES group tended to score higher on the Affective Inhibition scale. Similarly, while international findings suggest consistently elevated levels of alexithymia in the PNES population, the difference is not always found to be significant enough to warrant its use as a differentiator between PNES and ES (Bewley, Murphy, Mallows, & Baker, 2005; Brown et al., 2013; Myers et al., 2013; Tojek et al., 2000), warranting further research into this factor.

The Affective Disturbance scale items (Table 5) showed that the ES group scored higher on item IBQ18 "Do you find that you get anxious easily?" and both groups answered "Yes" similarly often to item IBQ12 "Do you have trouble with your nerves?", suggesting a possibly slightly greater tendency to feel anxiety and/or sadness in the ES group in terms of the above mentioned items (Pilowsky & Spence, 1983), unlike in the case of the discussed items in the study by Stone, Binzer, and Sharpe (2004) where the two groups scored the same on this subscale. This finding would also go against the BAI-PC findings in the present study (discussed below), which indicate a significantly higher prevalence of anxiety, depression and/or PTSD symptoms among the PNES participants when compared to those with ES. Furthermore, due to only two out of the total five scale items being used in this study, this finding must be interpreted preliminarily.

Lastly, concerning items on the Irritability scale (Table 5), the PNES group scored higher on item IBQ17 "Does your illness affect the way you get along with your family or friends a great deal?" when compared to ES patients, and both groups scored similarly in terms of item IBQ4 "Are you easiest to get along with when you are ill?" (reverse scored – "No"), suggesting a possibly greater tendency for angry feelings and interpersonal friction in the PNES group in terms of the two items (Pilowsky & Spence, 1983). However, Stone, Binzer, and Sharpe (2004) found their ES group scoring slightly higher on this factor yet found the difference to be non-significant. While studies investigating PNES patients' style of interpersonal relationships directly are few (Holman, Kirkby, Duncan, & Brown, 2008), difficulties in interpersonal relationships and early interpersonal trauma is widely accepted as an important aetiological factor in PNES development (Alsaadi & Marquez, 2005; Brown & Reuber, 2016b; LaFrance Jr, Reuber, et al., 2013; Mcouns, Schofield, & Middleton, 2010) and is further supported by the wide prevalence of Cluster B personality disorders among the

PNES population, which are denoted by instability of interpersonal relationships (Galimberti et al., 2003; LaFrance, Deluca, MacHan, & Fava, 2013; LaFrance & Devinsky, 2002).

6.2.4 BAI-PC Results

Time and time again people with PNES have been shown to experience higher psychiatric comorbidity when compared to those with ES (Hovorka et al., 2007; Mökleby et al., 2002), with PTSD, depression and anxiety being the most common of the disorders (Abubakr et al., 2003; Alsaadi & Shahrour, 2014; Diprose, Sundram, & Menkes, 2016; Griffith & Szaflarski, 2010; LaFrance & Devinsky, 2002; Reuber, 2008a). The current study confirms previous findings in demonstrating that the PNES group scored significantly higher on the BAI-PC when compared to ES (p=0.04) and combined ES and oNES (p=0.03). As mentioned earlier, trauma is prevalent among the PNES population and has even lead some to speculate that PNES might be a special type of PTSD (Betts & Boden, 1992; Fiszman et al., 2004), which may be partly responsible for the measure being able to predict PNES with high sensitivity (80%) and specificity (89%) in this seizure population. Indeed, even in such a small sample, the PNES group exhibited clear differences when compared to patients with ES and oNES. Furthermore, the finding of a 12 point cut-off score for PNES is especially useful and may prove to be an indispensable as well as quick and easy tool in PNES screening in primary care contexts when combined with other information.

6.5 Limitations and Recommendations for Future Research

Perhaps the most obvious limitation of the study is its small sample size curbing the power of the study to detect true effect – a problem that tends to be prevalent internationally when PNES research is still in its early stages (Brown & Reuber, 2016a; Cragar et al., 2002). The small sample size can largely be attributed to the delays in getting ethics approvals and difficulties in reaching key contacts in the two clinics that were approached. This is the first study in South Africa where data from PNES, ES and oNES patients was gathered at a clinic during their hospital vEEG monitoring – a vulnerable population at a vulnerable time. Furthermore, due to there being a paucity of vEEG monitoring facilities in the Western Cape, with Tygerberg Neurology Unit being the only government hospital, and Constantiaberg Medi-Clinic being the only private hospital to offer these services. Hence, The Constantiaberg Medi-Clinic Neuroscience Unit and the staff of this hospital are extremely busy and difficult to get hold of, where sometimes contacting a relevant staffer for their approval or input could take weeks. These two factors largely account for the difficulty of gaining access to the patients and the associated delays in data collection commencement, which led to a collection of a smaller than expected sample. Furthermore, due to the double-blind approach this study used when it came to knowledge of the diagnosis, it was impossible

to ensure a certain diagnostic distribution in any way other than collecting data longer. Nevertheless, despite the eventual small sample size, valuable knowledge was gained about the personality, illness behaviour and psychopathology profiles of the PNES (and ES) population and useful differences were found between PNES and other seizure populations that provide a stepping stone for further alternative diagnosis and descriptive research.

Secondly, despite collecting questionnaire data from the Tygerberg Neurology Unit, the researcher was unable to obtain the patients' diagnoses due to a backlog at the hospital. Hence, once the diagnoses do become available, this collected data should be presented within a scope of a larger study, which partly replicates the current one. Furthermore, having data only from one of the centres limited the applicability of collected data. The present sample was mainly White and consisted of people able to afford private healthcare, representing a minority in the South African context (Pretorius, 2016).

Likewise, the sample may not be reflective of the general PNES population, since it consisted solely of men. While there is no South African data on general prevalence of PNES, the latest epidemiological data seems to suggest that South Africa follows the international 3:1 proportion, when it comes to women dominating the condition (Anderson et al., 2017). Hence, while the data collected in the abovementioned study at one private clinic in Johannesburg may not necessarily be applicable to the Western Cape, it is highly likely that a considerable proportion of South Africans with PNES are women, as indicated by most international research (Noe et al., 2012; Szaflarski et al., 2000). Thus, again, a longer data collection period should be afforded to ensure that an adequately representative sample can be collected. Related is the fact that the current study used a data collection approach novel to South African PNES research. The study sought to approximate the situation of a patient with a seizure complaint visiting a clinic for a diagnosis. This meant that at the moment of questionnaire administration the researcher, the participant and the neurologist were blind to the diagnosis. While such an approach works great to ensure excellent external validity, the trade-off is the control the researcher has over their ultimate sample.

Fourth limitation is due to the clerical error that prevented a part of the IBQ questionnaire to be used. While Pilowsky himself advocates the use of IBQ as an item pool (Pilowsky, 1993) especially when it comes to his decision to keep the items that do not actually load on any of the IBQ scales (Pilowsky et al., 1984). Furthermore, as mentioned earlier, a few researchers have found different items useful for different populations and have accordingly shortened the questionnaire (Main & Waddell, 1987; Prior & Bond, 2014). Nevertheless, using the full extent of the questionnaire would have been useful in getting a

greater item pool, better insight into subscale results and would have provided the possibility to do more complex statistical analyses with the data.

Lastly, this study largely made use of reporting and comparing means between the groups. However, the reporting of averages within the PNES population is not always considered to be the best approach. While the PNES population shares similarities, it has perhaps even more differences and focusing on the averages may hide the important variation within this population. This is especially the case in studies with small samples. As an example, on average the PNES group in this study scored in the 54th percentile for Agreeableness, indicating an average score. However, upon closer look, one can see that two participants in the group scored either low or very low and the other three scored high or very high. Hence, ideally, a study like this would have a bigger sample and would try to cluster individuals with similar PNES aetiological mechanisms in data analysis as well as compare these clusters individually to ES patients.

6.6 Significance of the Present Study

In light of the discussed limitations it is important to discuss the valuable aspects of the present study. The present study used an innovative research design in South African PNES research, which involved the researcher, patient and healthcare provider being blind to the patient's diagnosis during the data collection period. This, in turn allowed a recreation of circumstances in which a patient would find themselves if they came to get a diagnosis for their seizures, suggesting high external validity. Additionally, this is the first South African study to gather personality, illness behaviour, anxiety, PTSD, and/or depression comorbidity data in South Africa. Hence, this study presented some novel results in the quest for greater understanding of the South African PNES (and ES) population and shed some light on some of the factors underlying PNES.

Furthermore, the study presented some findings that showed potential for differentiating between PNES and ES or oNES and should be investigated further. Likewise, another strength of the study was the inclusion of patients with oNES. Using only epilepsy controls has been criticised in PNES literature before (Reuber, 2008b).

While this cannot be seen as a direct outcome, simply getting such a close and unadulterated access to the PNES population was unprecedented. It made it possible to collect data from seizure patients before them actually knowing their diagnosis. Literature suggests that finding out the diagnosis often involves a considerable mind-shift in terms of the relationship PNES patients have with their condition (LaFrance Jr, Reuber, et al., 2013).

Hence, for the purpose of using the collected data for future PNES screening, being able to get access to PNES patients before they are diagnosed has been invaluable.

Lastly, this is one of the very few South African studies on PNES (Anderson et al., 2017; Cronje & Pretorius, 2013; Pretorius, 2016; Pretorius & Cronje, 2015; Pretorius & Sparrow, 2015), and apart from providing information on the PNES population is also intended to raise awareness of PNES in South Africa.

6.7 Conclusion

The present study aimed to examine if South African individuals with PNES differed from individuals with ES and oNES in terms of demographic and seizure characteristics, personality traits, illness behaviours and depression, anxiety and PTSD in statistically significant ways. Furthermore, if significant differences were to be revealed in terms of these factors between the PNES and ES or oNES samples, the aim was to test if these differences can be utilised in predicting PNES. Other than the demographic and seizure-related questions, the NEO Five Factor Inventory – 3 (NEO-FFI-3) was used to measure the Big Five personality domains, the Illness Behaviour Questionnaire (IBQ) was used to measure abnormal illness behaviours, and Beck Anxiety Inventory – Primary Care to measure depression, anxiety and/or PTSD comorbidity in the sample.

While the sample consisted of only 24 patients and can be considered somewhat unrepresentative of the PNES population in South Africa if one is to look at South African epidemiological research (Anderson et al., 2017) with its predominance of ES patients and the predominance of males in the PNES group, certain significant and important differences still emerged. The data analysis showed that those with PNES tended to experience more monthly seizures when compared to those with ES or oNES. Furthermore, individuals with PNES tended to report significantly more pain than those with epilepsy or oNES and experience significantly more comorbid depression, anxiety and/or PTSD. These findings suggest that individuals with PNES in South Africa tend to live even more debilitated lives than those with epilepsy, which is concurrent with international findings (Rawlings et al., 2017; Testa, Schefft, Szaflarski, Yeh, & Privitera, 2007). Furthermore, BAI-PC emerged as a potentially useful tool in screening for PNES in those who experience seizures and warrants further investigation with a larger sample.

While no significant differences emerged between the groups in terms of personality, certain tendencies could be noted in the PNES sample in terms of personality domains, illness behaviours and psychiatric comorbidity, thus painting a much more detailed picture of PNES in this country than previously known. Individuals with PNES in the present sample tended to

score high on Neuroticism, Extraversion and Openness to Experience scales, and average on the Agreeableness and Conscientiousness scales. This was different to the ES group where on average participants tended to score within the average range for each domain. High scores on the Neuroticism, Extraversion and Openness to Experience scales suggested individuals who are prone to negative affect, have an active imagination, are attentive to inner feelings and experience emotion keenly, as well as prefer stimulation and socialising in large groups.

The IBQ revealed a certain pattern of illness behaviours in the PNES population where, while perceiving psychological and somatic factors to be of similar importance in their illness, a tendency not to deny life stresses, this group also has a greater tendency to experience anger, yet inhibit their feelings. Furthermore, while, unlike the ES group, the PNES participants did not tend to be phobically pre-occupied with their health, once something felt wrong, they tended to preoccupy themselves with bodily symptoms to the point of rejecting medical reassurance of their health.

Lastly, while both the ES and PNES groups tended to score above the cut-off point on the BAI-PC, indicating a presence of depression, anxiety and/or PTSD symptoms, those with PNES exhibited these symptoms significantly more, suggesting a considerable psychological burden. The BAI-PC proved to be a useful tool in screening for PNES in a seizure population and a cut-off score of 12 was established to be able to predict PNES with high sensitivity (80%) and specificity (89%).

This study is a first of its kind in South Africa and serves as a basis for future research on this topic. Being able to screen for PNES in a more time and cost-effective way than vEEG is still of paramount importance and such research is extremely necessary. The discussed findings presented a profile of an individual with PNES in South Africa in terms of personality, illness behaviours and psychiatric comorbidity and presented factors that exhibit potential in the quest for developing a PNES screening instrument in the future.

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Appendices

Appendix A: Demographic and Seizure-related Questionnaire

Demographic information:

1) **Sex:** ☐ Female ☐ Male ☐ Other (please specify) _____

2) **Age:** _____

3) **To what population group do you belong?**

    ☐ Black

    ☐ Brown/Coloured

    ☐ White

    ☐ Indian

    ☐ Other (please specify) _____

4) What language do you speak at home?

    ☐ English

    ☐ Afrikaans

    ☐ Xhosa

    ☐ Other (please specify) _____

5) What is your highest education level?

Before Grade 3	
Before Grade 12	
Grade 12	
Tertiary Diploma	
University Degree (Bachelor's)	
Master's degree	
PhD	
Other (please specify)	

Seizure-related information:

6) How old were you when you had your **FIRST** event/episode/seizure? (Not including seizures which occurred due to high fever as a child)

    _____

7) How many events/episodes/seizures have you had in the **LAST 4 WEEKS**?

_____
Appendix B: Permission to Use NEO-FFI-3

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May 6, 2016

Chrisma Pretorius, PhD
Stellenbosch University
Department of Psychology
Private Bag X1
Matieland 7602
South Africa

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Appendix C: Sample from NEO-FFI-3

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SAMPLE ASSESSMENT ITEMS

SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE

NEO-FFI-3
NEO Five-Factor Inventory-3

Paul T. Costa, Jr., PhD and Robert R. McCrae, PhD

Form S–Adult

SELF-REPORT

Fill in (SD) if you *strongly disagree* or the statement is definitely false.

Fill in (D) if you *disagree* or the statement is mostly false.

Fill in (N) if you are *neutral* on the statement, if you cannot decide, or if the statement is about equally true and false.

Fill in (A) if you *agree* or the statement is mostly true.

Fill in (SA) if you *strongly agree* or the statement is definitely true.

1. I am not a worrier.
2. I like to have a lot of people around me.
3. I enjoy concentrating on a fantasy or daydream and exploring all its possibilities, letting it grow and develop.
4. I try to be courteous to everyone I meet.

SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE SAMPLE

Appendix D: Illness Behaviour Questionnaire

1.	Do you worry a lot about your health?	YES	NO
2.	Do you think there is something seriously wrong with your body?	YES	NO
3.	Does your illness interfere with your life a great deal?	YES	NO
4.	Are you easiest to get along with when you are ill?	YES	NO
5.	Does your family have a history of illness?	YES	NO
6.	Do you think you are more liable to illness than other people?	YES	NO
7.	If the doctor told you that he could find nothing wrong with you would you believe him?	YES	NO
8.	Is it easy for you to forget about yourself and think about all sorts of other things?	YES	NO
9.	If you feel ill and someone tells you that you are looking better, do you become annoyed?	YES	NO
10.	Do you find that you are often aware of various things happening in your body?	YES	NO
11.	Do you ever think of your illness as a punishment for something you have done wrong in the past?	YES	NO
12.	Do you have trouble with your nerves?	YES	NO
13.	If you feel ill or worried, can you be easily cheered up by the doctor?	YES	NO
14.	Do you think that other people realize what it is like to be sick?	YES	NO
15.	Does it upset you to talk to the doctor about your illness?	YES	NO
16.	Are you bothered by many pains and aches?	YES	NO
17.	Does your illness affect the way you get along with your family or friends a great deal?	YES	NO
18.	Do you find that you get anxious easily?	YES	NO
19.	Do you know anybody who has had the same illness as you?	YES	NO
20.	Are you more sensitive to pain than other people?	YES	NO
21.	Are you afraid of illness?	YES	NO
22.	Can you express your personal feelings easily to other people?	YES	NO
23.	Do people feel sorry for you when you are ill?	YES	NO
24.	Do you think that you worry about your health more than most people?	YES	NO
25.	Do you find that your illness affects your sexual relations?	YES	NO
26.	Do you experience a lot of pain with your illness?	YES	NO
27.	Except for your illness, do you have any problems in your life?	YES	NO
28.	Do you care whether or not people realize you are sick?	YES	NO
29.	Do you find that you get jealous of other people's good health?	YES	NO
30.	Do you ever have silly thoughts about your health which you can't get out of your mind, no matter how hard you try?	YES	NO
31.	Do you have any financial problems?	YES	NO
32.	Are you upset by the way people take your illness?	YES	NO
33.	Is it hard for you to believe the doctor when he tells you there is nothing for you to worry about?	YES	NO
34.	Do you often worry about the possibility that you have got a serious illness?	YES	NO
35.	Are you sleeping well?	YES	NO
36.	When you are angry do you tend to bottle up your feelings?	YES	NO

37. Do you often think that you might suddenly fall ill?	YES	NO
38. If a disease is brought to your attention (through the radio, television, newspapers or someone you know) do you worry about getting it yourself?	YES	NO
39. Do you get the feeling that people are not taking your illness seriously enough?	YES	NO
40. Are you upset by the appearance of your face or body?	YES	NO
41. Do you find that you are bothered by many different symptoms?	YES	NO
42. Do you frequently try to explain to others how you are feeling?	YES	NO
43. Do you have any family problems?	YES	NO
44. Do you think there is something the matter with your mind?	YES	NO
45. Are you eating well?	YES	NO
46. Is your bad health the biggest difficulty of your life? 47.	YES	NO
47. Do you find that you get sad easily?	YES	NO
48. Do you worry or fuss over small details that seem unimportant to others?	YES	NO
49. Are you always a co-operative patient?	YES	NO
50. Do you often have the symptoms of a very serious disease?	YES	NO
51. Do you find that you get angry easily?	YES	NO
52. Do you have any work problems?	YES	NO
53. Do you prefer to keep your feelings to yourself?	YES	NO
54. Do you often find that you get depressed?	YES	NO
55. Would all your worries be over if you were physically healthy?	YES	NO
56. Are you more irritable towards other people?	YES	NO
57. Do you think that your symptoms may be caused by worry?	YES	NO
58. Is it easy for you to let people know when you are cross with them?	YES	NO
59. Is it hard for you to relax?	YES	NO
60. Do you have personal worries which are not caused by physical illness?	YES	NO
61. Do you often find that you lose patience with other people?	YES	NO
62. Is it hard for you to show people your personal feelings?	YES	NO

Appendix E: Beck Anxiety Inventory – Primary Care

Beck Anxiety Inventory – Primary Care

Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by each symptom during the past two weeks, including today, by circling the number in the corresponding space in the column next to each symptom.

Symptoms	NOT AT ALL	MILDLY It did not bother me much	MODERATELY It was very unpleasant, but I could stand it	SEVERELY I could barely stand it
Unable to relax	0	1	2	3
Fear of worst happening	0	1	2	3
Terrified	0	1	2	3
Nervous	0	1	2	3
Fear of losing control	0	1	2	3
Fear of dying	0	1	2	3
Scared	0	1	2	3

Appendix F: Informed Consent Form

STELLENBOSCH UNIVERSITY

CONSENT TO PARTICIPATE IN RESEARCH

Personality Traits, Illness Behaviours and Psychiatric Comorbidity in Individuals with Psychogenic Non-Epileptic Seizures (PNES), Epilepsy and Other Non-Epileptic Seizures (oNES): Differentiating Between the Conditions

Individuals Experiencing Seizures

You are asked to participate in a research study carried out by a Masters student and her supervisor; Gabriele Vilyte (BA Hons) and Dr Chrisma Pretorius (PhD), from the Psychology department at University of Stellenbosch. Information collected during this study will form part of a Master's thesis. You were selected as a possible participant in this study because you are an adult who is experiencing seizures.

1. **PURPOSE OF THE STUDY**

Some seizures originate from physical causes and others from psychological ones. Unfortunately, it can often be difficult to tell apart between these different types of seizures without expensive technology, which can lead to an incorrect diagnosis where such technology is not immediately available. Hence, the purpose of this study is to explore whether learning about the personality traits, illness behaviour and presence or absence of certain psychiatric conditions in individuals with seizures can be used to tell apart between the different types of seizures and thus make appropriate treatment accessible sooner.

2. PROCEDURES

If you volunteer to participate in this study, we would ask you to do the following things:

1. A demographic and seizure-related questionnaire to get some background information about you and your seizures.
2. The Beck Anxiety Inventory - Primary Care (BAI-PC) subscale which has seven items that cover common anxiety, depression and post-traumatic stress disorder (PTSD) symptoms.
3. The NEO-Five-Factor Inventory 3 (NEO-FFI-3) which has 60 items and measures common personality traits.
4. The Illness Behaviour Questionnaire (IBQ) which has 62 items and looks at how you relate to your health.

It should take you approximately 20-30 minutes to complete the survey, but you can take as long as you need. If you are at the hospital you can complete it in your hospital room or otherwise at home.

3. POTENTIAL RISKS AND DISCOMFORTS

If you experience any discomfort during the research process to the point where counselling is required, you will be referred by the researchers to one of two psychologists who specialize in working with people who experience seizures. These psychologists work closely with Dr. Butler, the neurologist who provided you with information about this study. The contact details of these psychologists are: Dr. Jacqui Bean (021 761 6332) and Ms. Elspeth Burke (021 7021633). In the unlikely event that you have to be referred for counselling, the researchers will take responsibility for any cost involved.

4. POTENTIAL BENEFITS TO SUBJECTS AND/OR TO SOCIETY

There may be no direct benefits to you for participating in this study.

However, the study will give us information that could be helpful in making sure that individuals who experience seizures are diagnosed correctly quicker, as well as information on the personality and illness behaviours of people experiencing seizures in South Africa. This information will hopefully help us gain a better understanding of such patients in this country and may help them receive appropriate treatment sooner in the long term.

5. PAYMENT FOR PARTICIPATION

You will not receive payment for participating in the study.

6. CONFIDENTIALITY

Any information that is collected in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or as required by law. Confidentiality will be maintained by means of assigning you with a participant ID specific to this study, linking any personal information you give us to this ID in a separate computer file and by keeping collected information on a password protected computer where only we as researchers will have access to it. The hard copies of the information you provide (the questionnaires) will be kept securely in a locked cabinet in the research supervisor's office. The results of the study may be published in academic literature, however, you will never be identified as an individual.

7. PARTICIPATION AND WITHDRAWAL

You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise which warrant doing so.

8. IDENTIFICATION OF INVESTIGATORS

If you have any questions or concerns about the research, please feel free to contact the principal investigator for the study Gabriele Vilyte [18794912@sun.ac.za; 074 485 1097] or the study supervisor Dr Chrisma Pretorius [chrismapretorius@sun.ac.za; 021 808 3453].

9.   RIGHTS OF RESEARCH SUBJECTS

You may withdraw your consent at any time and discontinue participation without penalty. You are not waiving any legal claims, rights or remedies because of your participation in this research study. If you have questions regarding your rights as a research subject, contact Ms Maléne Fouché [mfouche@sun.ac.za; 021 808 4622] at the Division for Research Development.

SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE

The information above was described to me by Gabriele Vilyte in English and I am in command of this language. I was given the opportunity to ask questions and these questions were answered to my satisfaction.

I hereby consent voluntarily to participate in this study and to have my diagnosis shared by Dr. Butler, with the investigator. I have been given a copy of this form.

_____

Name of Subject/Participant

_____   _____

Signature of Subject/Participant   **Date**

SIGNATURE OF INVESTIGATOR

I declare that I explained the information given in this document to _____ [*name of the subject/participant*]. [*H*e/she] was encouraged and given ample time to ask me any questions. This conversation was conducted in English and no translator was used.

_____   _____

Signature of Investigator   **Date**

Appendix G: Invitation to Participate in Research Study: Individuals with seizures

We want to ensure that the correct diagnosis for individuals experiencing seizures is reached earlier in South Africa and we would like you to help us!

You are invited to take part in the research study "Personality Traits, Illness Behaviours and Psychiatric Comorbidity in Individuals with Psychogenic Non-Epileptic Seizures (PNES), Epilepsy and Other Non-Epileptic Seizures (oNES): Differentiating Between the Conditions", conducted by Gabriele Vilyte (Masters student) and Dr Chrisma Pretorius (supervisor; PhD) from University of Stellenbosch.

Some seizures originate from physical causes and others from psychological ones. Unfortunately, it can often be difficult to differentiate between these different types of seizures without sophisticated technology, which can lead to misdiagnosis where such technology is not immediately available. Hence, the purpose of this study is to investigate whether learning about the personality traits, illness behaviour and psychiatric comorbidity of individuals with seizures can be used to distinguish between the different types of seizures and thus make appropriate treatment accessible sooner.

If you agree to participate and are suitable for our study we will invite you to go through an informed consent form to ensure that you understand what the study entails. Once you have provided written consent (permission) for your participation, we will ask you to complete a survey that consists of the following:

1. A demographic and seizure-related questionnaire to obtain background information about you and your seizures.
2. The Beck Anxiety Inventory - Primary Care (BAI-PC) subscale which consists of seven items that measure common anxiety, depression and post-traumatic stress disorder (PTSD) symptoms.
3. The NEO-Five-Factor Inventory 3 (NEO-FFI-3) which is comprised of 60 items and measures common personality traits.
4. The Illness Behaviour Questionnaire (IBQ) which entails 62 items and looks at how you relate to your health.

It will take you approximately 20-30 minutes to complete the survey. You can complete the survey at hospital or at home.

To participate in this study you will need to be 18 years or older.

Your participation is entirely voluntary and you are free to decline to participate. You will also be free to withdraw from the study at any point, even if you do agree to take part. This study has been approved by the Health Research Ethics Committee at Stellenbosch University.

If you are interested, please contact Gabriele Vilyte via phone on 0744851097 or e-mail on 18794912@sun.ac.za .

If you are interested, please contact Gabriele Vilyte via phone on 0744851097 or e-mail on 18794912@sun.ac.za .

Appendix H: Approval Notice from REC

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

Approval Notice
Response to Modifications- (New Application)

23-Sep-2016
Vilyte, Gabriele GB

Proposal #: SU-HSD-002711

Title: Personality Traits, Illness Behaviours and Psychiatric Comorbidity in Individuals with Psychogenic Non-Epileptic Seizures
(PNES), Epilepsy and Other Seizure Disorders: Differentiating Between the Conditions

Dear Miss Gabriele Vilyte,

Your **Response to Modifications** - *(New Application)* received on **06-Sep-2016**, was reviewed by members of the **Research Ethics Committee:
Human Research (Humanities)** via Expedited review procedures on **19-Sep-2016** and was approved.
Please note the following information about your approved research proposal:

Proposal Approval Period: **19-Sep-2016 -18-Sep-2017**

Please take note of the general Investigator Responsibilities attached to this letter. You may commence with your research after complying fully with
these guidelines.

Please remember to use your **proposal number** (SU-HSD-002711) on any documents or correspondence with the REC concerning your research
proposal.

Please note that the REC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor
the conduct of your research and the consent process.

Also note that a progress report should be submitted to the Committee before the approval period has expired if a continuation is required. The
Committee will then consider the continuation of the project for a further year (if necessary).

This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki and the Guidelines for Ethical
Research: Principles Structures and Processes 2004 (Department of Health). Annually a number of projects may be selected randomly for an external
audit.

National Health Research Ethics Committee (NHREC) registration number REC-050411-032.

We wish you the best as you conduct your research.

If you have any questions or need further help, please contact the REC office at .

Appendix I: Institutional Permission from Constantiaberg Medi-Clinic

MEDICLINIC

MEDICLINIC OFFICES
STRAND ROAD
STELLENBOSCH
7600

PO BOX 456
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7599

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F +27 21 809 6756
ETHICS LINE 0800 005 316

www.mediclinic.co.za

14 November 2016

Ms G Vilyte
25 Weltevreden Avenue
RONDEBOSCH
7700

Dear Gabriele

PERMISSION TO CONDUCT RESEARCH AT MEDICLINIC CONSTANTIABERG

Your research proposal entitled *"Personality Traits, Illness Behaviours and Psychiatric Comorbidity in Individuals with Psychogenic Non-Epileptic Seizures (PNES), Epilepsy and Other Seizure Disorders: Differentiating between the conditions"* refers.

It is in order for you to conduct your research at Mediclinic Constantiaberg, and I wish you success with this project.

Yours sincerely

DR ESTELLE COUSTAS
Nursing Executive

MEDICLINIC (PTY) LTD
REG. NO. 1968/009218/07

Appendix J: Institutional Permission from the Western Cape Government

Western Cape
Government

Health

TYGERBERG HOSPITAL
REFERENCES: Research Projects
ENQUIRIES: Dr GG Marinus
TELEPHONE NO.: 021 938 5752

Ethics Reference: SU-HSD-002711

TITLE: Personality Traits, Illness Behaviours and Psychiatric Comorbidity in
Individuals with Psychogenic Non-Epileptic Seizures (PNES), Epilepsy and
Other Seizures Disorders: Differentiating Between the Conditions

Dear Miss G Vilyte

PERMISSION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL

1. In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009,
   permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg
   Hospital.

2. Researchers, in accessing Provincial Health Facilities, are expressing consent to provide the
   National Health Research Department with an electronic copy of the final feedback within six
   months of completion of research. This can be submitted to the Provincial Research Co-Ordinator
   (Health.Research@westerncape.gov.za)

DR GG MARINUS
MANAGER: MEDICAL SERVICES [RESEARCH CO-ORDINATOR]

DR D ERASMUS
CHIEF EXECUTIVE OFFICER

Date: 6 February 2017

Administration Building, Francie van Zijl Avenue, Parow, 7500
Tel: +27 21 938 9752   Fax: +27 21 938 4980

Private Bag X3, Tygerberg, 7505
www.capegateway.gov.za

TYGERBERG HOSPITAL

Ethics Reference: SU-HSD-002711

Title: Personality Traits, Illness Behaviours and Psychiatric Comorbidity in
               Individuals with Psychogenic Non-Epileptic Seizures (PNES), Epilepsy
               and Other Seizures Disorders: Differentiating Between and Conditions

BY   _____
             An authorized representative of Tygerberg Hospital

NAME _____Dr DErasmus_____

TITLE _____Ceo_____

DATE _____6 February 2017._____

Appendix K: Permission from Elsevier to Use Figure 1

**ELSEVIER LICENSE
TERMS AND CONDITIONS**

Feb 05, 2018

This Agreement between Mrs. Gabriele Vilyte ("You") and Elsevier ("Elsevier") consists of your license details and the terms and conditions provided by Elsevier and Copyright Clearance Center.

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