Emotion regulation in patients with Functional Neurological Disorder

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In loving memory of my mother, Rosie.

Dulcius ex asperis

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Abstract

Functional Neurological Symptom Disorder (FND) is defined in the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013) as one or more symptoms of altered voluntary motor or sensory function. In the absence of any clear structural or physiological aetiology, FND has long been believed to have an emotional cause. However, the relationship between emotion regulation and FND has received relatively little attention from the scientific community. The overall aim of my project was empirically to test hypotheses concerning emotion dysregulation generated from the Extended Process Model of emotion regulation (EPM) (Gross, 2015) in patients with FND, using a combination of self-report, behavioural, and physiological measures. Additional aims were to explore other important issues, including whether emotion dysregulation is related to specific manifestations of FND, and whether changes in emotion regulation can be tracked across psychotherapeutic intervention by self-report.

A systematic review of the available literature on emotion dysregulation in patients with Nonepileptic Attack Disorder (NEAD) (N = 52), suggested that this patient group exhibit impairments in the identification of their own emotional states, as well as a tendency to select and implement maladaptive regulatory strategies. Studies also suggested that patients with NEAD experience biased cognitive-affective processing of exteroceptive emotional information, which may further impede the implementation process. However, these impairments appear to be heterogeneously spread throughout the population, and linked to other clinical / aetiological factors such as psychological trauma.

Study One aimed to explore whether emotion dysregulation and co-morbid psychopathology is linked to whether or not patients self-report Impairment of

Consciousness (IOC) as part of their disorder. 163 patients with FND completed self-report measures of emotion dysregulation (The Emotional Processing Scale – 25; EPS-25), as well as measures of Major Depressive Disorder (PHQ-9), Generalized Anxiety Disorder (GAD-7), Somatization Disorder (PHQ-15), and Post-Traumatic Stress Disorder (PCL-5) symptomology. Patients with IOC scored significantly higher on the GAD-7 (p = .03), PHQ-15 (p = .002), and PCL-5 (p = .02) but there were no between-group differences on the EPS-25 (p = .45, both groups exceeding healthy norms). These results support the view that FND is associated with emotion dysregulation, but suggest that clinical presentations including IOC are related to symptoms of anxiety, Somatization disorder, and Post-Traumatic Stress Disorder.

Study Two aimed to experimentally test the hypothesis that patients with FND are impaired in their ability to identify their own emotional states, and that this impairment would be further exacerbated by stress. Twenty-six patients with FND and 27 healthy controls participated in the Heart Beat Detection Task (HBDT; Schandry, 1981) at baseline and following stress-induction with the Cold Pressor Test (Lovallo, 1975). The 'impoverished emotional experience' subscale of the EPS-25 was included as a self-report measure of participants' ability to identify their own emotional states. Patients were significantly impaired on the HBDT compared to controls (p = .04) and reported significantly greater difficulties on the 'impoverished emotional experience' subscale. However, there were no significant main effects of stress-induction on HBDT performance. These results suggest that patients with FND are impaired in the identification stage of the EPM, as characterised by reduced interoceptive sensitivity and insight into their emotional experiences, but that impairments in interoception are not exacerbated by the kind of stress induced by the Cold Pressor Test.

Study Three aimed to experimentally test the hypothesis that patients with FND habitually select and implement a maladaptive regulatory strategy, expressive suppression. Twenty-six patients and 28 healthy controls completed a picture viewing paradigm designed to elicit negative affect, and were instructed to either passively view the pictures or suppress their responses to the images. Facial responses to the images were measured using electromyography, implicit emotional responses to the images were measured with the Implicit Positive and Negative Affect Task (Quirin, Kazen, & Kuhl, 2009), and explicit emotional responses were measured with a self-report scale. The Emotion Regulation Questionnaire (Gross & John, 2003) assessed self-reported habitual implementation of expressive suppression. Patients reported an increased tendency to select / implement expressive suppression on the ERQ (p = .005), and experienced less positive emotion in response to the pictures (implicitly) than healthy controls (p = .002), consistent with the hypothesis that patients with FND are 'habitual suppressors'. However, facial electromyography recordings were greater in the second (p = .02) and third (p = .04) post-stimulus second epochs for patients than controls when instructed to suppress. These results suggest that patients with FND perceive themselves to be habitual suppressors, but struggle to suppress the physiological expression of their emotions.

Study Four aimed to examine emotion dysregulation in patients with FND by comparing a physiological measure of chronic autonomic arousal (resting Heart rate Variability; HRV) against healthy controls. This study also aimed to explore for associations between HRV and the other measures of emotion dysregulation and psychopathology used in this thesis. Five minute ECG recordings from 26 patients and 28 healthy controls were analysed for vagal and sympathetic HRV indices. Vagal, but not sympathetic HRV components were found to be lower in patients than controls (p

= .02). Vagal tone correlated negatively with self-reported symptoms of emotion dysregulation (r_s = -.27) and PTSD (r_s = -.31), and positively with HBDT performance across both groups (r_s = .36 - .39). These results suggest that patients with FND experience chronic autonomic arousal, associated with emotion dysregulation and psychological trauma.

Finally, Study Five sought to assess whether changes in emotion regulation following Brief Augmented Psychodynamic Interpersonal Therapy for FND could be assessed with a self-report measure, i.e. The EPS-25. Self-report data from 44 patients who returned pre- and post-intervention questionnaires including the EPS-25 were analysed. EPS-25 scores were significantly lower following intervention (p = .049), suggesting that emotion dysregulation improved following psychotherapy. Treatment-associated changes in EPS-25 scores correlated positively with change scores in psychological distress (CORE-10; partial correlation = .57) and mental health-related quality of life (SF-36 MHS subscale; partial correlation = .31) sharing 45% and 40% of variance respectively. These results suggest that this EPS-25 is sensitive to therapy-associated change in patients with FND.

The question of whether FND is caused by emotion dysregulation cannot be answered by this thesis. However, the associations found in these studies suggest that patients with FND experience emotion dysregulation as defined by the EPM, that clinical presentation is linked to co-morbid psychopathological symptoms, and that emotion dysregulation might be successfully treated in this population.

Table of Contents

List of Figures

List of Tables

Glossary of Abbreviations

ANS	Autonomic Nervous System
BIPQ	Brief Illness Perception Questionnaire
CODES	Cognitive Behavioural Therapy for Dissociative (Non-Epileptic) Seizures A Randomised Controlled Trial
CORE-10	Clinical Outcome in Routine Evaluations
CPT	Cold Pressor Test
CSI	Cardiosympathetic Index
CVI	Cardiovagal Index
DAPP-PQ	Dimensional Assessment of Personality Pathology
DDF	Difficulty Describing Feelings
DERS	Difficulties with Emotion Regulation Scale
DES	Dissociative Experiences Scale
DIF	Difficulty Identifying Feelings
DIS-Q	Dissociative Questionnaire
DSM-V	Diagnostic and Statistical Manual of Mental Disorders - 5
EEG	Electroencephalography
EMG	Electromyography
EOT	Externally Oriented Thinking
EPM	Extended Process Model of Emotion Regulation
EPS-25	Emotional Processing Scale -25
EPS-38	Emotional Processing Scale -38
ERQ	Emotion Regulation Questionnaire
ES	Epilepsy Control Group
FMD	Functional Motor Disorder(s)
fMRI	Functional Magnetic Resonance Imaging
FND	Functional Neurological Symptom Disorder
FNS	Functional Neurological Symptom(s)
GAD-7	Generalized Anxiety Disorder – 7 questionnaire
HBDT	Heart Beat Detection Task
HC	Healthy Control Group
HF	High frequency component of HRV
HRQoL	Health-related Quality of Life
HRV	Heart Rate Variability
ICD-10	International Classification of Diseases - 10
IOC	Impairment(s) of Consciousness
IOC-	Without Impairment(s) of Consciousness
IOC+	With Impairment(s) of Consciousness
IPANAT	Implicit Positive and Negative Affect Test

IS	Interoceptive Sensitivity
LF	Low frequency component of HRV
MASC	Movie for Assessment of Social Cognition
MHS	Mental Health Summary Scale of the SF-36
MMPI	Minnesota Multiphasic Personality Inventory
MUS	Medically Unexplained Symptom(s)
NEA	Nonepileptic Attack(s)
NEAD	Nonepileptic Attack Disorder
NEO-PI-R	NEO Personality Inventory Revised
NHS	National Health Service
NN50	Number of NN intervals that differ by more than 50 ms
PCL-5	Post-Traumatic Stress Disorder Checklist for the DSM-V
PHQ-15	Patient Health Questionnaire - 15
PHQ-9	Patient Health Questionnaire -9
PHS	Physical Health Summary Scale of the SF-36
PNES	Psychogenic Nonepileptic Seizures
pNN50	The percentage of NN intervals that differ by more than 50 ms
PNS	Parasympathetic Nervous System
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analysis
PTSD	Post-Traumatic Stress Disorder
rCBF	Regional Cerebral Bloodflow
RCSC	Reliable and Clinically Significant Change Analysis
RMSSD	Root Mean Squared of Successive Differences
RR	Two consecutive R waves in an ECG
RSA	Respiratory Sinus Arrhythmia
SF-36	The Short Form – 36
SNS	Sympathetic Nervous System
TAS-20	Toronto Alexithymia Scale
TSI-2	Trauma Symptom Inventory -2
vEEG	Video Electroencephalography
vmHRV	Vagally Mediated Heart Rate Variability
WOCS	Ways of Coping Scale

Glossary of terms as they will be used in this thesis

Term	Definition
Disorder *(noun)*	A pathological symptom or set of symptoms caused or characterised by a disruption to 'normal' (as defined by social norms or diagnostic manuals such as the DSM or ICD) functioning, which causes significant distress and / or impedes daily activities of living.
Psychological *(adjective)*	Relating to all cognitive processes, including but not limited to: behaviour, action-selection, emotion, movement, executive function, memory, sensation, meta-cognition, social cognition, learning, agency
Mental *(adjective)*	Synonymous with psychological.
Physical *(adjective)*	Relating to physiological processes, or a structure located within, the human body.
Neurological *(adjective)*	Relating to physical processes involving the brain or nervous system which currently fall under the remit of the medical speciality of neurology (e.g., epileptiform activity, Parkinson's disease).
Psychiatric *(adjective)*	Referring to psychological processes in the brain or nervous system causing disorders which currently fall under the remit of the medical speciality of psychiatry (e.g., "Major Depression is a psychiatric disorder.").
Medical *(adjective)*	Referring to physical and psychological processes associated with the manifestations of disorders which currently fall under the remit of medical specialities (including general internal medicine, psychiatry, and neurology).
Functional Neurological Disorder *(noun)*	A disorder with neurological symptoms associated with no easily identifiable physical cause / mechanism which would be consistent with traditional / existing accounts of neurological disorder, for example limb weakness in absence of a lesion to the motor cortex or descending motor projections.
Conversion Disorder *(noun)*	Neurological symptoms brought about by the transference of 'unspeakable' psychological distress / dilemma into 'physical' symptoms. This is a psychiatric concept most recently described in the DSM-V.

Psychogenic *(adjective)*	Describes a 'physical' symptom (e.g., tremor) caused by psychological / mental factors (e.g., psychological trauma), assuming that psychological processes are separate from physical processes. Psychogenic symptoms are commonly associated with psychiatric disorders.
Somatoform *(adjective)*	Referring to psychogenic symptoms resembling those of medical disorders (e.g., Irritable Bowel Syndrome).
Medically unexplained *(adjective)*	A symptom that cannot be accounted for by known / presently understood medical aetiological mechanisms.
Substance dualism *(noun)*	A philosophy of the mind which states that mental and physical processes / substances are two distinct, separate entities (i.e. that mental phenomena are non-physical).
Nonorganic *(adjective)*	A disorder not caused by a physical process – implies a disorder caused by psychological / mental dysfunction.
Dissociative *(adjective)*	Describes a symptom that is caused by a breakdown in the integration of normally integrated psychological / mental processes for example, movement and agency.

Publications arising from the project

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Poster presentations

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Statement of contributions

Chapter 2: Emotion dysregulation in patients with Nonepileptic Attack Disorder: a systematic review based on the Extended Process Model

Isobel Williams conducted the literature search, quality assessment, study categorisation, data analysis, and wrote the article. Dr. Liat Levita second-rated the study categorisation. Prof. Markus Reuber conducted the second quality assessment.

Chapter 3: Impairment of consciousness and emotion regulation in patients with Functional Neurological Disorder (Study 1)

Isobel Williams designed the study, recruited participants, collected and analysed the data, and wrote the article.

Chapter 4.2: The identification stage: Interoceptive sensitivity in patients with Functional Neurological Symptoms (Study 2)

Isobel Williams designed the study, recruited participants, collected and analysed the data, and wrote the article.

Chapter 4.3: The selection and implementation stages: Expressive suppression in patients with Functional Neurological Disorder (Study 3)

Isobel Williams designed the study, recruited participants, collected and analysed the data, and wrote the article. Dr. Luis Mannseur assisted with programming the MATLAB pre-processing and analysis script, as well as advising on experimental design.

Chapter 4.4: Resting Heart Rate Variability in patients with Functional Neurological Disorder (Study 4)

Isobel Williams designed the study, recruited participants, collected and analysed the data, and wrote the article.

Chapter 5: Changes in emotion processing following Brief Augmented Psychodynamic Interpersonal Therapy for Functional Neurological Symptoms (Study 5)

Data for this study were collected as part of a service evaluation in Neurology Psychotherapy Services between January 2010 and September 2012 (prior to the start of this PhD project in 2015) by other research assistants and administrative staff. Isobel Williams analysed and interpreted the data, and wrote the article. Stephanie Howlett delivered the intervention.

Prof. Markus Reuber and Dr. Liat Levita supervised the overall project, and provided feedback on all of the work presented in this thesis.

1. Introduction

1.1. Functional Neurological Symptom Disorder

Functional Neurological Symptom Disorder (FND) is defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (American Psychiatric Association, 2013) as one or more symptoms of altered voluntary motor or sensory function. In order for a diagnosis of FND to be given, clinical findings must demonstrate incompatibility between the Functional Neurological Symptom (FNS) and other known medical conditions. The symptoms must also cause clinically significant distress / impairment in a patient's functioning which warrants medical evaluation. FND can affect motor or sensory function. As such the DSM-V criteria also specify a range of FND symptom types, which may be short- or long-lasting and occur with or without a psychological stressor (Figure 1). Most patients diagnosed with FND by the DSM-V would also be classified as having a Dissociative Disorder in the International Classification of Diseases (ICD-10) (World Health Organization, 2016), a definition which also excludes malingering / conscious simulation of symptoms.

The DSM-V definition of FND is subsumed within a new category called 'Somatic Symptom and Related Disorders' (previously called 'Somatoform |Disorders'). This category contains what are proposed to be related, but categorically different diagnoses, including Illness Anxiety Disorder, Factitious Disorder, and Somatic Symptom Disorder. In the context of the DSM-V, a 'somatic' symptom refers to symptoms of 'physical' illness, such as fatigue or pain, which cannot be fully explained by another medical or psychiatric disorder. In order for a diagnosis of Somatic Symptom Disorder to be given, a patient must experience one or more somatic symptoms that are distressing and disrupt the patient's daily life, as well as

excessive thoughts, feelings, or behaviours related to the symptom(s) or associated health concerns (e.g., persistent thoughts, health anxiety, excessive time/energy devoted to health concerns). The somatic symptom should also be persistent – typically longer than six months – to meet diagnostic criteria. The DSM-V separates FND from Somatic Symptom Disorder by emphasising loss of function in FND and the distress caused by the symptom in Somatic Symptom Disorder. However, in practice, there is considerable overlap between the two diagnoses (the experience of pathological symptoms with no obvious identifiable structural or functional cause and an association with psychological factors being two examples), and many patients with FND also experience somatic symptoms such as chronic pain and fatigue. This diagnostic ambiguity is reflected in more recent theoretical models of functional somatic symptoms (e.g., Van den Bergh, Witthoft, Petersen, & Brown, 2017), which make no real distinction between the two diagnoses in terms of presumed aetiology and mechanism (see section 1.3 for further discussion). This example illustrates one of the limitations of the DSM-V definition of FND – that in reality, the boundaries between FND and other disorders are not as clearly defined as the DSM-V might suggest.

Nevertheless, FND are one of the most frequently diagnosed conditions in neurology outpatient clinics (Stone et al., 2010). While it is difficult to formally establish the exact frequency of individual FNS, Nonepileptic Attack Disorder (NEAD) seems to be the most common. NEAD is a condition in which the patient experiences paroxysmal seizure-like episodes often involving alterations in consciousness. While nonepileptic attacks superficially resemble epilepsy, epileptiform activity is absent in Video Electroencephalographic (vEEG) recordings (LaFrance, Baker, Duncan, Goldstein, & Reuber, 2013). In a breakdown of 587

'psychological / functional' patients diagnosed in Scottish neurology outpatient clinics over approximately 14 months, the largest group (n = 85) were patients with NEAD. This was followed by patients with Functional Sensory Symptoms (n = 68, including hemisensory and visual deficits), and Functional Movement Disorders (FMD) (n = 56, including weakness, movement disorder, and gait disturbances) (Stone et al., 2010). In reality, many patients with FND exhibit multiple FNS, with new ones developing or existing ones evolving over time.

Specify symptom type:
With weakness or paralysis (e.g., Functional Hemiparesis)
With abnormal movement (e.g., Functional Tremor)
With speech symptom (e.g., Functional Dysphonia)
With attacks or seizures (e.g., Nonepileptic Attack Disorder)
With anaesthesia or sensory loss (e.g., Functional Hypoesthesia)
With special sensory symptom (e.g., Persistent Postural-Perceptual Dizziness)
With mixed symptoms

Specify if:
Acute episode: Symptoms present for < 6 months
Persistent: Symptoms occurring for ≥ 6 months

Specify if:
With psychological stressor
Without psychological stressor

Figure 1. DSM-V FND symptom types and specifications.

Historically, there have been numerous different synonyms for FND, many of which imply a psychological aetiology; 'Psychogenic', 'Hysterical', and 'Psychosomatic' have all been used to indicate that a neurological symptom is considered functional. Commonly used alternative names for nonepileptic attacks include 'Pseudoseizures', 'Psychogenic Nonepileptic Seizures' and 'Dissociative Seizures'. Indeed, both the current ICD-10 (Dissociative Disorder) and DSM-V (Conversion Disorder) definitions allude to a psychological symptom or a psychological aetiology (conversion of psychological distress into physical

symptoms). While in the last iteration of the Diagnostic and Statistical Manual of Mental Disorders the presence of a psychological stressor was removed as a necessary condition, many experts maintain the view that psychological factors play an important role in the genesis and maintenance of symptoms for the majority of people with FND (Carson et al., 2012). However, psychological factors may not always appear relevant; many patients do not show any signs of other psychopathology and do not report any traumas or dilemmas which could be related to the symptoms (van der Hoeven et al., 2015). Moreover, a 'psychological' prefix overshadows biological and social factors which are likely involved in the genesis and maintenance of FND (Ejareh Dar & Kanaan, 2016).

Other synonyms for FND such as 'Non-organic' or 'Medically Unexplained Symptoms' simply state what the condition is not, containing no indication of the presumed or likely cause (Stone et al., 2011). These 'negative diagnoses' may risk giving patients the impression that the diagnosing clinician does not know what the diagnosis really is, even though there are an increasing number of positive diagnostic indictors for FND, such as Hoover's sign for functional weakness (McWhirter, Stone, Sandercock, & Whiteley, 2011) or the typical semiology of NEAD (Duncan, 2016).

The prefix 'Functional' is used to describe a problem with the workings of, and not the structure of, the Nervous System. It makes no assumptions about aetiology but likens FND to a problem with the software and not the hardware of a computer. Indeed, a recent meta-analysis of functional neuroimaging studies in FND implicated altered activity within a number of brain regions associated with motor-planning, motor-selection, and autonomic responding (Boeckle, Liegl, Jank, & Pieh, 2016), which seems consistent with this analogy. Furthermore, patients with NEAD find 'functional' more acceptable and less offensive than psychological or negative labels

(Stone et al., 2003). However, even the term ‘functional’ is not without issue; there is now also evidence of structural brain changes in patients with NEAD (McSweeney, Reuber, & Levita, 2017). It is therefore most likely that structural alterations can be implicated in the genesis and / or maintenance of FND, although they are yet to be elucidated. What is more, the nervous system is an adaptive biological system in which certain patterns of functioning (such as learning a new skill) can cause demonstrable structural changes, so the analogy with software problems has clear limitations. Nevertheless, the term ‘Functional Neurological Disorder’ (FND) is currently least problematic and will be used to refer to Functional Neurological Symptom Disorder throughout this thesis.

1.2. Epidemiology and prognosis of FND

Issues surrounding definition and case ascertainment of FND have obfuscated the attempts of large-scale studies to establish incidence and prevalence. For example, should an epidemiological study recruit only patients with medically unexplained neurological symptoms, or only those thought to have a psychogenic disorder? Furthermore, a diagnosis of FND can only be confirmed following neurological examination, meaning that studies are likely to miss individuals not in contact with neurology services. Despite this, FND are one of the commonest reasons why patients consults a neurologist (Stone et al., 2010). In a prospective cohort study of 300 new neurology outpatients, one third were found to have neurological symptoms not explained by any known ‘organic’ pathology (Carson et al., 2000). In a community sample, reported incidence rates range between 4 and 12 per 100,000 per year (Akagi & House (2001) cited in Carson et al., 2012). These estimates are comparable to the incidence of Multiple Sclerosis, which is one of the most common disabling neurological disorders (Mackenzie, Morant, Bloomfield, MacDonald, & O'Riordan,

2014). Based on information extracted from population-based case registers, lower estimates of the prevalence rate of FND reaches 50 in 100,000 members of the population (Akagi & House (2001), cited in Carson et al., 2012). Based on a calculation, Benbadis and Hauser (2000) estimated the prevalence of NEAD as between 1 in 50,000 and 1 in 3000. However, these figures likely under-represent the true incidence and prevalence of FND.

Broadly speaking, FND are more frequently diagnosed in women than men, with estimates of up for 75% of patient samples being female, although this figure may exaggerate true differences in the population prevalence as women are 1.5 times more likely than men to present to health services (Carson & Lehn, 2016). Age of symptom onset for FND in a series of 3781 newly referred patients to NHS neurological centres in Scotland, tended to be between 35 and 50 years of age (Stone et al., 2010). However, other reports suggest that NEAD symptom onset is earlier, frequently occurring in adolescence and early adulthood (Asadi-Pooya & Sperling, 2015). Nevertheless, FND can begin at any age, in any gender.

Outcomes from studies conducted in specialist centres often associate FND with significant disability and a poor prognosis. Patients with 'Medically Unexplained Neurological Symptoms' in a Scottish cohort were found to be more disabled, more distressed, and in receipt of more disability-related benefits than their medically-explained counterparts (Carson et al., 2011). However, it should be noted that these studies do not include patients who present to their General Practitioner or Accident and Emergency departments with symptoms that remit quickly, hence there are likely many patients with FND who have good outcomes. Nevertheless, having the belief that one will not recover, rejecting the influence of psychological factors on health, and the receipt of disability-related benefits have been shown to predict poor outcome

at one year post-consultation (Sharpe et al., 2010). Many patients with FND are initially misdiagnosed, and face a long wait before their diagnosis is corrected. One study found that, for patients ultimately found to have NEAD, it took an average of 7.2 years from manifestation to diagnosis. In the meantime, most of these patients had been subjected to unnecessary treatment with antiepileptic drugs, and many had undergone interventions such as intubation or the emergency administration of intravenous medications associated with a significant risk of iatrogenic harm (Reuber, Fernandez, Bauer, Helmstaedter, & Elger, 2002). Conversely, data suggests that once a diagnosis of FND is made, it is rarely changed at follow-up (Stone et al., 2009).

In view of its prevalence and the risk of poor outcomes, FND represent a significant challenge for healthcare provision. The cost of healthcare provision for somatizing patients is estimated to be £3 billion (equating to 10% of the NHS budget in 2008), and the cost of sickness and decreased health-related quality of life is estimated to exceed £14 billion (Bermingham, Cohen, Hague, & Parsonage, 2010). Unfortunately for these patients, FND is a diagnosis that has been stigmatized both by society and the medical profession (Rommelfanger et al., 2017), to the extent that in a survey of neurologists, FND came last on a list of neurological symptoms that neurologists 'like to treat' (Evans & Evans, 2010). It is hoped that multi-disciplinary research embracing a biopsychosocial framework as well as the rejection of dualist approaches to medicine will help to eliminate this stigma and improve outcomes for patients with FND (Rommelfanger et al., 2017).

1.3. Theories of FND – a role for emotion dysregulation

Recent theories of FND adopt a multi-factorial perspective, in which psychological, biological, and social factors have the potential to predispose an individual to the disorder, precipitate, and / or perpetuate the symptoms (Reuber,

Howlett, Khan, & Grunewald, 2007). In a naturalistic study of aetiological factors recorded during a screening interview by a single psychotherapist, identified predisposing and precipitating factors included sexual trauma, non-sexual trauma, bereavement, social / family factors such as family dysfunction and life pressures, and health issues. Identified perpetuating factors included, bereavement, health anxiety or physical health problems, financial or social gain (i.e., through illness identity), Axis 1 affective disorders, sexual trauma, and social / family factors including life pressures and family dysfunction. Of note, there was a subgroup of patients for whom no predisposing, precipitating, or perpetuating factors could be identified, illustrating the heterogeneity of risk factors for FND. Of course, many of the factors listed above are generic risk factors for mental disorders. Hence, there remain open questions about what mechanisms specifically lead to FND. To date, a number of psychological theories concerning the genesis and maintenance of FND have been proposed, some of which will now be discussed.

The Integrative Cognitive Model of Medically Unexplained Symptoms (MUS) proposed by Brown (2004) incorporates the concepts of dissociation, conversion, and somatisation and interprets them within a cognitive psychological framework as disorders of perception and control. According to this theory, 'rogue representations' are essentially symptom representations acquired through the patient's own history of physical illness, exposure to illness in others, sociocultural transmission, or verbal suggestion. A malfunctioning attentional control system persistently activates and selects these 'rogue representations', which gives rise to symptoms characterised by altered perception (e.g., pain, anaesthesia, visual disturbance) or impaired control (e.g., tremor). These alterations may be misattributed to physical illness by the patient, consistent with a loss of agency and the perception

that symptoms are involuntary.

Computational neuroscientists have provided predictive coding accounts for the mechanism of FND (Edwards, Adams, Brown, Pareés, & Friston, 2012; Van den Bergh et al., 2017), in which prior expectations and attentional processes play a role. Within a Bayesian framework, the brain is constantly generating probabilistic internal models to infer the causes of sensory inputs (referred to as posterior beliefs), which are calculated from prior expectations (learned knowledge) about the world and current sensory input. Mismatches between prior expectations and sensory input result in 'prediction errors', which the brain will try to reduce either by adjusting the prior expectation to better fit the sensory data, or by adjusting the representation of sensory data (e.g., through increased or decreased attentional allocation) to better fit the prior expectation. This process is continuous and iterative, moving bi-directionally through a hierarchical structure such that lower levels represent basic properties of sensory input and higher levels represent more abstract and complex properties. Bottom-up prediction errors depend on top-down input from predictions (which are also influenced by previous prediction errors). Over time and experience, predictions and prediction errors build a level of confidence (variance around a mean distribution), which can also be thought of as 'precision' (smaller variance translating to greater precision). Precise prior expectations represent strong predictions, and the stronger the prior the more likely it is the inferred cause of the sensory input (posterior) will be weighted in favour of the prior prediction. Conversely, if the sensory input has high precision the posterior will be biased towards the sensory data. Consequently, as more sensory inputs are accumulated over time the prior will be updated to reflect the sensory data. The system also weights prediction errors based on how likely they are to be a result of noise or an accurate reflection of input. When precise sensory data is

expected (e.g., in the light) the posterior will be weighted more in favour of sensory input. However, if the sensory input is expected to be imprecise or noisy (e.g., in the dark) the posterior will remain biased towards the prior. Ultimately, this process will generate an optimal posterior model to infer the cause of sensory inputs.

Edwards et al. (2012) propose that in the case of FND, sensory and motor symptoms are generated by two disruptions to this process of inference. The primary failure of inference is that the perception of a sensation or movement (or lack thereof) is generated from abnormal prior expectations which are given too much weight by attentional processes. The second failure of inference is that because the resulting posterior perception was not predicted, it is falsely inferred to be a symptom. The theorised role of an imbalance between prior expectations and sensory input in the phenomenology of functional tremor has been supported by Parees et al. (2012), who demonstrated that patients with functional tremor overestimated the duration of their tremor throughout the day more so than patients with 'organic' tremor. This may be interpreted as the consequence of an overly precise prior expectation (that a tremor is present all day) over-riding sensory proprioceptive sensory data from the affected limb (which should inform the generative model that the tremor is intermittent). The undue influence of beliefs or prior expectations on FND patients' phenomenology is also demonstrated through curative response to placebo; Edwards, Bhatia, and Cordivari (2011) showed that fixed dystonia patients experienced symptomatic relief almost immediately following a Botox injection (i.e., because they believed it would work), when in reality Botox takes 72 hours to take effect. Abnormal prior symptom expectations may come about through a number of social and cultural influences such as illness exposure. Hotopf, Mayou, Wadsworth, and Wessely (1999) found that the presence of MUS in adulthood was related to parental ill-health in childhood which

could conceivably lead to increased symptom monitoring - this can also be thought of as the pathological direction of attention to an abnormal prior. The authors note however, that while affective factors may be related to attentional and belief-driven processes in FND, affective factors are not always necessary and are not sufficient to produce Functional Movement or Sensory Symptoms.

Van den Bergh et al. (2017) recently proposed a predictive coding model of symptom perception in MUS, which incorporates concepts from both the Edwards et al. (2012) Bayesian inference model with factors from the Integrative Cognitive Model (Brown, 2004). This model extends to all functional symptoms including autonomic dysfunction, functional syndrome, and other somatization problems but places greater emphasis on the role of interoception. Within this model, FND symptoms can be thought of as 'somatovisceral illusions' brought about by a generative system which gives too much weight to priors predicting the presence of pathological symptoms or the 'normal' interoceptive condition of the body, coupled with a reduction in the detailed processing of sensory input. This set of conditions leads to a large mismatch between the prior and sensory input (prediction error) and the patient experiences, "a subjectively real but objectively illusory," symptom. In this model, the abnormally precise priors result from an over-representation of previously learned experience about the cause of a particular interoceptive sensation, analogous to symptom representations in the Integrative Cognitive Model. The reduction in detailed processing of sensory cues is moderated by a number of factors including low interoceptive sensitivity, attentional modulation, sensitivity to contextual cues, and threat processing strategies (such as high trait negative affect) – all of which are relevant to emotion dysregulation.

Other theories attempting to explain the mechanism by which FND manifest

have been derived from neuroimaging research. Based on their review of such studies, Perez et al. (2015) propose that NEAD and FMD are brought about by alterations in neural networks mediating emotional expression, regulation, and awareness (Anterior Cingulate Cortex (ACC), ventromedial prefrontal cortex, insula, amygdala, vermis), cognitive control and motor inhibition (ACC, dorsolateral prefrontal cortex, inferior frontal gyrus), perceptual awareness (temporoparietal junction, posterior parietal cortex), and motor planning / coordination (supplementary motor area, cerebellum). They suggest that pathological changes to these circuits may be precipitated by chronic stress.

With respect to NEAD, Baslet (2011) proposed a conceptual framework in which psychopathological mechanisms (dissociation, somatization, and Post-Traumatic Stress Disorder (PTSD)), a narrow window of arousal tolerance, emotional deficits (alexithymia and avoidance), cognitive deficits (maladaptive attentional styles), and disrupted automaticity / volitional control interact to facilitate a predisposition to NEAD which may be triggered by emotionally salient stimuli. Other psychological theories place emphasis on factors such as fear avoidance (Goldstein et al., 2010), and family dysfunction (Salmon, Al-Marzooqi, Baker, & Reilly, 2003). Given the reported higher rates of trauma, anxiety, alexithymia, dissociation, and pathological personality traits in patients with NEAD (e.g., Driver-Dunckley, Stonnington, Locke, & Noe, 2011; Ekanayake et al., 2017; Reuber, Howlett, et al., 2007; Stone, Sharpe, & Binzer, 2004), it is generally considered that NEAD aetiology may be more closely related to emotion dysregulation than the aetiology of FMD or other FNS.

The theories discussed above do not constitute an exhaustive list of those put forward to explain FND. However, they do serve to illustrate the point that even

though purely psychological accounts of FND are now considered insufficient, current theories of FND either explicitly endorse or give space for factors relating to emotion regulation such as trauma, attentional biases, illness beliefs, or emotion processing deficits. These contributions represent an important step forward in the study of FND, but are limited by a failure to adequately explain how or why psychological factors may render an individual susceptible to one particular FNS (e.g., NEAD) and not another (e.g., functional tremor). Indeed, FND is a highly heterogeneous disorder, with variations in symptom presentation between and within individuals. This heterogeneity extends to patients' psychosocial history; many will endorse a history of trauma, some will categorically deny any predisposing or precipitating traumatic experiences. Likewise, Axis 1 and Axis 2 disorders can be identified in many patients, but the nature of these varies widely between patients. Whether patients with FND should be lumped together or split into individual diagnostic categories is a contentious issue. However, given that response to therapeutic intervention is likely to depend on symptom aetiology, elucidating the nature and causes of psychological and clinical heterogeneity in FND will hopefully help clinicians to better diagnose and treat this patient group.

One potential solution to tackling the issue of heterogeneity in FND research is to embed identified psychological deficits or risk factors within a more comprehensive model. Taking this structured approach could conceivably help to systematically explain some of the differences in the aetiology and phenomenology of FND, by allowing for the generation and testing of specific and related hypotheses. We propose the Extended Process Model (EPM) of emotion regulation (Gross, 2015) as a candidate model in which to constrain the conceptualisation of, and operationalise emotion dysregulation in FND.

1.4. What is an emotion?

Before introducing the Extended Process Model of emotion regulation, it is helpful to define what an emotion is. Given the vast array of emotions humans are capable of experiencing, it is easier to say what emotions have in common, than to say what they are not. According to Appraisal Theory (Lazarus, 1991), one core feature of an emotion is that it occurs when an individual attends to and evaluates a situation as being relevant to a particular goal. Another core feature of emotions is that they are multi-faceted whole-body phenomena involving loosely coupled changes in subjective experience, behaviour, and physiology (Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005). The Modal Model of emotion (Gross, 1998) is a simple, linear conceptualisation of the emotion generative process (Figure 2). Emotions begin with attentional allocation to a psychologically relevant situation, which is then appraised in reference to a particular goal, ending in experiential, physiological, and behavioural changes within an individual. This response may then serve to alter the original situation which gave rise to the emotion in the first instance. The Modal Model illustrates another core feature of emotions; that they unfold over time.

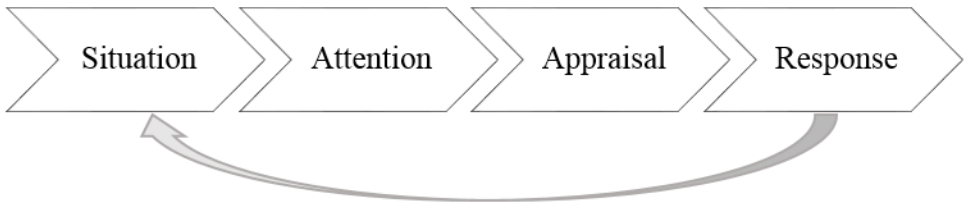

Figure 2. The Modal Model of Emotion (Gross, 1998b). Adapted from Gross (2014).

1.5. The Extended Process Model of Emotion Regulation

Emotion regulation can be defined as the process by which a person modifies or controls what emotions they are experiencing, when they have them, and the nature

in which they are experienced or expressed (Gross, 1998). The goal of emotion regulation can be to change emotion in oneself (intrinsic) or in another (extrinsic) (Zaki & Williams, 2013). The aim of emotion regulation is not necessarily to down-regulate negative emotions and up-regulate positive emotions; sometimes it is helpful to increase negative emotions, such as in the case of increasing fear to achieve the goal of successful threat-avoidance. Emotion regulation can be instrumental in achieving shorter- or longer-term goals, for example in the case of delayed-gratification during which one may down-regulate immediate pleasure in order to up-regulate pleasure in the future (Tamir, 2009). Emotion regulation may be explicit and effortful (such as instructing a participant to deliberately reappraise an upsetting stimulus) or implicit and automatic (such as a habitual tendency to avoid upsetting stimuli) (Gyurak, Gross, & Etkin, 2011). Emotion regulation can also aim to modify some specific aspect of the emotion, such as intensity or frequency (Sheppes, Suri, & Gross, 2015).

The Extended Process Model of Emotion Regulation (EPM) (Gross, 2015) is the most recent iteration of the popular 'Process Model of Emotion Regulation' (Gross, 2001). The Process Model is an information-processing model based on the Modal Model of Emotion, which reframes each step of the emotion generative process (i.e., Situation, Attention, Appraisal, Response) as a target for emotion regulation. This yields five general categories of emotion regulation strategies (Table 1). Response Modulation is considered a 'response-focused' general regulation category because it is used after the emotional response has been elicited. Accordingly, the other categories are considered 'antecedent-focused'.

Table 1- *General categories of emotion regulation strategies.*

Process Model Stage	**General Emotion Regulation Category**	**Description**
Situation	Situation Selection	Taking actions to increase / decrease likelihood of encountering situation (e.g., avoiding upsetting films).
	Situation Modification	Modifying an external situation to alter its emotional impact (e.g., physically distancing oneself from an argument).
Attention	Attentional Deployment	Directing attention to alter one's emotions (e.g., distraction).
Appraisal	Cognitive Change	Changing the way one thinks about an internal or external event (e.g, positively reframing criticism).
Response	Response Modulation	Directly influencing experiential, behavioural, or physiological components of the generated response (e.g., expressive suppression).

While the Process Model has been highly influential in the emotion regulation literature, it does not try to explain what initiates emotion regulation, or what would give rise to 'successful' or 'unsuccessful' emotion regulation – questions which are especially relevant to clinical research. Gross therefore presented the EPM (Gross, 2015) which essentially views emotion regulation a series of 'valuations' across three stages; identification, selection, and implementation (Figure 3). Each valuation begins with a representation of the internal or external environment (World) which is perceived (Perception) and compared against a goal-state (Valuation). If there is a sufficient discrepancy between the internal / external environment and the goal-state, the Action sub-step is triggered. The function of the Action sub-step is constrained by the stage of the EPM that the valuation system is within. During identification, an ongoing emotion is identified (e.g., disgust) and a decision is made whether or not to

regulate the emotion based on the discrepancy between the current emotion and goal emotional state. During selection, a general emotion regulation strategy (e.g., attentional deployment) is decided upon in light of the type and strength of the emotion identified. During the implementation stage, the general emotion regulation strategy is translated into specific tactics suitable for the current situation (e.g., distraction from the disgust-eliciting stimulus). In the case of successful emotion regulation, the process cycles through again until the emotion regulation goal is reached (e.g., the individual is no longer feeling disgusted). According to the EPM, emotion regulation is a continuous, multi-modal, and iterative process.

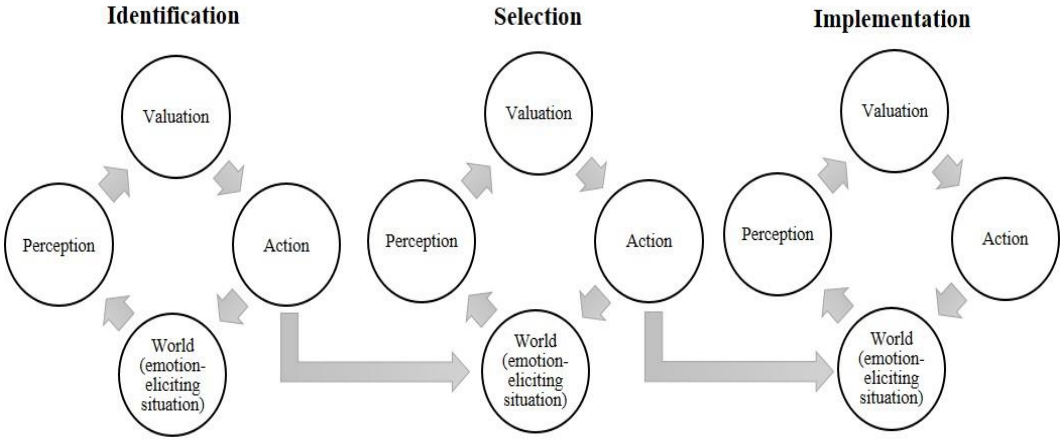

Figure 3. The Extended Process Model of Emotion Regulation (Gross, 2015).

The term 'emotion dysregulation' describes a disruption at any sub-step of these stages. Thinking about emotion dysregulation within this framework is helpful because this generates testable predictions about the nature of emotion dysregulation in FND. Sheppes et al. (2015) have already given examples of what emotion dysregulation would constitute in various forms of psychopathology according to the EPM, some of which are presented below.

Identification-stage difficulties result in trouble initiating emotion regulation. This can happen because the generated emotion is over- or under-represented

(Perceptual sub-step) or because of an erroneous analysis of the cost vs. benefits of maintaining an ongoing emotion (Valuation sub-step). Failures in the action sub-step would lead to the identified need to regulate not being translated into action. Panic attacks are an example of over-representation during the identification stage, during which current emotional states can be magnified resulting in unnecessary and maladaptive regulatory efforts. An example of under-representation is alexithymia – a personality type characterised by difficulty identifying and labelling emotional states (Taylor, 1984), which is likely to lead to a failure to regulate emotions at all.

Within the selection stage, a perceptual sub-step failure results in the mis-representation of available general regulatory categories. A valuation failure arises from an erroneous cost-benefit analysis associated with general regulatory categories; if a maladaptive category of strategies is given a strong-enough positive valuation, it will pass the threshold required for selection. An action sub-step impairment results in a failure to trigger the general regulatory category. Within this framework, a reliance on emotion-focused coping strategies could be considered an example of emotion dysregulation at the valuation sub-step, in that the immediate relief of negative affect passes the threshold of valuation, even though emotion-focused coping does little to resolve the initial cause of distress. It has been argued that non-suicidal self-injury is an example of this, because it is a harmful general category of tactics which are also a powerful distractor from even more distressing situations (McKenzie & Gross, 2014).

The implementation stage serves to execute a particular strategy from the general category of strategies yielded by the selection stage. Implementation-stage difficulties may arise through the misrepresentation of specific regulatory tactics (perceptual sub-step), erroneous valuations of the cost / benefits associated with a specific regulatory tactic, or a failure to enact the selected tactic. An example of the

latter can be seen in that the tactic of recalling positive memories to repair sad mood is impaired in dysphoric patients, but the ability to use distraction is intact (Joormann & Siemer, 2004).

Sheppes et al. (2015) also suggest that there can be deficits in the processing-dynamics of emotion regulation. For example, an individual may stop or switch to another regulatory tactic too soon, before the initially selected method has had time to work. This may happen because the individual has low regulatory self-efficacy (i.e., they believe they are not able to successfully implement regulation strategies), which has been linked to social anxiety (Thomasson & Psouni, 2010). Conversely, an individual may fail to stop or switch to another regulatory tactic even though it is ineffective. An example of this is the rigid style of thinking in Obsessive Compulsive Disorder, which can also be thought of as a failure to switch from strategies (e.g., repeated checking) that do not work.

1.6. Thesis aims

The overall aim of this thesis is to contribute to the existing knowledge of emotion dysregulation in patients with FND by taking a theoretically constrained, hypothesis driven approach set within a biopsychosocial perspective. The EPM (Gross, 2015) will be used to generate hypotheses about emotion dysregulation in FND, which will be tested with a combination of self-report, behavioural, and physiological measures. We also aim to investigate changes in self-reported emotion dysregulation and psychological distress over the course of a psychotherapeutic intervention for FND. A summary of the remaining chapter aims is outlined below:

Chapter 2 – A systematic review to synthesise the existing literature on emotion dysregulation in NEAD (emotion regulation is a likely to be a pertinent factor for FND in general (as for all medical conditions), but the literature suggests the link

to emotion dysregulation is particularly strong for NEAD).

Chapter 3 – To address this issue of heterogeneity in FND by exploring the relationship between FND symptom manifestation and emotion dysregulation. Self-reported emotion dysregulation and symptoms of psychopathology will be compared in FND patients with and without impairments of consciousness.

Chapter 4 – To generate and test hypotheses about the identification of emotions, as well as the selection and implementation of emotion regulation strategies in patient with FND. The identification stage will be studied using an interoceptive sensitivity paradigm, and the selection / implementation stages will be studied using a paradigm designed to investigate expressive suppression in patients with FND. Evidence of chronic autonomic arousal related to emotion dysregulation will also be studied in this chapter using a Heart Rate Variability paradigm.

Chapter 5 – To track changes in emotion dysregulation with a self-report measure in patients with FND pre- and post-psychotherapeutic intervention.

Chapter 6 – To synthesise and discuss the overall findings of this thesis as they relate to the EPM and emotion dysregulation in patients with FND.

2. Emotion dysregulation in patients with Nonepileptic Attack Disorder: a systematic review based on the Extended Process Model

2.1. Introduction

Nonepileptic Attacks (NEAs) are a paroxysmal FNS assumed to be a behavioural and experiential response to aversive triggers (Brown & Reuber, 2016a). Superficially resembling epileptic seizures, but un-associated with epileptiform activity, NEAs are relatively common, and are associated with long-term disability as well as a heavy economic burden (Asadi-Pooya & Sperling, 2015). While the causes of NEAD are yet to be elucidated, a biopsychosocial model attributes aetiology to a complex interaction of pre-disposing, precipitating, perpetuating, and triggering factors - several of which relate to an individuals' capacity to regulate their own emotions (Reuber, 2009). Examples of such relevant psychological and psychiatric factors include (but are not limited to) previous exposure to trauma, dissociation, coping, alexithymia, and interpersonal attachment styles (Brown & Reuber, 2016a). While there is an increasing trend for research on emotion regulation in NEAD, and an integrative psychological model has been proposed (e.g., Brown & Reuber, 2016b), it remains to be seen how observations of emotion dysregulation in NEAD can be fitted into a more general theory of emotion regulation. Therefore, the aim of this review is to synthesise the existing literature on emotion dysregulation in NEAD within the framework of the EPM (see section 1.5. for explanation of the EPM) (Gross, 2015).

2.2. Methods

A systematic review was conducted. Data were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist (Moher et al., 2015). The definition of emotion regulation and dysregulation was based on the EPM (Gross, 2015) and NEAD was defined as a clinical diagnosis identical to Psychogenic Nonepileptic Seizures (PNES). The diagnosis of NEAD does not map neatly onto any one of the nosological categories of the DSM-V, but usually fulfils the diagnostic criteria of FND (Conversion) Disorder (American Psychiatric Association, 2013) falling under the subtype of 'with attacks or seizures'. The diagnostic process clinically defining NEAD / PNES has been outlined in a consensus paper by the International League Against Epilepsy (LaFrance et al., 2013)

2.2.1. Search strategy

The electronic databases PubMed and Web of Science were searched on 18th January 2018 (years 1894 – 2017) using the following search terms: (nonepileptic NEAR attack*) OR (non-epileptic NEAR attack*)) OR (nonepileptic NEAR seizure*)) OR (non-epileptic NEAR seizure*)) OR pseudoseizure*) OR (dissociative NEAR seizure*)) OR (dissociative NEAR convulsion*)) OR pseudo- epilep*) OR (hysterical NEAR seizure*)) OR (hysterical NEAR convulsion*)) OR hysteroepilepsy*) OR (conversion NEAR seizure*)) OR (psychogenic NEAR seizure*)) OR (functional NEAR seizure*)) OR (nonepileptic NEAR event*)) OR (non-epileptic NEAR event*)) *AND* (((emotion NEAR regulation) OR emot*) OR mood)) *AND* (((((((((indentifi* OR alexithymi*) OR select*) OR avoid*) OR distraction) OR attention*) OR coping*) OR reapprais*) OR suppress*) OR implement*)). Search terms relating to NEAD were taken from a recent review article on NEAD (Wiseman & Reuber, 2015). Search terms relating to emotion dysregulation

were taken from or synonymous with keywords in the EPM (Gross, 2015). Further relevant articles were identified from the reference list of papers identified during the electronic database search.

2.2.2. Study selection

Titles and abstracts of the resulting articles were screened for relevance to the review topic by myself (IW) and compared against inclusion and exclusion criteria. Only original peer-reviewed research reports were included. Review articles, case studies, opinion pieces, conference abstract or posters, unpublished work, and articles not written in English were excluded from the review. No articles were excluded on the basis of study design. Studies not directly relevant to the mechanism of emotion regulation in patients with NEAD only (i.e. explicitly defined experimental / case groups with mixed FNS or with comorbid epilepsy) were also excluded at this stage. Studies of paediatric populations or treatment for NEAD, and studies that focused on patients' support networks were considered outside the scope of the review.The remaining full-text articles were then read in full by IW and MR. Articles were subsequently excluded because dependent variables were not quantitative psychological measures and were therefore incompatible with the quality rating system (Ding et al., 2014; Pick, Mellers, & Goldstein, 2016) or because the methods / methodologies used did not directly relate to a stage of the EPM (Del Bene et al., 2017; Holmes et al., 2001). Finally, each article was clustered to one or more specific stages of the EPM according to the methodologies or measures used (such that some studies are discussed in more than one section of this review, see Table 2 for list of measures grouped into EPM stage). The categorisation of each study / methodology into stages of the EPM was proposed by IW and confirmed by a second rater (LL).

2.2.3. Quality assessment

The selected papers were subjected to a formal quality assessment (Table 3).The articles were rated according to a bespoke appraisal tool designed specifically for quantitative psychological research in this field and published in a previous systematic review (Brown & Reuber, 2016a). This rating system clarifies whether i) all diagnoses of NEAD were confirmed with video-EEG (yes / no), ii) a diagnosis of epilepsy was explicitly ruled out in the group with NEAD (yes / no), iii) there was reference to a procedure to ensure that nonepileptic attacks could not have been misdiagnosed panic attacks (yes / no), iv) patients were recruited consecutively (yes / no), and v) dependent variables were standardised (yes / no). vi) Number, type, and gender ratio of control groups (where appropriate) were recorded to ensure that the control groups were matched and did not have a diagnosis of NEAD (yes / no) (a difference in gender ratio of less than 10% or mean age difference of less than five years between-groups was considered matched). Vii) Very few studies presented a formal power calculation to justify sample sizes, therefore we rated sample size according to the power and effect size conventions proposed by Cohen (1988) and used in a previous systematic review of NEAD (Brown & Reuber, 2016a). Study quality was calculated from a combination of ratings based on eight different quality criteria and sample power (Brown & Reuber, 2016a). Sample sizes for studies were rated as being very poor (<15 participants in each group; i.e., <80% power to detect a very large effect size, Cohen's d = 1.1), poor (<26 participants in each group; i.e., <80% power to detect a large effect size, d = 0.8), moderate (26–63 participants in each group; i.e., ≥80% power to detect a large effect size, d=0.8) or good (≥64 participants in each group; i.e., ≥80% power to detect a medium effect size, d = 0.5), assuming a two-tailed independent t test with alpha = .05. To establish inter-rater

reliability, each article was rated by IW and MR. Any disagreements on ratings were resolved following discussion. Studies which were rated as 'unacceptable' were subsequently excluded from the review.

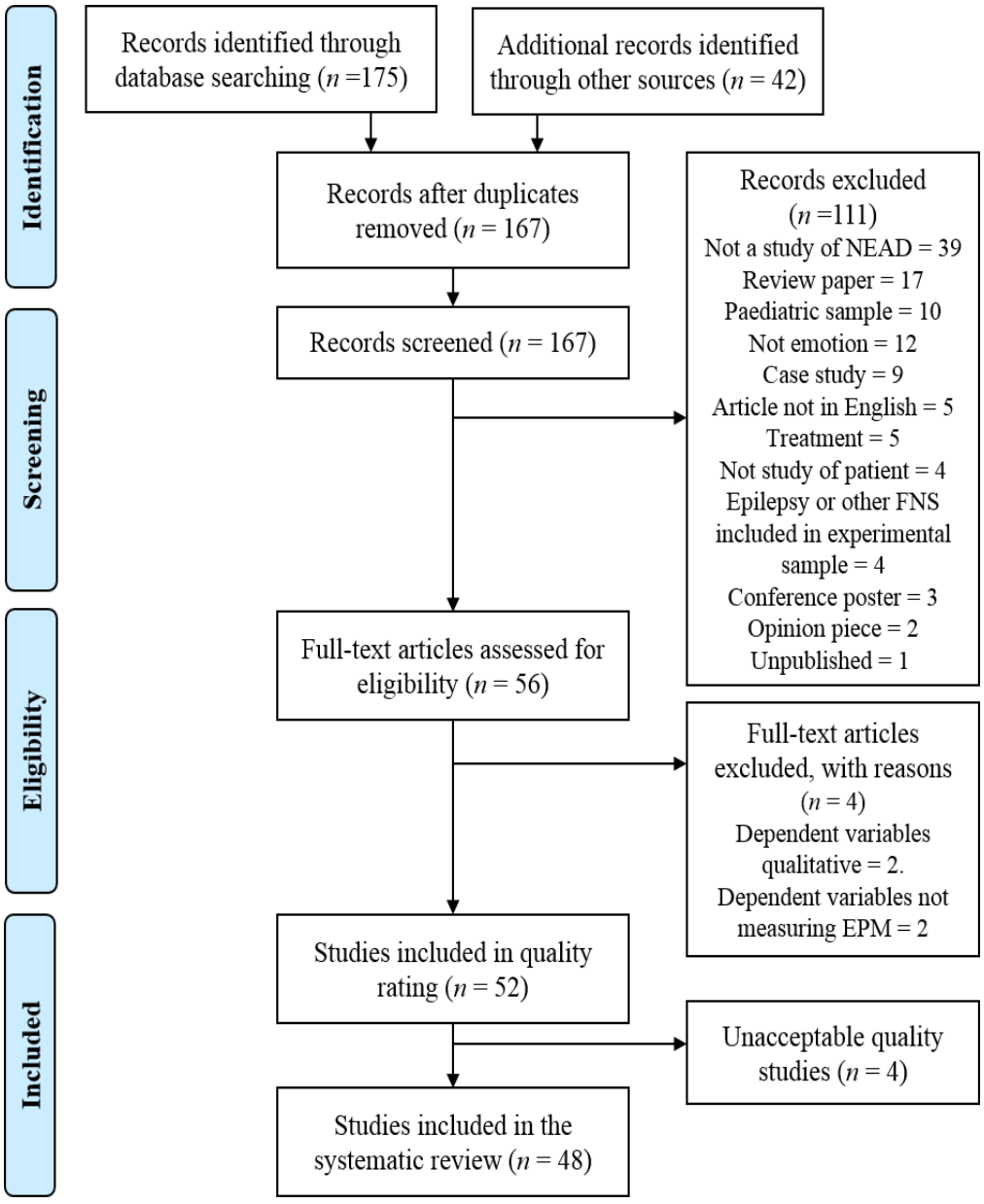

Figure 4. PRISMA flowchart

2.3. Results

2.3.1. Quality assessment

Fifty-two papers were included in the quality assessment (Table 3). Quality was rated as unacceptable in four (7.7%), low in 24 (46.2%), medium in 21 (40.4%), and high in 3 (5.8%) studies. The median size of case group included in the review was 30 but only 50% of studies (with a case-control design) were adequately powered (defined as moderate or good power). Sixteen of the 24 low quality studies would have been rated as medium quality if they had a sample size ≥26. Likewise, the four studies which were excluded were deemed inadmissible because of sample size of <15; all of these studies would have been classed as being of moderate to high quality on the basis of the other quality criteria. In terms of individual quality rating criteria, all dependent variables were standardised in 92%, an explicit reference to epilepsy being ruled out was made in 76%, all NEAD cases were confirmed with video-EEG in 71%, anxiety attacks were ruled out in 50%, and patients were recruited consecutively in 38% of studies subjected to the quality review. Forty eight studies were included in the final review.

2.3.2. Categorisation of studies

Twenty-three studies were categorised as relevant to the identification stage of the EPM because the measures and methodologies used captured participants' perception of their own emotional state. Thirty-four studies were deemed relevant to the selection and implementation stages (Table 2).

Table 2 - *Categorisation of measures and methodologies into stages of the Extended Process Model.*

EPM stage	Construct	Methodology / measures used
Identification	Emotional awareness / Alexithymia	TAS-20, EPS-25 impoverished emotional experience subscale, patient-endorsed ictal somatic panic symptoms versus panic item on HADS, patient-endorsed ictal emotions, BNI Screen for Higher Cognitive Function (affect subscale) vs. patient-reported irritability, The Heart Beat Detection Task
	Perceived stress	PERI (Life Events Scale), EPCL, LEC, PSS, NEO-PI-R Neuroticism subscale, DAPP-BQ
Selection and implementation	Regulatory / coping style	DERS, UCS, COPE Inventory, CERQ, WOC, MHLOC, ERQ, REM, MMPI, CISS, EPS-25, HRV, The Courthauld Emotional Control Scale
	Dissociation	DES, CADDS, DIS-Q, Somatoform Dissociation Questionnaire, SCID-D, CDS, patient-endorsed ictal dissociative symptomology, TSI-2 Dissociation subscale
	Avoidance	Short TCI (Avoidance subscale), WOC, MEAQ, Fear Questionnaire, CISS Avoidance subscale, EPS-25 Avoidance subscale
	Exteroceptive / others	Emotional N-Back Task, Emotional Stroop Task, Task-switching experiment (emotional categorisation), Animated Morph Task, Movie for Assessment of Social Cognition, HRV

Note. TAS-20 = Toronto Alexithymia Scale – 20, EPS-25 impoverished subscale = Emotional Processing Scale -25 impoverished emotional experience subscale, HADS= Hospital Anxiety and Depression Scale, PERI = Psychiatric Epidemiology Research Interview, EPCL = Everyday Problems Checklist, LEC= Life Events Checklist, PSS = Perceived Stress Scale, NEO-PI-R = NEO Personality Inventory Revised, DERS = Difficulties in Emotion Regulation Scale, UCS = Utrecht Coping Scale, DES = Dissociative Experiences Scale, CADDS = Clinician Administered Dissociative States Scale, DIS-Q = The Dissociation Questionnaire, CERQ = Cognitive Emotion Regulation Questionnaire, Short TCI = Short Temperament and Character Inventory, SCID-D = Structured Clinical Interview for Dissociative Disorders, WOC = Ways of Coping Scale, CDS = Cambridge Depersonalisation Scale, MEAQ = Multidimensional Experiential Avoidance Questionnaire, MHLOC = Multidimensional Health Locus of Control Scale, ERQ = Emotion Regulation Questionnaire, REM = Response Evaluation Measure, TSI-2 = Trauma Symptom Inventory, MMPI = Minnesota Multiphasic Personality Inventory, CISS = Coping Inventory for Stressful Situations, HRV = Heart Rate Variability, DAPP-PQ = Dimensional Assessment of Personality Pathology – Basic Questionnaire.

Table 3 - *Quality rating assessment of studies identified in the literature search.*

				Quality rating criteria									EPM stage	
Study	**Study design**	**Sample size** (<15 = very poor, 15-26= poor, 26-63= moderate, ≥63=good)	**Type of control group**	**Video-EEG**	**Epilepsy excluded**	**Anxiety excluded**	**Consecutive sampling**	**Standardised measures**	**≤10% difference in**	**≤5 years difference in**	**% of 'Yes' ratings**	**Overall rating**	Identification	Selection /implementation
Akyuz et al. (2004)	Case control	Moderate	ES	N	Y	Y	N	Y	Y	Y	71	Medium		✓
Alper et al. (1997)	Case control	Good	ES	Y	Y	Y	Y	Y	Y	Y	100	High		✓
Bakvis, Roelofs, et al. (2009)	Case control	Poor	HC	Y	Y	Y	N	Y	Y	Y	71	Low		✓
Bakvis, Spinhoven, et al. (2009)	Case control	Poor	HC & ES	Y	Y	Y	N	Y	N	N	57	Low		✓
Bakvis, Spinhoven, et al. (2011)	Case control	Very poor	HC	Y	Y	Y	Y	Y	N	N	57	Unacceptable	-	-
Bakvis et al. (2010)	Case control	Poor	HC	Y	Y	N	N	Y	Y	Y	100	Low		✓
Baslet et al. (2010)	Case series	-	-	N	N	N	Y	Y	-	-	29	Low		✓
Bewley et al. (2005)	Case control	Poor	HC & ES	Y	Y	N	N	Y	Y	Y	71	Low	✓	
Bodde et al. (2013)	Case series	-	-	Y	N	Y	Y	Y	-	-	57	Medium	✓	✓
Bodde et al. (2007)	Case series	-	-	Y	Y	N	Y	Y	-	-	57	Medium		✓
Bowman et al. (2000)	Case control	Poor	ES	Y	N	N	N	Y	Y	Y	57	Low		✓
Brown et al. (2013)	Case control	Moderate	ES	N	Y	N	N	Y	Y	Y	57	Medium	✓	
Cohen et al. (2014)	Case series	Moderate	-	Y	Y	Y	Y	Y	-	-	71	Medium		✓

Cragar et al. (2005)	Case control	Very good	ES	Y	Y	N	Y	Y	N	Y	71	Medium	✓	
Cronje & Pretorious (2013)	Case control	Poor	HC	Y	Y	N	N	Y	Y	Y	71	Low		✓
Demartini et al. (2016)	Case control	Poor	HC & FMD	Y	Y	Y	Y	Y	Y	Y	100	Low	✓	✓
Dikel et al. (2003)	Case control	Poor	ES	Y	N	N	N	Y	N	Y	43	Low		✓
Dimaro et al. (2014)	Case control	Moderate	HC & ES	Y	Y	N	N	Y	Y	Y	71	Medium	✓	✓
Ekanayake et al. (2017)	Case control	Moderate	FMD	Y	Y	N	Y	Y	Y	N	71	Medium	✓	✓
Fleisher et al. (2002)	Case control	Moderate	ES	Y	N	Y	N	Y	Y	Y	71	Medium		✓
Frances et al. (1999)	Case control	Moderate	ES & HC	N	Y	Y	N	Y	Y	Y	71	Medium	✓	✓
Goldstein et al. (2000)	Case control	Poor	HC	N	Y	Y	N	Y	Y	Y	71	Low		✓
Goldstein et al. (2006)	Case control	Poor	ES	N	Y	Y	N	Y	N	Y	57	Low	✓	✓
Gul and Ahmad (2014)	Case control	Good	HC	N	Y	Y	N	Y	Y	Y	71	Medium		✓
Hendrickson et al. (2014)	Case control	Good	ES	Y	Y	Y	Y	N	N	N	57	medium		✓
Hingray et al. (2011)	Case control	Very poor	NEAD - T	Y	N	Y	Y	Y	N	N	57	Unacceptable	-	-
Kaplan et al. (2013)	Case control	Good	ES	Y	N	N	N	Y	N	Y	43	Medium	✓	
Kuyk et al. (1999)	Case control	Good	ES	N	Y	N	N	Y	N	N	43	Low		✓
Lawton et al. (2008)	Case control	Moderate	ES	N	Y	N	N	Y	N	Y	43	Low		✓
Martino et al. (2017)	Case control	Very poor	MMDD	Y	Y	Y	Y	Y	Y	Y	100	Unacceptable	-	-
Mazza et al. (2009)	Case control	Moderate	ES & HC	Y	N	Y	Y	Y	Y	Y	86	Medium		✓
Myers, Fleming et al. (2013)	Case series	-	-	Y	Y	N	Y	Y	-	-	57	High	✓	✓
Myers, Matzner et al. (2013)	Case control	Moderate	ES	Y	Y	N	Y	Y	N	Y	86	Medium	✓	
Myers, Perinne, et al. (2013)	Case series	Good	NEAD - T	Y	Y	Y	Y	Y	Y	Y	86	High		✓
Novakova et al. (2015)	Case control	Moderate	HC	N	N	N	Y	Y	N	N	29	Low	✓	✓
O'Brien et al. (2015)	Case control	Poor	HC	Y	Y	Y	N	Y	Y	Y	86	low	✓	
Ozcetin et al. (2009)	Case control	Moderate	HC	Y	Y	Y	N	Y	Y	Y	86	Medium		✓
Ponnusamy et al. (2011)	Case control	Moderate	ES & HC	Y	Y	N	Y	Y	Y	Y	86	Medium		✓

Prigatano et al. (2002)	Case series	-	-	Y	N	N	N	N	-	-	14	Low		✓
Prigatano et al. (2009)	Case control	Poor	ES	Y	Y	N	N	N	N	Y	43	low		✓
Proenca et al. (2011)	Case control	Poor	ES	Y	Y	N	N	Y	Y	Y	71	low		✓
Prueter et al. (2002)	Case control	Poor	ES & ES+NEAD	N	Y	N	N	Y	N	N	29	Low		✓
Reuber et al. (2003)	Case control	Good	ES	N	Y	N	N	Y	N	Y	43	Medium		✓
Reuber et al. (2004)	Case control	Very good	ES & HC	Y	Y	N	Y	Y	N	Y	57	Medium	✓	
Roberts et al. (2012)	Case control	Poor	High T & Low T	Y	Y	Y	N	Y	N	Y	71	low		✓
Schonenberg et al. (2015)	Case control	Poor	HC	Y	Y	N	Y	Y	Y	Y	86	Low	✓	✓
Testa et al.(2012)	Case control	Moderate	HC & ES	Y	Y	Y	N	Y	N	Y	71	Medium	✓	✓
Tojek et al. (2000)	Case control	Poor	ES	Y	Y	N	N	N	Y	Y	57	low	✓	
Uliaszek et al. (2012)	Case series	-	-	N	N	Y	N	Y	-	-	29	Low	✓	✓
Urbanek et al. (2014)	Case control	Good	HC	N	N	N	N	Y	Y	N	29	Low	✓	
Van der Kruijs et al. (2012)	Case control	Very poor	HC	N	Y	Y	N	Y	Y	Y	71	Unacceptable	-	-
Wolf et al. (2015)	Case control	Good	ES	Y	Y	Y	N	Y	N	Y	86	Medium	✓	

Note. HC = healthy control, ES = epilepsy control, FMD = Functional Movement Disorder, NEAD-T= non-traumatised NEAD control, ES+NEAD= comorbid epilepsy and NEAD control, High T= high trauma control group, Low T= low trauma control group, MMDD = Mild Major Depressive Disorder - = not applicable, EPM = Extended Process Model of emotion regulation.

2.4. The identification stage

The identification stage describes the detection of an existing emotion followed by an evaluation of whether the emotion is negative or positive and whether the result of this evaluation is sufficiently discrepant with a goal state to warrant regulation (Gross, 2015). Based on this analysis, the goal to regulate an emotion will then be activated (or not). Studies pertaining to the identification of emotional state in patients with NEAD could be grouped into two themes: i) alexithymia / awareness of one's own emotional state and, ii) perceptions of stress.

2.4.1. Alexithymia / emotional awareness and NEAD

The ability of patients to detect and interpret their own emotional states has mostly been assessed with self-report measures of alexithymia in the NEAD population (e.g., The Toronto Alexithymia Scale -20 and the Emotional Processing Scale-25). Alexithymia is a psychological construct describing difficulties with the identification and description of feelings as well as their differentiation from sensations associated with physiological processes (Goerlich-Dobre, Votinov, Habel, Pripfl, & Lamm, 2015).Other studies have investigated the accuracy of patients' reporting on emotional states / feelings with the use of an interoceptive sensitivity paradigm or by comparing patients' self-reported feeling states against more objective measures of the same construct.

2.4.1.1. Self-report studies of alexithymia -The Toronto Alexithymia Scale.

The most frequently used measure of alexithymia in patients with NEAD was the twenty-item Toronto Alexithymia Scale-20 (TAS-20), which assesses patients' ability to identify their own emotions. There are three subscales measuring 'difficulty describing feelings (DDF)', 'difficulty identifying feelings (DIF)', and 'externally orientated thinking (EOT)' – the latter referring to a tendency to focus on external

rather than internal events and experiences (Bagby, Taylor, & Parker, 1994). Usually, an individual reporting a total TAS-20 score of ≥ 61 is considered 'alexithymic' and those scoring between 52 and 60 are considered 'possibly alexithymic' (Bagby et al., 1994).

Ten studies reporting a total TAS-20 score used a case-control design (Table 4). Of these ten studies, two classified the NEAD group as alexithymic (i.e. mean total TAS-20 >61) with approximately 90% and approximately 63% of the NEAD group scored above the clinical cut off for alexithymia respectively (Bewley, Murphy, Mallows, & Baker, 2005; Urbanek, Harvey, McGowan, & Agrawal, 2014). In seven studies, mean NEAD group scores were within the 'possibly alexithymic range' (Ekanayake et al., 2017; Kaplan et al., 2013; Myers, Matzner, Lancman, & Perrine, 2013; O'Brien et al., 2015; Schönenberg et al., 2015; Tojek, Lumley, Barkley, Mahr, & Thomas, 2000; Wolf et al., 2015). Patients with NEAD in five of these ten studies were compared against healthy controls, patients with epilepsy in five, or patients with FMD in two. The NEAD group scored more highly on the total TAS-20 score than healthy controls in all five of the studies which included a healthy control group (Bewley et al., 2005; Demartini, Goeta, et al., 2016; O'Brien et al., 2015; Schönenberg et al., 2015; Urbanek et al., 2014). NEAD patients only scored more highly than patients with epilepsy on the total TAS-20 in one of the three studies with an epilepsy control group (Kaplan et al., 2013). Of the two studies with a FMD control group, one found a significantly higher TAS-20 score in the NEAD group (Ekanayake et al., 2017). A total mean and standard deviation for total TAS-20 scores in each group in the nine studies was calculated (Table 6). This yielded a score of 58.6 (*SD* = 6.7). Overall, these data suggest that patients with NEAD are more alexithymic than healthy controls, with a tendency towards scoring in the high end of the 'possibly alexithymic'

range on the TAS-20.

Table 4 - *Mean and standard deviation (unless otherwise stated) of Total TAS-20 scores for patients with NEAD and control group(s).*

Study authors	**NEAD**	**HC**	**ES**	**FMD**
Bewley et al. (2005)	72.9 (11.8)	50.9 (11.9)[a]	68.6 (11.9)	-
Demartini et al. (2016)	50.6 (12.7)	40.9 (10.1)[a]	-	50.3 (12.6)
Ekanayake et al. (2017)	56.6 (12.2)	-	-	43.1 (10.3)[c]
Kaplan et al (2013)	56.2 (12.4)	-	51.9 (12.1)[b]	-
Myers, Matzner et al. (2013)	54.1 (1.7)	-	50.1 (2.4)	-
O'Brien et al. (2015)	54.7 (13.4)	39.6 (11.2)[a]	-	-
Urbanek et al. (2014)[1]	64.9 (30-9)	41.5 (22-8)[a]	-	-
Schönenberg et al. (2015)	54.6 (11.6)	43.9 (6.7)[a]	-	-
Tojek et al. (2000)	54.0 (11.9)	-	54.4 (10.4)	-
Wolf et al. (2015)	54.7 (11.9)	-	53.1 (10.8)	-
Total	57.3 (6.6)	43.4 (21.4)	55.6 (27.8)	46.7 (5.1)

Note. NEAD = Nonepileptic Attack Disorder, HC = Healthy controls, ES = epilepsy controls, FMD = Functional Movement Disorder controls. [a] = Healthy control group is significantly different from NEAD group. [b] = Epilepsy control group is significantly different from NEAD group. [c] = FMD control group is significantly different from NEAD group. [1] Values are median and range.

One study did not used the TAS-20 in a case / control design, but instead correlated the Total TAS-20 score against a measure of coping (as assessed by the Coping Inventory for Stressful Situations (Myers, Fleming, Lancman, & Perrine, 2013)). The authors found a small negative correlation (r = -.26) between the TAS-20 total score and task-focused coping, and a moderate-to-large positive correlation (r = .54) between the total TAS-20 score and emotion-focused coping, suggesting alexithymic traits in patients with NEAD may related to coping style (although the direction of effect cannot be inferred).

Six of the studies using the TAS-20 reported subscale values (Table 5). Four reported higher scores in the NEAD group on the DIF subscale compared to epileptic and healthy controls (Bewley et al., 2005; Kaplan et al., 2013; Schönenberg et al., 2015; Urbanek et al., 2014). Three reported higher scores on the DDF subscale compared to epileptic and healthy controls (Bewley et al., 2005; Kaplan et al., 2013; Urbanek et al., 2014). None of the studies found any between-group differences in

EOT scores. These results suggest that alexithymic traits in patients with NEAD might be restricted to a difficulty with identify and describing feelings, without a tendency to focus on external events.

In summary, the total TAS-20 results suggest that patients with NEAD are more alexithymic than healthy controls, and score close to the clinical cut-off for alexithymia. Given that the concept of alexithymia was developed to capture what was considered a core feature of psychosomatic disease (Sifneos, 1973) it is perhaps surprising that the total mean score of TAS-20 found in this review did not exceed the clinical threshold. However, the generally low sample size of studies in this field and the heterogeneity in psychological profiles of patients with NEAD (Baslet, Roiko, & Prensky, 2010), raise the possibility that the results in these studies could be an artefact of sampling bias or insufficient sample size. Alternatively, the present finding might reflect the fact that pre-existing beliefs about the role of alexithymia in the aetiology or FND are too generalised, when in reality alexithymia as measured by the TAS-20 is not ubiquitous throughout the NEAD population. Illustrating the psychological heterogeneity in NEAD, a subgroup analysis of patients with NEAD found no differences between patients with NEAD and patients with epilepsy, but yielded two subgroups of people with NEAD; one group (n = 11) characterised by high total TAS-20 scores, and a second group (n = 32) characterised by relatively low total TAS-20 scores (Brown et al., 2013). Therefore, it may be more appropriate for study designs using the TAS-20 to accommodate this heterogeneity with larger sample sizes and subgroup analyses. The conclusion that subscale score results suggest patients with NEAD might be impaired at identifying and describing their feelings, but do not exhibit a tendency to focus more on external experiences than control groups may also be called into question. Concerns have been raised about the reliability of the EOT

subscale and the validity of its application in patients with somatization disorders; a quantitative review of alexithymia and somatisation disorder demonstrated that the EOT subscale has lower internal consistency than the other subscales (De Gucht & Heiser, 2003). The review also showed that unlike the DIF and DDF subscales, the EOT is unrelated to the number of somatic symptoms patients report. The authors suggest that the aforementioned lower internal consistency might be attributed to a larger number of negatively keyed items on the EOT subscale than the DIF and DDF subscales, with the resulting unreliability generating mixed findings (some positive, some negative, some null) across studies. Furthermore, the conclusion that patients with NEAD don't focus on external events at the expense of internal events seems at odds with studies showing reduced attentional allocation to interoceptive information in patients with FND (Ricciardi et al., 2016; section 4.2) and cognitive biases towards exteroceptive emotional information (see section 2.5.4).

Table 5 - *Mean and standard deviation (unless otherwise indicated) of TAS-20 subscale scores for patients with NEAD and control groups.*

	Difficulty identifying feelings			**Difficulty describing feelings**			**Externally orientated thinking**		
	NEAD	**HC**	**ES**	**NEAD**	**HC**	**ES**	**NEAD**	**HC**	**ES**
Bewley et al (2005)	27.1 (6.3)	11.9 (5.8)*	25.2 (6.4)	18.5 (3.9)	12.1(4.0)*	15.7 (3.3*)	26.5 (4.8)	27.1 (4.4)	27.4 (4.6)
Brown et al (2013)[1]	24 (11)	-	18 (12.5)	16 (8)	-	12 (7)	23 (13)	-	21 (9)
Kaplan et al (2013)	20.9 (6.9)	-	18.5 (7.1)*	14.7 (4.6)	-	13.4 (4.1)*	20.61 (4.2)	-	20.0 (4.4)
Urbanek et al (2014)[2]	25 (11-35)	-	13 (7-32)*	18 (7-25)	-	11 (5-25)*	22 (9-34)	-	17 (9-28)
Schönenberg et al (2015)	17.6 (7.6)	12.6 (5.2)*	-	12.9 (4.1)	10.7 (2.6)	-	24.1(3.9)	24.8 (3.7)	-
Wolf et al (2015)	59.1 (12.1)	-	55.4 (13.2)	51.7 (11.6)	-	50.2 (11.2)	49.8 (11.1)	-	51.2 (9.5)

Note. * = statistically significantly different from NEAD values, HC = healthy control group, ES = epilepsy control group, [1] = Values are median and interquartile range, [2] = Values are median and range.

2.4.1.2. Other measures of alexithymia / emotional awareness in NEAD.

Other methodologies designed to assess emotion identification in patients with NEAD have yielded a more consistent pattern of deficiencies in emotion identification. A cross-sectional comparison of patients with NEAD against healthy controls using the Emotional Processing Scale-25 (Baker, Thomas, Thomas, Santonastaso, & Corrigan, 2015) found elevated scores on the 'impoverished emotional experience' subscale (Novakova, Howlett, Baker, & Reuber, 2015). This subscale describes a detached experience of one's emotions due to poor emotional insight. Uliaszek, Prensky, and Baslet (2012) also used the Difficulties with Emotion Regulation Scale (DERS) to delineate two subgroup profiles of patients with NEAD; one with higher than normative values on the 'emotional clarity' and 'emotional awareness' subscales of the DERS, and one with lower than normative values on the 'emotional awareness' subscale (Uliaszek et al., 2012), which supports the suggestion that patients with NEAD are unlikely to all have the same deficits in emotional regulation.

Comparisons of patients' self-reported emotional state against more objective measures also suggests that patients with NEAD are prone to difficulty with the identification of their emotions. Goldstein and Mellers (2006) noted that patients with NEAD reported more somatic symptoms of anxiety during seizures than patients with epilepsy, but did not report higher subjective levels of anxiety than patients with epilepsy. Similarly, Dimaro et al. (2014) observed a significant discrepancy between an implicit measure (Implicit Relational Assessment Procedure) and explicit measure (State-Trait Anxiety Inventory) of anxiety in patients with NEAD but not those with epilepsy. Likewise, Prigatano and Kirlin (2009) found that while patients with NEAD and epilepsy self-reported similar levels of psychopathology on the Personality

Assessment Inventory, patients with NEAD performed significantly worse on a neuropsychological measure of emotional regulation (the Barrow Neurological Institute Screen for Higher Cerebral Functions Affect subtest). While objective and subjective measures often fail to correlate strongly, the observed discrepancies in the NEAD but not epilepsy groups suggests that emotion identification may be a particular problem for patients with NEAD.

Finally, one other study has sought to measure patients' ability to identify their emotional state, using the well-established Heart Beat Detection Task (Schandry, 1981). This task requires the participant to count how many heartbeats they have within a time period (without manually checking) and is compared against how many they actually have, to generate an accuracy score. This test rests on the assumption that interoceptive processes are an important source of information for emotional identification (see section 4.2), and therefore a less accurate 'interoceptive sensitivity' score would suggest a more impaired ability to identify one's own emotions. Demartini, Goeta, et al. (2016) compared patients with NEAD against those with FMD and healthy controls on the Heart Beat Detection task, and found no significant between-groups difference (although TAS-20 scores were elevated in both patient groups compared to healthy controls). The same group had previously found reduced interoceptive sensitivity in a group of patients with FMD relative to healthy controls (Ricciardi et al., 2016), which we also replicate in a sample of patients with NEAD and other FNS in Chapter 4.2.

2.4.2. Perceptions of stress

It is important to note that impaired emotion identification does not mean that patients with NEAD experience an absence of affect. This is clearly reflected in studies investigating NEAD patients' perceptions of how stressful their lives are. Four studies

have demonstrated that patients with NEAD perceive their lives as more stressful than healthy controls or the general population (Bodde et al., 2013; Frances, Baker, & Appleton, 1999; Schönenberg et al., 2015; Tojek et al., 2000). One might argue that this is to be expected given the known detrimental effect of living with a disability on quality of life (Alonso et al., 2004). However, patients with NEAD subjectively rated stressful life events as more distressing than patients with epilepsy, even though objectively they did not experience any more stressful life events than epileptic and healthy controls (Testa, Krauss, Lesser, & Brandt, 2012). This finding suggests that patients with NEAD may have magnified perceptions of stress over and above that of individuals living with non-functional seizure disorders.

An increased tendency to perceive life as stressful is also reflected in measures of personality. Ekanayake et al. (2017) observed significantly higher scores on the neuroticism subscale of the NEO Personality Inventory Revised (NEO-PI-R) compared to patients with FMD – elevations on this subscale reflect a 'persistent, life-long tendency to experience events negatively.' Other assessments of personality in patients with NEAD have also shown that clusters of this group exhibit elevated levels of neuroticism compared to patients with epilepsy on the NEO-PI-R (Cragar, Berry, Schmitt, & Fakhoury, 2005), and as measured by the Dimensional Assessment of Personality Pathology – Basic Questionnaire (DAPP-PQ) (Reuber, Pukrop, Bauer, Derfuss, & Elger, 2004). Furthermore, these latter two studies of personality pathology went on to identify clusters of personality styles characterised by higher and lower levels of neuroticism. As such, it may be the case that only subgroups of patients with NEAD exhibit a personality style prone to perceive their lives as stressful.

2.4.3. Conclusions on the identification stage

The ability of patients with NEAD to identify their emotional state has been

assessed with a combination of self-report and behavioural measures. Findings generated from the TAS-20 suggest that patients with NEAD have a tendency towards alexithymia, approaching if not exceeding the clinical cut-off and characterised by difficulties identifying and describing feelings. Other self-report measures suggest that patients with NEAD experience a lack of emotional clarity / awareness and an impoverished emotional experience, and the discrepancy between self-report and objective measures of affect seem to corroborate this conclusion. However, difficulties with identification do not seem to prevent patients with NEAD from perceiving their lives as stressful, which is reflected in the elevated scores on personality questionnaires capturing neuroticism. Taken together, these studies suggest that emotional dysregulation in NEAD involves impairments in the identification stage of the EPM (Gross, 2015), although subgroups of patients who are more and less impaired in this respect are likely to exist.

2.5. The selection and implementation stages

During the selection stage of the EPM, potential emotion regulation strategies are represented and evaluated in relation to the strength of the emotion and the available cognitive and physiological resources (Gross, 2015). A general regulatory strategy is selected and fed-forward to the implementation stage, which is when the selected regulatory strategy is translated into specific tactics appropriate for the situation an individual is in (Gross, 2015). 'Selection' in this model does not necessarily imply a deliberate choice, as the decision to use a regulatory strategy can be made outside of conscious awareness, for example automatically turning away from an upsetting image. Emotion dysregulation may occur at this point because the individual has a limited repertoire of regulatory strategies or a pre-disposition to select maladaptive strategies. Alternatively, a failure to accurately appraise the external

world (e.g., interpreting another person's benign actions as deliberate) could result in a failure to implement a strategy which would otherwise successfully down-regulate negative affect (e.g., by reappraising another person's potentially harmful actions as unintentional).

Studies were identified relating to the selection and implementation of potentially maladaptive regulatory strategies (specifically emotion-focused coping, avoidance, and dissociation) and a tendency to misrepresent exteroceptive emotional information which could feasibly influence an individual's appraisal of the external world. Owing to the fact that no experimental designs identified in the literature search allowed for a clear distinction between the selection and implementation stages of the EPM (if that is indeed possible), the following section will discuss research pertaining to these two stages together.

2.5.1. Emotion-focused coping

Researchers frequently categorise coping as either emotion-focused, or problem-focused (Lazarus, 1984). Problem-focused coping describes attempts to relieve negative emotion by changing some aspect of the distress-causing situation. Emotion-focused coping however, describes attempts to reduce negative emotions (e.g., denial or venting), rather than modify their cause. Emotion-focused coping is therefore generally considered to be less adaptive than problem-focused coping (Lazarus, 1984) (although there are exceptions to this rule). Within the context of the EPM, emotion-focused coping would fall under the 'response-modulation' general category of regulatory strategies (Table 1).

Nine studies measuring emotion- and problem-focused coping tendencies in patients with NEAD were identified. Using the Ways of Coping Scale (WOCS) (Folkman & Lazarus, 1988), patients with NEAD were shown to be less likely to use

‘planful-problem solving’ than healthy controls (Frances et al., 1999). Other researchers administering the WOCS, observed greater scores on the ‘distancing-coping’ subscale in patients with NEAD relative to healthy controls, which negatively predicted health-related quality of life (Cronje & Pretorius, 2013). On the Utrecht Coping List (Schreurs, Van de Willige, Brosschot, & Tellegen, 1993), patients with NEAD self-reported a greater tendency towards a passive wait-and-see attitude in response to problems than healthy controls, suggesting that they felt unable to address the cause of their distress (Bodde et al., 2013). Accordingly, other studies have observed a greater use of emotional and expressive suppression in NEAD patients than healthy controls (Gul & Ahmad, 2014; Novakova et al., 2015; Testa, Schefft, Szaflarski, Yeh, & Privitera, 2007). An over-reliance on emotion-focused coping strategies may be explained by an external locus of health control; patients with NEAD have been demonstrated to perceive more situations as beyond their control and to have a stronger belief in an external locus of control over their health than healthy controls (Bodde et al., 2013; Goldstein, Drew, Mellers, Mitchell-O'Malley, & Oakley, 2000). Therefore, studies seem to suggest that, in comparison to healthy control groups, patients with NEAD have an increased tendency to select and implement maladaptive emotion-focused coping strategies to manage negative emotion, with some indication that this may be related to an external locus of control.

Studies including cluster and subgroup analyses provide a more nuanced picture of coping in NEAD by taking into account of the heterogeneity of the patient group as a whole. Myers, Perrine, Lancman, and Fleming (2013) categorised patients with NEAD according to several criteria, one of which being whether or not they had been traumatised. Traumatised patients were characterised by a significant elevation on the demoralization scale of the Dutch Short Minnesota Multiphasic Personality

Inventory (MMPI) (Luteijn & Kok, 1985), implying a 'persistent failure to cope internally or externally with life'. This suggested that only traumatised patients with NEAD had difficulties with coping in this study. In another subgroup analysis of emotion regulation profiles in patients with NEAD using the DERS (Gratz & Roemer, 2004), only one of the two sub-groups scored more highly than normative data on the strategies subscale. Items on this subscale indicate that the individual believes that little can be done to regulate negative emotions when one is upset (Uliaszek et al., 2012). Once again, it was not the case that all patients with NEAD felt they could not cope with negative emotions, only those belonging to the subgroup characterised by other measures of emotion dysregulation and psychopathology self-reported difficulties with coping. Myers, Fleming, et al. (2013) demonstrated that an increased tendency to rely on emotion-focused coping strategies in patients with NEAD was associated with co-morbid psychological symptoms, such a depression and somatic complaints. Conversely, the use of task-orientated coping was negatively associated with alexithymia and low positive emotions as measured by the MMPI. Taken together, these studies suggest that a predisposition to select and implement emotion-focused coping strategies is related to other psychological factors such as trauma and depression in sub-groups of patients with NEAD.

2.5.2. Avoidance

Avoidance can be defined as a disinclination to sustain contact with aversive private experiences (including emotions, thoughts, bodily sensations, memories, and behavioural predispositions) or action taken to alter experiences or the events that give rise to them (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). Within the context of the EPM, avoidance falls within the general regulatory category of 'situation selection' (Gross, 2015). A tendency to over-value and select avoidance often

becomes problematic because the short-term relief does little to relieve the cause of the emotion or emotion-eliciting situation. Nine studies investigated avoidance in patients with NEAD, all using self-report measures. With respect to the avoidance of events or emotion-eliciting situations, patients with NEAD endorsed a greater use of escape-avoidance strategies on the WOCS than healthy controls in two studies (Cronje & Pretorius, 2013; Goldstein et al., 2000). An increased self-reported avoidance of negative emotional triggers in patients with NEAD versus healthy controls has been reported on the EPS-25 (Novakova et al., 2015). Patients with NEAD also reported elevated scores on the harm-avoidance subscale of the Temperament and Character Inventory (Dutch version), indicating a personality style characterised by behavioural inhibition in response to signals of punishment and frustrative-non reward (Bodde et al., 2013) Furthermore, responses on the Fear Questionnaire (Marks & Mathews, 1979) indicated that patients with NEAD have a greater tendency to avoid situations that may elicit feelings of agoraphobia than those with epilepsy (Goldstein & Mellers, 2006). In addition, self-report measures have been used to assess patients' tendency to avoid aversive private experiences. Dimaro et al. (2014) demonstrated that patients with NEAD scored significantly higher on the Multidimensional Experiential Avoidance Questionnaire (Gamez, Chmielewski, Kotov, Ruggero, & Watson, 2011) than epileptic and healthy controls. Experiential avoidance scores positively correlated with explicit (i.e. self-reported) anxiety scores and seizure frequency in the NEAD group only. Furthermore, experiential avoidance and somatization scores delineated the two patient groups in a logistic regression model (Dimaro et al., 2014). Uliaszek et al. (2012) identified a subgroup of patients with NEAD who scored significantly lower than normative values on the DERS. The authors of the study interpreted this as reflecting a pre-disposition to being emotionally avoidant. Despite the variety of

avoidance measures used, elevated levels of avoidance endorsed by patients with NEAD is a relatively consistent finding.

A tendency to select and implement avoidance as an emotion regulation strategy may be related to previous psychological trauma, which is common in patients with NEAD (Beghi et al., 2015; Fleisher et al., 2002). For example, when patients with NEAD were categorised according to whether they self-reported trauma or not, the traumatised group also self-reported higher levels of 'defensive-avoidance' on the Trauma Symptom Inventory (TSI-2) than the non-traumatised group (Myers, Perrine, et al., 2013). Higher scores on the defensive-avoidance subscale indicate a tendency to make intentional efforts to avoid unwanted internal experiences and emotion-eliciting environments. Likewise, Bodde et al. (2013), also identified greater levels of 'harm avoidance' in a subgroup of patients with NEAD who had been traumatised than those who had not. Therefore, a predisposition in patients with NEAD towards the selection and implementation of avoidance as a regulatory strategy may also be a product of other psychological factors.

2.5.3. Dissociation

Nonepileptic attacks themselves have been conceptualised a dissociative response to overwhelming emotion (Roberts & Reuber, 2014; Stone & Carson, 2013). Dissociation, the breakdown in the normal integration of cognitive functions, has been considered such an important symptom of NEAD, that it is classified as a dissociative disorder in the ICD-10 (World Health Organization, 2016). However, the definition of dissociation and its relationship to NEAD is a contentious subject. For further explanation of this controversy see Roberts and Reuber (2014). Dissociative symptoms in NEAD have largely been investigated using self-report questionnaires. The Dissociative Experiences Scale (DES (Bernstein & Putnam, 1986)) is one such

instrument, which gives a total score and subscores measuring amnesic dissociation, absorption and imaginative involvement, depersonalization, and derealisation. Total scores of 20 or more are considered consistent with dissociative disorders, including Posttraumatic Stress Disorder, Dissociative Identity Disorder, and Schizophrenia (Bernstein & Putnam, 1986). However, the use of a clinical cut-off score of 20 has been challenged. Mueller-Pfeiffer et al. (2013) evaluated the performance of the DES as a screening tool for dissociative disorders in a population of psychiatric outpatients and day service patients, which resulted in cut-off scores of 12 and 20 for detecting any dissociative disorder or dissociative identity disorder respectively. Thirteen studies were identified in which the DES was administered to patients with NEAD (Table 6).

For ten out of the thirteen studies, patients with NEAD scored significantly higher on the DES total score than control groups (Akyuz, Kugu, Akyuz, & Dogan, 2004; Bowman & Coons, 2000; Demartini, Goeta, et al., 2016; Dikel, Fennell, & Gilmore, 2003; Goldstein et al., 2000; Goldstein & Mellers, 2006; Mazza et al., 2009; Proenca, Castro, Jorge, & Marchetti, 2011; Prueter, Schultz-Venrath, & Rimpau, 2002; Reuber, House, Pukrop, Bauer, & Elger, 2003). This suggests that patients with NEAD experience more dissociative symptoms than patients with epilepsy, FMD, or healthy controls. Although the mean DES score for patients with NEAD in Fleisher et al. (2002) was not significantly greater than that of controls with epilepsy, a significantly higher percentage of patients with NEAD than patients with epilepsy scored above the clinical cut-off (set at 30 in this case). Notably the Alper et al. (1997) study, which was rated as being of high quality and which has the largest sample size of all studies using the DES in this review, did not result in DES scores which exceeded the clinical-cut off, or scores which were greater than those of patients with

epilepsy. Likewise, the mean DES score did not exceed the cut-off in four other studies (Demartini, Goeta, et al., 2016; Ekanayake et al., 2017; Mazza et al., 2009; Reuber et al., 2003). However, when a mean total DES score was calculated for all studies (Table 6), this score was greater than the cut-off of twenty, which suggests that when all studies are taken together, patients with NEAD do experience levels of dissociative symptoms consistent with an understanding of NEAD as a dissociative disorder.

Table 6 - *Means and standard deviations (unless otherwise stated) of Dissociative Experience Scale scores included in review.*

Study	NEAD	ES	ES+ NEAD	FMD	HC
Akyuz et al. (2004)	29.8 (20.0)	17.6 (15.5)*	-	-	-
Alper et al. (1997)	15.1 (13.5)	12.7 (10.8)	-	-	-
Bowman et al. (2000)	20.2 (18.2)	10.7 (11.3)*	-	-	-
Demartini et al. (2016)	17.2 (10.6)	-	-	7.9 (13.9)*	8.2 (7.5)*
Ekanayake et al. (2017)	15.9 (12.2)	-	-	5.6 (5.1)*	-
Dikel et al. (2003)	22.8	14.11[a]	-	-	-
Fleisher et al. (2002)	22.7 (20.1)	15.1 (12.8)	-	-	-
Goldstein et al. (2006)	24.9 (16.5)	14.5 (10.2)*	-	-	-
Goldstein et al. (2000)	22.6 (16.4)	-	-	-	13.1 (11.8)*
Lawton et al. (2008)	20.2 (34.1)	11.8 (15.5)	-	-	-
Mazza et al. (2009)	17.6 (8.9)	6.4 (5.8)*	-	-	4.5 (2.9)*
Proenca et al. (2011)	54.3 (23.2)	22 (16.4)*	-	-	-
Prueter et al. (2002)	32.0 (26.8)	6.5 (2.9)*	17.9 (9.5)*	-	-
Reuber et al. (2003)	17.2 (14.0)	8.8 (8.1)*	-	-	-
Total Mean (*SD*)	23.75(10.1)	12.74 (4.7)	17.9 (9.5)	6.8 (1.6)	8.6 (4.3)

Note. NEAD = Nonepileptic Attack Disorder, ES = Epilepsy control group, ES + NEAD = Comorbid epilepsy and NEAD control group, FMD = Functional Movement Disorder control group, HC = Healthy control group, * = control group significantly different from NEAD group. [a] = SD not reported, women only.

The variability of findings pertaining to whether dissociation in NEAD exceeds a pathological cut-off may be due to the failure of single construct questionnaires such as the DES to capture the multiple forms of dissociation that are thought to exist (Brown, 2006). For instance, Alper et al. (1997) found that DES scores in NEAD patients were higher than in the general population, but did not differentiate between patients with NEAD and epilepsy. However, when total DES scores were

subjected to a principal components analysis, the resulting components did differentiate between patient groups. A depersonalisation-derealisation component accounted for more variance in DES scores in the NEAD group than the epilepsy group. An absorption-imagination component was only raised in patients who reported childhood abuse, irrespective of seizure diagnosis. Finally, an 'amnesic' factor was only raised in patients with epilepsy. This finding raises the possibility that perhaps some types of dissociation are unique to NEAD (in this case depersonalisation-derealisation). Accordingly, Demartini, Goeta, et al. (2016) compared patients with NEAD, patients with FMD, and healthy controls on three different types of dissociation; 'psychoform', 'compartmentalisation', and 'detachment' using the DES, the Somatoform Dissociation Questionnaire (SDQ-20) (Bernstein & Putnam, 1986), and the Cambridge Depersonalisation Scale (CDS) (Sierra & Berrios, 2000), respectively. Patients with NEAD scored significantly higher on the DES and CDS than both groups, but lower on the SDQ-20 than the group with FMD. These results suggest patients with NEAD can be differentiated from patients with other forms of FND, by a susceptibility to psychoform dissociation and compartmentalisation, but not detachment (Demartini, Goeta, et al., 2016). In summary, the type of dissociation pertinent to NEAD requires further clarification.

However, given that the grand total DES score calculated in Table 6 exceeded the clinical cut-off and that 75% of studies using the DES found elevated levels of dissociation in patients with NEAD compared to epileptic and / or healthy control groups, it can be concluded patients with NEAD are likely to select dissociation as a general regulatory strategy. Corroborating this interpretation, higher levels of dissociative symptoms in patients with NEAD than control groups have also been observed using other self-report measures including the Dissociation Questionnaire

(DIS-Q) (Kuyk, Spinhoven, van Emde Boas, & van Dyck, 1999), the TSI-2 (Myers, Matzner, et al., 2013) the SDQ (Kuyk et al., 1999), and using structured clinical interviews (Hendrickson, Popescu, Ghearing, & Bagic, 2015). A case series of patients with NEAD demonstrated that patients would recall upsetting memories from their childhood without expressing the emotion one would expect to be associated with such events, such as fear or anger. The authors argue this reflects a dissociation between memories and normally associated feelings (Prigatano, Stonnington, & Fisher, 2002), although it should be added that this study had a very small sample size (N = 15) and so these findings may not generalise to the wider NEAD population.

There is also evidence of other psychological factors interacting with dissociation. For example, a subgroup of patients with NEAD who scored more highly on measures of emotion dysregulation were also shown to self-report more dissociative symptoms (Uliaszek et al., 2012). Other researchers have found patients with NEAD and comorbid psychiatric impairment had more frequent dissociative experiences (Baslet et al., 2010), and 70.2% of variance in DES scores was explained by psychological distress as measured by the Brief Symptom Inventory (Cohen, Testa, Pritchard, Zhu, & Hopp, 2014). Lawton, Baker, and Brown (2008) also found compartmentalization scores did not differentiate between patients with NEAD and epilepsy after controlling for anxiety and depression. Similarly, the positive correlation between DES scores and a NEAD severity index lost significance when somatisation and psychopathology were controlled for. In another study, DES scores did not discriminate between patients with NEAD and epilepsy in a logistic regression model, whereas levels of somatization and psychopathology did (Reuber et al., 2003). Finally, when patients diagnosed with NEAD were followed up 4-6 years post-diagnosis, those with reduced seizure frequency also experienced fewer dissociative

symptoms (Bodde et al., 2007). Taken together, these findings suggest that the results of self-report measures of dissociation are closely related to current distress or psychopathology. Indeed, a relationship has been observed between dissociative symptoms and trauma or trauma-related distress in other populations (Gershuny & Thayer, 1999), raising the possibility that dissociation is selected and implemented as an emotion regulation strategy to mitigate negative affect in some patients with NEAD. Therefore, dissociation may not be a core feature of NEAD aetiology, rather, dissociative experiences are an artefact of the psychological distress which causes or is associated with NEAD.

2.5.4. Appraisal of external world

According to the EPM, successful implementation of an emotion regulation strategy relies on an accurate representation of the external world - including the agents or situations one is interacting with (Gross, 2015). For example, one might implement reappraisal to lessen feelings of anger if they perceived an apology to be sincere rather than insincere.

There is some evidence that patients with NEAD exhibit cognitive biases that could lead to an inaccurate or altered appraisal of exteroceptive emotional information. This evidence comes from experimental studies which include emotional imagery (pictures of faces or scenes) as stimuli. Roberts et al. (2012) compared responses to standard affective pictures in patients with NEAD against seizure free-individuals with high or low trauma levels. Groups did not differ in their pleasantness / unpleasantness ratings of the images but patients with NEAD reported more intense emotional experiences in reaction to the images and displayed less positive emotional behaviour. This is suggestive of altered processing of exteroceptive emotional information.

Altered processing of exteroceptive emotional information in patients with

NEAD has also been demonstrated by Bakvis, Spinhoven, Putman, Zitman, and Roelofs (2010) who showed that social distractors (happy, neutral, or angry faces) impaired working memory performance relative to healthy controls whether data were collected at baseline or following stress induction. Bakvis, Roelofs, et al. (2009) also demonstrated that when compared to healthy controls, patients with NEAD exhibited a preconscious positive attentional bias to angry faces during a masked emotional Stroop Test. Hypervigilance to negatively-valenced emotional information correlated positively with self-reported sexual trauma, indicating a potential mechanism by which hypervigilance to social threat may be mediated. Indeed, trauma is considered a contributory factor to hypervigilance in military and civilian samples (Kimble, Fleming, & Bennion, 2013). A further analysis of data from Bakvis, Spinhoven, and Roelofs (2009) found that basal cortisol levels correlated positively with threat vigilance in patients but not healthy controls, suggesting a relationship between the endocrine stress response and threat vigilance restricted to patients with NEAD. These results allude to a hypervigilant attentional system which is biased towards the processing of exteroceptive emotional information in NEAD and may be related to trauma exposure.

Affective-cognitive control may also be impaired in patients with NEAD. Gul and Ahmad (2014) asked participants to make emotional and non-emotional judgements about images of faces presented to them. Patients with NEAD had greater difficulty switching from emotional judgements to non-emotional judgements than healthy controls. This switching bias correlated positively with the use of a maladaptive emotion regulation strategy (expressive suppression) and negatively with healthier forms of emotion regulation (cognitive reappraisal). This observed deficit in affective-cognitive control also suggests an attentional system primed towards to

processing of exteroceptive emotional information related to impaired emotion regulation.

Cognitive-affective biases in NEAD may be related abnormalities in theory of mind. Schönenberg et al. (2015) found evidence of impaired theory of mind in patients with NEAD relative to healthy controls when observing the Movie for Assessment of Social Cognition (MASC). NEAD patients tended to over-mentalize the emotional meaning behind the actions of characters in the movie, a tendency which positively correlated with stress-vulnerability as measured by the Perceived Stress Scale. Critically, this was not a result of an impaired ability to identify emotional expression in others, as basal facial expression recognition was intact when viewing animated movies of neutral expressions slowly changing to full-blown emotions. However, it is worth nothing that Prigatano and Kirlin (2009) found that patients with NEAD were impaired in their ability to identify emotions in drawings of affective expressions relative to patients with epilepsy. This discrepancy in basal affect recognition in others might be explained by the greater cognitive demand imposed by interpreting emotional expression from more abstract representations of facial expressions. Therefore, these studies suggest that patients with NEAD can accurately recognise emotional expression in others, but they ascribe too much meaning to that emotional content – a phenomenon which could conceivably drive hypervigilance and impaired cognitive-affective control. Deficits in complex mentalizing ability have also been observed in another patient group characterised by emotion dysregulation - those with Borderline (emotionally unstable) Personality Disorder (Petersen, Brakoulias, & Langdon, 2016). Given that features of Borderline Personality Disorder are relatively common in patients with NEAD (Lacey, Cook, & Salzberg, 2007; Reuber et al., 2004), it is conceivable that there are overlapping mechanisms in both disorders causing

mentalizing deficits which could disrupt appraisal of the external world and precipitate emotion dysregulation.

Indirect support for the proposition that patients with NEAD exhibit signs of a nervous system on 'high alert' for threat comes from studies of vagal tone (see Chapter 4.4). According to the Polyvagal Theory, tonically low vagally mediated Heart Rate Variability (vmHRV) is considered to reflect a chronically aroused nervous system in a state of readiness to deal with external demands (Porges, 1995). Bakvis, Roelofs, et al. (2009) observed lower vmHRV in a group of patients with NEAD than healthy controls at baseline and in the recovery phase following a masked emotional Stroop Task. Similarly, Ponnusamy, Marques, and Reuber (2011) observed lower vmHRV in patients with NEAD than healthy controls. However, vmHRV did not differentiate between patients with NEAD and those with epilepsy. Likewise, Roberts et al. (2012) observed no significant difference in vmHRV between patients with NEAD and patients with high or low levels of PTSD symptoms in response to affective pictures, suggesting that patients with NEAD exhibit resting vagal tone similar to that of a clinical group with known pathological hypervigilance and hyperarousal (American Psychiatric Association, 2013). A limitation of these studies is that vmHRV was not correlated against measures of emotion dysregulation – therefore a relationship between vmHRV and emotion dysregulation in NEAD is speculative at this stage (see Chapter 4.4). Furthermore, it has also been proposed that vagal tone serves to influence perceptual processes (e.g., Park, Van Bavel, Vasey, & Thayer, 2013), and so may also relate to the identification stage of the EPM, by affecting perception of one's own emotional state. An aim of future studies of vagal tone in patients with NEAD could be to further explore the relationship between vmHRV and the three stages of the EPM.

2.5.5. Conclusions on the selection and implementation stages

In summary, there is evidence that patients with NEAD experience deficits in the selection and implementation of emotion regulatory strategies. In particular, the literature has focused on emotion-focused coping, avoidance, and dissociation as emotion regulation strategies in NEAD. Correlational data suggests that these deficits are likely related to other psychological factors such as trauma or distress. Experimental studies have also begun to demonstrate the existence of affective-cognitive biases relating to appraisal of exteroceptive information, which may also interfere with adaptive selection and implementation of regulatory strategies.

2.6. Discussion

The studies included in this review suggest that emotion dysregulation in patients with NEAD can be characterised as deficits in the identification, selection, and implementation stages of the EPM. Difficulties in the identification stage relate to an impaired ability to detect and understand one's own emotions as well as a heightened vulnerability to stress. While it was not possible to clearly separate the selection and implementation stages from the measures and methodologies included in the review, there is also evidence that patients with NEAD tend to select potentially maladaptive regulatory strategies (emotion-focused coping, avoidance, and dissociation). Altered processing of exteroceptive emotional information may also interfere with external world representations and impede the implementation stage.

A recurring theme throughout this was review was the biopsychosocial heterogeneity of NEAD. One explanation is that emotion dysregulation appears to be related to psychological factors such as trauma, personality, and current psychological distress – rather than NEAD diagnosis per se. Therefore, an individual with NEAD who has experienced greater trauma may also experience more severe symptomology

and emotion dysregulation than those who have experienced less trauma. As such, future studies employing subgroup analyses based on psychological or clinical variables (cf. Baslet, Tolchin, & Dworetzky, 2017; Bodde et al., 2013; Uliaszek et al., 2012)or including relevant psychiatric control groups (c.f. Martino et al., 2018; Roberts et al., 2012) would constitute useful designs to elucidate this potential source of heterogeneity in regulatory deficits.

Some studies included in this review found no differences in some measures of emotion dysregulation between patients with NEAD and patients with 'organic' seizure disorders (e.g., Alper et al., 1997; Brown et al., 2013; Fleisher et al., 2002; Wolf et al., 2015). These findings do not mean that patients with NEAD do not experience emotion dysregulation; rather it is possible that both groups have difficulties with emotion regulation, for some overlapping and some distinct reasons. For example, both patients with NEAD and epilepsy may carry a similar emotional burden associated with experiencing seizures and disabilities, although the two seizure disorders (or their consequences in terms of emotion dysregulation) are not the result of the same pathological process (Labate et al., 2012). Further exploration of neural correlates of emotion dysregulation in NEAD may help to clarify its neural substrate and further explain some of these differences; specific forms of emotion dysregulation may be related to particular structural or functional abnormalities. One study identified in the literature search has examined the neural correlates of dissociation in patients with NEAD (van der Kruijs et al., 2012), but was excluded due to insufficient sample size. The fact that patients with NEAD are a heterogeneous group reinforces the importance of and value in taking a person-centred and individualised approach to working with this population.

Given that emotion dysregulation is considered to play a role in the

precipitation and maintenance of affective disorders (e.g., depression and anxiety), and that these affective disorders are frequently co-morbid with NEAD (Brown & Reuber, 2016a), it is perhaps unsurprising that emotion dysregulation is also commonly observed in patients with NEAD. However, the case-control design of most of the studies discussed here makes it impossible to say with certainty whether emotion dysregulation is a cause, consequence, or correlate of NEAD. It is also unlikely that the relationship between emotion dysregulation and NEAD is the same for every patient. Nevertheless, despite open questions, emotion dysregulation is likely to be involved in the pathogenesis of NEAD and NEAD-associated disabilities for at least some patients. Further support for this proposition comes from the demonstrated effectiveness of psychotherapeutic techniques designed to target emotion regulation difficulties in NEAD (Conwill, Oakley, Evans, & Cavanna, 2014; Goldstein et al., 2010; Howlett & Reuber, 2009; LaFrance et al., 2009; Mayor, Howlett, Gruenewald, & Reuber, 2010; Williams, Howlett, Levita, & Reuber, 2018) although more work is needed to elucidate the mechanism of treatment action. Given the personal and societal cost of NEAD and the relevance of emotion dysregulation to psychological treatment, improving our understanding of emotion regulation in NEAD is clearly very important.

2.6.1. Limitations and recommendations

The number of studies which have been designed to investigate emotion regulation in NEAD has increased markedly over the last two decades, however, many are underpowered. Indeed, a small sample size was the only reason why some studies in this area were considered to be of such uncertain quality that they had to be excluded from this review (Bakvis, Spinhoven, Zitman, & Roelofs, 2011; Hingray et al., 2011; Martino et al., 2018; van der Kruijs et al., 2014). Small studies cannot account for the

obvious heterogeneity of the NEAD patient population. Although there may be particular problems with recruiting patients with NEAD to clinical studies (e.g., low patient numbers in single centres, problems with transport or engagement in research) the ongoing CODES treatment study in the UK, to which over 600 patients have been recruited to date, demonstrates that large-scale research is possible in this area with sufficient funding (Goldstein et al., 2015)

In addition to a need for larger studies, there is a need for higher standard of reporting in this area. There was a tendency for studies to not explicitly state methodological criteria of importance; such as whether NEAs had been formally differentiated from panic attacks or whether patients were recruited consecutively. As recommended elsewhere (Brown & Reuber, 2016a) work should draw on established publication guidelines (e.g., www.strobe-statement.org), to improve both the quality of study design and reporting in this area.

It is worth mentioning that while avoidance, emotion-focused coping, dissociation, and hypervigilance are considered maladaptive in this review, the utility of a regulatory strategy is context-dependent. For example, because reappraisal difficulty increases with emotional intensity and requires cognitive effort (Suri et al., 2017) an individual who is vulnerable or compromised might be better off implementing a 'maladaptive' strategy such as dissociation rather than not regulate at all. Furthermore, strategies that involve the redirection of attentional resources (like avoidance) are more effective in reducing short-term negative affect than reappraisal in high-emotional intensity conditions (Shafir, Schwartz, Blechert, & Sheppes, 2015). Although arguably, a tendency to habitually select these strategies irrespective of context might still be considered an example of dysregulation.

The studies reviewed here have not been designed explicitly to examine

emotion regulation according to the EPM, so we have clustered the literature post-hoc. While this categorisation was double-rated, this method does introduce risk of bias. Ideally, studies of emotion regulation in NEAD would be grounded in theory and designed to test specific models. However, the majority of studies in this area are based on observational data, which can be difficult to interpret within frameworks they were not designed to fit. Furthermore, the selection and implementation stages are arguably more difficult to isolate and study than the identification and selection stages. A possible approach to rectifying this issue could be adopted from other fields of psychopathology research; that is via the experimental manipulation of emotion regulation strategies. For example, other researchers have instructed healthy participants to suppress or enhance negative emotion elicited by unpleasant pictures (Jackson, Malmstadt, Larson, & Davidson, 2000). Versions of this paradigm have been applied to other patient populations characterised by emotion dysregulation, such as those with Major Depression (e.g., Heller et al., 2009). Designs such as this could present a powerful way to empirically test the selection and implementation stage of the EPM in patients with NEAD. There are of course, other models of emotion regulation which could facilitate our understanding of NEAD (Parkinson & Totterdell, 1999; Thayer, Newman, & McClain, 1994). In spite of the fact that there is at present only 'modest' support for the EPM and that the substeps require further empirical assessment (Sheppes et al., 2015), we chose the EPM as it is the most recent iteration of a well-established and widely used model of emotion regulation. The EPM may not bear up to future scientific scrutiny, however there is value in adopting the more structured approach of grounding studies within broader psychological theory.

2.7. Conclusion

Research conducted to date suggests that emotion dysregulation in patients

with NEAD can be characterised by deficits in the identification, selection, and implementation stages of the EPM (Gross, 2015). However, the spread of these deficits throughout the NEAD population is heterogeneous and likely linked to other psychological factors such as trauma, personality, and psychological distress. Future studies of emotion regulation in NEAD should seek to elucidate subgroups of NEAD patients based on the presenting style of emotion dysregulation, as well as the relationship between emotion dysregulation and other psychological or clinical variables.

3. Impairment of consciousness and emotion regulation in patients with Functional Neurological Disorder (Study 1)

3.1. Introduction

Functional Neurological Disorder (FND) is defined by the presence of at least one FNS, but symptoms can present with a wide range of different clinical manifestations. FNS may take the form of seizures, abnormal movements, sensory impairments or cognitive disruption. Most patients have more than one FNS, the same symptom (e.g., tremor) can present differently between patients, and FNS can also evolve over the course of time (e.g., a tremor can spread to another part of the body). There are open questions pertaining to the potential meaning behind this variability in FNS presentation. For example, whether or not overlapping aetiological factors mean that all presentations of FND (and indeed other functional somatic symptoms such as Irritable Bowel Syndrome or non-cardiac chest pain) should be included under one classification, or sub-divided into symptom-specific disorders is a contentious issue (Wessely & White, 2004). The DSM-V suggests classifying FND as separate from functional syndromes which affect other systems in the body, such as the digestive tract or the cardiovascular system, but does not comment on whether or not it is important for diagnosis and treatment to disambiguate between different FND presentations. The aim of this chapter is therefore to examine whether different FND symptoms are related to different forms of emotion dysregulation and psychopathology. Answering this question may give some indication as to whether all FNS should be considered part of the same syndrome or individual, symptom-specific syndromes.

The clinical heterogeneity of FND can be illustrated by considering NEAD. Nonepileptic Attacks (NEAs) are generally characterised by paroxysmal symptoms and signs which superficially resemble those associated with epileptic seizures, but are not associated with any abnormal cortical electrical discharges. However, despite being one of the most common FNS, the diagnostic criteria for NEAD lack specificity (LaFrance et al., 2013). This means that patients with very different seizures may all receive the same diagnosis of NEAD. For example, for some patients NEAs involve only motor symptoms, for others sensory, cognitive or combined manifestations may occur. Likewise, patients with NEAD may experience impairment of consciousness (or not) as part of their seizures.

Impairment of consciousness (IOC) is not a universally agreed diagnostic requirement although reported or observed impairment of awareness differentiates NEAD from other paroxysmal problems (such as panic attacks, tics, flashbacks or FMD). While IOC is therefore used an inclusion criterion in some research studies of NEAD (Reuber et al., 2011), other patient series include patients whose consciousness is never impaired in their NEAs. For instance, in one retrospective chart review study, 21 of 116 of NEAD patients were found not to experience alterations of consciousness (Driver-Dunckley et al., 2011), and 5 out of 30 patients with NEAD self-reported no alterations of consciousness in a study comparing psychological profiles between patients with NEAD and those with FMD (Hopp, Anderson, Krumholz, Gruber-Baldini, & Shulman, 2012). It is possible that patients classified as having NEAD without impairment of consciousness in an epilepsy clinic would have been diagnosed with FMD if they had presented to a movement disorders clinic. Conversely, some patients with a diagnosis of paroxysmal FMD (not labelled as having NEAD) do report impairments of consciousness; 3 of 56 of patients with FMD in one study (Driver-

Dunckley et al., 2011) and 32 of 104 in another (Hopp et al., 2012) were reported to experience alterations of consciousness. This raises the question, if these patients had presented to an epilepsy clinic, would they have been diagnosed with NEAD rather than FMD? When one considers that diagnosis is likely influenced by the medical speciality that the patient first makes contact with, and that both NEAD and FMD can manifest with paroxysmal motor symptoms (e.g., intermittent tremor or convulsions) with or without IOC, the boundary between NEAD and FMD becomes blurred.

NEAD and FMD are often managed by different subspecialists in neurology, so comparative studies are rare. While the few previous studies examining emotion regulation or psychopathology in NEAD versus FMD suggest that there are more commonalities than differences between these two types of FND (Erro et al., 2016), there are still some divergent findings between studies. For example, Driver-Dunckley et al. (2011) compared frequency of common psychiatric comorbidities between patients with NEAD and FMD, finding no difference in rates of depressive disorder but that patients in the NEAD group had more frequently been diagnosed with an anxiety disorder (Driver-Dunckley et al., 2011). Conversely, Stone et al. (2004) found no difference in the rate of Axis 1 disorders (including anxiety and depression) between the two groups. However, they did observe a greater incidence of Borderline (Emotionally Unstable) Personality Disorder (an Axis 2 disorder) in the patients with NEAD. With respect to somatic symptoms, Demartini, Goeta, et al. (2016) observed more unexplained physical symptoms in patients with FMD than those with NEAD, but Hopp et al. (2012) observed no significant difference in somatisation scores as measured by the Brief Symptom Inventory between the two groups. While there are several explanations for these discrepancies, the failure of FND diagnostic labels to

account for the variable ways in which these symptoms present is conceivably an important confound.

Given the lack of clear diagnostic boundaries between different FND presentations, it might be more useful to examine the relationship between objective clinical features and emotion regulation / psychopathology irrespective of diagnostic label. To date, authors have compared psychopathology in patients with NEAD according to higher or lower DES scores (Sarisoy et al., 2015) or altered ictal responsiveness (Baslet et al., 2017). Another clinical feature of theoretical interest, is whether or not the patients experience IOC as part of their FND. In NEAD, IOC is a semiological feature theorised to be a dissociative response to overwhelming emotion (Roberts & Reuber, 2014). We therefore aimed to compare deficits in emotion regulation and psychopathology in patients with FND who experience subjective impairment of consciousness (IOC+) against those who do not (IOC-), predicting that patients who experience IOC would self-report more severe emotion dysregulation than those who do not. We also hypothesised that the IOC+ group would report higher levels of comorbid psychopathological symptoms than the IOC- group.

3.2. Methods

3.2.1. Regulatory Approvals

This study was granted ethical approval by the Sheffield Local Research Ethics Committee (REC 16/YH/0196, 31st May 2016). Research governance approval was given by the research departments of the Sheffield Teaching Hospitals Foundation trust.

3.2.2. Participants

Adult patients with a diagnosis of FND under the care of a consultant neurologist at the Royal Hallamshire Hospital in Sheffield, United Kingdom (n = 70),

and adult patients responding to an online advertisement on UK- and US-based FND patient organisation websites (n = 94) were recruited to the study. For those recruited from the hospital, a clinical diagnosis of FND was established on the basis of all available evidence and the expert opinion of the patient's consultant neurologist. For patients recruited online, confirmation of the FND diagnosis was sought from a selected subgroup of the participants' General Practitioner or Consultant Neurologist, but these recruits were not excluded if confirmation of the diagnosis could not be secured. Patients were not eligible for the study if they had any neurological comorbidity which could partially or wholly account for their symptoms, if they were unable to complete the questionnaires, or if they were unable to give informed consent.

3.2.3. Measures

3.2.3.1. Demographics / IOC questionnaire. A questionnaire designed by the research team was used to capture information on demographics and relevant information regarding any FNS that the patient experiences. This included questions regarding the type and number of FNS, and whether or not the patient experienced IOC as part of their symptoms (Appendix 1). Patients indicated whether they experienced any of the following IOC by answering 'yes' or 'no' to the following questions:

i) I have spells in which I black out / lose consciousness completely.

ii) I have spells in which am aware of what is going on, but I am unable to respond to other people.

iii) I have spells in which I can perform actions, but I am not aware of what I am doing.

Patients were categorised as experiencing IOC if they experienced any of these phenomena.

3.2.3.2. The Emotional Processing Scale – 25 (EPS-25). The EPS-25 (Appendix 2), is a 25-item self-report scale measuring emotion processing styles and deficits. It is comprised of five subscales measuring suppression (excessive control of emotional experience and expression), signs of unprocessed emotions (intrusive and persistent emotional experiences), unregulated emotion (inability to control one's emotions), avoidance (of negative emotional triggers) and impoverished emotional experience (detached experience of emotions due to poor emotional insight) (Baker et al., 2009). Participants respond on a 0-9 Likert scale to indicate their response to a question. Higher scores indicate greater difficulties with emotion processing and regulation. This measure has previously been used in patients with lower back pain (Esteves, Wheatley, Mayall, & Abbey, 2013), Post-Traumatic Stress Disorder (Compare et al., 2012), and patients with NEAD (Novakova et al., 2015). The EPS-25 has also been demonstrated to be sensitive to psychotherapy-associated change in patient with FND (Williams et al., 2018).

3.2.3.3. Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 (Appendix 3) is a nine item self-report questionnaire measuring symptoms of Major Depressive Disorder over the past two weeks (Kroenke et al., 2001). The PHQ-9 has a sensitivity of 88% and a specificity of 88% for Major Depression. Respondents indicate the frequency of each symptom on a 0-3 Likert scale. The PHQ-9 is also a widely used clinical measure and has been administered to patients with NEAD (Chen et al., 2014).

3.2.3.4. Generalized Anxiety Disorder -7 (GAD-7). The GAD-7 (Appendix 4) is a seven item self-report questionnaire, designed to assess symptoms of Generalized Anxiety Disorder experienced over the past two weeks (Spitzer, Kroenke,

Williams, & Lowe, 2006). Participants indicate the frequency of each symptom on a 0-3 Likert scale. The GAD-7 has a sensitivity of 89% and a specificity of 82% for Generalized Anxiety Disorder, and is a widely used measure in psychiatric populations. It has also previously been administered to patients with functional somatic symptoms (Vijay, Avasthi, & Grover, 2014).

3.2.3.5. Patient Health Questionnaire-15 (PHQ-15). The PHQ-15 (Appendix 5) is a 15 item self-report questionnaire assessing the frequency and severity of Somatization Disorder symptoms experienced over the past four weeks (Kroenke, Spitzer, & Williams, 2001). Responses are indicated on a 0-2 Likert scale. The PHQ-15 has been administered to patients with NEAD and patients with other FNS previously (Novakova et al., 2015; Reuber, Burness, Howlett, Brazier, & Grunewald, 2007).

3.2.3.6. PTSD Checklist for DSM-V (PCL-5). The PCL-5 (Appendix 6) is a 20 item self-report questionnaire, which assesses 20 symptoms of Post-Traumatic Stress Disorder as defined by the DSM-V. It can be used as a screening tool and to measure change over time. Rating scale indicators range from 0-4 for each symptom, corresponding to 'not at all', 'a little bit', 'moderately', 'quite a bit', and 'extremely'. It has been validated for use in a range of clinical populations including US combat soldiers (Hoge, Riviere, Wilk, Herrell, & Weathers, 2014), problem drinkers (Keane et al., 2014), and natural disaster survivors (Gruebner, Lowe, Sampson, & Galea, 2015). The PCL-5 provides a total symptom severity score (0-80), with higher scores indicating a greater level of trauma. To the author's knowledge, the PCL-5 has not yet been administered to a population of patients with FND.

3.2.4. Design

This study used a between-subjects design, with IOC (+ / -) as the independent

variable and self-report scores on a measure of emotion regulation (EPS-25) and symptoms of psychopathology (PHQ-9, GAD-7, PHQ-15, and PCL-5) as the dependent variables.

3.2.5. Procedure

Patients were approached in four settings:

In outpatient clinics. A consultant neurologist identified patients and introduced them to the researcher. Patients were then provided with study information and the opportunity to ask questions. Patients were given as much time as they wished to consider whether they wanted to take part. Participants then completed the questionnaire pack either in clinic or at home, returning the pack in a stamped addressed envelope if they chose the latter option (n = 66).

From consultant caseloads. Consultant neurologists at the Royal Hallamshire Hospital identified patients with FNS from their case load. Suitable patients were mailed a Participant Information Sheet and an invitation letter with details of how to contact the researcher if they were interested in participating. Patients who made contact with the researcher to express interest in participation were then sent the questionnaire pack and consent forms to complete and return in freepost envelope (n = 1).

On the neurology ward. A consultant neurologist identified patients meeting the study inclusion criteria and introduced them to the researcher with the patient's permission. The researcher then explained the study to the patient with the information sheet and allowed them to ask any questions. The patient was given as much time as they wished to consider participation. If they chose to take part, written informed consent was obtained and the patient was given the questionnaire pack to complete during their inpatient stay (n = 3).

Online from patient organisation websites. The study was advertised on patient organisation websites (i.e. FND Hope and FND Action) along with a brief description and link to an online version of the study where participants could also view the information sheet and complete the consent form (hosted on Google Forms) *(n* = 93). A selection of patients' (i.e. those who reported taking medication which may also be prescribed for an 'organic' neurological condition such a Pregabalin or Sodium Valproate) consultant neurologists / General Practitioners were contacted in writing and asked to verify their patient's diagnosis of FND (*n* = 20).

3.2.6. Data collection and statistical analysis

All questionnaire data were scored and any missing data were handled according to their respective questionnaire scoring manuals. Patients were categorised as either experiencing IOC or not according to their responses in the demographic questionnaire. This categorisation was made irrespective of FND clinical presentation. Data were entered into SPSS (version 22) and screened for normality using the Kolmogorov-Smirnov test. All self-report measures were found not to be normally distributed ($p = <.05$) so parametric analyses of these responses were bootstrapped and reported with confidence intervals. Levene's test indicated equality of variance for all self-reported dependent measures ($p = >.05$). Alpha was set at $p = .05$. False discovery rate was controlled for using the Benjamini-Hochberg procedure (FDR = .05).

3.3. Results

3.3.4. Demographic and clinical characteristics

One hundred and sixty three patients participated in the study (70 were recruited from the Royal Hallamshire, 93 were recruited from online). 115 patients (56.9%) reported experiencing any IOC. Of these, 63 (31.2%) reported having spells during which they black out / lose consciousness completely, 90 (44.6%) reported

having spells during which they are aware of what is going on but are unable to respond, and 55 (27.2%) reported having spells during which they are responsive but unaware. Demographic and clinical features of the IOC+ and IOC- group are presented in Table 7. Groups were matched on gender, economic activity, whether they had previously received psychological treatment, the number of medications they were prescribed, and the duration of their symptoms. The IOC+ group were significantly younger and more likely to have a current diagnosis of NEAD than the IOC- group. Of note, 16.67% of the IOC- group had a current diagnosis of NEAD, and 19.13% of the IOC+ group did not have a diagnosis of NEAD.

Table 7- *Demographic and clinical comparison of patients with impairments of consciousness (IOC+) against those without (IOC-).*

Characteristic	**IOC- (*n* = 48)**	**IOC+ (*n* = 115)**	***p* value**
Mean age (*SD*)	45.9 (13.8)	40.4 (12.6)	.014[a]
Female (%)	83.0	81.2	.803[b]
Economically active (%)	50.0	42.1	.356[b]
Psychological Treatment (%)	58.7	68.1	.256[b]
Mean medication (*SD*)	3.4 (3.8)	2.9 (3.1)	.451[a]
Mean duration in months (*SD*)	79.7 (95.9)	89.76 (106.9)	.575[a]
First FNS (%)			
NEAD	14.5	53.0	<.001[b]
Paralysis / weakness	31.3	21.7	.198[b]
Sensory	10.1	3.5	.191[b]
Pain	8.3	2.6	.100[b]
Vestibular	4.2	.9	.153[b]
Tremor	16.7	12.2	.444[b]
Jerk / twitch	4.2	1.7	.361[b]
Fatigue	2.1	.0	.121[b]
Cognitive	4.2	.9	.153[b]
Spasm / rigidity	2.1	3.5	.638[b]
Current NEAD diagnosis	16.7	80.9	<.001[b]

Note. NEAD = Nonepileptic Attack Disorder, Mean medication = mean number of prescribed medications, Psychological treatment = patient has previously received psychological therapy, Economically active = in full - / part-time work / education or homemaker, *SD* = standard deviation, [a] = between-groups t test, [b] = Chi squared test of association.

3.3.5. Emotion dysregulation

A series of bootstrapped ANCOVAs with IOC+ / IOC- as the between-subjects factor were conducted on the EPS-25 total score and subscores. Given that the IOC+ group were significantly younger than the IOC- group, age was entered as a covariate. Scores were generally elevated above the 25th percentile for mental health norms – suggesting that both groups had deficits in emotion regulation (Table 8).

Table 8 - Descriptive statistics of EPS-25 total and subscale scores in the IOC+ and IOC- groups.

	IOC-				IOC+				CI		MH
EPS-25	***M***	***SD***	***M_{adj}***	***SE***	***M***	***SD***	***M_{adj}***	***SE***	***LL***	***UL***	
Suppression	5.1	2.2	5.1	.4	5.2	2.6	5.2	.2	-.87	.84	3.8
Unprocessed	4.9	2.6	5.0	.4	5.2	2.7	5.2	.3	-1.11	.70	5.0
Unregulated	3.7	1.9	.37	.4	4.2	2.5	4.2	.2	-1.20	.23	3.0
Avoidance	4.2	1.9	4.2	.3	4.5	2.4	4.2	.3	-1.03	.41	4.0
Impoverished	3.7	2.5	3.7	.4	4.2	2.6	4.2	.2	-1.33	.33	2.6
Total	4.4	1.9	4.4	.3	4.6	2.3	4.7	.2	-.99	.43	4.0

Note. IOC- = no impairment of consciousness, IOC+= impairment of consciousness, MH = 25th percentile for UK Mental Health Norms, *CI*= Bootstrapped 95% Confidence Interval; *LL* = lower limit, *UL* = upper limit, *M* = unadjusted means, M_{adj} = Adjusted mean.

Although the EPS-25 total score was slightly greater in the IOC+ group, this difference was not significant; $F(1, 160) = .57$, $p = .45$, $\eta_p^2 = .01$. Similarly, subscale scores were slightly elevated in the IOC+ group compared to the IOC- group, but these differences did not reach significance for suppression; $F(1,160) = .06$, $p = .79$, $\eta_p^2 = .00$, unprocessed emotions; $F(1,160) = .07$, $p = .78$, $\eta_p^2 = .00$, unregulated emotions; $F(1,160)$, $= 1.56$, $p = .21$, $\eta_p^2 = .01$, avoidance; $F(1,160) = .51$ =, p =.46, $\eta_p^2 = .00$, or impoverished emotional experience; $F(1,160) = 1.31$, $p = .26$, $\eta_p^2 = .01$. With the exception of the unprocessed subscale in the IOC- group, all scores exceeded the 25th percentile for UK Mental Health Norms. Therefore, the FND patients in this sample self-reported similar emotion regulation deficits, irrespective of whether or not they experienced IOC.

3.3.6. Psychopathology

Both groups exceeded the cut-off suggestive of moderate Major Depression on the PHQ-9 and moderate Somatisation Disorder on the PHQ-15 (i.e. ≥ 10). However, only the IOC+ group exceeded the clinical cut-off for moderate Generalised Anxiety Disorder on the GAD-7 (i.e. ≥10) and the cut-off for likely Post-Traumatic Stress Disorder (i.e. ≥33) (Figure 5). In order to assess the significance of differences in self-reported symptoms of psychopathology between the IOC+ and IOC- group, a series of bootstrapped between-subjects ANCOVAs were conducted on depression (PHQ-9), anxiety (GAD-7), number and severity of somatic symptoms (PHQ-15), and Post-Traumatic Stress symptoms (PCL-5) scores (Table 9). Patients with IOC scored significantly higher on the GAD-7; $F(1,159) = 3.63$, $p = .03$, $\eta_p^2 = .03$, PHQ-15; $F(1,157) = 10.47$, $p = .002$, $\eta_p^2 = .06$ and PCL-5; $F(1,153) = 4.38$, $p = .02$, $\eta_p^2 = .03$. Differences on the PHQ-9 were non-significant; $F(1,157) = .29$, $p = .09$, $\eta_p^2 = .02$. The observed between-groups differences in GAD-7, PHQ-15, and PCL-5 scores retained significance after controlling for false-discovery rate.

Self-reported symptoms of Generalized Anxiety Disorder, Somatization Disorder, and Post-Traumatic Stress Disorder were therefore greater in patients with IOC than those without. However, there was no difference in self-reported symptoms of Major Depressive Disorder between the two groups.

Table 9 - *Descriptive statistics of psychopathology in the IOC+ and IOC- group.*

	IOC-					IOC+					CI	
Measure	***n***	***M***	***SD***	M_{adj}	***SE***	***n***	***M***	***SD***	M_{adj}	***SE***	***LL***	***UL***
PHQ-9	47	11.2	7.1	11.3	1.1	113	13.5	7.4	13.5	.7	-4.61	.35
GAD-7	47	7.8	6.1	8.2	.9	115	10.6	6.5	10.5	.6	-4.39	-.32
PHQ-15	46	11.7	5.5	11.9	.9	114	15.6	6.6	15.5	.6	-5.71	-1.51
PCL-5	47	24.8	19.9	25.8	3.3	109	34.6	23.7	34.2	2.2	-16.81	-2.39

Note. CI = 95% Bootstrapped Confidence Interval; *LL* = Lower Limit, *UL* = Upper Limit, PHQ-9 = Patient Health Questionnaire – 9 (Major Depression), GAD-7 = Generalized Anxiety Disorder – 7, PHQ-15 = Patient Health Questionnaire – 15 (Somatization Disorder), PCL-5 = PTSD Checklist for DSM 5. *M* = unadjusted mean, M_{adj} = Adjusted mean.

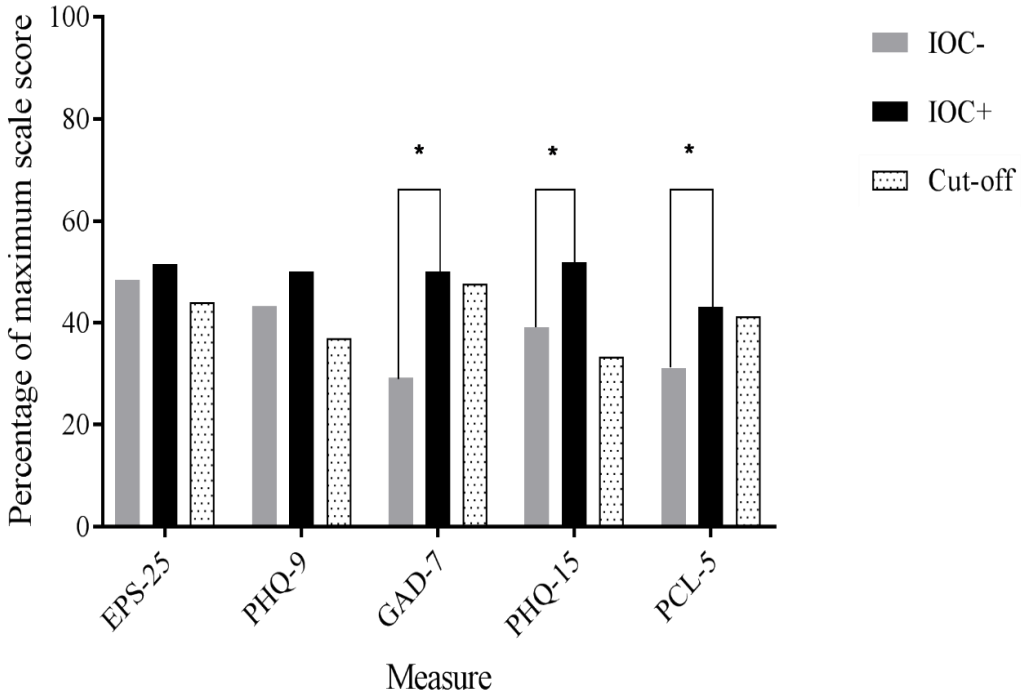

Figure 5. Mean emotion dysregulation and psychopathology symptom scale scores represented as percentage of maximum scale score for FND patients with and without IOC. Emotion dysregulation (EPS-25) cut-off = 25th percentile for mental health norms. Cut-off for PHQ-9, GAD-7, PHQ-15 = moderately severe symptoms of Major Depression (PHQ-9), Generalised Anxiety Disorder (GAD-7), Somatization Disorder (PHQ-15). Cut-off for PCL-5 = clinical cut-off for likely Post-Traumatic Stress Disorder (PCL-5). * = statistically significant difference.

3.3.7. Confirming diagnosis of patients recruited online

Fifteen out of 20 clinicians responded to our request to confirm their patient's diagnosis. All 15 of these confirmed the diagnosis of FND with no comorbid neurological disorder which could partially explain the patients' symptoms.

3.4. Discussion

The results give evidence of elevated levels of emotion dysregulation, whether or not the patient experiences IOC as part of their FND. However, higher levels of Generalized Anxiety Disorder and Post-Traumatic Stress symptomology, as well as an increased number and severity of somatic symptoms, were observed in patients

with IOC compared to those without (Figure 6). These findings corroborate the putative association between emotion dysregulation and FND, and suggest that a symptomatology including IOC, may be related to anxiety, somatization, and psychological trauma. By associating these measures of psychological functioning and previous experiences with FNS presentation, this study represents a step towards elucidating some of the psychological heterogeneity in FND. This has implications for treatment of FND; if a patient reports IOC as part of their FND, they might be more likely to benefit from psychological interventions targeting anxiety, somatization, and psychological trauma than those who do not report IOC. Given that patients with IOC are also more likely to self-report psychopathology, they may also be more likely to accept psychological accounts of their FND and understand the rationale for psychotherapy (Howlett, Grunewald, Khan, & Reuber, 2007; Howlett & Reuber, 2009).

Although EPS-25 scores were slightly greater in patients with IOC, they did not differ significantly between-groups. This is perhaps not surprising given that several psychological constructs measured by the questionnaire, including avoidance (Cronje & Pretorius, 2013; van Beilen, Griffioen, & Leenders, 2009), alexithymia (Ekanayake et al., 2017; Steffen, Fiess, Schmidt, & Rockstroh, 2015), and suppression (Gul & Ahmad, 2014; Steffen et al., 2015) have previously been shown to be elevated in patients with either NEAD or FMD relative to healthy controls. These findings therefore lend support to the view that there is some overlap between patients with FND with different clinical manifestations – at least in terms of emotion regulatory style. In order to help address the question of whether FND should be included in the same category as other assumed somatization disorders, it would be useful to

administer the EPS-25 to other relevant patient populations, such as those with Irritable Bowel Syndrome or Fibromyalgia to compare emotion regulation profiles.

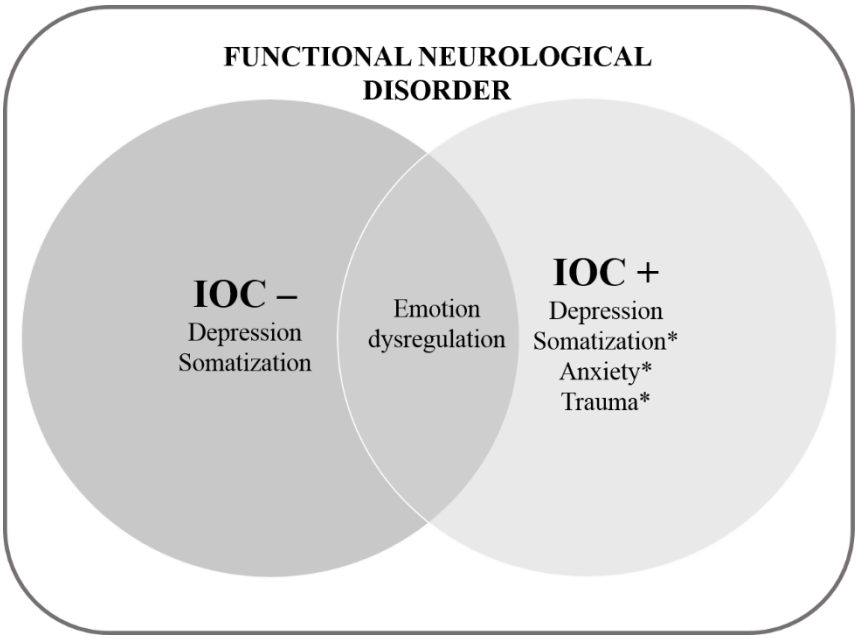

Figure 6. Diagrammatic representation of IOC findings. Patients with Impairments of Consciousness (IOC+) reported symptoms exceeding the cut-off for moderately severe Major Depressive Disorder, Somatization Disorder, Generalized Anxiety Disorder, and Post-Traumatic Stress Disorder Symptoms. Patients without Impairments of Consciousness (IOC-) reported symptoms of moderately severe Major Depressive Disorder and Somatization Disorder. Both groups reported levels pathological levels of emotion dysregulation. * = significant between-groups difference.

To our knowledge, there have been no other studies comparing emotion dysregulation and psychopathology in FND patients with and without IOC. One recent study has compared emotion regulation and psychopathology in patients with NEAD who experience altered responsiveness (defined as patient not responding, verbally or otherwise, and not remembering three words given to them during at least one of their vEEG recorded events during hospital admission) during their attacks against those who don't. Lower emotional resilience / tolerance was observed in patients with altered responsiveness, but no differences were found in measures of dissociation, somatization, mood, trauma, or psychiatric co-morbidity (Baslet et al., 2017). However, due to the patient group being comprised totally of patients with NEAD (i.e.

patients with predominantly episodic, seizure-like symptoms), these findings cannot be directly compared with our own.

Studies with the most similar design and patient group to the present study have compared psychopathology in patients with NEAD with those with FMD. How do our findings concerning anxiety and depression compare with previous work? We found significantly higher self-reported levels of Generalized Anxiety Disorder symptomology (GAD-7) in the IOC+ group which exceeded the threshold for moderately severe symptoms. However, the IOC- group mean score on the GAD-7 fell within a non-clinical range. We also found that levels of depressive symptomology did not differ between the groups (as measured by the PHQ-9), but both exceeded the cut-off suggestive of moderately severe Major Depression. These findings are partially consistent with a study by Grimaldi, Dubuc, Kahane, Bougerol, and Vercueil (2010) who found that levels of depressive symptomology, as measured by the Beck Depression Inventory, did not differ in group of eight patients with NEAD compared with a group of nine patients with FMD. However, they only found a trend towards higher levels of anxiety in the NEAD group as measured by the Spielberger State-Trait Anxiety Inventory (although the small sample size should be noted). Also in accordance with the present findings, Hopp et al. (2012) observed no between-group differences on the depression subscale of the Brief Symptom Inventory (a measure of overall psychiatric symptoms) in patients with NEAD and those with FMD (the authors do not report findings on the anxiety subscale). However, in direct contrast to our findings, Driver-Dunckley et al. (2011) found that patients with FMD were significantly more likely to have a pre-existing psychiatric diagnosis of anxiety than patients with NEAD, and Stone et al. (2004) observed no difference in rates of any Axis 1 disorder between the two patient groups. Therefore, our findings on depression

and anxiety in patients with and without IOC do not clearly align with pre-existing findings on depression and anxiety in patients with NEAD compared to those with FMD.

Regarding somatization, we observed higher scores on the PHQ-15 in the IOC+ group (which exceeded the cut-off for severe Somatization Disorder) than the IOC- group (which still exceeded the cut-off for moderately severe somatization disorder). These data are at odds with those of Hopp et al. (2012), who found no differences between patients with FMD and NEAD on the somatisation subscale of Brief Symptom Inventory. It is possible that IOC represent a more severe somatic symptom, which drives the increased somatization scores in our data, an effect which is diluted by the use of diagnostic category as an independent variable by Hopp et al. (2012). However, Baslet et al. (2017) manipulated an objectively more severe semiological feature as an independent variable, altered responsiveness during nonepileptic attacks, and found no differences in somatization as indexed by the PHQ-15. A key difference between the methodology used by Baslet et al. (2017) and our own is that impaired responsiveness was assessed by a clinician whereas IOC in our data were self-reported. Indeed, over 50% of observers report that patients with NEAD 'always' completely lose consciousness during their attacks, whereas only 30% patients endorse this ictal phenomenology (Reuber et al., 2011). It is therefore possible that reporter biases influencing how patients are categorised into groups partially account for the difference between our PHQ-15 findings and those of Baslet et al. (2017).

As previously mentioned, inconsistent findings on depression, anxiety, and somatization in patients with NEAD versus those with FMD may be due to the fact that these diagnostic labels are not clearly defined and that patients have

heterogeneous biopsychosocial and clinical profiles. For example, Duncan and Oto (2008) demonstrated that patient endorsement of antecedent trauma to the development of NEAD was predicted by a later age of onset and having additional medically unexplained symptoms. However, having a Learning Disability predicted an absence of patient-reported antecedent trauma. Furthermore, different forms of antecedent trauma were related to different predictors; bullying was predicted by early onset of NEAD, whereas health-related trauma was predicted by late-age onset, sexual abuse was predicted by female gender, physical abuse, self-harm and other medically unexplained symptoms. These findings resonate with our own, and raise the possibility that categorising patients according to objective clinical characteristics or features which are demonstrably linked to psychopathology might therefore be more fruitful than using labels such as FMD or NEAD in future research. This approach could also have important ramifications for the psychological treatment of FND – given the unclear boundaries between diagnostic categories and clinical presentation, might symptom manifestation give more important clues about aetiology than the diagnostic label? Indeed, IOC were not restricted to patients with NEAD; in the present study 19.13% of patients with NEAD did not report experiencing any IOC, and 16.67% of the IOC- group reported a diagnosis of NEAD.

Our finding of significantly higher levels of PTSD symptomology in the IOC+ group than the IOC- group is consistent with the literature. Not only were self-reported symptoms of trauma higher in the IOC+ group, but PCL-5 (PTSD symptomology) scores fell within a non-clinical range in the IOC- group. Psychological trauma is one of the most commonly cited psychological risk factors for NEAD. Antecedent trauma is reported in up to 70% of patients with NEAD (Proenca et al., 2011). Furthermore, trauma seems to be a more pertinent aetiological factor to NEAD than FMD. A

retrospective chart review of 116 patients with NEAD and 56 with FMD found patients with NEAD were more likely to report one or more traumatic events that precipitated or exacerbated symptoms (Driver-Dunckley et al., 2011). Similarly, Reuber, Howlett, et al. (2007) found psychological trauma to be more common in patients with NEAD than those with other FNS. Stone et al. (2004) compared clinical characteristics in patients with NEAD against FMD, and found that patients with NEAD reported a greater number of traumatising events, including a lower perception of parental care, incest, parental divorce, and as higher number negative life events relating to changes in family life in 12 months prior to symptom onset. Although trauma is reported in patients with FMD, it appears be less frequent than one might expect in a supposedly 'psychogenic' disorder (Kranick et al., 2011). If FND accompanied by IOC were viewed as more intense dissociative symptoms than FND without IOC, then the suggestion that traumatic experiences could serve to intensify dissociative symptoms in FND but are not necessary for the disorder to manifest (Kienle et al., 2017), would seem appropriate.

Our findings therefore suggest that IOC in FND symptomology appears to be related to increased self-reported symptoms of anxiety, somatization, and psychological trauma. However, an emotion regulatory style characterised by avoidance, suppression, impoverished emotional experience, unregulated emotions, and unprocessed emotions is common to patients at with FND (at group level) whether or not they experience IOC. This conclusion is consistent with the theory that IOC in NEAD represent a dissociative response to overwhelming emotion (Roberts & Reuber, 2014).

The neural mechanism driving IOC in FND is not yet known, but Roberts and Reuber (2014) have proposed three mechanisms which may occur in isolation, or in

combination. Firstly, IOC may represent a "side-effect" of excessive emotion inhibition in reaction to overwhelming emotions, which the individual may have learned over time or may be biologically predisposed to. Secondly, overwhelming emotion may directly trigger IOC. Thirdly, minor emotional fluctuations may be conditioned to elicit the behavioural response of IOC.

While our data do support the idea of a relationship between psychopathology and FND symptom semiology, it is important to stress that the cross-sectional study design does not allow for a causal interpretation. It may be that IOC is brought about by a deficient emotion regulatory style in combination with trauma, a tendency to experience more and more severe somatic symptoms, and higher levels of anxiety. It may also be the case that the IOC themselves are psychologically traumatizing, and result in the kind of bodily symptoms described in the PHQ-15, or that living with IOC induces feelings of anxiety that are captured by the GAD-7.

3.4.1. Limitations

One potential limitation of this study is that approximately half of the sample were recruited online and not directly from consultant neurologists who were able to verify the diagnosis at entry to the study. This is a particular concern, as the reliability of patients with Medically Unexplained Symptoms to report previous functional and 'non-functional' medical diagnoses has been brought into question (Schrag, Brown, & Trimble, 2004). However, this approach did enable us to recruit a good sample size and we have contacted a selection of patients' clinicians to confirm their diagnosis. Reassuringly, all of the clinicians who responded (15 / 20) confirmed the diagnosis of FND with no comorbid neurological conditions which could partially account for their symptoms. The range of recruitment methods used also increases the generalizability

of our findings to the wider population of patients with FND, many of whom may not currently be attending specialist clinics.

The methodology might also be criticised for a failure to ask patients what 'stressful event' they were referring to when completing the PCL-5. This was a conscious decision, designed to protect patients completing the study measures without any immediate recourse to emotional support from the researchers as far as possible from the potentially harmful effects of reactivating trauma memories. However, given the subjective nature of trauma, it can be argued that it is not always necessary to know the exact nature of the traumatic stressor when assessing Post-Traumatic Stress symptomology.

Given that IOC was conceptualised as a dissociative response, the study design might have benefited from the inclusion of a measure of dissociation. However, there are concerns over the validity of self-report measures of dissociation in patients with NEAD (Roberts & Reuber, 2014). Other authors have argued that given the complex nature of dissociation, multiple measures of dissociation (e.g., compartmentalization, depersonalisation, and derealisation) might be needed when studying dissociation in patients with FND (Alper et al., 1997; Lawton et al., 2008). Others have argued that dissociation as measured by the Dissociative Experience Scale is not necessarily relevant for all patients with NEAD, and the tendency to express psychosocial distress through unexplained medical symptoms is a more relevant aetiological factor (Reuber et al., 2003). Therefore, a measure of dissociation may not have added any value to the findings. We were keen not to make the questionnaire pack too lengthy for patients to complete, and so concede that this study cannot come to any firm conclusions about the role of dissociation in IOC.

A final consideration is the unequal sample sizes of patients with and without IOC. While this is interesting in that it suggests more patients with FND are likely to experience IOC than those who don't, unequal sample sizes can affect the homogeneity of variance assumption of the ANOVA model. However, Levene's test of homogeneity of variance was non-significant in the present data, therefore the unequal sample sizes recruited to the study should not invalidate the findings.

3.5. Conclusion

There is evidence of emotion dysregulation in patients with FND, whether or not they experience IOC as part of their symptom. Both groups also reported elevated levels of Major Depressive Disorder symptomology. However, patients with IOC reported more symptoms of Generalized Anxiety Disorder, Somatization Disorder, and Post Traumatic Stress Disorder than patients without IOC. Despite the limitation of the cross-sectional design, our study suggests that differences in patients' psychopathological profiles and their histories of traumatic experiences may contribute to shaping the symptomology of their FND.

4. Testing the Extended Process Model of emotion regulation in patients with Functional Neurological Disorder

4.1.1. Introduction

The experimental work presented in this chapter used a combination of self-report, physiological, and behavioural measures to test the EPM (Gross, 2015) in patients with FND compared to healthy controls. This chapter is organized in three subsections. Section 4.2 examines the identification stage through assessing interoceptive sensitivity in patients with FND compared to healthy controls. The selection and implementation stage are addressed in section 4.3, which examines the use of expressive suppression as an emotion regulation strategy in patients with FND relative to healthy controls. Section 4.4 assesses for physiological evidence of chronic autonomic dysregulation in patients with FND (resting Heart Rate Variability (HRV)) and its relationship measures of emotion dysregulation, emotion identification, as well as emotion regulation strategy selection and implementation assessed in the previous two sections. The chapter begins with a description of the overall procedure and a comparison of the participants on demographics and self-report measures of emotion dysregulation and psychopathology.

All studies presented in this chapter received ethical approval from the Sheffield Local Research Ethics Committee on the 31st May 2016. All patient participants who completed Study One (Chapter 3) were given the opportunity to express their interest in studies two, three, and four, and all of those who expressed interest were invited to attend the University of Sheffield Department of Psychology for testing. Healthy controls were recruited via the university volunteer email list. The

overall procedure is depicted in Figure 7. The experimental set up is depicted in Figure 8.

4.1.2. Participants

Twenty-six patients diagnosed with FND by a consultant neurologist and 28 healthy controls with no known medical (including mental health) diagnoses were recruited to the study. The control group was gender-matched to the patient group, but significantly younger. The control group were also more economically active, taking fewer prescribed medications, and less likely to have received psychological treatment than the patient group (Table 10) which was unsurprising given the poor social, economic, and health outcomes associated with FND (Carson et al., 2011).

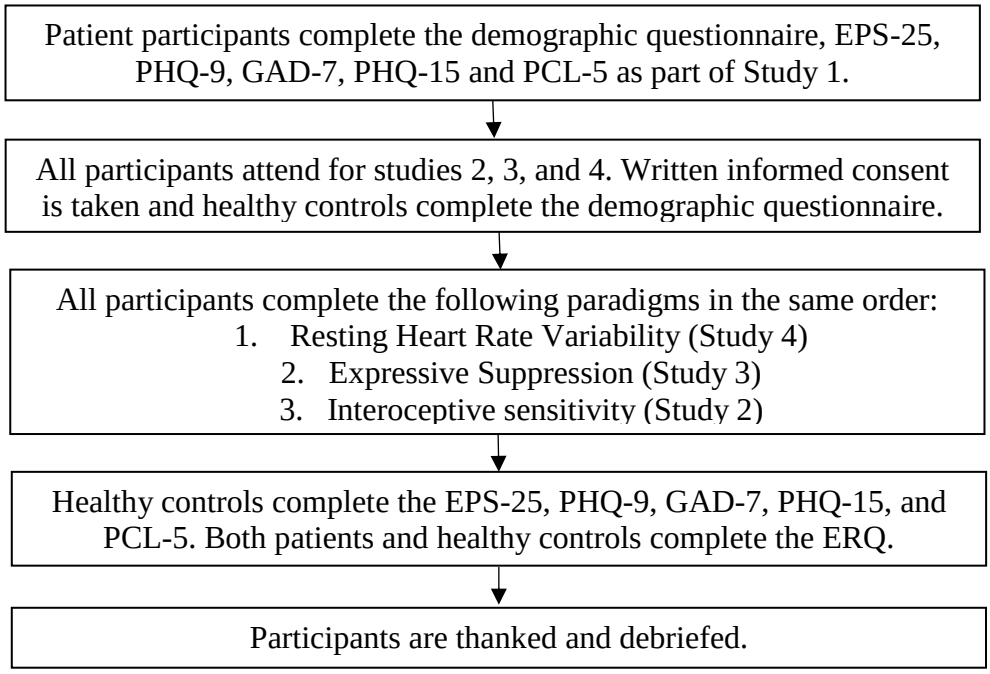

Figure 7. Outline of Stage Two procedure

Figure 8. Experimental set up. The participant is seated on the right in front of a computer monitor with a keyboard. A privacy screen separates the experimenter who would be sat on the left.

Table 10 – *Comparison of demographic details between the patient and control group.*

Characteristic	***n***	**Control**	***n***	**Patient**	***p* value**
Mean age (*SD*)	28	33.3 (11.6)	26	41.6 (14.3)	.021[a*]
Female %	28	78.6	26	88.5	.330[b]
Economically active %	28	100	26	36.0	<.001[b*]
Mean medication (*SD*)	28	.4 (.6)	26	2.3 (2.7)	<.001[a*]
Psychological treatment %	28	14.3	25	68.0	<.001[b*]

Note. 'Mean Age' = mean age in years, 'Economically active' = in full- or part-time work or education or a homemaker, 'Mean medication' = mean number of medications, 'Psychological treatment'= previously received psychological treatment, [a] = t-test. [b] = chi-squared test of association. * = p <.05.

The most commonly reported FND in the sample was NEAD (Table 11). Other symptoms included movement and sensory disturbances. FND were chronic (Mean duration = 99.7 months, *SD* = 126.4). Over half of the sample had been diagnosed with NEAD (n = 15) and the mean number of Nonepileptic Attacks in the past month was 19.8 (*SD* = 26.6). The majority of patients reported experiencing impairments of consciousness as part of their FND (n = 19).

Table 11- *FNS characteristics in patient group*

FNS Characteristics		*n*
First symptom		
	NEAD	12
	Paralysis / weakness	7
	Sensory	1
	Vestibular	1
	Tremor	1
	Jerk / twitch	2
	Spasm / rigidity	1
Impairments of consciousness		
	Blackout	11
	Unresponsive	15
	Unaware	10
	Total	19

Note. NEAD = Nonepileptic Attack Disorder, Blackout = patient 'blacks out' / loses consciousness completely, Unresponsive = patient has periods during which they are conscious but unresponsive, Unaware = patient has periods during which they are responsive but unaware.

Patients also reported significantly greater emotion regulation deficits (EPS-25) as well as more symptoms of Major Depression (PHQ-9), Generalised Anxiety Disorder (GAD-7), Somatization Disorder (PHQ-15), and Post-Traumatic Stress Disorder (PCL-5) than healthy controls (Table 12).

Table 12- *Comparison of emotion processing and psychopathology between patients and healthy controls.*

Measure	**Control**			**Patient**						***CI***	
	n	***M***	***SD***	***n***	***M***	***SD***	***df***	***t***	***p***	***LL***	***UL***
EPS-25	28	2.8	1.3	26	5.0	1.6	52	-5.5	<.001	-2.9	-1.4
PHQ-9	28	3.2	2.7	26	10.9	4.9	37.6	-7.0^{v}	<.001	-9.9	-5.5
GAD-7	28	3.7	4.8	26	11.0	5.0	52	-5.4	<.001	-9.8	-4.5
PHQ-15	28	4.8	3.4	26	13.5	4.6	45.7	-7.8^{v}	<.001	-10.7	-6.6
PCL-5	28	8.2	9.7	26	34.5	18.2	37.6	-6.7^{v}	<.001	-34.3	-18.4

Note. EPS-25 = Emotional Processing Scale- 25, PHQ-9 = Patient Health Questionnaire – 9, GAD-7 = Generalised Anxiety Disorder – 7, PHQ-15 = Patient Health Questionnaire- 15, PCL-5 = PTSD Checklist – 5. *CI* = Bootstrapped confidence interval; *LL* = Lower Limit, *UL* = Upper Limit. ^{v} = equal variances not assumed.

4.2. The identification stage: Interoceptive sensitivity in patients with Functional Neurological Symptoms (Study 2)

4.2.1. Introduction

Successful emotion regulation depends on an individual's ability to identify the emotion they are experiencing (Gross, 2015), and there is evidence to suggest that emotion dysregulation in FND might be characterised by deficits in the identification of patients' own emotions. For example, several self-report studies using the TAS-20 have found raised levels of alexithymia in patients with NEAD (see section 2.4.1) compared to healthy controls and patients with epilepsy. Similar results have also been observed when comparing patients with FMD to healthy controls and those with 'organic' movement disorders (Demartini, Petrochilos, et al., 2014; Demartini, Ricciardi, Crucianelli, Fotopoulou, & Edwards, 2016). However, significant differences are not always observed between patient and control groups when using the TAS-20 (Brown et al., 2013; Ricciardi et al., 2016; Wolf et al., 2015). This may be because alexithymia is not as ubiquitous in FND as has previously been suggested and there are subgroups of patients who are not alexithymic, or because of issues with the validity and reliability of the TAS-20. Indeed, concerns have been raised about the validity of the Externally Oriented Thinking subscale of TAS-20, which reflects a tendency to focus on details of the external world rather than focus attention on internal states (e.g., Gignac, Palmer, & Stough, 2007). It is also possible that a group of patients who have difficulty reflecting on their emotional experiences would not reliably be able to accurately self-report on their emotional experiences – in which case, a more objective non-self-report measure of alexithymia would be preferential.

The aim of this chapter was therefore to test the hypothesis that patients with FND have a deficit in the identification of their own emotions using measures other than the TAS-20.

One such alternative approach to assessing emotion identification is to examine interoception - the sensation and representation of the physiological state of the body (Craig, 2002), which has historically been regarded as integral to emotional experience. One of the earliest theories of emotion, the James-Lange theory, held that emotions resulted from the perception of physiological changes within the body which had been elicited by emotional stimuli – and that this perception itself constitutes an emotion (James, 1994). While the James-Lange theory does offer a role for interoception in emotion identification, it has been criticised for being too simplistic and received numerous other challenges. For example, Cannon (1927) severed afferent sympathetic nerves in cats and found that the animals still displayed emotional behaviours when provoked, demonstrating that the perception of physiological states was not necessary for emotional experience - as the James-Lange theory asserts. Instead, Cannon (1927) argued that these physiological states are actually caused by emotions, and not the other way around. As a result, later theories of emotion give a more nuanced account of the role of interoception in emotion identification. For example, Schachter and Singer (1962) famously demonstrated that emotional experience also depended on one's cognitive appraisal of their physiological state. Peripheral injections of adrenaline causing a state of physiological arousal elicited either elation or anger in participants depending on the presence of an elated or irritated confederate. More recently, The Somatic Marker Hypothesis (Damasio, 1996) proposed that physiological sensations over time become consciously and / or unconsciously associated with corresponding emotions (e.g., a rapid heartbeat with

anger or a churning stomach with anxiety). These physiological sensations therefore become 'somatic markers' which serve to inform the individual about what emotion they are experiencing and help to guide decision making. While the major theories differ in their accounts of the specific process by which emotions are generated and identified, all agree that the ability to perceive ones internal physiological milieu has an important role to play in emotion identification. In doing so, these theories offer a possible mechanism for alexithymia in FND – impaired interoception.

Several lines of converging evidence support the assumed relatedness between interoception and alexithymia. During a widely used behavioural measure of interoception, the 'Heart Beat Detection Task' (Schandry, 1981), participants are instructed to silently count their heartbeats over a period of time without any manual checking. The number of counted heartbeats is compared against the actual number of heart beats and an accuracy score is calculated. More accurate responses are considered a measure of greater interoceptive sensitivity which is related to how well an individual can identify and label their emotions. Herbert, Herbert, and Pollatos (2011) demonstrated a negative correlation between self-reported measures of alexithymia (TAS-20) and interoceptive sensitivity in a sample of 155 healthy volunteers. In support of this association, there is also growing behavioural evidence that individuals with alexithymia are impaired on the Heart Beat Detection Task (e.g., Shah, Hall, Catmur, & Bird, 2016). From a neuroanatomical perspective, interoception and emotion processing appear to be supported by overlapping neural systems, including both the anterior insula and cingulate cortices (Medford & Critchley, 2010). Alexithymia has been associated with abnormalities of these structures; Goerlich-Dobre, Bruce, Martens, Aleman, and Hooker (2014) demonstrated that greater cortical thickness in the anterior cingulate and posterior insula cortices were associated with

worse scores on self-report measures of alexithymia in healthy participants. Furthermore, abnormal interoception and alexithymia have been observed to co-occur in a number of conditions in which emotion dysregulation are a common factor, such as chronic pain (Di Lernia, Serino, & Riva, 2016) and eating disorders (Garfinkel, Moldofsky, Garner, Stancer, & Coscina, 1978; Rozenstein, Latzer, Stein, & Eviatar, 2011). It is therefore possible that if patients with FND are alexithymic according to self-report measures, they will also have impaired interoceptive sensitivity.

An interoceptive deficit could have two consequences for emotion identification in patients with FND; i) problems with differentiating physiological sensations from emotions could result in the misattribution of emotions to physical symptoms leading to 'disease conviction' and the rejection of psychological factors as being related to health (e.g., Binzer, Eisemann, & Kullgren, 1998), or ii) attenuated intensity of emotional experience, rendering emotional states more difficult to detect, identify, and differentiate from one another. An attenuated emotional experience seems less likely given findings which suggest that patients with NEAD perceive their lives as more stressful than the general population (e.g., Frances et al., 1999; Schönenberg et al., 2015; Testa et al., 2012; Tojek et al., 2000). One research group have proposed that impaired interoception, in conjunction with physical or psychological stress may be important in the development of FND (Demartini, Goeta, et al., 2016; Demartini, Petrochilos, et al., 2014). They propose that when emotional arousal becomes overwhelming in alexithymic patients, they are not able to interpret the accompanying automatic arousal correctly and confuse feelings of anxiety or panic with 'physical' symptoms. This breakdown in the normal integration of emotion processing with sensorimotor processing represents a dissociative response – in the case of NEAD this is would take the form of detachment (loss of consciousness) and

in FMD this would take the form of compartmentalisation (somatization).

Accordingly, researchers have begun to investigate interoceptive sensitivity in patients with FND – with mixed results. Ricciardi et al. (2016) have demonstrated reduced interoceptive sensitivity in a group of patients with FMD relative to healthy controls, but have not found any group differences in interoceptive sensitivity between patients with FMD, patients with NEAD, and healthy controls (Demartini, Goeta, et al., 2016). The aim of the present study was therefore to test the hypothesis that patients with FND have an impaired ability to identify their emotions, characterised by reduced interoceptive sensitivity (Heart Beat Detection Task) and less insight into their emotional experiences than healthy controls. Given that psychological stress has been endorsed as triggering factor for FND, we elaborated on the paradigm by including a stress induction procedure to test the idea that interoception in patients with FND is vulnerable to psychophysiological arousal. Owing to self-report literature that has found patients with FND to be alexithymic and the theoretical relationship between alexithymia and interoception, we hypothesised that patients with FND would exhibit lower interoceptive sensitivity than healthy controls. Given the proposed interaction between stress and interoception in FND (Demartini, Goeta, et al., 2016; Demartini, Petrochilos, et al., 2014), we hypothesised that the interoceptive sensitivity deficit would be exacerbated by stress. We also hypothesised that patients would self-report higher levels of alexithymia (as measured by the EPS-25) than healthy controls.

4.2.2. Methods

4.2.2.1. Participants

Twenty-six patients with FND and 28 healthy controls performed the study. Data from one healthy control was excluded due to a technical malfunction, resulting

in a final sample of 26 patients and 27 healthy controls.

4.2.2.2. Materials / apparatus

4.2.2.2.1. Stimuli. Task instructions, including when to start and stop counting, were presented to the participant on a computer monitor positioned in front of them, running an E-Prime (2.0) script coded specifically for the experiment (Psychology Software Tools, 2012). The instructions to start and stop counting were accompanied by an audible tone (.01 seconds, 44.1 kHz) played on speakers.

4.2.2.2.2. ECG recording. The number of heartbeats within each trial was recorded with an electrocardiogram (ECG). The ECG was arranged in a Lead II configuration, with electrodes (EL503 Biopac systems) applied with electrode gel (Signagel, Biopac Systems) placed on the participant's right inner arm (negative lead), left ankle (positive lead), and right ankle (ground lead) to form an Einthoven's triangle. The ECG leads (SS2L BSL Shielded Electrode Assembly, Biopac Systems) fed into a Biopac MP36R amplifier. The ECG trace was recorded with AcqKnowledge 4.4 software (BIOPAC Systems, Inc., Goleta, CA) and sampled at a rate of 2000 Hz (preset .05 - 35Hz, gain x 2000). Triggers sent from the Eprime script running on the participant's computer marked the start and finish of trials. One heartbeat was defined as one complete R-R interval. The number of R-R intervals within each epoch was calculated using the cycle detection algorithm within AcqKnowledge.

4.2.2.2.3. The Cold Pressor Test (Lovallo, 1975). A 20 litre cooler filled with 5 litres of ice-water (0 - 4˚C) was used for the Cold Pressor Test (CPT). Water temperature was checked and recorded immediately prior to the test. Length of handimmersion was timed using a stop watch. The researcher verbally indicated when the participant should submerge their hand.

4.2.2.3. Measures

4.2.2.3.1. The Emotional Processing Scale – 25. Participants' responses to the 'Impoverished Emotional Experience' subscale on the EPS-25 were employed as a measure of alexithymia. This subscale captures a, "detached experience of ones emotions due to poor emotional insight" and higher scores indicate difficulty with awareness, labelling, and linking of emotional experience (Cronbach's Alpha = .82) (Baker et al., 2009).

4.2.2.3.2. Interoceptive Sensitivity. Interoceptive Sensitivity was measured using the Heart Beat Detection Task (Schandry, 1981), which yields an Interoceptive Sensitivity (IS) score, ranging between 0 – 1 (1 being more accurate). The IS score is calculated from the number of verbally reported (counted) heartbeats and the number of recorded heartbeats averaged across the three trials using the following calculation:

$$IS = \frac{1}{3}\Sigma[(1 - (|\text{recorded heartbeats} - \text{counted heartbeats}|/ \text{recorded heartbeats}))]$$

4.2.2.4. Design

A mixed-measures design was used. There were two independent variables; group (patient versus healthy control) as the between-subjects variable, and stress-induction (pre- versus post - CPT) as the within - subjects variable. There were two dependent variables; 'interoceptive sensitivity' score, and baseline 'impoverished emotional experience' score on the EPS-25. All participants took part in all conditions of the experiment.

4.2.2.5. Procedure

Participants were seated and viewing a computer monitor running the EPrime 2.0 script, which presented the following task instructions for the Heart Beat Detection Task (Schandry, 1981):

"*We will ask you to silently count how many heart beats you can feel during a period of time. Please do this by paying attention to your body only. Do not take your pulse to count. If you feel unable to do this, please try to guess*."

The beginning of each trial was signalled to the participant by an audio tone and the instructions 'start counting' presented on the screen. At the end of the trial, another audio tone was played and the instructions to 'stop counting' were presented on the monitor screen. The participant then verbally reported the number they had counted to the researcher, who was sat behind a privacy screen (Figure 8).

Participants had a 15 second practice trial to familiarise themselves with the procedure, after which they were instructed to count their heartbeat in three experimental trials which differed in duration, lasting 25, 35, or 45 seconds (order randomised). There was a 30 second break in-between trials. Participants were not informed of the length of each trial or given any feedback on their performance. This Heart Beat Detection Task was performed before and after the Cold Pressor Test (CPT) which is known to elicit a strong physiological stress response (Lovallo, 1975). During the CPT participants were instructed to immerse their non-dominant hand into cold water (0-4^{0}C) to above the wrist, for as long as possible (but up to three minutes). This was repeated three times, with 30 second intervals in-between immersions.

4.2.2.6. Statistical analysis

Data were screened for normality. IS scores were normally distributed, as assessed by Shapiro-Wilk's test of normality (p >.05). There was homogeneity of variance as assessed by Levene's test of homogeneity of variances (p >.05) and covariance as assessed by Box's M (p >.05). Therefore, parametric analyses were used to analyse the IS data. The EPS-25 violated the assumption of normality (Shapiro-Wilk p <.05), and so all analyses of the EPS-25 and its subscales were bootstrapped

and reported with confidence intervals. Alpha was set at p <.05 but adjusted to control for False Discovery Rate (FDR = .1) for the exploratory correlational analyses.

4.2.3. Results

4.2.3.1. Interoceptive sensitivity

To investigate group differences in interoceptive sensitivity as well as the effect of physiological stress on interoceptive sensitivity, a 2x2 ANCOVA with Group (Healthy Control vs. Patient) as the between-subjects factor and stress-induction (Pre- vs. Post-CPT) as the within-subjects factor was conducted on mean IS scores. Owing to the significant difference in age between groups, age was entered as a covariate.

There was a significant main effect of group; $F(1, 50) = 4.60$, $p = .04$, $\eta_p^2 = .08$, revealing that patients had significantly lower IS than healthy controls (Table 13). There was also a significant main effect of stress-induction; $F(1,50) = 5.06$, $p = .03$, $\eta_p^2 = .09$. IS became more accurate after stress induction (Table 13). The interaction effect was non-significant; $F(1,50) = .27$, $p = .61$, $\eta_p^2 = .01$, suggesting that the effect of stress-induction on IS did not vary as a function of group (Figure 9).

4.2.3.2. Self-reported alexithymia

To assess for differences in self-reported levels of alexithymia, a between-subjects ANCOVA was conducted on the Impoverished Emotional Experience subscale of the EPS-25. Patients reported significantly greater impairments ($M = 3.99$, $SD = 2.13$) than healthy controls ($M = 1.74$, $SD = 1.30$); $F(1, 51) = 20.00$, $p = <.001$, $\eta_p^2 = .28$, 95% CI [-3.38, -1.49]. Patients' mean reported Impoverished Emotional Experience scale score exceeded the 75th percentile for UK healthy norms (3.8) and the 25th percentile for UK Mental Health norms (2.6) suggesting a pathological lack of insight into emotional experience.

Table 13- *Interoceptive Sensitivity Scores for healthy controls and patients, pre- and post- stress-induction with the Cold Pressor Test.*

	Pre – Cold Pressor Test trials								**Post- Cold Pressor Test trials**							
	25 seconds		**35 seconds**		**45 seconds**		**All**		**25 seconds**		**35 seconds**		**45 seconds**		**All**	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Healthy control	.76	.16	.66	.26	.73	.16	.71	.17	.76	.16	.76	.20	.76	.18	.76	.17
Patient	.65	.22	.70	.22	.65	.23	.67	.21	.69	.24	.69	.24	.65	.26	.67	.22
Total	.69	.19	.67	.24	.69	.21	.68	.19	.72	.21	.72	.22	.69	.24	.71	.21

Note. *M* = Unadjusted mean, *SD* = Standard Deviation, 25 seconds = 25 second trial, 35 seconds = 35 seconds trial, 45 = 45 second trial, All = mean of 25, 35, and 45 second trials.

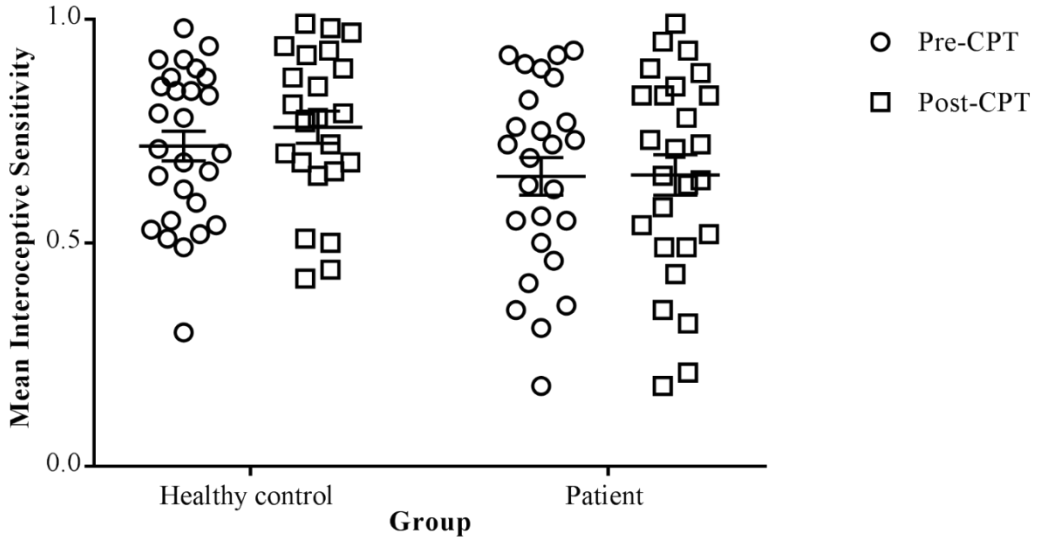

Figure 9. Healthy Control and Patient Interoceptive Sensitivity scores pre- (Pre-CPT) and post- stress-induction (Post-CPT) with the Cold Pressor Test. Higher scores indicate greater accuracy on the Heart Beat Detection Task. Error bars are Standard Error of the Mean.

4.2.3.3. Manipulation checks

To ensure that the stress-induction was administered equally between groups, between-subjects t tests were conducted on water temperature and length of hand immersion during the CPT. Water temperature did not differ significantly between the healthy control group (M = .35 °C, SD = 1.72) and the patient group (M = .16, SD = 1.51); $t(49) = .41$, $p = .68$. Similarly, the mean time (secs) that participants kept their hand immersed during the CPT (Table 14) also did not differ significantly between healthy control and the patient group; $t(51) = -.17$, $p = .91$. Therefore, any observed group-differences cannot be explained by differences in the intensity of cold exposure or its duration.

Table 14 - *Cold Pressor Test hand immersion times (seconds) over the three trials.*

	Cold Pressor Test Immersion Time (seconds)							
	1st trial		**2nd trial**		**3rd trial**		**Total**	
	M	***SD***	***M***	***SD***	***M***	***SD***	***M***	***SD***
Healthy control	37.2	45.3	30.5	52.1	29.2	48.6	32.3	47.3
Patient	32.9	31.2	32.3	64.6	36.0	67.9	33.9	51.8

Note. M = Mean, SD = Standard Deviation, Total = Mean of all three trials.

It is also possible that lower IS in patients may be explained by difficulties sustaining attention. If this were the case, one would predict IS to decrease as trial length increased and that this effect would be larger in patients than controls. To that end, a mixed ANCOVA with Trial Length (25, 35, and 45 seconds) and Stress-Induction (Pre- versus Post-CPT) as the within-subjects variables, Group (Healthy Control versus Patient) as the between-subjects variable, and age as a covariate was conducted on IS scores. As expected, there was a significant main effect of Stress-Induction, meaning that IS increased following stress-induction (Table 13); $F(1,48) = 5.59$, $p = .02$, $\eta_p^2 = .10$. However, there was no significant main effect of Trial Length; $F(2,96) = .11$, $p = .11$, $\eta_p^2 = .05$ (Greenhouse-Geisser correction applied) meaning that

IS did not systematically decrease as trial length increased. Moreover, the Trial Length * Group interaction was non-significant; $F(2,96) = 2.59$, $p = .09$, $\eta_p^2 = .05$ (Greenhouse-Geisser correction applied). Therefore, patients' lower IS cannot be explained by a relative deficit in sustaining attention over longer time periods.

4.2.3.4. Exploratory correlational analyses

To explore for potential relationships between interoceptive sensitivity and an impoverished emotional experience / psychopathology, a series of bootstrapped Pearson's correlations were conducted on IS scores pre- and post-stress induction, and all self-report measures (Table 15). There were no significant correlations between IS and any of these measures

Table 15- *Correlations between Interoceptive Sensitivity and self-report measures of psychopathology in Patients, Healthy Controls, and across both groups.*

	Bootstrapped Pearson correlation coefficients					
	Healthy control		**Patients**		**All**	
	Pre-	**Post-**	**Pre-**	**Post-**	**Pre-**	**Post-**
Impoverished	-.19	-.18	.26	.15	-.02	-.11
PHQ-9	-.13	-.21	.21	-.01	.03	-.18
GAD-7	.01	.00	.28	.18	.09	-.03
PHQ-15	.06	-.19	.06	-.04	-.01	-.20
PCL-5	-.23	-.14	-.05	-.08	-.12	-.19

Note. Pre- = Pre-stress induction, Post- = Post-stress induction. Impoverished = Impoverished Emotional Experience subscale of the Emotional Processing Scale-25, PHQ-9 = Patient Health Questionnaire- 9, GAD-7 = Generalised Anxiety Disorder – 7, PHQ-15 = Patient Health Questionnaire- 15, PCL-5 = PTSD Checklist – 5.

4.2.4. Discussion

In support of our hypothesis, we found reduced interoceptive sensitivity in patients with FND relative to healthy controls. We also found that interoceptive sensitivity improved following the Cold Pressor Test in both groups, suggesting that patients' interoceptive sensitivity is not differentially sensitive to stress. Patients did self-report higher scores on the impoverished emotional experience subscale of the

EPS-25 than controls. Taken together, these findings support the hypothesis that patients with FND exhibit impairments in the identification stage of the EPM (lower IS and higher levels alexithymia), but suggest that this deficit does not interact with the kind of stress induced by the Cold Pressor Test.

Our finding of reduced IS in patients with FND is consistent with one other study examining interoception in FND. Ricciardi et al. (2016) also observed lower IS during the Heart Beat Detection Task in a group of 17 patients with FMD relative to healthy controls. However, the same lab did not find significant group differences in IS between 20 patients with NEAD, 20 with FMD, and 20 age-matched healthy controls (Demartini, Goeta, et al., 2016). The reason for this discrepancy is unclear, but might be attributed to heterogeneity in FND samples – which is illustrated by the relatively greater spread of IS scores in patients relative to controls (Figure 9). Nevertheless, impaired interoception has also been observed in other disorders associated with emotion dysregulation, such as Major Depressive Disorder (Furman, Waugh, Bhattacharjee, Thompson, & Gotlib, 2013) and chronic pain (Di Lernia et al., 2016). Conversely, increased interoceptive sensitivity has been associated with an increased tendency to relate bodily responses to emotional experience in healthy controls (Dunn et al., 2010). Overall, these findings support the suggestion that reduced interoceptive sensitivity may be a marker of, or confer vulnerability to, emotion dysregulation in FND.

Indeed, greater impairments in IS have been associated with more severe symptoms of psychopathology. In a sample of patients with Panic Disorder, 'frequent panicers' were shown to have lower interoceptive awareness than patients who panicked less frequently (Zoellner & Craske, 1999). Similarly, IS negatively correlated with more severe depressive symptomology in patients with Major

Depressive Disorder (Avery et al., 2014) as well as more severe somatic symptoms in patients with Major Depressive Disorder (Avery et al., 2014) and somatoform disorders (Schaefer, Egloff, & Witthoft, 2012). During the exploratory correlational analyses, we did not find any association between IS and the self-report measures of psychopathology used in this study (Anxiety, GAD-7; Depression PHQ-9; Somatisation Disorder, PHQ-15; Post-traumatic Stress Disorder, PCL-5) or alexithymia (impoverished emotional experience) in patients or controls. This finding suggests that impaired IS in patients with FND may not be related to these forms of comorbid psychopathology. Likewise, other studies have also found no correlation between interoceptive awareness and self-report measures of psychopathology in healthy participants (Fairclough & Goodwin, 2007; Ricciardi et al., 2016). Ricciardi et al. (2016), did find a significant negative correlation between IS and depression as measured by the Montgomery Asberg Depression Rating Scale when FND patient data were pooled with healthy control participants' data, but we found no associations between IS and depression or the other measures of psychopathology with FND and matched control data combined – this may be due to the fact that we used different self-report measures of depressive symptomology. The lack of significant correlation between our self-report measure of alexithymia and IS score may be because the impoverished emotional experience subscale and interoceptive sensitivity paradigm measure different components of an identification impairment (for example, cognitions about emotions versus sensitivity to bodily feelings respectively). However, owing to the fact that the EPS-25 is a relatively new scale which has not previously been correlated with IS scores (unlike the TAS-20 which has been more extensively used in interoception paradigms), it is difficult to be confident about why these measures were not significantly associated. Unfortunately, the sample size in our

study was too small for sub-group analyses, but one potential avenue for future research might be to categorise patients with FND into 'good' and 'poor' IS categories and test for group differences in psychopathology or the type of emotion regulation strategies patients tend to habitually select.

Turning to the self-report findings on alexithymia, patients reported a significantly more impoverished emotional experience relative to controls. This subscale of the EPS-25 measures a "detached experience of one's emotions due to lack of insight", which is analogous to a difficulty in labelling and identifying emotions as measured by the Toronto Alexithymia Scale (Bagby et al., 1994). Alexithymia has long been regarded a risk factor for the development of functional symptoms, and raised levels of alexithymia in patients is one of the more robust findings in the emotion regulation literature on FND. We have previously shown elevated scores on the impoverished emotional experience subscale of the EPS-25 in a group of patients with NEAD relative to healthy controls (Novakova et al., 2015). The present data extend this finding to include a group of patients with other forms of FND. Numerous studies have found raised levels of alexithymia in patients with NEAD relative to healthy controls (see section 2.4.1). Higher levels of alexithymia have also been reported in patients with Conversion Disorder (Gulpek, Kelemence Kaplan, Kesebir, & Bora, 2014) and a quantitative review found patients suffering from somatoform conditions were significantly more alexithymic, with medium to large effect sizes (De Gucht & Heiser, 2003). Alexithymia has also been implicated in the development of FMD, through a phenomenon called emotional overmodulation. According to this theory, patients have difficulty differentiating emotions from physical sensations and so misattribute their symptoms of anxiety (e.g., tremor) to physical illness' (Demartini, Petrochilos, et al., 2014). Our findings raise the possibility that emotional

overmodulation may also apply to patients with NEAD as well, although replication of this study in a sample comprised purely of patients with NEAD would be needed to confirm this.

Contrary to our hypothesis, we did not observe an interaction between stress-induction and IS. The emotional overmodulation model suggests that alexithymic traits become particularly problematic for patients with FND during conditions of high emotional arousal. While patients' IS scores remained lower than healthy controls' throughout the study, they were not further decreased by stress induction. As we did not include a self-report measure of stress, it is possible that participants did not find the CPT stressful. It is also possible, that the type of stress induced by the CPT is not particularly pertinent to the genesis of FND. Other forms of stress, such as psychosocial stress, might be more salient for patients. Bakvis, Roelofs, et al. (2009) combined the Trier Social Stress Test with an emotional Stroop paradigm in a group of patients with NEAD, and found a positive attentional bias towards masked angry faces relative to healthy controls at baseline, but not following stress induction. Another option might be to use a more cognitive stressor, such as a mental arithmetic task which has been shown to reduce interoceptive accuracy in healthy females (Fairclough & Goodwin, 2007). A natural next step would therefore be to repeat the present study with a different form of stress induction to the physiological stressor employed here. However, it is also possible that stress is not problematic for patients with FND because it disrupts interoception, but that it is the combination of low interoceptive sensitivity as a trait and the presence of a stressor that results in emotion dysregulation.

Other possibilities for future work on interoception in FND could be to take advantage of the different interoceptive paradigms and measures that have been

developed since the Heart Beat Detection Task (Schandry, 1981). For example, the Heartbeat Discrimination Task (Störmer, Heiligtag, & Knoll, 1989), in which participants have to decide whether or not their heart beat is synchronised with an auditory or visual stimulus, requires the integration of interoceptive and exteroceptive information (whereas Heart Beat Detection Task performance relies only on interoceptive processing). Performance on the Heartbeat Discrimination Task has previously been shown to be adversely effected by the Cold Pressor Test, whereas Heart Beat Detection Task performance is enhanced (Schulz, Lass-Hennemann, Sütterlin, Schächinger, & Vögele, 2013). Given the theorised pre-existing imbalance between exteroceptive and interoceptive affective processing in patients with NEAD (see Chapter Two), and relationship between stress and FND, one might predict patients with FND to be further impaired on Heartbeat Discrimination Task performance following stress-induction than healthy controls.

The late Heartbeat Evoked Potential (HEP) might also provide further insight into interoceptive deficits in FND. The late HEP is an EEG component that occurs 400-600 msecs after the ECG R wave, and has been interpreted as a Central Nervous System representation of sensory information processing related to cardiac interoceptive sensitivity (Pollatos & Schandry, 2004). The late HEP has been more recently related to aspects of interoception including 'worrying about body sensations' (Baranauskas, Grabauskaitė, & Griškova-Bulanova, 2017). As proposed by Bayesian accounts of FND (Edwards et al., 2012; Van den Bergh et al., 2017), 'worrying about body sensations' could conceivably result from a combination of pathological prior beliefs about the causes of sensation and vague imprecise sensory interoceptive sensory data. The additional advantage of using the late HEP to study interoception in FND would be that this approach would circumnavigate the need for verbal

responses and the associated risk of bias introduced by these.

Finally, an alternative approach could be to investigate the different dimensions of interoception proposed by Garfinkel, Seth, Barrett, Suzuki, and Critchley (2015), in patients with FND. These include interoceptive accuracy, interoceptive sensibility (defined as an individual's "self-perceived tendency to be internally self-focused and interoceptively cognisant"), and interoceptive awareness (metacognitive awareness of interoceptive accuracy). Bayesian accounts of FND (Edwards et al., 2012; Van den Bergh et al., 2017) would predict low interoceptive accuracy, high interoceptive sensitivity, and therefore low interoceptive awareness as being mechanistic in the generation of functional symptoms.

4.2.4.1. Limitations

While we have demonstrated that patients' IS is not differentially sensitive to the kind of stress induced by the CPT, the cross-sectional design of our study means that we cannot know whether the lower IS observed in patients with FND is a cause or consequence of the disorder. Also, we cannot say whether reduced IS causes alexithymia or vice versa, or both are produced by a third factor– we can only say that the two impairments co-exist in this sample.

In addition, while we did well to recruit a respectable sample size of patients with FND in a group with recognised barriers to recruitment (n = 26), the sample size was too small to conduct sub-group analyses. Given that our findings in Chapter 3 show that there are subgroups of patients with FND according to whether or not they experience impairments of consciousness, it is possible that subgroups of patients with higher or lower IS are obscured by the analysis – indeed, patients with FND do seem to have a slightly larger variance in IS scores than healthy controls.

A further arguable limitation is that we did not measure Body Mass Index in

participants – there is some evidence to suggest that IS is attenuated in overweight and obese individuals (Herbert & Pollatos, 2014). However, reduced IS has also been reported in patients with Anorexia Nervosa who are underweight (Mean BMI = 16.59) (Pollatos et al., 2008), suggesting that IS does not necessarily decrease as body weight increases. Therefore, a failure to measure Body Mass Index in this study may not be a critical confound.

4.2.5. Conclusion

Interoceptive Sensitivity was lower and self-reported levels of alexithymia were higher in a group of patients with FND relative to healthy controls. Interoceptive Sensitivity improved in both groups following stress induction with the Cold Pressor Test. Taken together, these findings suggest that patients with FND experience deficits in the identification of their own emotional states, which may be associated with a deficit in detecting physiological changes related to emotional states and / or lacking insight into emotions.

4.3. The selection and implementation stages: Expressive suppression in patients with Functional Neurological Disorder (Study 3)

4.3.1. Introduction

During the 'selection stage' of the EPM, a conscious or unconscious choice is made about which general regulatory strategy category should be used in response to the identified emotion. The purpose of the implementation stage is to enact a specific strategy from this general category (Gross, 2015). Two of the most studied and well-defined regulatory strategies in emotion regulation research are expressive suppression and cognitive reappraisal. Cognitive reappraisal refers to changing the way an emotion-eliciting situation is construed in order to lessen the emotional impact, and is considered to belong to the 'cognitive change' category (Table 1). With respect to the EPM (Gross, 2015), cognitive reappraisal occurs relatively early in the emotion-generative process, and is therefore considered an 'antecedent-focused' strategy (Gross, 1998). Conversely, expressive suppression, can be defined as the inhibition of ongoing emotional-expressive behaviour in response to an emotion-eliciting situation, with no attempt to change the way the situation is construed (Gross, 1998). As such, expressive suppression belongs to the 'response modulation' category (Table 1). This strategy tends to be employed later in the emotion-generative process and is therefore also categorised as a 'response-focused strategy' (Gross, 1998). The stage at which these emotion regulation strategies are employed is not the only difference between them; expressive suppression is (with some exceptions) considered a less healthy emotion regulation strategy than cognitive reappraisal (John & Gross, 2004). It has been argued that patients with NEAD have a tendency habitually to select emotion

regulatory strategies which would be considered as maladaptive in many circumstances and which could be related to the high levels of emotion dysregulation found in many of these patients (see section 2.5). The aim of this chapter is therefore to investigate whether patients with FND are more likely than healthy controls to select and implement a maladaptive emotion regulatory strategy - expressive suppression.

The automatic or deliberate inhibition of negative emotions has long been held to have negative consequences for health. Folk-wisdom advising against 'bottling up your emotions' has been corroborated by over 70 years of research. With respect to physical health, expressive suppression has been linked to a number of illnesses including asthma and hypertension (Gross, 1998). Expressive suppression has been repeatedly shown to increase sympathetic activation (e.g., heart rate) (Dan-Glauser & Gross, 2015; Gross, 1998; Gross & Levenson, 1993; Krantz & Manuck, 1984) which can cumulatively have adverse effects on health over time, and is one of the assumed mechanisms by which habitually suppressing emotions can lead to 'physical' ill health. The extent to which an individual selects or implements expressive suppression and cognitive reappraisal can be measured with the self-report scale, The Emotion Regulation Questionnaire (ERQ) (Gross & John, 2003).

To date, the ERQ has been used in several experimental studies to demonstrate how the habitual implementation of expressive suppression can also result in more disadvantageous psychological, social, and cognitive outcomes for an individual than cognitive reappraisal. In the development of the ERQ, Gross and John (2003) found that there were systematic individual differences between people who were habitual 'suppressors' or 're-appraisers'. In line with the view that habitual suppression has deleterious effects on mental health, more frequent 'suppressors' were shown to experience less positive emotion, have less clarity about their feelings in general, and

possess less favourable views about their emotions. Regarding social outcomes, more frequent suppressors were shown to report having more closed and less emotionally intimate relationships than people who suppressed less. Intuitively, expression suppression could therefore also impact negatively on wellbeing by limiting an individual's access to social support through increasing isolation and weakening relationships (Butler et al., 2003). With respect to cognition, Richards and Gross (2000) had previously demonstrated that the recruitment of expression suppression lead to impaired recall of information presented in films and slides, and that expressive suppression was associated with poorer objective and self-reported memory – probably owing to the distracting effect of consciously inhibiting emotional expression interfering with encoding. In spite of the potentially high biological, psychological, cognitive, and social cost of habitually suppressing ones emotions, expressive suppression has been shown to have no effect on the subjective experience of negative emotions (Gross & Levenson, 1993; Roberts, Levenson, & Gross, 2008), while simultaneously decreasing the experience of positive emotions (e.g., Brans, Koval, Verduyn, Lim, & Kuppens, 2013). In light of this information, expressive suppression can therefore be considered a maladaptive emotion regulation strategy to habitually select and implement.

The tendency to habitually select and implement expressive suppression might be one form of emotion dysregulation relevant to patients with FND, constituting a potential pre-disposing, precipitating, or perpetuating factor within a multifactorial biopsychosocial account (Reuber, 2009). Anecdotally, patients and psychotherapists report a tendency for individuals with FND to have difficulty showing their emotions to others. This observation seems to be reflected in studies which have examined expressive suppression in patients with FND. Gul and Ahmad (2014) demonstrated

that compared to healthy controls, patients with NEAD self-reported an increased tendency to regulate their emotions with expressive suppression relative to healthy controls. Urbanek et al. (2014) administered the Courtauld Emotional Control Scale (which measures emotional control and expression) to patients with NEAD and healthy controls. Patients reported a significantly greater tendency to control their emotional expression in response to feelings of sadness and anxiety. Similarly, Roberts et al. (2012) showed that fewer patients with NEAD expressed positive emotional behaviour to pleasant, but not unpleasant pictures than healthy controls. These initial findings corroborate the suggestion that patients with FND are inclined to suppress their emotional expression, even though this regulatory strategy is associated with unchanged negative affect (Gross & Levenson, 1993), reduced positive affect (Brans et al., 2013), and increased autonomic arousal (Dan-Glauser & Gross, 2015).

While the studies described above do support the idea that patients with FND could be habitual suppressors, no researchers have yet adopted the powerful experimental design of manipulating expressive suppression as an independent variable in this patient group. Inspired by paradigms adopted by researchers in the emotion regulation field (e.g., Dan-Glauser & Gross, 2015), the primary aim of the present study was to test the hypothesis that patients with FND have an increased tendency to select and implement expressive suppression in response to negative emotions as compared to healthy controls. Participants were instructed to respond as they 'normally would' to negatively valenced affective stimuli, or deliberately suppress their responses (expressive behaviour). If patients are 'habitual suppressors', one might expect reduced expressive behaviour at baseline compared to healthy controls (reflecting a natural tendency to suppress), and even less expressive behaviour

when instructed to suppress relative to healthy controls (because habitual suppressors would be well-practiced in inhibiting their facial expression, they would implement this strategy more effectively). A secondary aim was to explore for task-related changes and group differences in emotional experience. Our third aim was to assess whether patients self-report a habitual tendency to select expressive suppression as an emotion regulation strategy relative to healthy controls, and to explore for associations between the endorsement of these strategies and self-reported emotion dysregulation (as measured by the EPS-25). Specifically, we hypothesised that:

1. ***Expressive behaviour*** - Based on anecdotal reports and experimental findings (Gul & Ahmad, 2014; Roberts et al., 2012; Urbanek et al., 2014), patients with FND would express less emotion (facial expression as measured by electromyography) than healthy controls in response to negative affective stimuli, both spontaneously and when instructed to implement expressive suppression.
2. ***Emotional experience*** - Owing to the association between expressive suppression and unchanged negative affect but decreased positive affect (Brans et al., 2013; Gross & Levenson, 1993) patients will exhibit similar levels of negative affect in response to negative affective stimuli but decreased positive affect relative to healthy controls.
3. ***Habitual expressive suppression*** - Patients with FND will self-report an increased tendency to habitually select expressive suppression and a decreased tendency to habitually select cognitive reappraisal relative to healthy controls as measured using the ERQ (Gross & John, 2003).

4.3.2. Methods

4.3.2.1. Participants

Twenty six patients with FND and 28 healthy controls participated in the study. See section 4.1.2. for demographic and clinical details.

4.3.2.2. Materials / apparatus

4.3.2.2.1. Task presentation. The task was presented on a computer monitor. EPrime 2.0 software presented all stimuli, instructions and recorded participants' responses to measures of emotional experience. The ERQ (Gross & John, 2003) was completed with pen and paper at the end of the experiment.

4.3.2.2.2. Stimuli. We chose to elicit negative emotion, and selected disgust because it is considered a relatively 'universal' and well-studied emotion (e.g., Chapman & Anderson, 2012). Twelve 'disgusting' pictures were identified from a database of images used and validated during a master's degree project (Walsh, 2012). The images were rated on a scale of 1-100 (least – most) for four valences: pleasantness, unpleasantness, disgusting, and agreeableness. Given the elevated levels of self-reported trauma and anxiety we expected to find in the patient group, images which depicted injury or images which were rated as extremely disgusting (i.e. a disgust rating of >90) were not selected for inclusion. The mean disgust ratings for the passive (M = 75.43, SD = 4.23) and suppress (M = 75.78, SD = 5.07) conditions were matched; $t(10) = -1.3$, $p = .90$, 95% CI [-5.03, 5.78]. See Appendix 8 for further details.

4.3.2.2.3. EMG recording. EMG recordings were taken with reusable 4-mm standard silver / silver-chloride electrodes filled with conductive gel (Larsen, Norris, & Cacioppo, 2003). EMG signals were relayed through shielded cable to an MP36R

Biopac amplifier (Biopac Systems, Inc., Santa Barbara, CA), amplified x5000, and sampled at 2000Hz. Electrodes were positioned according to recommendations set out by Fridlund and Cacioppo (1986), and skin was prepared with sterile saline wipes.

4.3.2.3. Measures

4.3.2.3.1. Expressive behaviour (facial). Facial EMG was recorded over the corrugator supercilii (brow) on the right side of the face (Figure 10). We chose this site as negative affective states can reliably be distinguished based on the activity of this muscle – activity is facilitated during negative affective states and simultaneously inhibited during positive affective states (Larsen et al., 2003).

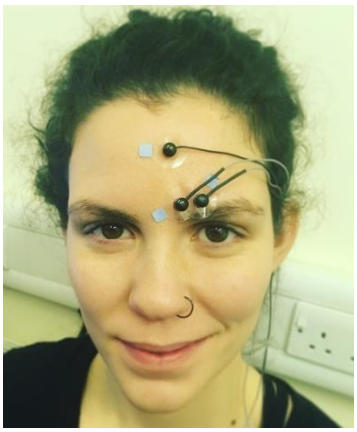

Figure 10. Image of electrode placement for facial EMG recording of corrugator supercilii face muscle activity.

4.3.2.3.2. Emotional Experience. Measures of explicit and implicit affect were taken.

Explicit affect. Explicit affect was measured using a Likert scale adapted from the Positive and Negative Affect Scale, which is a self-report measure designed to capture to what extent the participant feels each of 20 emotions in the moment (Watson, Clark, & Tellegen, 1988). For brevity, participants were only asked to

indicate how ‘positive’ and how ‘negative’ they were feeling ‘right now’ by pressing a key on scale from 1-5 (1 = very slightly or not at all, 5 = extremely).

Implicit affect. Owing to the possibility that alexithymic traits might prevent patient participants from reporting accurately on their emotional state, we included the Implicit Positive and Negative Affect Test (IPANAT) (Quirin, Kazen, & Kuhl, 2009). The IPANAT indirectly measures affect by asking participants to rate how much an artificial word reflects a mood word. Six artificial words (SAFME, VIKES, TUNBA, TALEP, BELNI, SUKOV) are presented along with each of three positive (happy, cheerful, energetic) and three negative (helpless, tense, inhibited) mood words (e.g., BELNI-Happy, BELNI-Helpless or VIKES-Tense). The IPANAT has been shown to have good internal consistency ($\alpha = .81$) for implicit positive and negative affect. Test-retest reliability over a week was also good for positive affect ($\alpha = .72$) and negative affect ($\alpha = .76$) (Quirin, Kazen, & Kuhl, 2009). To our knowledge, the IPANAT has never been administered to patients with FND.

4.3.2.3.3. Habitual use of expressive suppression. The Emotion Regulation Questionnaire (ERQ) is designed to measure how individuals regulate their emotions in daily life, using either cognitive reappraisal or expressive suppression (Gross & John, 2003) (Appendix 7). It consists of 10 items which the participant responds to on a 1-7 Likert scale indicating whether or not they use each strategy. The ERQ subscales have good internal consistency; $\alpha = .73$ for reappraisal and $\alpha = .69$ for suppression. The ERQ has previously been administered to patients with NEAD (Gul & Ahmad, 2014).

4.3.2.3.4. The Emotional Processing Scale - 25. See section 3.2.3.2.

4.3.2.4. Design

This was a mixed design study with ‘emotion regulation’ (passive or regulate)

as the within-subjects factor, and 'group' (healthy control or patient) as the between-subjects factor. The dependent variables were expressive behaviour (normalised facial EMG of the corrugator supercilii), emotional experience (explicit affect ratings and IPANAT scores), and self-reported use of expressive suppression / cognitive reappraisal (ERQ). Responses on the EPS-25 were also included in an exploratory correlational analyses.

4.3.2.5. Expressive suppression paradigm

The present study was a picture-viewing paradigm with an emotion regulation manipulation. It was adapted from a previous study which investigated emotional experiences and expression when healthy participants were instructed to passively attend, and accept or suppress their emotional responses when viewing pictures (Dan-Glauser & Gross, 2015). However, due to time constraints the present experiment included 'passively attend' and 'suppress' conditions only.

4.3.2.6. Procedure

Participants were seated in front of a computer monitor. Facial EMG electrodes were then applied (ECG electrodes had already been applied during for the HRV study (section 4.4)), and participants were instructed to follow the on-screen instructions. Participants completed one practice block to familiarise themselves with the procedure. The following instructions, taken and adapted from Dan-Glauser and Gross (2015), were then presented for each condition:

Passive:

> *"We would like you to simply view the pictures and let any emotions you feel come and go naturally, as you did during the practice training. We want you*

to respond as you would if you encountered this picture during your daily life. Do whatever you would normally do."

Suppress:

"*In this part of the study, when you see the aversive pictures your task is to try your best to strongly decrease any bodily and facial reactions you might have in response to the images. Even if you feel emotion, try to act as if there is no emotion present, so that no-one watching your responses or your face would know what you are feeling*."

Each block consisted of six trials (Figure 11). During each trial, the participant viewed a fixation cross (presented for one second) which preceded a disgusting image (presented for three seconds). The participant then performed one IPANAT trial (i.e. one fictional word presented with six mood words sequentially in a pseudorandom order). The fixation cross – picture – IPANAT trial procedure was repeated six times in each block, with different pictures and fictional words each trial (order pseudorandomised). At the end the blocks, participants were asked to explicitly indicate how positive or negative they were feeling (Figure 11). At the end of the study, participants completed the Emotion Regulation Questionnaire (Gross & John, 2003).

4.3.2.7. Data analysis / reduction

4.3.2.7.1. Expressive behaviour. The EMG signal recorded was checked for artefacts (e.g., due to movement) and noise. To that end, the EMG signal was subjected to a FIR bandpass filters offline (low frequency fixed at 20Hz, high frequency fixed at 400Hz, no of coefficients = 400) (Biopac Systems, 2014; van Boxtel, 2001) to remove noise and recording-associated artefacts. The resulting signal was saved as a

.txt file and exported to MATLAB for pre-processing. A specifically coded MATLAB script rectified and normalised the signal (divided trial activity by mean activity in the final 500 msecs of the fixation period) to correct for any non-task-related potentials. The same script also averaged the data and split it into three different post-stimulus one-second epochs to allow for statistical analysis of changes in muscle activity over time.

4.3.2.7.2. Emotional experience.

Implicit affect. Scores for single mood words were calculated with the average of all six artificial word judgments that refer to the respective mood word (e.g., average ratings of 'helpless' presented alongside ratings of SAFME, VIKES, TUNBA, TALEP, BELNI, & SUKOV). Then, scale scores for positive and negative affect were calculated by averaging mood word scores taken from positively valenced mood words and negatively valenced mood words, respectively.

Explicit affect. Mean positive and negative affect scores were calculated from participant's responses to the explicit affect questions.

4.3.2.8. Statistical analysis

For all analyses, alpha was set at p =.05, unless otherwise stated. Post-hoc Bonferroni corrections were used to correct for the inflated risk of type I error associated with multiple comparisons. Parametric analyses are bootstrapped as appropriate.

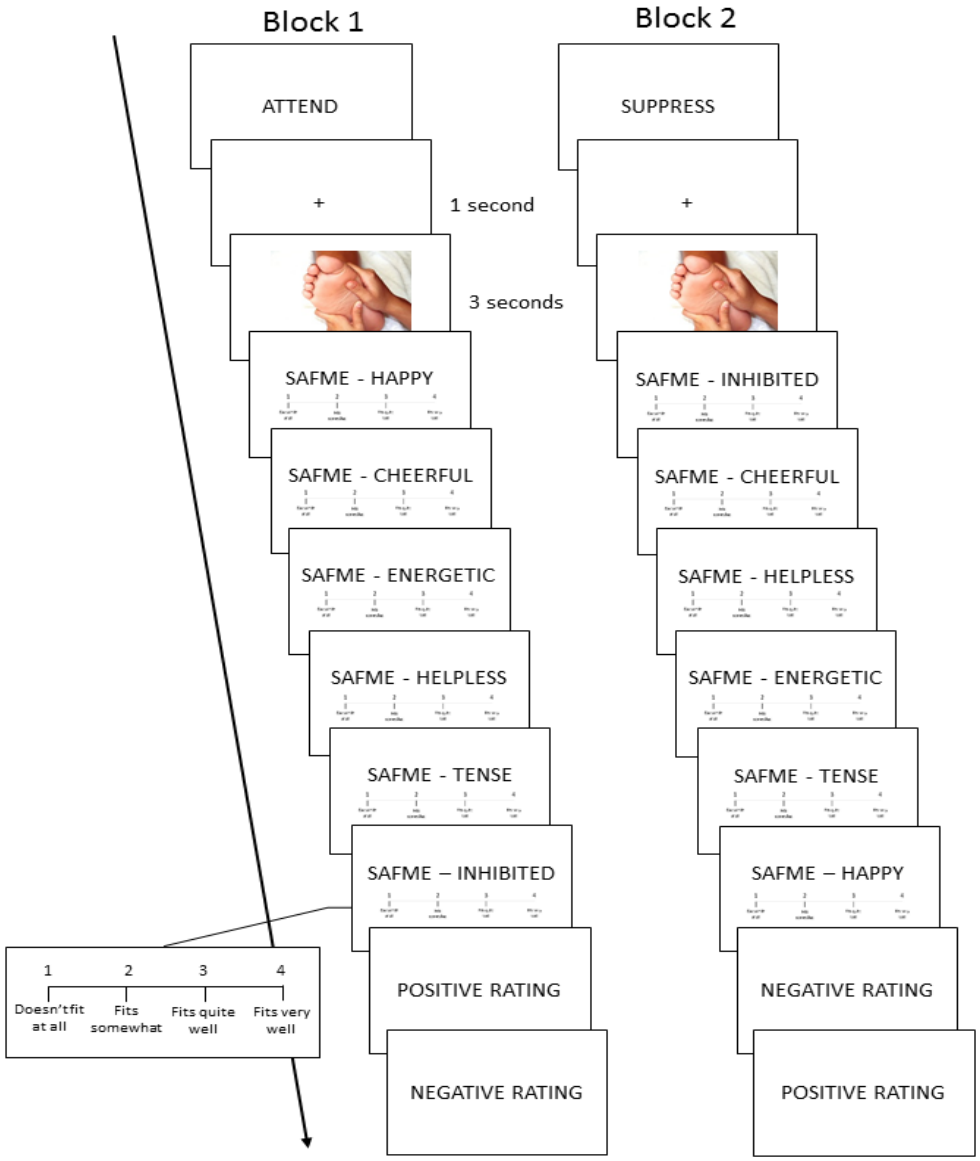

Figure 11. Expressive suppression paradigm trial structure. Blocks began with the instruction to either passively attend to the pictures or suppress emotional responses (order counterbalanced between participants). One trial consisted of one picture and six IPANAT judgements. There were six trials per block. At the end of each block, participants gave an explicit positive and negative affect rating.

4.3.2.8.1. Expressive behaviour. EMG values were found to be non-normally distributed (Shapiro-Wilk p = <.05). One univariate outlier was identified (3 z scores > 3) but was retained in the analysis to preserve statistical power. The assumption of equality of variances for the first and second epochs in both conditions was violated (Levenes's p <.05). The assumption of homogeneity of covariance matrices was also

violated (Box's M p <.05). There was a linear relationship between the covariate and all levels of the dependent variable as assessed by scatterplots. The assumption of sphericity was not violated (Mauchley's test p >.05). No non-parametric test would allow for as fine-grained analysis controlling for age difference as an ANCOVA, and ANOVA models are considered robust to violations of normality with equal group sizes (Tabachnick, 2001). We therefore continued to analyse the data with the planned mixed ANCOVA with group as the between-subjects factor, two within-subjects factors (condition and post-stimulus epoch), age as the covariate, and normalised facial EMG activity as the dependent variable.

4.3.2.8.2. Emotional experience.

Implicit. IPANAT scores for each condition were normally distributed apart from patients' responses to positive words (Shapiro-Wilk p <.05), which were positively skewed (as assessed by inspection of histogram). These values were not transformed as this may have represented a 'floor effect' and the remaining values were normally distributed. No outliers were identified in boxplots. There was an approximately linear relationship between the covariate and each level of the dependent variable as assessed by scatterplots. The assumption of equal covariance matrices was met for both valences of affect (Box's M p >.05). The assumption of equal error variances was also met for both valences of affect (Levene's p > .05). The data were therefore analysed with two mixed ANCOVAs; one for positive and one for negative affect with group as the between-subjects factor, condition as the within-subjects factor, and age as the covariate.

Explicit affect. Positive and negative explicit affect scores were non-normally distributed in both conditions (Shapiro-Wilk p <.05). There was a linear relationship between covariates and levels of the dependent variables as assessed by visual

inspection of scatterplots. There were no outliers, as assessed by boxplots. The assumption of equal covariance matrices was met for both valences of affect (Box's M p >.05). The assumption of equal error variances was also met for both valences of affect (Levene's p > .05). The data were therefore analysed with a mixed ANCOVA with group as the between-subjects factor, condition as the within-subjects factor, and age as the covariate.

4.3.2.8.3. Habitual use of expressive suppression. Expressive suppression and cognitive reappraisal subscale scores were normally distributed (Shapiro-Wilk p >.05). There was equality of error variances (Levene's p >.05) and equality of covariance matrices (Box's M p >.05). The relationships between dependent variables and covariates were approximately linear as assessed by scatterplots. There was homogeneity of regression slopes as assessed by the interaction term (p >.05). There were no multivariate outliers as assessed by Mahalanobis distances (cut-off = 13.82). Therefore responses on the ERQ were analysed with a between-subjects MANCOVA with cognitive reappraisal and expressive suppression subscale scores as the dependent variables, group as the independent variables, and age as the covariate.

4.3.3. Results

4.3.3.1. Manipulation check

To check that participants adhered to the task instruction and suppressed their facial expression when asked to do so, normalised EMG activity in the passive and regulate conditions (averaged all three epochs) was compared with a within-subjects bootstrapped t-test. Mean normalised EMG activity was significantly lower in the suppress condition (M = .92, SD = .05) than the passive condition (M = 1.06, SD = .15); t (51) = 3.38, p = .04, cohen's d = .28, 95% CI [.03, .10]. These results suggest that participants adhered to the instructions.

4.3.3.2. Expressive behaviour

To test for group differences in facial emotional expression across the three one-second post-stimulus epochs, a mixed ANCOVA with group (patient or control) as the between-subjects factor, instruction (passive or regulate) and post-stimulus epoch (1st second, 2nd second, and 3rd second) as the within subjects factors, and age as the covariate was conducted on normalised facial EMG activity. There was no significant main effect of instruction; $F(1,49) = .00$, $p = .96$, $\eta_p^2 = .00$, or epoch; $F(2,98) = .91$, $p = .41$, $\eta_p^2 = .02$. There was also no significant between-groups difference; $F(1,49) = .06$, $p = .80$, $\eta_p^2 = .01$. However, there was a significant three-way interaction between epoch, instruction, and group; $F(2,98) = 3.99$, $p = .02$, $\eta_p^2 = .08$.

To explore this interaction further, a series of post-hoc bootstrapped within-subjects ANCOVAs were conducted to compare normalised facial EMG activity in the regulate and passive conditions during each epoch for each group in both conditions. Regarding the passive condition, group-differences on normalised facial EMG activity were non-significant in the first epoch; $F(1,49) = 1.52$, $p = .22$, $\eta_p^2 = .03$, 95% CI [-.03, 12], second epoch; $F(1,49) = 1.67$, $p = .20$, $\eta_p^2 = .03$ 95% CI [-.04, .27], and third epoch; $F(1,49) = .01$, $p = .95$, $\eta_p^2 = .00$, 95% CI[-.11, .09]. Regarding the suppress condition, between-group differences were non-significant for the first epoch; $F(1,49) = .61$, $p = .44$, $\eta_p^2 = .01$, 95% CI[-.01, .03]. However, between-group differences were significant for the second epoch; $F(1,49) = 6.27$, p = .016, $\eta_p^2 = .11$, 95% CI [-.07, -.008], and the third epoch; $F(1,49) = 3.52$, p = .044, $\eta_p^2 = .07$, 95% CI [-.08, -.01]. These differences retained significance after controlling for multiple comparisons with the Benjamnini-Hochberg procedure (FDR = .1). Inspection of descriptive statistics (Table 16) shows greater activity in the corrugator supercilii

muscle in patients than controls during the second and third post-stimulus presentation epoch in the suppress condition. Therefore, the three-way interaction between epoch, instruction and group, can be explained by patients suppressing their facial expression less than healthy controls during the second and third seconds following the disgust image in the suppress condition.

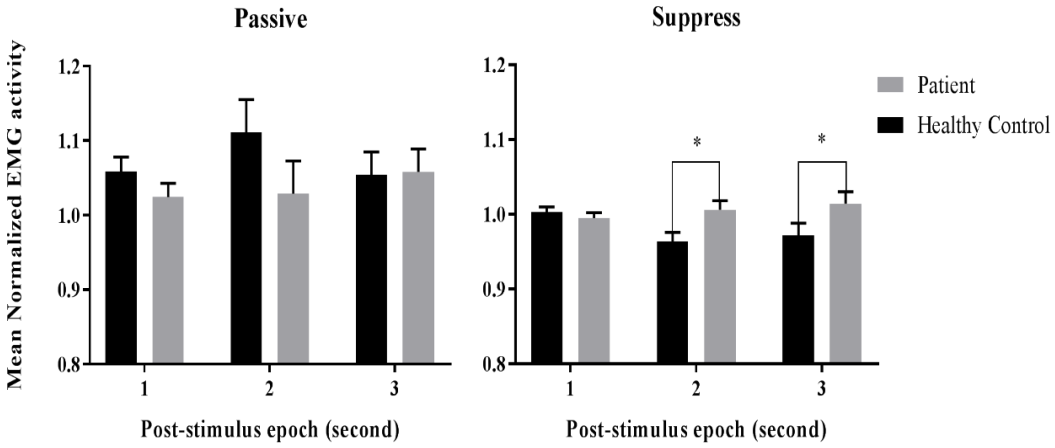

Figure 12. Adjusted Mean normalised EMG activity over the corrugator supercilii during the Passive and Suppress conditions. Error bars represent Standard Error of the adjusted mean. * = p <. 05

4.3.3.3. Emotional experience

To assess for differences in emotional experience between groups and across conditions, two mixed ANCOVAs were conducted on explicit negative and positive affect scores with group as the between-subjects factor (healthy control vs. patient) and condition (passive vs. suppress) as the within-subjects factor. The same process was repeated for the implicit measure.

Regarding the explicit measure of negative affect, there was a significant main effect of instruction; $F(1,49) = 5.08$, $p = .03$, $\eta_p^2 = .09$, whereby participants reported feeling more negative affect in the suppress condition. However, the was no significant main effect of group; $F(1,49) = .53$, $p = .47$, $\eta_p^2 = .01$, and the group*instruction interaction was also non-significant; $F(1,49) = .89$, $p = .35$, $\eta_p^2 = .02$. With respect to

the implicit measure of negative affect, there was no significant effect of condition; $F(1,49) = 3.05$, $p = .08$, $\eta_p^2 = .06$. There was also no significant effect of group; $F(1,49) = 1.43$, $p = .24$, $\eta_p^2 = .03$. The interaction effect was non-significant; $F(1,49) = .11$, $p = .74$, $\eta_p^2 = .00$. A Bonferroni post-hoc adjustment was applied to control for the increased risk of a Type 1 error associated with multiple comparisons, such that $p < .008$ would be considered statistically significant. Following this adjustment, negative affect (explicit or implicit) did not differ between groups and was not affected by the task.

Regarding the explicit measure of positive affect, there was no significant main effect of instruction; $F(1,49) = 1.11$, $p = .29$, $\eta_p^2 = .04$, or group; $F(1,49) = 2.37$, $p = .13$, $\eta_p^2 = .05$. In addition, the interaction between group and instruction was also non-significant; $F(1,49) = 1.04$, $p = .31$, $\eta_p^2 = .02$. With respect to the implicit measure of positive affect, there was also no significant effect of condition; $F(1,49) = 3.13$, $p = .08$, $\eta_p^2 = .06$, and the interaction effect was non-significant; $F(1,29) = .52$, $p = .47$, $\eta_p^2 = .01$. There was however, a significant effect of group; $F(1,29) = 10.18$, $p = .002$, $\eta_p^2 = .17$. A Bonferroni post-hoc adjustment was applied to control for the increased risk of a Type 1 error associated with multiple comparisons, such that $p < .008$ would be considered statistically significant. The difference in implicit positive affect retained significance. These responses suggest that patients felt less positive (implicitly) than healthy controls (Table 18), but there were no between- or within-subjects differences in explicit affect (Table 17).

Table 16 - *Normalised facial EMG activity in the three stimulus presentation epochs across passive and suppress conditions in healthy controls (n = 26) and patients (n = 26).*

		Passive condition				**Suppress condition**			
Epoch	**Group**	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***
1	Healthy control	1.06	.13	1.06	.02	1.00	.05	1.00	.01
	Patient	1.03	.05	1.02	.02	.99	.02	.99	.01
2	Healthy control	1.09	.30	1.11	.04	.96	.07	.96	.01
	Patient	1.04	.06	1.03	.04	1.01	.04	1.01	.01
3	Healthy control	1.05	.19	1.05	.03	.97	.07	.97	.02
	Patient	1.06	.11	1.06	.03	1.02	.07	1.01	.02

Note. *M* = Mean, *SD* = Standard deviation, M_{adj} = Adjusted Mean, *SE* = Standard Error of adjusted mean.

Table 17 - *Explicit positive and negative affect scores for healthy controls and patients in both passive and suppress conditions.*

	Passive condition									**Suppress condition**							
		Negative				**Positive**				**Negative**				**Positive**			
	n	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***
Healthy control	27	2.14	1.29	2.12	.24	3.07	1.14	3.16	.19	2.15	1.13	2.02	.19	2.85	1.19	2.89	.21
Patient	25	2.16	1.07	2.19	.25	2.72	.79	2.63	.19	2.24	1.01	2.37	.21	2.64	.91	2.60	.22
Total	52	2.15	1.18	2.16	.17	2.90	.99	2.89	.13	2.19	1.07	2.19	.14	2.75	1.06	2.75	.15

Note. *M* = Mean, *SD* = Standard deviation, M_{adj} = Adjusted Mean, *SE* = Standard Error of adjusted mean.

Table 18 - *Implicit Positive and Negative Affect test scores for healthy controls and patients in both passive and suppress conditions.*

	Passive condition									**Suppress condition**							
		Negative				**Positive**				**Negative**				**Positive**			
	n	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***
Healthy control	27	1.84	.46	1.81	.08	2.14	.49	2.14	.11	1.87	.48	1.84	.09	2.13	.51	2.14	.12
Patient	25	1.63	.39	1.66	.09	1.64	.61	1.63	.11	1.66	.42	1.69	.09	1.62	.65	1.59	.12

Note. *M* = Mean, *SD* = Standard deviation, M_{adj} = Adjusted Mean, *SE* = Standard Error of adjusted mean.

4.3.3.4. Habitual use of expressive suppression

To assess for group differences in the self-reported habitual use of expressive suppression and cognitive re-appraisal, a between-subjects MANCOVA was conducted on ERQ expressive suppression and cognitive reappraisal subscale scores, with group (healthy control or patient) as the between-subjects factor and age as the covariate. There was a significant main effect of group; $F(2,48) = 8.35$, $p = .001$, Wilks's $\Lambda = .74$, $\eta_p^2 = .26$. Follow up univariate ANCOVAS were performed. A Bonferroni adjustment was made such that statistical significance was accepted when $p < .025$. Patients reported significantly greater use of expressive suppression than healthy controls; $F(1,49) = 8.55$, $p = .005$, $\eta_p^2 = .15$ (Table 19). Conversely, patients reported using cognitive reappraisal less than healthy controls; $F(1,49) = 12.96$, $p = .001$, $\eta_p^2 = .21$ (Table 19).

Table 19 - *Descriptive statistics for expressive suppression and cognitive reappraisal subscale scores of the ERQ in healthy controls and patients.*

	Expressive suppression				**Cognitive reappraisal**			
	M	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***
Healthy control	12.5	5.1	12.6	16.7	32.9	5.7	33.0	1.4
Patient	16.8	4.5	16.7	1.0	25.7	8.1	25.7	1.5

Note. M = Mean, SD = Standard deviation, M_{adj} = Adjusted Mean, SE = Standard Error of adjusted mean.

4.3.3.5. Exploratory correlational analyses.

To explore the relationship between the habitual use of cognitive reappraisal and expressive suppression as emotion regulation strategies and their relationship to other forms of emotion dysregulation in all participants, a series of bootstrapped Pearson's correlations were conducted on expressive suppression, EPS-25 total and subscores. The same process was repeated for cognitive reappraisal. A Benjamini-Hochberg correction was applied to control for False Discovery Rate (set at .1). Perhaps unsurprisingly, a moderate positive correlation was observed between

expressive suppression as measured by the ERQ and the suppression subscale of the EPS-25; $r(50) = .43$, $p = .002$, 95% CI [.18, .62]. A small-to-medium positive correlation was also observed between the Total EPS-25 score and expressive suppression as measured by the ERQ; $r(50) = .31$, $p = .03$, 95% CI [.08, .51]. There were significant small-to-medium correlations between the cognitive reappraisal subscale of the ERQ and the unprocessed subscale $r(50) = -.29$, $p = .04$ 95% CI [-.49, -.06], unregulated subscale $r(50) = -.32$, $p = .02$ 95% CI [-.51, -.07], and the avoidance subscale of the EPS-25 $r(50) = -.31$, $p = .03$ 95% CI [-.09, -.49]. There were also significant moderate correlations between cognitive reappraisal as measured by the ERQ and the EPS-25 total score, $r(50) = -.48$, $p = <.001$ 95% CI [-.62,-.29], the suppression subscale $r(50) = -.46$, $p = .001$, 95% CI [-.63, -.27]. Finally, there was a strong significant negative correlation between the cognitive reappraisal and the impoverished emotional experience subscale of the EPS-25; $r(50) = -.54$, $p = <.001$ 95% CI [-.71,-.38].

Table 20 – *Exploratory Spearman's rank correlational analyses between the ERQ subscales and EPS-25 total score and subscale scores in healthy controls and patients.*

	Suppression	**Unprocessed**	**Unregulated**	**Avoidance**	**Impoverished**	**Total**
Expressive suppression	.42*	.23	.17	.25	.18	.31*
Cognitive reappraisal	-.46*	-.29*	-.32*	-.31*	-.54*	-.47*

Note. *p <.008. N = 52.

4.3.4. Discussion

The aim of this study was to employ a combination of self-report, physiological, and behavioural measures to experimentally test the hypothesis that patients with FND have an increased tendency to select and implement expressive suppression as an emotion regulation strategy relative to healthy controls. In line with

our hypothesis, patients self-reported a greater use of expressive suppression and decreased use of cognitive reappraisal in their daily lives than healthy controls on the ERQ; this suggests that patients with FND perceive themselves to be habitual suppressors. With regards to emotional experience, we predicted that there would be no between-groups differences in the experience of negative affect, but consistent with the habitual tendency to select and implement expressive suppression, patients would experience less positive affect than healthy controls. In line with our hypothesis, the implicit measure of affect suggested that patients experienced less positive emotion than healthy controls with no difference in negative emotion. Additionally, no task-related or between-groups differences were observed in negative affect. In contrast to the above findings, patients' self-reported relative tendency to select expressive suppression as a regulatory strategy was not reflected in the facial EMG responses elicited during the experiment. This was the case both when instructed to respond to negative affective stimuli as they 'normally would' (no difference significant difference between patients and controls), or when instructed to suppress their facial responses (increased facial muscle activity relative to healthy controls). Contrary to our hypothesis, these data suggest that patients express their emotions facially *more* than healthy controls in response to negative affective stimuli when instructed to suppress. Hence, these results give mixed support to the hypothesis that patients with FND are 'habitual suppressors' of their emotions.

The self-report findings on the ERQ are consistent with other studies in patients with FND, which have also shown an increased tendency to conceal one's emotions rather than try to change them by thinking about them differently (Gul & Ahmad, 2014; Urbanek et al., 2014). Why might patients tend to 'select' an arguably more maladaptive emotion regulation strategy? One possible explanation is that the

ability to implement cognitive reappraisal relies on the correct identification of one's emotional state in the first instance (Moyal, Henik, & Anholt, 2013). In chapter three we have demonstrated that patients with FND display a deficit in the identification of their own emotional states. Moreover, the strong negative correlation between the cognitive reappraisal subscale of the ERQ and the impoverished emotional experience subscale of the EPS-25 identified in this chapter (Table 20), suggests that individuals with more alexithymic traits are also less likely to use cognitive reappraisal. Conversely, the significant positive correlation between the expressive suppression subscale of the ERQ and the suppression subscale of the EPS-25, suggests that individuals who tend to use expressive suppression also exert excessive control over their emotional experience and expression. In the event that patients are unable to detect or make sense of their emotions, they may be forced to select and implement other (albeit less effective) regulatory strategies which do not require a good understanding of or flexible control of their emotions, such as expressive suppression (or indeed emotion-focussed coping, dissociation, or avoidance (See section 2.5)).

The finding of significantly increased corrugator supercilii activity in patients relative to controls seems to contradict the self-report findings, which suggest a habitual tendency to suppress emotional expression. Instead, these data suggest that patients with FND exhibit greater emotional expressive behaviour as measured by facial electromyography in response to negative affective stimuli than healthy controls (and therefore implement less expressive suppression). There are several potential explanations for this finding.

Firstly, reduced facial expressive suppression may reflect increased 'physical' reactivity to affective stimuli, which has previously been observed in patients with FMD who exhibited a potentiated startle response to positive emotional stimuli

(Seignourel et al., 2007). However, this would not explain why patients did not also exhibit greater facial muscle activity in the passive condition.

Secondly, it is possible that patients with FND are less able to follow instruction or implement the emotion regulation strategy when instructed to do – even if it is considered maladaptive. However, the manipulation check did suggest that, overall, participants followed the instruction to suppress.

A final potential explanation for the discrepancy between ERQ responses and facial EMG findings is that these measures may be capturing different aspects of expressive suppression. Items in the ERQ ask about emotional expression in a general sense and do not specify whether the expression takes on a behavioural, physiological, or verbal form (e.g., Item 9. "When I am feeling negative emotions, I make sure not to express them."). On the other hand, facial EMG of the corrugator supercilii is a specific physiological measure of acute voluntary facial emotional expressive suppression. It is possible that when patients self-report an increased tendency to expressive suppression on the ERQ, they are referring to verbal or other forms of expression. Indeed, when investigating the social consequences of habitual suppression in a sample of college students, Gross and John (2003) observed a negative correlation between scores on the suppression subscale of the ERQ and 'social sharing with others', which was defined as, "…when you talk about your feelings with others in order to change how you are feeling. An example of sharing feelings is telling your partner how irritated you are at someone else to calm yourself down." One could avoid talking about their emotions with others without suppressing their facial emotional reactions. Therefore, the present observed discrepancy between facial muscle activity when instructed to suppress and responses to the suppression subscale score on the ERQ, might suggest that with patients with FND perceive

themselves to be habitual suppressors because they don't talk about their feelings with others, but they are relatively poor at suppressing acute facial emotional expression. The lack of awareness around acute changes in facial expression might be explained by general deficits in interoceptive sensitivity throughout the body, which is not restricted to detection of heart beat (as demonstrated in Chapter 4.2), and extends to facial muscles. Indeed, somatic symptoms and Conversion Disorder have been conceptualised as the physical expression of psychological distress (Hurwitz, 2004), and patients with FND have repeatedly been shown to endorse more severe somatic symptomology than patients with "medically-explained" "equivalent" conditions (e.g., Brown & Reuber, 2016a; Defazio et al., 2017). To investigate this potential cause of a discrepancy between self-reported and physiological measures of emotional expression further, an experimental paradigm and self-report measure of expressive suppression might be designed to capture all modalities of emotional expression.

How do our findings on emotional experience fit with the literature? With respect to the explicit measures of affect, our findings are consistent with Roberts et al. (2012), who also found no difference between NEAD patients' and seizure-free controls' negative response to negative pictures. However, Roberts et al. (2012) did not examine patients' positive responses to negative pictures, so our positive explicit data cannot be compared. According to the wider expressive suppression literature, the task-related or habitual implementation of expressive suppression should have no influence on negative affect, but result in diminished positive affect (Cutuli, 2014). In line with this, we did not observe any task-induced changes to measures of explicit or implicit negative affect. We also did not observe a task-related reduction in implicit or explicit positive affect, however there was a significant between-groups difference in implicit positive affect. Reduced implicit positive affect in patients aligns with the

broader theory that habitual suppressors tend to experience less positive affect (Gross & John, 2003). The observed lack of difference in implicitly-measured negative affect between patients with FND and controls without FND, is also consistent with the similar levels of implicit anxiety and implicit self-esteem reported between patients with NEAD and epilepsy (Dimaro et al., 2014; Dimaro et al., 2015). As the present study represents a novel design (emotion regulation manipulation with implicit and explicit measures of emotional experience), it is difficult to draw clear comparisons with the rest of the literature. However, trait-reduced implicit positive affect in patients compared to healthy controls does seem to fit with the theory that patients with FND habitually suppress their emotions.

It is not possible to know whether the habitual selection and implementation of expressive suppression is a cause or consequence of reduced positive affect or alexithymia. However, increasing the repertoire of available adaptive emotion regulatory strategies for patients to select from and training them in successful implementation may constitute a useful therapeutic strategy. Approaches such as Cognitive Behaviour Therapy and Cognitive Analytic Therapy which help patients learn how to label and re-appraise their emotions, and therefore regulate them in such a way that would minimise psychological distress, might therefore be effective. Indeed, there is emerging evidence that Cognitive Behavioural Therapy alongside standard medical care is more effective in reducing nonepileptic seizure frequency than standard medical care alone (Goldstein et al., 2015). Expressive suppression and cognitive reappraisal therefore warrant further investigation as psychotherapeutic targets.

4.3.4.1. Limitations

There are a number of limitations to this study which the results need to be

considered in light of. Firstly, the EMG data were very noisy, which meant that a number of parametric assumptions were violated. Unfortunately, these issues could not be corrected without loss of statistical power, and no other statistical test would have allowed for a mixed-design comparison over multiple epochs while controlling for the between-groups difference in age. As a result, the results of the EMG analysis should be interpreted with some caution. Relatedly, a number of analyses were conducted on a relatively small sample size - even though Bonferroni corrections were applied as appropriate, our findings are at risk of a type I error. The small sample size may have also concealed subgroups of patients with FND with opposing emotion regulatory profiles who are likely to exist (Uliaszek et al., 2012). In addition, the generalizability of these findings may also be questioned due to low ecological validity, as the testing scenario was artificial and the presence of facial electrodes may have unduly influenced participants' responses. Future studies can address this by videoing participants' facial expressions and later coding them (c.f. Roberts et al., 2012) – although this approach is also at risk of bias from the experimenters' interpretation of facial expression. In addition, our measure of explicit affect was developed purely for the purposes of this study and, as such, has not been validated elsewhere. We also did not check that the participants perceived the pictures as negative – although the perceived valence of images has been validated in a student sample (Walsh, 2012). A more theoretical criticism is that, although a self-report measure of the tendency to select expressive suppression and a physiological measure of participants' ability to implement expressive suppression was included in this paradigm, the study design does not clearly isolate and manipulate the selection stage independently from the implementation stage of the EPM. Furthermore, the inclusion of a cognitive reappraisal manipulation as well as positive affective stimuli in the

paradigm would have allowed for a more complete comparison with the rest of the emotion regulation and FND literature.

4.3.5. Conclusion

This study aimed to test the hypothesis that emotion dysregulation in patients with FND is characterised by a tendency to select and implement a maladaptive emotion regulatory strategy – expressive suppression. Self-report responses on the ERQ suggested that patients do tend to select expressive suppression instead of cognitive reappraisal as a regulatory strategy in their daily lives, and that this tendency may be related to a tightly controlled regulatory style as well as alexithymic traits. Consistent with endorsed habitual suppression, patients exhibited less positive emotional experience during the study. However, the self-reported tendency to conceal emotions was not reflected in facial EMG responses, which were potentiated relative to controls when participants with FND were instructed to implement expressive suppression.

4.4. Resting Heart Rate Variability in patients with Functional Neurological Disorder (Study 4)

4.4.1. Introduction

The previous chapters in this thesis have found evidence of emotion dysregulation in patients with FND with and without impairments of consciousness (Chapter 3), which is characterised by deficits in the identification of their emotional states (Chapter 4.2) and a self-reported tendency to select / implement maladaptive emotion regulatory strategies (Chapter 4.3). The aim of the research presented in this chapter is to explore if the emotion dysregulation identified through self-report and behavioural measures is also reflected in patients' baseline level of autonomic arousal as captured by resting Heart Rate Variability.

Heart Rate Variability (HRV) is a physiological measure that has been extensively applied in emotion regulation research. HRV can be defined as the oscillation in time interval between consecutive normal heart beats (RR intervals, originating from depolarisation of the sino-atrial node) (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). The heart - like all internal organs in the human body - is innervated by the autonomic nervous system (ANS). The ANS has two branches; the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS), which stimulate or inhibit heart function respectively, working antagonistically to control heart rate and therefore also influencing the variation in time between successive RR intervals (Berntson, Cacioppo, & Quigley, 1991). Regarding sympathetic influence on heart function, sympathetic nerves leave the medulla of the brainstem and project down the spinal cord to synapse with preganglionic fibres. These

in turn exit the spinal cord and project to the sinoatrial node (the heart's pacemaker) via sympathetic ganglia. Sympathetic influences on heart rate are mediated by norepinephrine and manifest relatively slowly – reaching a peak after approximately four seconds and returning to baseline 20 seconds from onset. The vagal nerve is responsible for parasympathetic control of heart rate. Efferent fibres of the vagal nerve originate from the nucleus ambiguus and dorsal nucleus in the brainstem. These nuclei exert tonic inhibitory control over heart rate by rapidly inhibiting or disinhibiting the sino-atrial node. Increasing vagal influence on the sinoatrial node causes the RR interval to become longer (slower heart rate) and is also associated with higher HRV. Conversely, reducing vagal influence causes the RR interval to become shorter (quicker heart rate) and is associated with lower HRV (Porges, 2007). In contrast to the relatively slow-acting sympathetic influence on heart rate, parasympathetic influences are mediated by acetylcholine and act quickly, reaching peak at 0.5 seconds from onset and returning to baseline after one second. The short latency of vagal heart rate control permits rapid and flexible physiological responses to changing environmental demands (Appelhans & Luecken, 2006) and introduces high-frequency variability to heart rate. It also means that the PNS is considered the most prominent influence over cardiac autonomic flexibility - and therefore HRV (Dyavanapalli, Dergacheva, Wang, & Mendelowitz, 2016).

There are two main complementary theories relating to autonomic adjustment to emotional experience and arousal as measured by HRV; the Polyvagal Theory (Porges, 2003) and the Theory of Neurovisceral Integration (Thayer & Lane, 2000). Both theories emphasise the significance of vagal influences on HRV and the overlapping or interconnected neural control of emotion and HRV. However, both theories approach emotion and autonomic control from different perspectives.

Porges' Polyvagal Theory (Porges, 2003) originates from an evolutionary perspective and proposes that autonomic control of the heart results in physiological states that support different types of behaviour in response to environmental demands. The Polyvagal Theory asserts that the human ANS evolved in three stages, each stage representing the acquisition of a new branch of the vagal nerve with a specific role in social processes (i.e. freezing, 'fight or flight', and then social engagement). Porges refers to vagal inhibitory control of the heart as the 'vagal brake', which is constantly being increased or decreased according to changing environmental demands (Kemp & Quintana, 2013). For example, when the vagal brake is activated, heart rate decreases and the body is placed in a more relaxed physiological state which would support social engagement behaviours. Conversely, when the vagal brake is withdrawn, heart rate increases and the body is physiologically prepared for the mobilisation behaviours of 'fight or flight'. Therefore, lower 'vagal tone' is considered a physiological index of stress and stress vulnerability because the body is prepared for 'fight or flight' (Porges, 1995). The relationship between vagal tone and social engagement behaviours is physiologically mediated via afferent connections between the nucleus ambiguus and nuclei of facial and trigeminal nerves, which also facilitate socially relevant behaviours such as facial expression and vocalisation. As part of the Polyvagal Theory, Porges also proposed a mechanism called 'neuroception' (Porges, 2003), which acts outside of conscious awareness to determine whether an environment is safe by 'deciding' if environmental features should elicit mobilisation or social-engagement behaviours. A brain network supporting neuroception would include regions of the temporal cortex which decode biological movement and the intentions of others during social interactions (Van Overwalle & Baetens, 2009). According to the Polyvagal Theory then, fluctuations in vagal tone are intimately

related to behaviour and motivation.

The Theory of Neurovisceral Integration (Thayer & Lane, 2009) is grounded in dynamical systems perspective, and also proposes a relationship between autonomic control and emotion. According to this theory, conscious emotional experience relies on the transmission of affective information from subcortical to cortical brain regions, the latter exerting top-down influence on subjective emotional experience. Regions of the insula as well as prefrontal and cingulate cortices hold the amygdala under tonic inhibition. When the central nucleus of the amygdala is disinhibited, there is further downstream disinhibition of sympathetic neurons (rostral ventrolateral medulla) and increased inhibition of neurons in the nucleus ambiguus and dorsal vagal motor nucleus which control the parasympathetic system. This results in increased heart rate and therefore lower HRV. The activity of this network is associated with emotional arousal. For example, Lane et al. (2009) showed that regional cerebral bloodflow (rCBF) in the right superior prefrontal cortex, left rostral anterior cingulate cortex, right dorsolateral prefrontal cortex and right parietal cortex positively correlated with vagally-mediated HRV during an emotion induction paradigm. Importantly, self-reported emotional arousal was negatively associated with HRV and rCBF in these regions. Therefore, during conditions of emotional arousal, cortical regions are deactivated resulting in a cascade of autonomic changes that lower HRV by increasing heart rate (Appelhans & Luecken, 2006). As such, brain networks that control HRV and emotional experience are anatomically and functionally integrated and HRV can serve as a proxy of emotional arousal.

Both the Polyvagal Theory and the Theory of Neurovisceral Integration argue that low HRV / vagal tone is indicative of high emotional arousal. If this is the case, then low vagal tone could also be an indicator of emotional dysregulation. Indeed,

several studies have associated lower resting vagal tone with trait emotional dysregulation, for instance in patients with panic disorder (Friedman & Thayer, 1998), Generalized Anxiety Disorder (Thayer, Friedman, & Borkovec, 1996), Post-Traumatic Stress Disorder (Meyer et al., 2016), Borderline (emotionally unstable) Personality Disorder (Koenig, Kemp, Feeling, Thayer, & Kaess, 2016), and trait-negative affect (elevated levels of self-reported depression and anxiety) (Bleil, Gianaros, Jennings, Flory, & Manuck, 2008). Lower vagal tone has also been positively associated with emotion dysregulation as measured by the DERS in both resting HRV and 24 hour ambulatory HRV data from healthy participants. Specifically, the inability to accept negative emotions (DERS subscale) showed the strongest negative association with vagally mediated HRV (vmHRV) in a student sample (Visted et al., 2017). Another study also found a negative association between vmHRV and DERS subscale scores, namely 'emotional clarity' and 'impulse control', in healthy volunteers (Williams et al., 2015). Although the direction of effect has varied in different studies, HRV can also be measured as a state variable during emotion regulation tasks. For example, vmHRV in students has been demonstrated to decrease prior to an exam versus rest, with simultaneous increases in state anxiety as measured by the State Trait Anxiety Inventory (Dimitriev, Saperova, & Dimitriev, 2016). State HRV reactivity can also interact with trait emotional characteristics. For example, healthy subjects were categorised into high or low neuroticism groups and performed an emotion regulation task where participants were instructed to down-regulate negative affect. The more neurotic group presented with lower vmHRV during down-regulation of negative affect than participants rated as low in neuroticism (Di Simplicio et al., 2012). The results from these studies therefore support the idea that reduced vagal tone as measured by HRV is a considered a universal measure of

emotion dysregulation.

Whether reduced vagal tone is a cause or consequence of emotion dysregulation is unclear. However, there is a strong body of evidence suggesting that reduced resting vagal tone may predispose an individual to maladaptive perceptual processing of emotional information. Park, Van Bavel, Vasey, and Thayer (2012) demonstrated that healthy participants with low (versus high) resting vmHRV were less able to disengage from images of fearful faces in order to perform a novelty search during an Inhibition of Return paradigm. Healthy participants with lower resting vmHRV have also been shown to exhibit faster attentional engagement to fearful faces than those with higher resting HRV (Park et al., 2013), reflecting an attentional bias to negative emotional information in individuals with reduced vagal tone. Park, Vasey, Van Bavel, and Thayer (2014) have also suggested that lower resting HRV may render an individual susceptible to inappropriate stress responses. Healthy participants performed a letter detection task with fearful distractors (images of faces) under lower and higher load conditions. During the low-load condition, participants with higher resting HRV showed phasic enhancement of HRV in response to fearful distractors during a letter detection task – suggesting a self-regulatory effort. Conversely, participants with lower resting HRV showed further, phasic suppression of HRV during the low-load condition. During the high-load condition, there was no significant change in phasic HRV for participants with high resting HRV (suggesting that participants redirected all of their attention away from the emotion-eliciting stimulus and towards the task-relevant stimuli). However participants with low-resting HRV still exhibited phasic suppression in response to the fearful faces, meaning that these participants continued to process the affective stimulus at the expense of task-performance. These results suggest that individuals with lower resting HRV are prone

to a potentiated autonomic stress response, even when a stress reaction is not required or appropriate (as in the case of the low perceptual load condition) (Park et al., 2014). It is therefore conceivable that the afferent effects of low vagal tone may serve to enhance or sustain physiological arousal / psychological distress. As such, reduced vagal tone may constitute a cause or a consequence of emotion dysregulation.

Given the putative role of emotion dysregulation in FND, researchers have begun to investigate HRV in patients with these symptoms. Patients with FMD have been shown to have lower resting vmHRV than healthy controls (Maurer et al., 2016). Likewise, patients with NEAD have been demonstrated to have lower resting vmHRV than healthy controls (Ponnusamy et al., 2011) or controls with low levels of Post-Traumatic symptoms (Roberts et al., 2012). Sympathetic tone has been shown to increase in the five minutes preceding a nonepileptic attack, with a subsequent increase in vmHRV during and following the attack, supporting the hypothesis that nonepileptic attacks may function as an emotion regulation strategy ameliorating increased emotional arousal (van der Kruijs et al., 2016). Bakvis, Roelofs, et al. (2009) found lower vmHRV in a group of patients with NEAD at rest and during recovery from the Trier Social Stress Test than in healthy controls. What remains to be seen, is whether vmHRV correlates with emotion dysregulation (for instance measured by the EPS-25) and with particular manifestations of comorbid psychopathology in patients with FND.

The aim of the present study was therefore to compare HRV in patients diagnosed with FND against healthy controls, and to explore whether HRV measures were associated with measures of emotion dysregulation and psychopathology in patients and controls. We hypothesised that patients with FND would have lower vmHRV than healthy controls, but that vmHRV would be significantly associated with

measures of emotion regulation and psychopathology in all participants.

4.4.2. Methods

4.4.2.1. Participants

Twenty six patients with FND and 28 healthy controls participated in this study. For demographic and clinical details see Table 10.

4.4.2.2. Materials / Apparatus

4.4.2.2.1. ECG recording. See section 4.2.2.2.2.

4.4.2.3. Measures

4.4.2.3.1. Heart Rate Variability. HRV is operationalised through various measures resulting from analyses of RR intervals and there are several different methods for measuring HRV: time domain, frequency domain, and non-linear methods. Power spectral density analysis of RR interval time yields two main frequency components; high (.15 - .40Hz) and low (.01 – .15Hz) frequency components which reflect vagal tone, and both sympathetic influence and vagal tone respectively. These metrics are referred to as frequency domain measures. Alternatively, time domain measures employ different statistical or geometric techniques to express the variance of successive RR intervals, which have been shown to reflect different combinations of ANS control of heart rate. Toichi, Sugiura, Murai, and Sengoku (1997) developed a non-linear technique for assessing cardiac autonomic function, which they suggested was more reliable than time or frequency domain measures. This method is based on the construction of a Lorenz plot, in which the variation in consecutive RR intervals is represented on a two-dimensional plane with two axes; the longitudinal axis (*L*) which is parallel to the plane, and the transverse axis (*T*) which is vertical to the plane. A measure of sympathetic tone, the Cardiosympathetic Index (CSI), is calculated as *L*/*T*. Conversely, a measure of

parasympathetic tone, the Cardiovagal Index (CVI), is calculated as $\log_{10}$ (T x L). Although there are many different measures of HRV, each with their respective advantages and disadvantages (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996), to avoid the increased risk of Type 1 error associated with multiple comparisons, and owing to their proposed increased reliability as compared to time and frequency domain measures (Toichi et al., 1997), we selected CVI and CSI as the dependent measures for the present study.

4.4.2.3.2. Emotion regulation measures.

The Emotional Processing Scale. See section 3.2.3.2.

Interoceptive Sensitivity. The IS scores generated in Chapter 4.2 were included in the exploratory analysis.

The Emotion Regulation Questionnaire. See section 4.3.2.3.3.

4.4.2.3.3. Psychopathology symptom measures.

The Patient Health Questionnaire – 9. See section 3.2.3.3.

Generalized Anxiety Disorder – 7. See section 3.2.3.4.

The Patient Health Questionnaire – 15.See section 3.2.3.5.

Post-Traumatic Stress Disorder Checklist – 5.See section 3.2.3.6.

4.4.2.4. Design

A between-subjects design was used. The independent variable was group (Patient versus Healthy Control) and the dependent variables were CSI and CVI, self-reported emotion dysregulation (EPS-25), interoceptive sensitivity pre- and post-Cold Pressor Test (ISpre and ISpost) symptoms of Major Depressive Disorder (PHQ-9), symptoms of Generalized Anxiety Disorder (GAD-7), frequency and severity of somatic symptoms (PHQ-15), and Post-Traumatic Stress Disorder symptoms (PCL-

5).

4.4.2.5. Procedure

Participants were seated in a chair with their feet placed on the floor and their arms uncrossed. They were positioned in front of a computer monitor (approximately 60cm away) running an E-Prime 2.0 script (Psychology Software Tools, 2012), which presented the following onscreen instructions:

"We would like you to sit and relax for five minutes. During this time, we will be recording your heart beat. Nothing else will happen. Please get comfortable, with your hands resting on the desk in front of you and your legs uncrossed. Try to remain like this during the recording. When you are ready to begin, press any key to continue."

The E-Prime script also informed participants when recording started and stopped. A privacy screen separated the experimenter and the recording equipment from the participant. Participants were seated for several minutes before recording began.

4.4.2.6. Data analysis

Triggers sent from the E-prime 2.0 script running on the participant's computer marked the start and finish of five minutes in the ECG trace. These five minute sections of the ECG recording were then selected and exported to Kubios HRV Software for Windows (Tarvainen, Niskanen, Lipponen, Ranta-Aho, & Karjalainen, 2014) for pre-processing and analysis.

4.4.2.6.1. Pre-processing. Kubios (Tarvainen et al., 2014) is Matlab-based software which uses a QRS detection algorithm to calculate time domain, frequency domain, and non-linear HRV parameters from ECG recordings (Figure 13). Recordings were visually inspected for technical and physiological artefacts, and slow linear

trends – all of which may interfere with HRV analysis. A threshold for rejection of recordings from the final analysis was set at 5% of beats, however no traces contained more than 5% artefacts. We identified ectopic beats (physiological artefacts) in five recordings, which were reduced by applying the lowest possible level of artefact correction to the RR series. Slow baseline fluctuations in the RR series trend were corrected with the smoothness priors method (lower bound of LF band = <.04Hz, Lambda = 500). These pre-processing steps are recommended by Kubios (Tarvainen, Ranta-Aho, & Karjalainen, 2002).

Figure 13. Screenshot of the Kubios HRV interface.

4.4.2.7. Statistical analysis

Data were screened for normality in SPSS. CVI and CSI and Heart Rate scores were found to be normally distributed (Levene's $p > .05$). There was a linear relationship between CVI and CSI and all other dependent measures as assessed by visual inspection of a scatterplot. There was homogeneity of regression slopes, as assessed by the interaction term between age and group, $F(2,48) = .78$, $p = .46$. There was homogeneity of covariances, as assessed by Box's M test ($p = >.05$). There were

no multivariate outliers as assessed by Mahalanobis distance (critical value = < 13.82). Therefore, HRV was analysed with a MANCOVA. PHQ-9, GAD-7, PHQ-15, and PCL-5 responses were found to be non-normally distributed (Levene's $p > .05$). However, inspection of scatterplots revealed a monotonic relationship between all variables. Therefore a series of Spearman's correlation coefficients were used to analyse the relationship between HRV and self-report measures of emotion dysregulation and psychopathology.

4.4.3. Results

4.4.3.1.Heart Rate Variability

To assess for group differences in HRV, a MANCOVA with group (healthy control versus patient) as the between-subjects variable was conducted on CSI and CVI as the dependent variables. Means and adjusted means are presented in Table 21. Measures of HRV appear to be lower in the patient group than the healthy control group. Selected Lorenz plots depicting the balance between sympathetic and parasympathetic tone in one patient and one healthy control are displayed in Figure 14. These plots suggest an imbalance in vagal and sympathetic tone in patients but not healthy controls.

Table 21 - *Means, Adjusted Means, Standard Deviations, and Standard Errors for Cardiovagal Index and Cardiosympathetic Index in patients and healthy controls.*

	HRV							
	CSI				**CVI**			
Group	***M***	***SD***	M_{adj}	***SE***	***M***	***SD***	M_{adj}	***SE***
Healthy control	2.38	.60	2.44	.12	2.97	.38	2.92	.09
Patient	2.12	.60	2.05	.13	2.49	.66	2.56	.10

Note. CSI = Cardiosympathetic Index, CVI = Cardiovagal Index, *M* = mean, *SD* = Standard Deviation, M_{adj} = Adjusted Mean, *SE* = Standard Error of the Adjusted Mean.

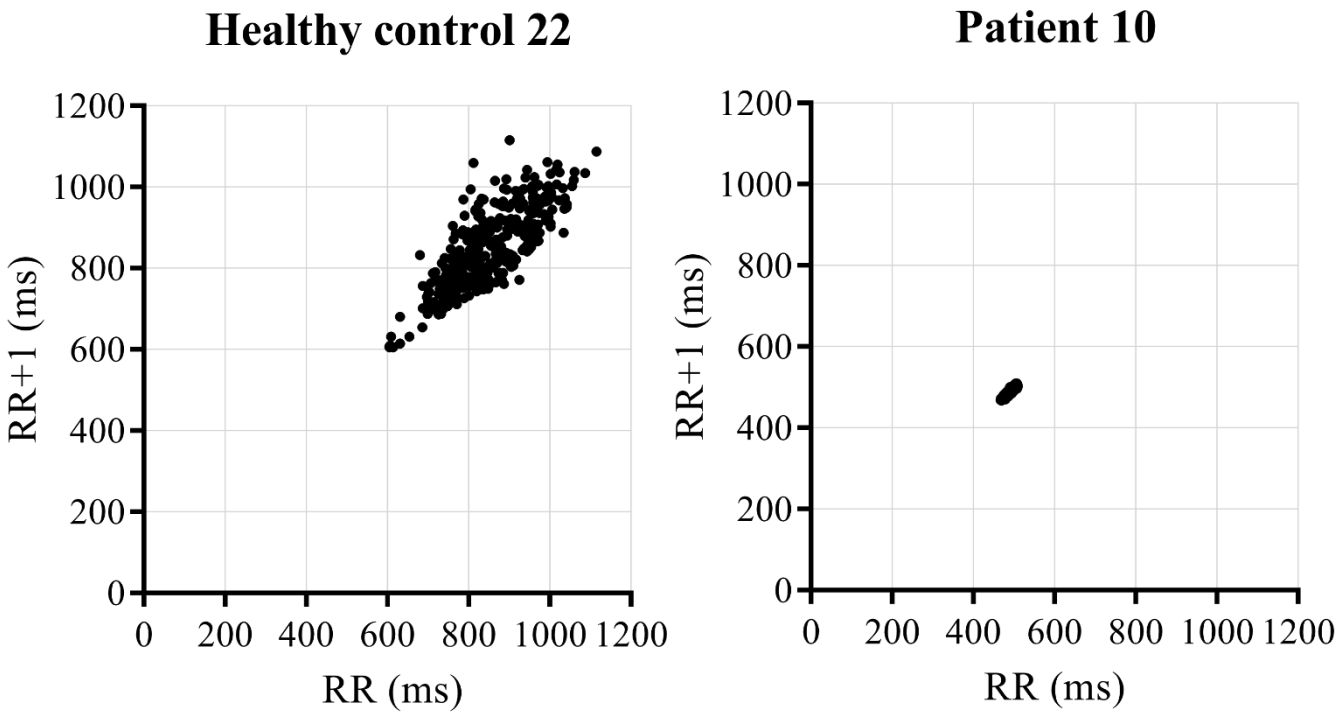

Figure 14. Lorenz plot generating a cardiac vagal index (CVI) and cardiac sympathetic index (CSI) in a healthy control and patient participant. The increased spread of points in the healthy control graph indicates greater variability in time between consecutive RR intervals. The more elliptical shape in the healthy control graph indicate a normal balance between sympathetic and parasympathetic tone. The spread of points in the patient scatterplot are tightly bunched around the longitudinal access indicating low parasympathetic tone.

The one-way MANCOVA showed that there was a statistically significant difference in HRV between-groups after controlling for age; $F(2,50) = 7.61$, $p < .001$, Wilks' $\Lambda = .77$, $\eta_p^2 = .23$. Follow up univariate one-way ANCOVAs were performed. A bonferroni adjustment was made such that statistical significance was accepted when $p < .025$. There were statistically significant differences in the adjusted mean for CVI; $F(1,51) = 6.08$, $p = .02$, $\eta_p^2 = .11$,but not for CSI; $F(1,51) = 4.93$, $p = .03$, $\eta_p^2 = .09$ (Figure 15). Inspection of the descriptive statistics reveals that CVI was lower in the patient group than the healthy control group. Heart rate did not differ significantly between-groups; $t(52) = -1.06$, $p = .29$ [95% CI, -11.47 to 3.55], and so could not account for this discrepancy. Therefore, the significantly lower HRV in patients relative to controls was driven by reduced vagal tone.

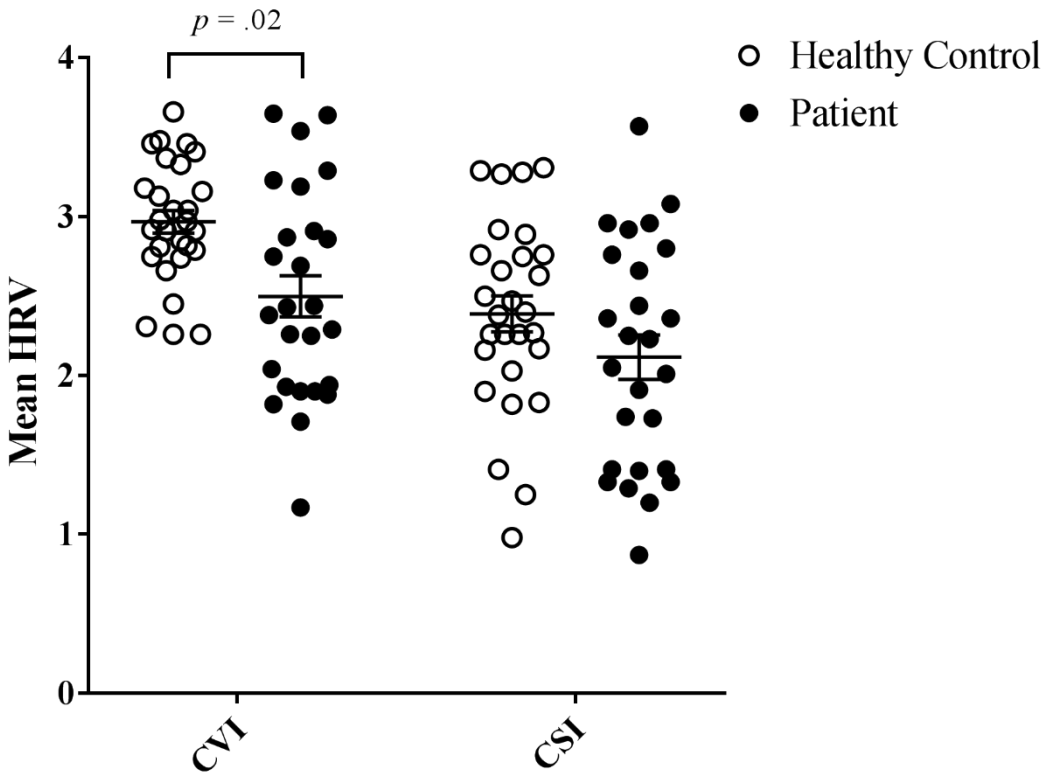

Figure 15. CVI and CSI scores for patients and healthy controls. Error bars represent Standard Error of the mean.

4.4.3.2.The effect of cardioactive medication and ECG artefacts on HRV

Eight patients reported being prescribed and taking medication that have been associated with altered HRV (e.g., Tricyclic anti-depressants (Kemp et al., 2010), Benzodiazepines (Agelink, Majewski, Andrich, & Mueck-Weymann, 2002)). To investigate the possibility that decreased HRV in patients was caused by these medications, the MANCOVA was repeated with these patients' data removed. While the effect size was slightly reduced, the between-subjects difference in HRV retained significance; $F(1,43) = 5.28$, $p < .01$, Wilks $\Lambda = .79$, $\eta_p^2 = .20$, suggesting that reduced HRV in patients was not chiefly explained by the effect of cardioactive medication.

ECG recordings from six participants required correction for artefacts (e.g., ectopic beats). Given the sensitivity of HRV analysis to the presence of artefacts or their correction, the MANCOVA was repeated again with these traces excluded. The model remained significant; $F(2,45) = 6.91$, $p < .01$, Wilks $\Lambda = .26$, $\eta_p^2 = .24$, suggesting that inclusion of corrected ECG traces did not confound the analysis.

4.4.3.3.Exploratory correlational analyses

To explore for potential relationships between HRV, emotion dysregulation, and psychopathology a series of Spearman's rank order correlations were conducted on CSI, CVI and EPS-25, PHQ-9, GAD-7, PHQ-15, PCL-5 scores, and ERQ subscale scores (Table 22). CSI did not correlate significantly with any of the self-report measures. However, there was a small-to-moderate negative correlation between CVI and the EPS-25; $r_s(52) = -.27$, $p = .049$. There was also a small-to-moderate correlation between CVI and the PCL-5 scores; $r_s(52) = -.31$, $p = .02$. Significant positive correlations were also observed between CVI and interoceptive sensitivity pre-CPT; $r_s(52) = .39$, $p < .01$, and interoceptive sensitivity post-CPT; $r_s(52) = .36$, $p < .01$. These correlations indicate that participants with lower vagal tone reported

greater emotion dysregulation and PTSD symptoms. Conversely, participants with higher vagal tone exhibited greater interoceptive sensitivity pre- and post- CPT. All CVI correlations retained significance after controlling for the False Discovery Rate (set at 0.1) with a Benjamini-Hochberg correction.

Table 22 - *Spearman's Rank Order correlation coefficients between HRV scores and measures of emotion dysregulation and psychopathology.*

	HRV	
Measure	**CSI**	**CVI**
EPS-25	-.02	-.27*
PHQ-9	-.03	-.21
GAD-7	-.15	-.15
PHQ-15	-.19	-.11
PCL-5	-.08	-.31*
IS pre	-.03	.39*
IS post	-.07	.36*
Cognitive Reappraisal	.24	.14
Expressive Suppression	-.20	-.24

Note. EPS-25 = Emotional Processing Scale, PHQ – 9 = Patient Health Questionnaire-9, GAD-7 = Generalized Anxiety Disorder-7, PHQ-15 = Patient Health Questionnaire-15, PCL-5 = PTSD Checklist for DSM-V. IS pre = Interoceptive Sensitivity pre-stress induction. IS post = Interoceptive Sensitivity post-stress induction, Cognitive reappraisal = Cognitive Reappraisal subscale of the Emotion Regulation Questionnaire, Expressive Suppression = Expressive Suppression subscale of the Emotion Regulation Questionnaire. * = statistically significant correlation

4.4.4. Discussion

The aim of this study was to test the hypothesis that patients with FND would have lower resting HRV than healthy controls, and that reduced HRV (in particular vagal tone) is related to emotion dysregulation and psychopathology. Lower vagal tone was observed in patients relative to healthy controls, and reduced vagal tone was found to be associated with increased emotion dysregulation and symptoms of Post-Traumatic Stress Disorder. Conversely, increased vagal tone was associated with greater interoceptive sensitivity. Sympathetic tone did not differ significantly between-groups and did not correlate with any self-report measures of emotion dysregulation or psychopathology. These results suggest that patients with FND experience chronic autonomic arousal and support the view that vagal tone is related

to emotion regulation and psychological health. They also raise the possibility that reduced vmHRV may be a potential biomarker of emotion dysregulation in FND.

A few other studies have compared vagal tone in patients with FND against healthy controls. In line with our findings of reduced vagal tone in patients with FMD relative to healthy controls, Ponnusamy et al. (2011) also observed lower CVI in 52 patients with NEAD admitted to a video telemetry unit, as compared to 35 healthy controls. However, unlike Ponnusamy et al. (2011), we did not observe significantly higher sympathetic tone in patients. Potential explanations for this are differences in sample size and the testing scenario – in the Ponnusamy et al. (2011) study, patients were tested under arguably more stressful conditions (video telemetry unit) than the present setting, which may have led to a greater discrepancy between vagal and sympathetic tone. However, our results are consistent with studies of vagal tone in patients with FND as assessed by other HRV metrics. Maurer et al. (2016), found decreased resting vagal tone in patients with FMD, as measured by time (RMSSD, NN50, pNN50) and frequency (HF, LF/HF) parasympathetic components. Lower RMSSD and lower RSA (both measures of vagal tone) have also been reported in patients with NEAD relative to healthy controls (Bakvis, Roelofs, et al., 2009; Roberts et al., 2012). Therefore, our data are consistent with other findings that vagal tone is reduced in patients with FND. According to the Theory of Neurovisceral Integration and Polyvagal Theory, this would mean that patients with FND exhibit a biomarker of stress-vulnerability. Indeed, other studies have demonstrated increased sensitivity to affective information suggestive of greater stress-vulnerability in patients with FND. For example, Voon et al. (2010) demonstrated impaired amygdala habituation and altered functional connectivity between the right amygdala and the right supplementary motor when patients with Conversion Disorder viewed emotional

stimuli. Similarly, Seignourel et al. (2007) demonstrated that patients with FMD exhibited an atypical pattern of potentiated startle response to both positive and negative pictures (healthy controls exhibit a slight inhibition in response to positive pictures). Taken together, these studies suggest that patients with FND exhibit chronic emotion dysregulation and autonomic arousal consistent with an increased susceptibility to stress.

To our knowledge, no other studies have reported significant correlations between vmHRV and measures of emotion regulation or psychopathology in patients with FND. However, the present observation that impaired vagal tone is associated emotion dysregulation, impaired interoceptive sensitivity, and PTSD symptomology is consistent with theory and work conducted in other clinical populations, which will now be discussed.

The observed relationship between emotion dysregulation as measured by the EPS-25 and vagal tone in participants supports the Neurovisceral Integration Theory – which proposes that successful emotion regulation (i.e., the ability to flexibly up- or down-regulate positive / negative affect appropriately in response to changing contexts) requires a flexible autonomic nervous system to effect the response. As decreased HRV is considered a marker of inflexible autonomic control, individuals with lower resting HRV are less able to produce adaptive regulatory responses (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012) and are more vulnerable to stress (Porges, 1995). Indeed, patients' difficulty in the implementation of adaptive regulatory responses is evidenced in the current study by elevated scores on the EPS-25 (which captures the use of avoidance, suppression, and presence of unregulated and unprocessed emotions).

The observed correlation between vagal tone and IS is also consistent with the

theory that flexible vagal modulation of heart rate and the production of adaptive regulatory responses is reliant on the ability to accurately perceive emotional arousal from interoceptive inputs (Porges, 2003). The correlation between CVI and interoceptive sensitivity both pre-and post-stress induction suggests that individuals with greater vagal tone are more able to accurately detect their emotional states. This would be advantageous for the adaptive selection and implementation of emotion regulatory strategies (Gross, 2015), and corroborates the link between vagal tone and emotion regulation – specifically the identification of emotional states.

Consistent with the observed correlation between PTSD symptomology and CVI, Meyer et al. (2016) found a negative correlation between RMSSD (time-domain measure of parasympathetic control) and self-reported early-life maltreatment as measured by the Childhood Trauma Questionnaire in patients with PTSD or Borderline (emotionally unstable) Personality Disorder. Other studies have also reported negative correlations between PTSD symptom severity and resting vagal tone (e.g., Chang et al., 2013). These data raise the possibility of an aetiological overlap between PTSD and FND, which may represent components of a biopsychosocial account of FND (Reuber, 2009) in which low vagal tone confers a susceptibility to the genesis of symptoms in trauma-exposed individuals. Alternatively, reduced resting vagal tone could reflect a state of hypervigilance which would constitute an adaptive response to traumatic experiences. Interestingly, low vagal tone has been demonstrated to amplify the association between childhood trauma and internalizing psychopathology (e.g., depression and anxiety) in adolescents (McLaughlin, Rith-Najarian, Dirks, & Sheridan, 2015) – a similar mechanism may be at work in patients with FND, although longitudinal data would be needed to confirm or disprove this possibility. Therefore, these results support the conclusion that vagal tone is more

specifically related to emotion dysregulation and trauma in patients with FND.

Notably, however, we did not find any significant relationship between vagal tone and the self-reported used of expressive suppression / cognitive reappraisal as measured by the ERQ, and severity of Generalized Anxiety Disorder, Major Depression, and Somatization Disorder symptomology – the reason for this is unclear, but given the number of correlations performed on a relatively small sample, it is possible that the significant correlations observed in this exploratory analysis represent a Type 1 error. The rate of False Discoveries was controlled for using a Benjamini-Hochberg procedure, but a more highly powered, confirmatory analysis is required to investigate this possibility further.

If reduced vagal tone is indeed a biomarker of emotion dysregulation in patients with FND, a natural question is whether or not vmHRV could be used to assist in the diagnostic process. Unfortunately, it is too soon for this question to be answered fully. Existing research comparing HRV in patients with FND against their neurological equivalents (e.g., NEAD versus epilepsy) has shown that resting vagal tone is lower in both groups and therefore not unique to FND (Ponnusamy et al., 2011). However, differences in changes between resting and ictal vagal tone has been observed between patients with NEAD and epilepsy (the change is less marked in NEAD) (Ponnusamy, Marques, & Reuber, 2012). Future work would be well-placed to compare HRV in relevant patient groups (e.g., those with 'medically explained equivalents' or similar psychiatric diagnoses) at different stages of symptom activity. This would allow for the generation of data which could potentially assist in the differential diagnostic procedure. Vagal tone could also conceivably be used as a biomarker when assessing the effect of psychological interventions for FND.

4.4.4.1.Limitations

A potential limitation of this study is that vagal tone may have been influenced by cardioactive medications that the patients were taking (Laborde, Mosley, & Thayer, 2017). We therefore repeated the analysis without patients who reported taking medication and the MANCOVA model retained significance, with a slightly reduced effect size. However, given that many patients were taking combination therapy it was not possible to examine the effects of individual medications on HRV in this sample. It is therefore possible that some of the group difference in vagal tone is attributable to the effects of medication.

A further potential limitation of this study is the inclusion of ECG traces which were not artefact-free (n = 6). Even though HRV analysis is sensitive to artefacts, we decided to retain these cases to preserve statistical power and correct them using the recommended inbuilt algorithm in the Kubios software (Tarvainen et al., 2014). However, even the application of these corrections may have a biasing effect on HRV. Reassuringly, the MANCOVA model also remained significant with these cases removed. Therefore artefact correction did not seem to confound our results.

With respect to the exploratory correlational analysis between HRV parameters and measures of interoception, emotion dysregulation and psychopathology, these correlations were relatively small (.27-.39). This indicates a fairly weak relationship between those variables with statistically significant correlations. Correlational analyses also do not inform us about the direction of association and the effect of other latent variables on the relationship cannot be ruled out.

Owing to a lack of previous research in this area at the time of study design, it was not possible to perform an a-priori power analysis. However, a recent systematic

review by Quintana (2017) suggested that in order to achieve 80% power, samples of 233, 61, and 21 participants per group are required to detect small, medium, and large effect sizes respectively. Given the large effect size produced in this present study (η_p^2 =.23) and the group sizes (patients = 26, healthy controls = 28), we can be somewhat confident that the study was sufficiently powered to compare resting HRV between patients and healthy controls. However, the sample size was not large enough to allow for subgroup comparisons, which is important as FND is likely to be an aetiologically heterogeneous disorder.

4.4.5. Conclusion

The present findings suggest that patients with FND have lower resting vagal tone than healthy controls, and that reduced vagal tone is associated with emotion dysregulation, PTSD symptomology, and impaired interoceptive sensitivity. These observations support the suggestion that vagally mediated HRV serves as a potential biomarker of emotion dysregulation in patients with FND (Ponnusamy et al., 2011). Future comparative studies of HRV in patients with FND and other patient groups would help to establish the utility of HRV in the diagnostic process and assessment of treatment response.

5. Changes in emotion processing following Brief Augmented Psychodynamic Interpersonal Therapy for Functional Neurological Symptoms (Study 5)

The previous chapters in this thesis lend support to the commonly held assumption that patients with FND experience pathological emotion dysregulation. The putative view that emotional dysregulation is pertinent to the aetiology and maintenance of FND means that in spite of the relative lack of research demonstrating the efficacy of psychotherapeutic interventions, the mainstay of treatment for FND has been psychotherapy (Carson et al., 2012). Lately, the number of studies investigating the efficacy of psychological investigations for FND has increased. A recent meta-analysis of 13 studies investigating the effectiveness of psychological intervention for NEAD revealed that 47% of patients were seizure-free upon completion of therapy (Carlson & Nicholson Perry, 2017). There is also some evidence that psychological interventions can help patients with other FNS such as FMD (Reuber, Burness, et al., 2007) (although evidence is mounting that multi-disciplinary interventions including physiotherapy and occupational therapy are also effective for FND (Demartini, Batla, et al., 2014; Gardiner, MacGregor, Carson, & Stone, 2017; Nielsen et al., 2015)). However, open questions remain about how emotion dysregulation might best be measured during the course of psychotherapeutic intervention. The aim of the work in this chapter was to assess whether a newly developed self-report measure called the Emotional Processing Scale (EPS-25) (Baker et al., 2015) might be a useful tool to track changes in emotion dysregulation and psychopathology following a psychotherapeutic intervention. Emotional processing as defined by Baker et al. (2015), bears similarities to the model of emotion regulation proposed by Gross (2015). The Emotional Processing Model describes a process in which an emotional

event is detected and appraised (c.f. the identification stage of the EPM), and the resulting emotional experience is expressed or controlled (c.f. the selection and implementation stages of the EPM). Therefore, both models conceptualise emotion regulation / processing as a multi-faceted and iterative process. The remainder of the work in this chapter is presented as it was accepted to the Journal of Behavioural and Cognitive Psychotherapy (with permission from the publisher, Cambridge University Press).

5.1. Abstract

Background: Functional Neurological Symptoms (FNS) are considered non-volitional and often very disabling, but are not explainable by neurological disease or structural abnormalities. Brief Augmented Psychodynamic Interpersonal Therapy (BAPIT), was adapted to treat the putative emotion processing deficits thought to be central to FNS aetiology and maintenance. BAPIT for FNS has previously been shown to improve levels of distress and functioning, but it is unknown whether improvements on such measures correlate with changes in emotion processing - which this treatment focuses on.

Aim

To determine a) whether the recently developed Emotional Processing Scale-25 can be used to demonstrate BAPIT-associated changes in patients with FNS, and b) whether changes in the EPS-25 are associated with changes in previously validated outcome measures.

Method

44 patients with FNS completed questionnaires including the EPS-25 and measures of clinical symptomology (health-related quality of life (SF-36), somatic

symptoms (PHQ-15), psychological distress (CORE-10), illness understanding (BIPQ)) pre- and post-therapy.

Results

At group level emotion processing improved following therapy (p = .049). Some measures of clinical symptomology also improved, namely health-related quality of life (p = 0.02) and illness understanding (p = 0.01). Improvements in the EPS-25 correlated with improvements in mental health-related quality of life and psychological distress.

Conclusion

Emotion processing and some measures of clinical symptomology improved in patients with FNS following BAPIT. The EPS-25 demonstrated changes which correlated with previously validated outcome measures. The EPS-25 is a suitable measure of psychotherapy-associated change in the FNS patient population.

Keywords: Functional Neurological Symptoms, Emotion processing, Psychopathology, Quality of life

5.2. Introduction

Functional Neurological Symptoms (FNS) are manifestations of altered motor or sensory functions not caused by readily identifiable structural or pathophysiological changes in the nervous system (Carson et al., 2012)The DSM-V refers to FNS as 'Conversion Disorder' (American Psychiatric Association, 2013) and the ICD-10 as 'Somatoform Disorder' (World Health Organization, 2016). In both nosologies FNS should not be better explained by other known diagnoses. FNS may present as movement disorders, including weakness and tremor. FNS may also affect sensory processing and include symptoms such as anaesthesia or visual deficits. Nonepileptic Attack Disorder (NEAD), is a paroxysmal FNS involving episodes of altered consciousness. Approximately one third of neurology outpatients present with FNS (Stone, 2013). The long-term prognosis is variable but often poor, as FNS are associated with as much or more significant disability, distress, and unemployment as other "medically explained" conditions presenting to neurologists (Carson et al., 2011).

The existing categorization of FNS as a 'Conversion Disorder' reflects the on-going assumption that psychological difficulties may contribute to their aetiology (American Psychiatric Association, 2013). Indeed, an interaction between pre-disposing, precipitating, and perpetuating factors linked to abnormal emotion processing has been proposed as mechanistic in FNS aetiology (Carson et al., 2012) . 'Emotion processing' describes the process by which, "emotional disturbances are absorbed, and decline to the extent that other experiences and behaviours can proceed without disruption." (p.51) (Rachman, 1980). According to this model, abnormal emotion processing occurs when emotional disturbances are not satisfactorily absorbed by an individual. Disrupted emotion processing may be evident through

direct signs, including intrusive thoughts, irritability, or inappropriate expressions of emotion. Rachman argues that there are also 'indirect' signs of unsatisfactory emotion processing, including fatigue, insomnia, and anorexia (Rachman, 1980). Abnormal emotion processing theoretically contributes to the symptomatology of multiple mental health difficulties and personality disorders, including anxiety and emotionally unstable (borderline) personality disorder (Kret & Ploeger, 2015).

Emotion processing is a multi-faceted concept; consequently there are multiple instruments measuring different aspects of emotion processing, such as the Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004) and the Toronto Alexithymia Scale (Bagby et al., 1994). The Emotional Processing Scale (EPS-38)(Baker, Thomas, Thomas, & Owens, 2007) was developed to create one unified, psychometrically sound measurement of emotion processing (Baker et al., 2007). It has been used to demonstrate improvements in emotion processing and sensitivity to changes in alexithymia as well as psychiatric symptom severity following Cognitive Behavioural Therapy (Baker et al., 2012). The Emotional Processing Scale (EPS-25) (Baker et al., 2015) was later created as a shortened version of the EPS-38, with subscales measuring five key variants of abnormal emotion processing; namely suppression, signs of unprocessed emotion, unregulated emotion, avoidance, and impoverished emotional experience.

Several self-report and experimental studies have provided evidence of abnormal emotion processing in patients with FNS. This research has primarily focused on NEAD (Roberts & Reuber, 2014). In a study by Novakova et al. (Novakova et al., 2015) patients with NEAD exhibited greater impairments in emotion processing on the EPS-25 than healthy controls. Impairments in emotion processing correlated with more severe somatic symptoms, greater psychological distress, and a poorer

illness understanding, supporting the validity of this measure of emotion processing in a patient group with paroxysmal functional neurological symptoms. Another study demonstrated that patients with NEAD have greater difficulty in describing and identifying their emotions as well as possessing more negative beliefs about emotions than healthy controls (Urbanek et al., 2014). Abnormal attentional biases to emotional information and altered physiological markers of autonomic arousal are also evident in this population (Bakvis, Roelofs, et al., 2009). Likewise, disrupted emotion processing is evident in patients with functional motor symptoms. Using event-related fMRI, Aybek et al. demonstrated an increased amygdala response amplitude to fearful imagery, suggesting altered emotion regulation (Aybek et al., 2015). Furthermore, patients with such symptoms have greater difficulty in identifying and describing emotions than controls (Demartini, Petrochilos, et al., 2014). Patients with functional motor symptoms also have lower interoceptive accuracy than healthy controls, elucidating a mechanism by which difficulties in emotion identification and processing could manifest (Ricciardi et al., 2016). Given the multiple forms of emotion processing impairments that have been identified in the FNS population, the administration of a single questionnaire in clinical or research settings may therefore be an efficient approach to capturing the range of emotional difficulties in this population.

The putative links between abnormal emotion processing and FNS suggest that patients could benefit from psychotherapeutic interventions aiming to improve emotion processing. Indeed, there is some evidence that Psychodynamic Interpersonal Therapy (PIT) can help patients with FNS; a brief course of PIT was effective in a randomised control trial of patients with 'multisomatoform disorder' which included at least one FNS (Sattel et al., 2012). Brief Augmented Psychodynamic Interpersonal

Therapy (BAPIT), is an augmented version of traditional PIT, with elements of somatic trauma therapy. BAPIT was adapted specifically to address FNS (Howlett & Reuber, 2009; Sattel et al., 2012) and assumes that psychological difficulties result from interpersonal conflicts in early life. Deep-rooted and commonly occurring issues in this population, such as childhood trauma or neglect are addressed (Reuber, Howlett, et al., 2007). The therapeutic targets of BAPIT include deficits in emotion processing (including the naming, tolerance, and expression of emotions) thought to play a role in FNS aetiology. BAPIT has been associated with significant improvements in psychological distress, mental health, physical health, and healthcare utilization in patients with FNS (Reuber, Burness, et al., 2007). In patients with NEAD, BAPIT has also been associated with sustained improvements in seizure control and healthcare utilisation (Mayor et al., 2010). However, whilst BAPIT aims to improve emotion processing, it has not yet been examined whether the treatment-associated improvements in outcome measures are associated with similar improvements in emotion processing. What is more, the EPS-25 is a novel questionnaire, and it has not yet been demonstrated whether it is sensitive to therapy-associated changes in emotion processing in the FNS population.

The aim of the present study was therefore to explore whether BAPIT associated changes in emotion processing can be picked up the EPS-25. We also aimed to see whether changes seen in health-related quality of life (HRQoL) and some measures of relevant clinical symptomology (psychological distress, illness understanding, and somatic symptoms) correlated with changes in the EPS-25 scores. Finally, we aimed to see whether EPS-25 change scores were sensitive to changes in the measures of clinical symptomology used in this study. Given the theorised causal links between abnormal emotion processing and FNS, we predicted that patients

would experience therapy-associated improvements in emotion processing, HRQoL, and clinical symptomology. We also predicted that changes in EPS-25 scores would correlate with changes in measures of HRQoL and measures of clinical symptomology.

5.3. Methods

5.3.1. Regulatory approvals

This study was granted ethical approval by the Sheffield Local Research Ethics Committee (REC 09/H1308/2; 01/05/2009). Research governance approval was given by the research departments of the Sheffield Teaching Hospitals Foundation Trust and the Barnsley Hospital NHS Foundation Trust.

5.3.2. Participants

Patients with FNS were recruited consecutively from referrals to Neurology Psychotherapy Services at the Barnsley Hospital and the Royal Hallamshire Hospital between January 2010 and September 2012. The FNS diagnosis was formulated by Consultant Neurologists on the basis of all available clinical information. Neurologists were sufficiently certain about this diagnosis to recommend psychological treatment and withdraw treatment for alternative neurological diagnoses (e.g., antiepileptic drugs). All patients provided written informed consent.

5.3.3. Treatment

BAPIT is based on an adapted version of PIT (Hobson, 1985), which assumes that dysfunctional interpersonal patterns originating from childhood are mechanistic in the development of abnormal emotion processing. We have described this approach in greater detail elsewhere (Howlett & Reuber, 2009). BAPIT is intended to improve emotion processing, increase symptom control, change illness perceptions, and improve quality of life through increasing independence and encouraging self-care. In

view of the heterogeneous pre-disposing, precipitating, and perpetuating factors contributing to the aetiology of FNS, BAPIT is based on a personalised assessment of each patient and can also include elements traditionally associated with Cognitive Behavioural Therapy such as goal-setting, exposure, and relaxation. If the patient has problems with hyper- or hypo-arousal (often occurring in the context of a trauma history), elements of Somatic Trauma Therapy, designed to allow patients to control autonomic arousal, identify personal triggers, and process traumatic memories, are incorporated (Rothschild, 2000). Help from carers may be recruited if appropriate (Howlett & Reuber, 2009).

In practice, therapists employ 'here and now' techniques to help the patient notice, tolerate, and understand emotions arising in the session. The patient is encouraged to stay with emotions as they manifest, notice their location in the body, and describe what they feel as a way of linking the emotion to associated physical symptoms / sensations e.g., "I wonder where you can feel that anger in your body right now?" Linking hypotheses are used to connect between current and other feelings both inside and outside the therapy room e.g., "You say you're feeling angry and frustrated now. I wonder if that's a bit like you used to feel as a child when that teacher showed you up in front of the class?"

A single psychotherapist delivered therapy. Psychotherapy duration was tailored to the patients' needs but was intended to be brief (with a notional maximum number of 20 sessions). The initial session lasted two hours. All remaining sessions lasted 50 minutes. Progress was reviewed after six-eight sessions. Further sessions were offered if the patient was considered to have engaged with therapy and if there was a therapeutic need for further sessions agreed upon by both the patient and the therapist. The end of therapy was agreed upon between the two parties when the 20-

session limit was reached or when both parties agreed that therapy was complete (in four cases, the therapy was extended beyond 20 sessions because of individual patients' particular needs and circumstances).

5.3.4. Design and procedure

This was a prospective, uncontrolled study with a within-subjects design. Study information was sent to patients along with their first psychotherapy assessment appointment letter. FNS diagnosis was re-explained at assessment. Patients were screened for factors suggesting they should be excluded from outpatient psychotherapy at this point (including risk of suicide, serious psychiatric conditions or current addictions). Patients were then given a range of symptom-appropriate self-help strategies, a relaxation CD, and self-help literature. Patients were telephoned to check whether their symptoms persisted and to arrange regular therapy sessions two months from assessment. Pre-intervention questionnaires were posted along with the appointment letter to those who agreed to further sessions. Patients were asked to return the questionnaire battery in a pre-paid envelope. Patients failing to do so were given an opportunity to complete the pre-intervention questionnaires immediately before the first therapy session. The first therapy session took place approximately three months after the initial assessment visit.

Immediately after discharge (either planned or following a failure to attend and contact), participants were sent a post-intervention self-report questionnaire battery to complete and return using a pre-paid envelope. To reduce attrition, participants were mailed another copy of the questionnaires if they had failed to return the initial post-intervention questionnaires. Pre- and post-intervention data were collected by an assistant who had not been involved in the administration of psychotherapy. Patients who did not complete and return the post-intervention questionnaire pack were

classified as ‘study non-completers’ and excluded from the analysis.

5.3.5. Measures

5.3.5.1. Demographic, referral and psychotherapy questionnaires. Demographic and clinical information was provided by patients, referring neurologists, and the psychotherapist. Information regarding the FNS diagnosis was provided by the neurologist. Personal information was provided by the participant. An ‘end of therapy summary’ including information about the number of sessions, reason for the end of therapy, and the issues tackled in therapy was provided by the psychotherapist.

5.3.5.2. The Emotional Processing Scale (EPS-25). The EPS-25 is a standardised 25-item self-report scale measuring emotion processing styles and deficits. There are five subscales: suppression, signs of unprocessed emotions, unregulated emotion, avoidance, and impoverished emotional experience (Baker et al., 2009). The EPS-25 has been used in patients with lower back pain (Esteves et al., 2013), Post-Traumatic Stress Disorder (Compare et al., 2012), and patients with NEAD (Novakova et al., 2015) but not in a sample of patients with mixed FNS. Responses are given on a 0-9 Likert scale. There are also three open-ended questions. Higher scores indicate greater difficulties with emotion processing. As per the administrator’s manual, single missing items were replaced by the mean of the subscale (Baker et al., 2015).

5.3.5.3. The Short Form- 36 (SF-36). The SF-36 is a standardised 36-item self-report questionnaire that measures nine areas of Health Related Quality of Life (HRQoL): physical functioning, role limitation - physical, role limitation - emotional, general health, mental health, bodily pain, vitality, health transition, and social functioning. Responses are given on scales ranging from three to ten options.

Higher scores indicate a better HRQoL. Missing items were dealt with as recommended by the user manual (Ware, Kosinski, & Gandek, 2000). Remaining scores were recoded and standardised using norm-based scoring. Scores were combined into physical (PHS) and mental health (MHS) summary scales, as per the procedure detailed in the manual.

5.3.5.4. Clinical Outcome in Routine Evaluations (CORE-10). The CORE-10, is a standardised ten-item self-report scale measuring global psychological distress, taken from the 34 item CORE-OM (Outcome Measure)(Connell & Barkham, 2007). It has been used in studies of patients with FNS (Reuber, Burness, et al., 2007). On a Likert scale (0-4), higher responses indicate a higher level of psychological distress experienced over the last week. The CORE-10 is known to correlate strongly with the Beck Depression Inventory (Beck, Erbaugh, Ward, Mock, & Mendelsohn, 1961; Connell & Barkham, 2007).

5.3.5.5. Patient Health Questionnaires (PHQ-15). The PHQ-15 is a standardised 15-item self-report questionnaire designed to measure common somatic symptoms, for example, stomach pain or trouble sleeping (Kroenke, Spitzer, & Williams, 2002). Participants indicate how bothered they have been by a symptom over the past week, on a three-point Likert scale. Higher scores indicate that participants have been bothered more by a particular symptom. A pattern of missing items emerged, whereby items 4 and 11 were not responded to by 14 and 8 participants respectively. These items may not have been relevant to the participants and so were dropped from the analysis, replicating the procedure adopted in a previous paper (Novakova et al., 2015).

5.3.5.6. Brief Illness Perception Questionnaire (BIPQ). The BIPQ is a standardised nine-item self-report scale measuring emotional and cognitive

representations of illness (Broadbent, Petrie, Main, & Weinman, 2006). For eight items, participants respond on a 0-10 Likert Scale. The 9th item is an open-ended question. The items represent nine dimensions of illness perception including consequences, personal control, treatment control, timeline, illness concern, coherence, identity, emotional representation, and causation. Responses were scored and missing items were dealt with as per the scoring instructions.

5.3.6. Statistical analysis

Given that this was an exploratory study and that there no previous studies using the EPS-25 have been undertaken in this patient group with this measure, no formal power calculation was undertaken. However, one similar prospective study using the EPS-38 (a longer and earlier version of the EPS-25) in patients with depression found an effect size of .74. On this basis a study involving a group of 44 (our sample size) should be able to detect an effect size of .99 with power set at 0.8 and a two-tailed alpha of 0.05. Data were analysed using SPSS Version 22.0 (IBM Corp, 2013). Prior to the use of inferential statistics, all scales scores were screened for normality. The EPS-25 and SF-36 scale scores were non-normally distributed. Therefore, all analyses of scale scores were bootstrapped using 95% confidence intervals based on 1000 samples to control for non-normality. The *p* value was set at $p = 0.05$ (two-tailed hypothesis). Otherwise, the inflated risk of Type 1 error associated with multiple comparisons was controlled for using the Holm-Bonferroni method to correct *p* values when more than one comparison or correlation was being made.

Within-subjects t-tests and repeated measures ANOVAs with Bonferroni corrections were used to compare group mean and / or subscale scores on the EPS-25 and SF-36 self-report scales pre- versus post-intervention. The ANOVA model is robust to violations of normality when group sizes are equal, as is the case in the

present study (Field, 2013). Change scores were calculated such that positive values corresponded to improvements in functioning across all scales. Pearson's product moment correlation coefficients were used to calculate the relationship between change scores on the EPS-25 and the other clinical variables. Partial correlation coefficients were used to explain the amount of variance shared between EPS-25 change scores and any significantly correlated clinical symptomology / HRQoL scores. To complement our analysis of the EPS-25 we included a Reliable and Clinically Significant Change (RCSC) analysis (Jacobson, Roberts, Berns, & McGlinchey, 1999). This method was used to categorise patients according to whether or not changes on the EPS-25 could be considered both statistically reliable and clinically meaningful. We then compared patients who made RCSC against those who did not on the study outcome measures.

5.3.6.1. Internal consistency of the Emotion Processing Scale- 25. Responses on the EPS-25 were combined into total scores for pre- and post-intervention and assessed for internal consistency reliability. Internal consistency was excellent when administered both before ($\alpha = .962$) and after ($\alpha = .967$) intervention.

5.4. Results

5.4.1 Patient characteristics

One hundred and eighteen patients consented to the study. Of this group, 72 returned the pre- and 44 also the post-intervention questionnaire (Figure 16). The final sample therefore consisted of 44 patients. 77.3% (34) were female and the mean age was 41.5 years (*SD* = 13.5). 63% of the sample were economically inactive (defined as unemployed, in receipt of disability benefits, or being retired due to ill-health or old age). Mean symptom duration was 5.4 years (*SD* = 10.8). The mean time between completion of the pre- and post-intervention questionnaires was 11.0 months.

Patients had different main FNS. To explore the justification of analysing patients with different FNS together, we divided the total group into two subgroups (NEAD and 'other FNS'). We compared these two groups on key demographic and therapy variables. There were no differences between the two groups on the mean number of sessions they completed, the number who completed therapy, economic activity, gender, and age at the start of therapy (Supplementary Table 1). Mean pre-intervention total EPS-25 scores did not differ between these FNS groups; $t(42) = .11$, $p = .91$, 95% CI [-1.17, 1.49].

The patient sample also included those who had completed therapy in the judgement of the therapist ($n = 26$) and those who had not ($n = 17$). Reasons for non-completion of therapy included therapy was non-appropriate ($n = 2$), the patient was not progressing ($n = 2$), the patient improved after the initial session ($n = 1$), the patient dropped out ($n = 9$), and 'other' ($n = 2$). To explore the justification of including both patients who completed therapy and those who did not in the analysis, both groups of patients were compared on baseline emotion processing and clinical symptomology (Supplementary Table 2). There were no differences between the two groups on any of these measures.

On the basis that the remaining 44 patients with FNS did not differ significantly on baseline measures of emotion processing and clinical symptomology, irrespective of FNS semiology or therapy completion, we analysed the group as a whole.

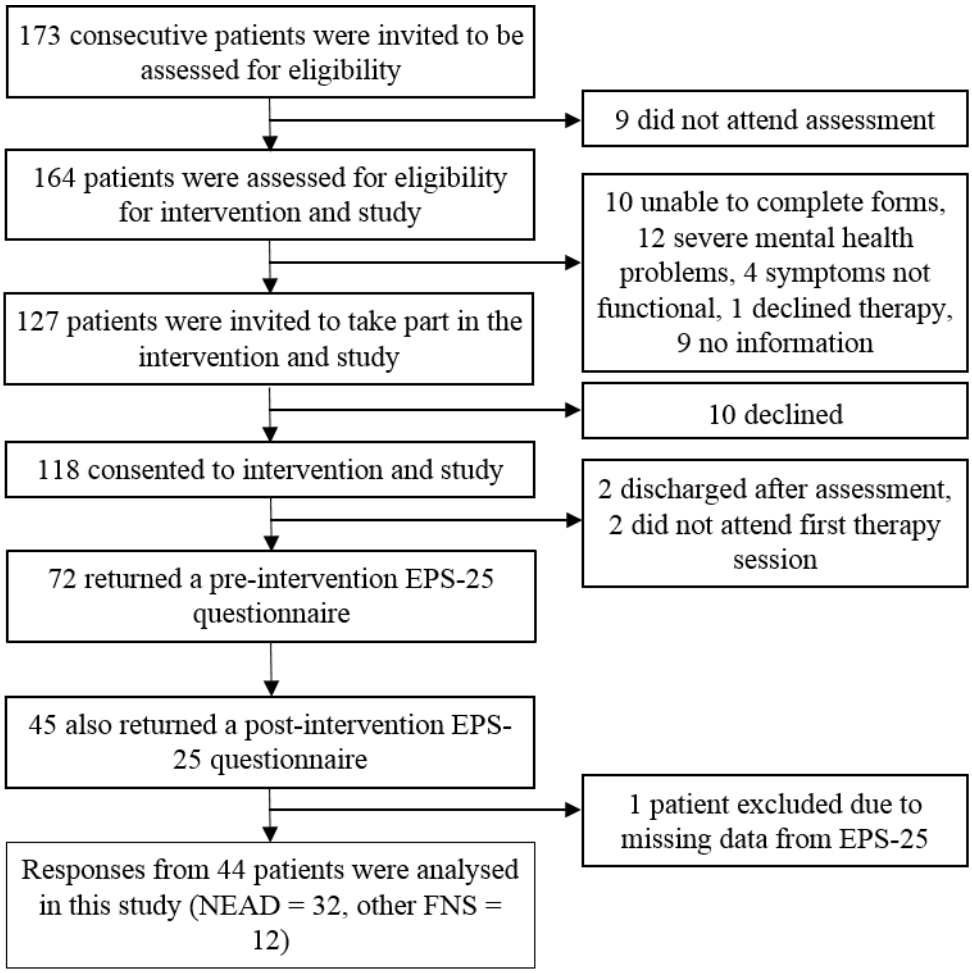

Figure 16. Flowchart of patient attrition

5.4.2. Treatment-associated changes in emotion processing

Patients' pre-intervention EPS-25 scores indicated levels of emotion processing problems above normative healthy values for the UK, with the mean total EPS-25 scores of the FNS sample falling within the top 25th percentile of normative values, and well within pain and mental health norms (M = 4.96, SD = 2.26) (Baker et al., 2015). This indicates that emotion processing problems were common in this patient group before the intervention.

The EPS-25 total score and subscale scores were lower post-intervention (Table *23*). A within-subjects t-test on pre-versus post-intervention mean EPS-25

scores confirmed the statistical significance of therapy associated change; $t(43) = 2.02$, $p = .049$, 95% CI [.043, 1.21], $d = .31$. A two-way repeated measures ANOVA with time point (pre- and post-intervention) and EPS-25 subscale (suppression, unprocessed emotion, unregulated emotion, avoidance, and impoverished emotional experience) as the within-subjects factors showed that there was a significant main effect of time point; $F(1,43) = 4.09$, $p = .049$, $\eta_p^2 = .09$, indicating that emotion processing improved significantly post-intervention. There was also a significant main effect of subscale; $F(4,172) = 10.13$, $p < .001$, $\eta_p^2 = .19$, suggesting that the mean scores on each subscale differed from each other both pre- and post-intervention. There was no significant interaction between time point and subscale, indicating that the relationship between the mean subscale scores did not vary over time; $F(4,172) = .923$, $p = .45$, $\eta_p^2 = .02$. Therefore, as measured by the EPS-25, emotion processing improved following BAPIT.

Table 23- *Pre- and post-intervention EPS-25 total and subscale scores.*

	Pre-intervention		**Post-intervention**	
EPS-25 scores	***M***	***SD***	***M***	***SD***
Suppression	5.43	2.58	4.69	2.83
Unprocessed emotion	5.56	2.86	4.72	2.73
Unregulated emotion	4.40	2.34	4.10	2.38
Avoidance	5.07	2.29	4.53	2.28
Impoverished emotional experience	4.33	2.64	3.64	2.55
Total	4.96	2.26	4.33	2.31

Note. EPS-25 = Emotional Processing Scale-25. $N = 44$.

5.4.3. Treatment-associated changes in routine outcome measures

HRQoL improved following intervention. The post-intervention PHS score ($M = 38.10$, $SD = 11.95$) was greater than the pre-intervention PHS score ($M = 36.24$, $SD = 11.45$). Likewise, the post-intervention MHS score ($M = 42.31$, $SD = 11.12$) was

greater than the pre-intervention MHS score (*M* = 40.10, *SD* = 10.11). A two-way repeated measures ANOVA conducted on the SF-36 summary scales (PHS and MHS) with time point (pre- and post-intervention) as the within-subjects factors showed a significant main effect of time point, indicating that SF-36 scores were significantly higher (better quality of life) for both the MHS and PHS scores post-intervention; $F(1,38) = 5.94$, $p = .02$, $\eta_p^2 = .14$. There was no significant main effect of SF-36 summary scale; $F(1,38) = 2.69$, $p = .11$, $\eta_p^2 = .07$. There was no significant interaction effect; $F(1,38) = .018$, $p = .89$, $\eta_p^2 = .00$.

Post-intervention BIPQ scores (*M* = 48.83, *SD* = 15.79) were lower than pre-intervention scores (*M* = 55.51, *SD* = 11.84). This improvement in illness understanding was significant; $t(32) = 2.95$, $p = .01$, 95% CI [2.57, 12.39] (critical *p* value = .016). While CORE-10 scores were also lower post-intervention (*M* = 17.05, *SD* = 10.43) than pre-intervention (*M* = 19.19, *SD* = 9.39), this reduction in psychological distress was not statistically significant; $t(42) = 1.54$, $p = .13$, 95% CI [-.69, 4.76] (critical *p* value = .05). Similarly, while PHQ-15 scores were lower post-intervention (*M* = 12.14, *SD* = 6.32) than pre-intervention (*M* = 14.05, *SD* = 5.35), reductions in the number and severity of somatic symptoms only approached significance following Holm-Bonferroni correction; $t(36) = 2.31$, $p = .03$, 95% CI [.35, 3.43] (critical *p* value = .025).

5.4.4. Did treatment-associated changes on the EPS-25 correlate with changes in treatment outcome measures?

To assess whether improvements on the EPS-25 were associated with improvements in the measures of clinical symptomology and HRQoL of life used in this study, a series of correlational analyses were conducted on the scale change scores (Table 24). There were moderate to strong positive correlations between EPS-25

change scores, CORE-10, and MHS scale change scores. However, there were no significant correlations between EPS-25 change scores, PHQ-15 scores, BIPQ scores or PHS change scores. This suggests that improvements in emotion processing were associated with improvements in psychological distress and the mental health domain of the SF-36, but not with a better understanding of symptoms, fewer somatic symptoms or improved scores on the physical health domain of the SF-36. EPS-25 change scores did not significantly correlate with the number of sessions received, therefore improvements in emotion processing cannot be explained by contact-time with the therapist; r = .024, n = 43, p = .878, 95% CI [-.184, .289].

Table 24 - *Bootstrapped Pearson's Correlations (r - values) between pre- and post-intervention questionnaire change scores.*

Measure	**EPS-25**	**PHQ-15**	**CORE-10**	**BIPQ**	**MHS**	**PHS**
EPS-25	-					
PHQ-15	.467	-				
CORE-10	.673*	.282	-			
BIPQ	.160	.199	.024	-		
MHS	.634*	.342	.331	.313	-	
PHS	.167	.461	-.122	.307	-.010	-

Note. *significant at adjusted p value (p < .008) using the Holm-Bonferroni correction. CORE-10 = Core Outcome in Routine Evaluation-10, BIPQ= Brief Illness Perceptions Questionnaire, PHQ-15= Patient Health Questionnaire- 15, MHS= SF-36 Mental Health Summary Scale, PHS= SF-36 Physical Health Summary Scale.

Partial correlation coefficients were calculated to elucidate the relationship between the CORE-10 / MHS total scores and the EPS-25 total score when either CORE-10 or MHS-specific variance was controlled for. After controlling for the MHS total difference score, the correlation between the EPS-25 total difference score and the CORE-10 total difference score was smaller, and the amount of shared variance decreased, but the correlation was still statistically significant [partial correlation = .57, r^2 = .32, p < .001, 95% CI [.23, .83]]. Similarly, when controlling for the change in MHS scores, the correlation between the EPS-25 total difference scores and the

CORE-10 total difference score was reduced, and the amount of shared variance reduced, but the correlation remained significant [partial correlation = .56, r^2 = .31, p < .001, 95% CI [.31, .84]. These results indicate that EPS-25 change scores accounted for 45% and 40% of variance in CORE-10 and MHS change scores respectively.

In order to provide a more detailed picture of how patients' emotion processing changed following therapy, we ran a RCSC analysis on EPS-25 scores (Jacobson et al., 1999). 22.7% made a clinically significant improvement, 29.5% made an improvement which was not clinically significant, 20.5% did not change, 18% deteriorated, and 10% experienced a clinically significant deterioration. There were no significant differences on any of the outcome measures between patients who achieved a RCSC and those who did not.

5.4.5. Study non-completers

Seventy-four patients consented for the intervention did not provide complete follow-up data (Figure 16). Therefore, to examine whether attrition biased the results as far as possible, study completers were compared against study non-completers on a series of key variables. There were no associations between whether a patient completed the study and the demographic variables of gender, economic activity, and FNS type. However, study non-completers were younger (M = 34.2 years, SD = 11.6) than study completers (M = 41.4 years, SD = 13.5); $t(75) = 2.48$, p = .02, 95% CI [-12.96, -1.87]. Study non-completers were also less likely to complete therapy (38.2% completed therapy, 61.8% did not complete therapy) in the judgement of the therapist; $\chi^2(1) = 5.91$, p = .02. However, the absence of clear differences between study completers and non-completers in terms of emotion processing and other baseline measures suggests that study completers were representative of the total consented sample on the available psychological parameters (Table 25).

Table 25 - *Comparison of patients who completed the study and those who did not complete the study on baseline emotion processing and clinical symptomology measures.*

	Completers		Non-completers					95% CI	
Measure	***M***	***SD***	***M***	***SD***	***df***	**t**	***p***	***LL***	***UL***
EPS-25	4.96	2.64	5.10	1.92	75	.18	.84	-.76	1.04
PHS	36.24	11.45	37.25	10.84	68	.38	.71	-.43	6.10
MHS	40.10	10.11	35.48	12.80	68	1.70	.31	-10.46	1.26
CORE-10	19.20	9.40	19.50	10.40	75	.14	.09	-3.80	5.30
PHQ-15	12.80	5.60	14.30	4.90	45	.96	.360	-1.52	4.49
BIPQ	56.10	11.10	48.70	10.30	54	2.52	.02	-12.78	-.074

Note. *significant at adjusted *p* - value ($p < .008$) using the Holm-Bonferroni correction. Completers = patients who completed the study. Non-completers = patients who did not complete the study CI = Bootstrapped confidence interval; LL = lower limit; UL = upper limit. EPS-25 = Emotion Processing Scale-25 Total Score, CORE-10 = Core Outcome in Routine Evaluation-10, BIPQ = Brief Illness Perceptions Questionnaire, PHQ-15 = Patient Health Questionnaire- 15, MHS = SF-36 Mental Health Summary Scale, PHS = SF-36 Physical Health Summary Scale.

5.5. Discussion

Abnormal emotion processing is an important target for psychotherapy in patients with FNS because it may contribute to FNS aetiology (Novakova et al., 2015), and appears to be related to a poorer quality of life and understanding of the disorder (Baker et al., 2007). Therefore, the aim of this study was investigate whether emotion processing improved in patients with FNS following a course of BAPIT. We also explored the extent to which changes in emotion processing correlated with treatment-associated changes in HRQoL and other measures of clinical symptomology.

As predicted, emotion processing improved post-intervention; the pre-intervention total mean EPS-25 score (4.96) fell within mental health norms (4.0 – 5.9), and was elevated above healthy norms (2.2 – 4.4). However, the post-intervention score (4.33) fell within healthy UK norms. In view of the chronicity and severity of FNS, this supports our interpretation that EPS-25 outcome data represent a clinically meaningful change for participants. This conclusion is also supported by the improved HRQoL and illness understanding following intervention. Although psychological distress and other somatic symptoms failed to improve significantly, change scores on

the EPS-25 correlated positively with change scores on the CORE-10 and MHS sharing 45% and 40% of variance respectively. This suggests that improvements captured by the EPS-25 are not simply of academic interest but clinically meaningful to patients.

To our knowledge this the first study to examine therapy-associated changes in emotion processing in patients with FNS. The significant improvement in HRQoL observed in our patient group is consistent with our previous observations in this patient population (Reuber, Burness, et al., 2007). However, this time we did not observe significant improvements in somatic symptoms or psychological distress. This discrepancy could be due to the smaller sample size in the present study reducing statistical power. Illness understanding was not measured in the previous study but we did observe a significant improvement in the present patient cohort. One earlier study in a much larger sample showed that having a poor illness understanding of FNS as measured by the Illness Beliefs Questionnaire (including a non-attribution of functional symptoms to psychological factors), is a strong predictor of poor patient outcome on a 'Clinical Global Improvement Scale' at twelve month follow-up (Sharpe et al., 2010).

The present pre-intervention EPS-25 scores support previous observations that many patients with FNS experience abnormal emotion processing. Group mean pre-intervention total EPS-25 scores fell within the top 25th percentile for UK normative values and well within the range for mental health patients (Baker et al., 2007). When administered to patients with NEAD only, Novakova et al. observed similar abnormalities in emotion processing (Novakova et al., 2015). Here we extend this finding to include patients with other forms of FNS including functional motor and sensory symptoms.

The breadth of emotion processing styles assessed by the EPS-25 is a strength of this study. It could be argued that other forms of emotion processing measurement fail to reflect the multi-faceted nature of emotion perception, regulation, and expression (Baker et al., 2007). Therefore, the EPS-25 is likely to be well-suited to detecting the heterogeneous abnormalities of emotion processing which other studies have found to be associated with FNS (Carson et al., 2012). The fact that the EPS-25 was sensitive to changes scores in psychological distress and the mental health domain of the SF-36, corroborate the usefulness of this scale in clinical and research settings of patients with FNS.

5.5.1. Limitations

The high attrition rate is a regrettable limitation of this study. As is often the case with postal-questionnaire designs, a significant proportion of data were lost by patients' failure to return the follow-up questionnaires. Another limitation is the lack of control group or a pre-treatment monitoring period demonstrating a lack of spontaneous improvements in emotion processing. Although spontaneous clinical improvements may be considered unlikely in view of the chronicity of the functional disorders treated in this study (mean duration of 5.8 years (*SD* = 10.8)), these limitations introduce the possibility that any improvements in emotion processing, HRQoL, and clinical symptomology could simply reflect regression to the mean. Furthermore, mechanism or direction of therapeutic change cannot be inferred.

Although twice as many patients met the threshold of "reliable and clinically significant improvement" on the EPS-25 as self-reported "reliable and clinically significant deterioration", at first sight, the results of the RCSC analysis are not particularly encouraging. However, it is important to point out that the EPS-25 was not designed or intended to be used here as an outcome measure. As stated above,

emotion processing deficits may be a core feature of FNS. Patients who habitually over-controlled their emotions may have become more aware of the emotional aspects of their disorder and distress through the process of psychotherapy, which may have led to an apparent deterioration of their total EPS-25 score. Interestingly (and in support of this interpretation), all four patients who reported reliable and clinically significant deteriorations on the EPS-25 also reported increases on the 'unregulated' subscale of the EPS-25 (there was no consistent pattern on the other subscales). These observations suggest that, given the wide range of emotion processing problems which the EPS-25 captures, it is likely to be important to look at change profiles rather than the total EPS-25 score to understand psychotherapy-associated changes at an individual patient level.

Although we only found an age difference between the patient groups completing and not completing BAPIT, the generalizability of our study findings is diminished by the fact that older patients were more likely to complete treatment than younger ones. This age disparity in therapy completion resonates with earlier studies noting a greater probability of older patients engaging in specialist psychotherapy for FNS (Howlett et al., 2007). It is possible that older patients are better able to appreciate or tackle the relationship between emotions and functional symptoms. Alternatively, a younger presentation with FNS may be associated with greater levels of dysfunction and disability, creating additional barriers for the patient to complete treatment and return outcome data (Edlund et al., 2002).

In view of the lack of a control group and the relatively high attrition rates in this study, the influence of BAPIT on emotion processing requires further clarification. Furthermore, being practice-based evidence, the therapist's adherence to BAPIT is uncertain. However, therapy was delivered by a single, highly-trained

therapist with extensive experience in this particular clinical field who has described her therapeutic approach in previous publications (SH) – a fact which should provide some assurance of uniformity of the intervention (Hobson, 1985; Howlett & Reuber, 2009). The absence of treatment data generated by other therapists also limits the generalizability of the findings presented here.

The fact that not all patients who contributed follow-up data had completed therapy and that these patients were retained in the analysis should be considered a strength of this study. The inclusion of these patients in our analysis should mean that the findings of our study come closer to the sort of effects on emotion processing BAPIT might achieve in real-life rather than research settings.

We were also able to exclude some other biases. Patients with NEAD and those with other FNS were matched on key demographic variables irrespective of FNS semiology, minimising the risks of bias associated with analysing a small and heterogeneous population as whole. Consecutive recruitment of participants from two sites further reduced risk of bias introduced by patient selection.

5.6. Conclusion

In this prospective, uncontrolled study of patients with FNS we provide preliminary evidence that emotion processing improves following a course of BAPIT, with simultaneous improvements in HRQoL and illness understanding. Improvements in emotion processing correlated with a reduction in psychological distress as well as improved scores on the mental health domain of the SF-36. We conclude that the EPS-25 shows promise as a tool for the investigation of emotion processing deficits in patients with FNS. We are not proposing that, in patients with FNS, the EPS-25 be used as an outcome measure – however, our study demonstrates that the EPS-25 is a measure sensitive to therapy-associated changes in emotion processing. Future

research should aim to replicate these preliminary findings in controlled studies with larger sample sizes.

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Ethical statements

The authors have abided by the Ethical Principles of Psychologists and Code of Conduct as set out by the APA.

Conflict of interests

Ms Isobel Williams, Ms Stephanie Howlett, Dr.Liat Levita, and Prof. Markus Reuber have no conflict of interest with respect to this publication.

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Supplementary Table 1 - *Comparisons of demographic and therapy characteristics between patients with NEAD (n = 32) and patients with 'other FNS' (n = 12).*

Characteristics	NEAD	Other FNS	Statistic
Female (%)	77.4	76.9	$\chi^2(1) = .001$, $p = .979$
Mean age at start of therapy (*SD*)	40.42 (14.55)	44.32 (10.12)	$t(42) = -.-.853$, $p = .398$
Economically active (%)	67.7	53.8	$\chi^2(1) = .764$, $p = .382$
Mean sessions (*SD*)	10.90 (11.05)	14.42 (10.48)	$t(41) = -.948$, $p = .349$
Completed therapy (%)	56.7	69.2	$\chi^2(1) = .599$, $p = .439$

Note. NEAD = Nonepileptic Attack Disorder, Other FNS = hemiparesis, jerking, memory problems, dizziness. Mean sessions = number of sessions received by patients.

Supplementary Table 2 -*Comparison of emotion processing and outcome measure scale scores from patients who completed therapy (completers) versus those who did not complete therapy (non-completers).*

	Completers		Non-completers					95% CI	
Measure	***M***	***SD***	***M***	***SD***	***df***	***t***	***p***	***LL***	***UL***
EPS-25	5.33	2.10	4.68	2.28	41	-.96	.36	-2.03	0.66
PHQ-15	13.75	5.35	14.63	5.52	35	.47	.64	-2.78	4.52
CORE 10	19.82	9.20	18.00	9.94	41	-.60	54	-7.96	4.10
BIPQ	53.52	10.50	60.50	11.30	31	1.80	.08	-.38	14.26
MHS	39.72	9.94	40.72	10.70	37	.30	.80	-5.90	7.67
PHS	36.60	11.80	35.88	11.34	37	-.15	.86	-7.44	7.75

Note. *significant at adjusted p - value Holm-Bonferroni correction. CI = confidence interval; LL = lower limit; UL = upper limit. CORE-10 = Core Outcome in Routine Evaluation-10, BIPQ= Brief Illness Perceptions Questionnaire, PHQ-15= Patient Health Questionnaire- 15, MHS= Mental Health Summary Scale, PHS= Physical Health Summary Scale.

6. Discussion

FND are one of the commonest reasons patients will consult a neurologist (Stone et al., 2010). FND have also been associated with greater disability and distress than equivalent neurological symptoms which are explained by diseases characterised by clear structural or pathophysiological changes (Carson et al., 2011). Furthermore, medical problems not associated with these changes, such as FND, are estimated to cost the UK economy more than dementia (approximately £18 billion) (Bermingham et al., 2010; Edwards & Bhatia, 2012). In spite of these facts, FND is relatively unheard of by the general public, and has received comparatively little academic attention. Traditional explanations of FND aetiology highlight the importance of overwhelming emotions. Therefore, the aim of this thesis was to contribute to the existing knowledge of emotion dysregulation in this putatively 'psychogenic' disorder, by taking a structured and theoretically-driven approach. I set out to empirically test hypotheses concerning emotion dysregulation in FND using a combination of self-report, behavioural, and physiological measures. Some of these predictions were generated from the EPM (Gross, 2015), but I also wanted to address other important clinical questions such as whether or not emotion dysregulation is related to clinical symptomology, and whether changes in emotion dysregulation can be meaningfully tracked throughout therapy using patients' self-report.

6.1. Key findings

Chapter Two consisted of a systematic review synthesising the existing research on emotion dysregulation in NEAD – which has been the most widely researched form of FND. The studies identified by the literature search were subjected to a bespoke quality assessment and synthesised according to the stages of the EPM

(Gross, 2015). The majority of studies were found to be of low quality, an appraisal largely driven by small sample sizes. Nevertheless, the systematic review suggested that emotion dysregulation in NEAD is characterised by deficits in the identification of the patients' own emotional states, as well as the selection and implementation of maladaptive regulatory strategies which may be related to abnormalities in the processing of exteroceptive emotional information. A key conclusion was that the NEAD population are psychologically heterogeneous; subgroups of patients with NEAD seem to exist, characterised by quantitatively different deficits in emotion regulation which are also likely related to other psychological or clinical factors such as trauma and current distress.

Chapter Three further delineated some of this heterogeneity. A cross-sectional study showed that patients who experience impairments of consciousness (IOC) as part of their FND exhibited more severe psychopathology than those who do not. However, similar profiles of emotion dysregulation were observed in both groups, suggesting that patients with and without IOC exhibit a similar maladaptive style of emotion regulation characterised by high levels of avoidance, dysregulated emotional responding, suppression, unprocessed emotions, and an impoverished emotional experience. These findings emphasise the importance of understanding the patient as an individual and the symptoms they present with, rather than working with the diagnosis alone.

In Chapter Four, I began to experimentally test the stages of the EPM in a smaller group of patients with FND. An interoceptive sensitivity paradigm was used to test the hypothesis that patients with FND experience deficits in the identification of their emotions (Chapter 4.1). A stress induction (The Cold Pressor Test) was included to test the prediction that interoceptive sensitivity would be adversely

affected by stress in patients but not healthy controls. Patients with FND were observed to have lower interoceptive sensitivity and a more impoverished emotional experience (EPS-25 subscale) than healthy controls. Contrary to our hypothesis, interoceptive sensitivity was enhanced by stress in both groups. We concluded that patients with FND are impaired in the identification of their own emotional states, but that this is not further impaired by the kind of stress induced by the Cold Pressor Test.

The work presented in Chapter 4.2 aimed to test the selection and implementation stages of the EPM in patients with FND. Anecdotal and self-report findings suggested that patients with FND have a tendency to select and implement a maladaptive regulatory strategy - expressive suppression. Patients and healthy controls took part in a picture-viewing paradigm designed to elicit negative affect. Participants were instructed either to respond as they normally would if they came across such an image in their daily lives, or to try and suppress their response. Explicit and implicit measures of affect in response to the pictures were taken, and participants were also given a self-report measure of their habitual use of expressive suppression and cognitive reappraisal (ERQ). Consistent with the experimental hypothesis, patients self-reported an increased tendency to use expressive suppression on the ERQ. Implicit and explicit measures of affect suggested that patients with FND implicitly felt less positive than healthy controls, which is consistent with the habitual selection and implementation of expressive suppression. However, patients exhibited greater facial reactivity in response to negative pictures than healthy controls when instructed to suppress their expression, suggesting they are impaired in their ability to implement expressive suppression. We therefore found mixed support for the hypothesis that patients with FND exhibit a tendency to select and implement the (arguably) maladaptive regulatory strategy, expressive suppression.

The aim of Chapter 4.3 was to test the hypothesis that patients with FND have lower resting Heart Rate Variability (HRV) than healthy controls. In this part of the research project, we tested the potential of using HRV as a biomarker of emotion dysregulation in FND. Exploratory correlational analyses were also conducted on two measures of HRV: Cardiosympathetic Index (sympathetic tone) and Cardiovagal Index (vagal tone). As predicted, vagal tone was lower in patients with FND than healthy controls. Exploratory correlational analyses showed that vagal tone negatively correlated with self-report measures of emotion dysregulation and Post-Traumatic Stress Disorder Symptomology across both groups. Vagal tone also positively correlated with interoceptive sensitivity (measure of the identification stage), suggesting that patients with FND experience chronic autonomic arousal, which may be related to emotion dysregulation, trauma, and decreased interoceptive sensitivity.

Finally, Chapter Five examined if the newly developed Emotional Processing Scale – 25 (EPS-25) could be used to track changes in emotion dysregulation associated with a course of Brief Augmented Psychodynamic Interpersonal Therapy for FND. As measured by the EPS-25, emotion regulation improved following intervention, and changes in emotion dysregulation correlated with changes in mental health related quality of life and psychological distress. These data suggest that emotion dysregulation and psychopathology can be treated in FND and that these changes can be captured by a self-report measure (EPS-25). Nevertheless, further work is required to elucidate the relationship between these changes and FND symptomology, as well as to more rigorously assess the effectiveness of the intervention in a more highly-powered and controlled study.

6.1.1. Conclusions from key findings. The work presented in this thesis suggests that patients with FND appear to exhibit signs of emotion dysregulation,

characterised by deficits in the identification of their emotional state, a tendency to select and implement maladaptive emotion regulatory strategies, and chronic autonomic arousal. However, the data also suggest that the precise nature of psychological distress is heterogeneous across patients suffering from FND and that there is some association between particular functional symptoms and certain abnormalities of emotion regulation.

In particular, my work identified a theme of impairments at the identification stage (Gross, 2015). Raised levels of alexithymia as measured by the TAS-20 and other self-report measures, as well as discrepancies between self-reported and objective measures of affect and a tendency to perceive life as unduly stressful were found in the systematic review (Chapter Two). Study One (Chapter Three) found that in a group of patients with FND, scores on the 'impoverished emotional experience' subscale of the EPS-25 were raised above healthy norms, and did not differ significantly whether FND patients experienced impairments of consciousness or not. Likewise, the sample of patients included in studies Two, Three, and Four (recruited from Study One) also exhibited significantly higher scores on the impoverished emotional experience subscale of the EPS-25 than healthy controls. Furthermore, in Study Three, we found that the impoverished subscale score on the EPS-25 negatively correlated with participants' self-endorsed use of cognitive reappraisal, suggesting that individuals who are more impaired in identifying their own emotions are less likely to select and implement cognitive reappraisal as a regulatory strategy. In Study Two we demonstrated that this groups of patients with FND had significantly lower interoceptive sensitivity than healthy controls, and so are less able to perceive physiological information, which assists in the identification of emotions. In Study Four, we demonstrated that vagal tone correlates positively with interoceptive

sensitivity pre- and post-stress induction, suggesting that individuals with greater vmHRV are more sensitive to their internal physiological milieu and therefore theoretically more able to identify their own emotional state. Finally, in Study Five we demonstrated that impoverished emotional experience subscale scores improve following a course of psychotherapy, raising the possibility that patients' ability to have insight into their own emotional experiences might be successfully treated with Brief Augmented Psychodynamic Interpersonal Therapy (which includes techniques such as encouraging patients to notice the location of feelings in their body or to link emotions that arise in the therapy session to other emotions inside and outside of therapy (Howlett & Reuber, 2009)). The work presented in this thesis has therefore shown that, i) individuals who are better at identifying their emotions are more likely to select and implement healthier regulatory strategies and have more adaptive vagal control of their autonomic nervous system, but also that ii), patients with FND are generally more impaired at identifying and making sense of their emotions that healthy controls.

With respect to the selection and implementation stages of the EPM, the work presented in this thesis provides less conclusive evidence. The systematic review (Chapter 2) showed that patients with NEAD have a tendency to select and implement maladaptive regulatory strategies, such as emotion-focused coping, avoidance, and dissociation – a tendency which is likely related to other psychological factors such as current distress. The review also discussed experimental work suggesting that patients with NEAD may exhibit cognitive biases with the potential to disrupt the implementation process. Study One showed that patients with FND self-report an increased tendency to select and implement suppression and avoidance and experience unregulated emotions (as measured by the EPS-25), irrespective of whether or not they

experience impairments of consciousness. Similarly, the sample of patients with FND who participated in studies Two, Three, and Four scored more highly on these subscales of the EPS-25 than healthy controls. Study Three showed that patients with FND endorse greater selection and implementation of expressive suppression and less frequent selection and implementation of cognitive reappraisal than healthy controls. However, when instructed to suppress their facial expression in response to negative stimuli, patients were less able to implement expressive suppression than healthy controls. The significantly lower vagal tone in patients with FND than healthy controls and the significant negative correlation between CVI and the EPS-25 scores (Study Four) suggest that patients with FND experience chronic autonomic arousal associated with emotion dysregulation – which is consistent with the proposition that patients with FND habitually select and implement maladaptive regulatory strategies or fail to implement adaptive regulatory strategies, but is not direct support for this proposition. Finally, Study Five demonstrated that suppression and avoidance subscale scores on the EPS-25 improved following psychotherapy and that changes in the EPS-25 correlated with improvements in psychological distress and mental-health related quality of life. An important point to make is, whether or not an individual successfully selects and implements an adaptive regulatory strategy depends on the correct identification of their emotional state and the activation of the goal to regulate. Given that the work presented in this thesis strongly suggests impairments in the identification stage in patients with FND, it is possible that impairments in the selection / implementation stage stem from a failure to accurately identify one's own emotions in the first instance.

The findings regarding identification can be mapped onto the predictive coding model of symptom perception in 'Medically Unexplained Symptoms' (MUS) put

forwards by Van den Bergh et al. (2017). This theory takes account of previous models including that of a 'Bayesian Account of Hysteria' (Edwards et al., 2012) and the 'Integrative Cognitive Model' of MUS (Brown, 2004), but focuses more closely on interoception. According to Van den Bergh et al. (2017), when vague and imprecise interoceptive input is interpreted in the context of abnormally strong pathological prior beliefs about the causes of the sensory input, the patient experiences MUS. In other words, what the patient expects to feel outweighs what they actually feel because they have strong, abnormal prior expectations about what particular sensory inputs means and are not good at correctly checking expectations against actual sensory inputs. This causes patients to experience innocuous physiological sensations as pathological symptoms (i.e., FND) or a, "subjectively real but objectively illusory experience" (Edwards et al., 2012). Van den Bergh et al. (2017) also propose that reduced interoceptive sensitivity is moderated by high-trait negative affect and threat processing strategies. While we did not set out to test a Bayesian model of FND or measure trait-negative affect in this thesis, our findings of raised psychopathology (i.e. symptoms of depression, anxiety, and somatization disorder) are in line with the account that patients with FND exhibit high trait-negative affect. Furthermore, the raised levels of PTSD symptomology we observed may also serve to have an impact on threat-processing, which would contribute to negative affect (hypervigilance is a recognised symptom of PTSD (American Psychiatric Association, 2013)). Therefore, the work presented in this thesis fits in with predictive coding accounts of FND (Edwards et al., 2012; Van den Bergh et al., 2017). Future work should seek to test these models more directly and examine patients' prior beliefs about the causes of interoceptive sensations more closely.

6.2. Limitations

There are several caveats that should be borne in mind when interpreting the conclusions of this thesis. Some are methodological and some are theoretical. These will now be discussed below.

The first general methodological limitation is that the sample sizes recruited to or retained in each study are relatively small; the number of patients recruited to studies Two, Three, and Four are at the lower-bound of what we would define as a moderately-powered sample size (See section 2.2.3.). This combined with the number of analyses performed on the data means that our conclusions run the risk of representing false positives (even though FWER and FDR were controlled for as appropriate). Equally, due to the lack of pre-existing research in this area a priori power analyses were not conducted, and so we cannot be certain that the studies are sufficiently powered. When one takes into consideration the heterogeneity of the group (symptom type, duration, demographic, psychological, medical history, etc.), the importance of recruiting sufficient sample sizes and a-priori power analyses becomes more apparent. However, given the known barriers to recruitment in the FND patient population, it could be argued that we did well to recruit 26 patient participants for studies Two, Three, and Four. Furthermore, the effect sizes generated in this thesis should enable a-priori power analyses for future studies to be conducted. As such, these results do not represent the 'final conclusion' on emotion regulation in FND, but provide a foundation on which future researchers may build.

A further source of methodological bias is that the individuals who participated in these studies may have been more willing to endorse psychological factors as relevant to their disorder than those who declined or did not respond to advertisement. Efforts were made to advertise the study in a clear but neutral tone, but nevertheless it

is possible that the sample is biased towards individuals who feel that emotion dysregulation is more pertinent to their symptoms. Another source of bias is that the patients who attended the university for studies Two, Three, and Four, although clearly disabled by their symptoms, were well enough to travel and participate. Indeed, there were a few patients who initially accepted the invitation to attend but later dropped out owing to poor health. Many of the patients who attended for these studies had also previously received psychotherapy (68%). This means that that our findings may only pertain to a subgroup of patients with FND who are relatively well and accepting of psychological accounts of the disorder. Therefore the findings in this thesis should not be generalised to the wider FND population in an uncritical fashion.

The first theoretical limitation also relates to the interpretation of our findings. While the work presented in this thesis gives evidence of emotion dysregulation in patients with FND, the cross-sectional nature of studies One, Two, Three, and Four mean that it cannot answer the question of whether or not FND is indeed 'psychogenic'. Emotion dysregulation is still likely a relevant predisposing, precipitating, or perpetuating factor for FND, but should be considered within the context of other biological (e.g., genetic, structural / metabolic) and social (e.g., quality of close relationships) factors.

A second theoretical limitation is that, at present, there is only 'modest' empirical support for the EPM (Sheppes et al., 2015). Each stage of the EPM (identification, selection, implementation) relies on the same three basic processes (perception, valuation, action) working on different types of information. This makes it difficult isolate and test individual stages of the EPM as similar processes are happening in each stage – indeed it was realised throughout the course of the PhD project that it was difficult to separate existing studies or measures that assessed the

selection and implementation stages in isolation (Chapter Two), or indeed to delineate these stages in the studies reported in this thesis (Studies Two, Three, and Four). Testing the stages directly might be improved by a self-report measure assessing each stage individually, but at present no such scale exists. Future research could potentially help to address these issues by testing and developing measures of the individual EPM stages.

On a related point, the manner in which emotion regulation strategies or examples of emotion dysregulation have been categorised in this thesis might be called into question. Firstly, regulatory strategies have been framed as adaptive or maladaptive, but in reality individual regulatory strategies are not dichotomously 'good or bad'. For example there are cases where putatively maladaptive strategies would be adaptive – such as expressive suppression in settings where displaying emotion would be considered inappropriate and the associated negative consequences would outweigh the harmful effects of suppression (e.g., stifling nervous laughter). Furthermore, forms of emotion dysregulation can map onto more than one stage of the EPM. For example, a tendency towards experiential avoidance can represent a deficit in the Valuation substep of the identification stage (i.e., overvaluating the cost of emotional states) (Sheppes et al., 2015) or a deficit in the perception substep of the selection stage (i.e., reflecting the over-representation of maladaptive strategies to select from). These issues are particularly relevant to the interpretation of our findings regarding selection and implementation of regulatory strategies in FND.

6.3. Strengths

In spite of the theoretical limitations of the EPM discussed above, the use of the EPM to structure this research should also be considered a strength of the thesis. To my knowledge, this is the first body of research on emotion regulation in FND to

have been theoretically constrained by an over-arching model of emotion regulation. This has allowed for an empirical approach, in which theory has been used to generate testable hypotheses is a systematic manner. While there are issues with the EPM, it is at present the most recent version of the widely tested and studied theory of emotion regulation. A further related strength of this thesis, is that emotion regulation research in psychopathology has tended to focus on the problems incurred by disrupted implementation – by using the EPM to structure our approach, we have also generated findings regarding the identification stage. Furthermore, in taking a theoretically driven approach, we are able to gain a clearer understanding of what might be disrupting emotion regulation in FND and / or how this might be happening. If other studies were also to take this theoretically-driven approach, researchers in the field might be able to collaborate more closely and more rapidly advance our understanding of emotion dysregulation in FND.

A further strength of this project was the inclusion of experimental studies and multiple forms of measurement including self-report, behavioural, and physiological methods. Each approach has its respective advantages and disadvantages, but by using different measurement modalities in conjunction we are able to capitalise on the benefits of each approach while mitigating some of the draw-backs. For example, self-report measures are quick and easy to administer and give information about what an individual perceives but are subjective and prone to bias. Physiological measures are highly objective but more difficult to administer and may be interpreted in too reductionist a light. However, by combining various methods, we are able to build a more nuanced and complete picture of the construct (emotion regulation) under question.

6.4. Implications for future research

Future work should also aim to take a theoretically driven approach. One option would be further to examine the EPM in patients with FND. Alternatively, future research could aim to test predictions made by other accounts of FND / MUS, such as the predictive coding models proposed by Edwards et al. (2012) and Van den Bergh et al. (2017), or the Integrative Cognitive Model of Psychogenic Nonepileptic Seizures proposed by Brown and Reuber (2016b). The generation of testable predictions embedded within a wider theory might afford a clearer understanding of how emotions may be dysregulated in FND. A further advantage of pursuing a theory-driven approach is the increased ease of comparison and synthesis with other studies based on the same model. This would allow for easier collaboration between researchers and for the field to advance as a whole towards an improved understanding of emotion regulation in FND.

The work presented in this thesis also illustrates the importance of taking into account heterogeneity in the FND population. For example, in Chapter Two, studies were identified that showed how there are subgroups of patients with NEAD characterised by quantitatively different emotion regulation profiles (e.g., Brown et al., 2013; Uliaszek et al., 2012). Other studies showed that the extent of emotion dysregulation in patients with NEAD correlated with other psychological or clinical factors (e.g., Dimaro et al., 2014; Urbanek et al., 2014). The work presented in Chapter Three showed that irrespective of FND subtype (e.g. NEAD, FMD), patients who experience impairments of consciousness as part of their FND also self-reported higher levels of psychopathology (symptoms of Generalised Anxiety Disorder, Somatization Disorder, and PTSD) than those who did not. Moreover, both patients with and without NEAD reported impairments of consciousness (and vice versa.), and

so this finding illustrates the point that an individual person's clinical symptomology may also give clues about the relevance of emotion dysregulation, over and above that of the diagnostic label. Therefore, future studies should also seek to elucidate some of this psychological and clinical heterogeneity.

6.5. Potential for translational research

The ultimate aim of improving our understanding of emotion dysregulation in FND is to improve treatment and outcomes for patients. The work presented in this thesis showed that, while patients with FND do appear to have similar styles of emotion dysregulation (as measured by the EPS-25), they do not have homogenous psychopathological profiles or indeed all report a history of trauma. This means that clinicians should not make assumptions about an assumed psychological aetiology, and instead take a person-centred approach. Our findings also allude to two interesting potential avenues for treatment / monitoring outcomes: emotion identification and HRV.

With respect to emotion identification, Study Two showed that patients with FND report having less insight into their emotions and were also observed to have lower interoceptive sensitivity than healthy controls (as recorded by the Heart Beat Detection Task). We concluded that this was indicative of an impairment in the identification stage. It stands to reason that if an individual cannot detect or make sense of their own emotions, they are limited in their ability to regulate them effectively. A therapeutic aim may therefore be to improve patients' ability to detect and identify their emotions by using mindfulness techniques, such as those described in Study Five, which teach the individual to notice physiological sensations arising in their body and link them to emotions or thoughts. This technique is already taught as one of the first steps towards seizure control in patients with NEAD attending The Royal Hallamshire

Psychotherapy Services, although Biofeedback methods (such as those focusing on heart rate or vmHRV) may present one potential complement to this intervention, which patients could utilise at home. The Heart Rate Tracking task may also represent a useful pre-and post-intervention measure, but a prospective controlled study to establish the effectiveness of this approach in relation to symptom frequency and severity would be needed.

The use of vmHRV in diagnosis and as an outcome measures also warrants further exploration. vmHRV could be used to distinguish between an epileptic or nonepileptic episode. It could also be compared pre- and post-psychotherapeutic intervention to assess whether the patient's autonomic arousal and therefore emotion dysregulation has decreased. However, more work is needed to verify the relationship vmHRV and emotion dysregulation, as well as its relationship to FND symptomology.

Moreover, the development of a unified FND symptom rating scale similar to the UPDRS for Parkinson's disease (Goetz et al., 2008) or the Liverpool Seizure Severity Scale for epilepsy (Baker, Smith, Jacoby, Hayes, & Chadwick, 1998) could facilitate the assessment of interventions. At present, other scales such as the PHQ-15 are used to assess levels of somatic symptomology, but this measure might be criticised for being non-specific to FND. Given that many patients with FND experience more than one type of symptom, a unified FND symptom severity questionnaire might be a more parsimonious and easier-to-compare measure.

As a more general point, research on FND speaks to the issue of dualism in medicine, which has traditionally treated the mind and the brain as two separate entities. This much is reflected in the fact that two different specialisms exist (i.e., neurology and psychiatry) for treating neurological disorders and mental disorders, in spite of the fact that both commonly co-occur and both are disorders of the brain.

While there has been a recent trend towards neurologists and psychiatrists identifying themselves as 'neuropsychiatrists', neuropsychiatry is not a clearly defined speciality. Equally, FND is still considered a 'medically unexplained symptom', even though there are many other medical problems that are defined by the very fact that their cause is unknown (e.g., Juvenile Idiopathic Arthritis, idiopathic Parkinsons' disease), but that are not labelled as 'medically unexplained' or 'functional' or 'psychogenic'. These issues may stem from the relative discrimination against mental health in medicine (Giandinoto, Stephenson, & Edward, 2018), which has also been internalised by patients with FND (Rommelfanger et al., 2017). To the patient, a diagnosis of FND can mean they feel disbelieved or that they are 'going mad' - because of the negative connotations associated with mental health, and ultimately rejection of the diagnosis. A fuller exploration of this issue is beyond the scope of this thesis, but it is hoped that as our scientific understanding of FND improves, so will the experience and treatment of patients with FND.

6.6. Conclusion

The work presented in this thesis aimed to contribute towards the current understanding of emotion dysregulation in FND by taking a theoretically-constrained, empirical approach, using a combination of self-report, behavioural, and physiological measures. Evidence of emotion dysregulation characterised by difficulties in the identification of one's own emotional state, as well as the selection and implementation of maladaptive regulatory strategies was observed. Another key finding was that psychopathology or specific forms of emotion dysregulation in the FND population is heterogeneously distributed and likely related to other psychological or clinical variables. The final study presented in this thesis demonstrated that emotion dysregulation in patients with FND can be tracked

throughout intervention using a self-report tool, and suggested that emotion dysregulation may respond to psychotherapeutic treatment. The question of whether FND is caused by emotion dysregulation cannot be answered by this thesis. However, it is likely that emotion dysregulation is a predisposing, precipitating, and perpetuating factor for many patients with FND.

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Appendices

Appendix 1

Patient Demographic Questionnaire

Personal Information

Please answer the following questions about yourself. The information you are giving us will be treated as confidential. Personally identifiable data (such as your name, address and date of birth) will not be stored and analysed together with the data provided on the self-report questionnaires.

1. Full name: _____
2. Address: _____

   _____

   _____

   _____
3. Post code: _____
4. Home phone number: _____
5. Mobile phone number _____
6. Email address: _____
7. Date of birth: _____
8. Age today: _____
9. Gender (please tick the correct option):

   Male ☐ Female ☐

   Other please specify: _____

10. How would you describe your ethnic background?

Please tick the box that applies to you, or write an answer in the space provided.

White- English/Welsh/Scottish/Northern Irish/ British	
White- Irish	
White- Gypsy or Irish Traveller	
White- Any other white background	
Mixed/ multiple ethnic group- White and Black Caribbean	
Mixed/Multiple ethnic group - White and Black African	

Mixed/Multiple ethnic group - White and Asian	
Mixed/Multiple ethnic group	
Any Other Mixed/multiple ethnic background	
Asian/Asian British – Indian	
Asian/Asian British – Pakistani	
Asian/Asian British – Bangladeshi	
Asian/Asian British – Chinese	
Asian/Asian British - Any other Asian background	
Black/African/Caribbean/Black British – African	
Black /African/Caribbean/Black British – Caribbean	
Any other Black / African / Caribbean background	
Other ethnic group – Arab	
Any other ethnic group (please specify)	

11. How would you describe your current employment status? Please tick the box(es) that applies/apply to you or write an answer in the space provided.

In full-time paid work	
In part-time paid work	
In full-time education	
In part-time education	
Full-time carer/homemaker	
On leave/out of work due to illness or disability	
Retired	
Other (please specify):	

12. What is your highest educational qualification? Please tick the box(es) that applies/apply to you or write an answer in the space provided.

No educational qualifications	
Standard grades, O grades, O levels, GCE/GCSEs	
Highers, advanced highers, A levels	
Vocational qualification (e.g. SVQ, NVQ, SCOTVEC)	
HNC/HND	
Degree (e.g., BA, BSc)	
Postgraduate qualification (e.g. MSc, PhD)	
Professional qualification (e.g. CAEW, CIIA)	
Other (please specify):	

13. When did you first experience a functional neurological symptom (e.g. psychogenic nonepileptic seizure, tremor)?

    (For example, 6 months ago or 3 years ago)

    _____months ago

    _____years ago

14. What functional neurological symptom was it (e.g. tremor, weakness, seizure)?

_____

15. Do you experience any other functional neurological symptoms? If so, please list them below.

_____

_____

_____

16. a) Do you experience nonepileptic attacks (also known as dissociative seizures/ psychogenic nonepileptic seizures) (please tick)?

☐ YES ☐ NO

b) If the answer is 'yes', how many have you had **in the last month**?

_____

17. Do you ever experience any of the following as part of your functional neurological symptom(s) (please tick)?

	YES	NO
I have spells during which I black out/ lose consciousness completely.		
I have spells during which am aware of what is going on, but I am unable to respond to other people.		
I have spells during which I can perform actions, but I am not aware of what I am doing.		

18. a) Are you currently taking any medication (please tick)?

☐ YES ☐ NO

b) If yes, please list your medication below:

_____

_____

_____

_____

19. Have you received or are receiving any form of psychological treatment (please tick)?

☐ YES ☐ NO

20. a) Would you like to be contacted about stage 2 of this study (please tick)?

☐ YES ☐ NO

b) If you would like to be contacted about stage 2 of this study, how would you like to be contacted (e.g. on my mobile phone, by email) and at what time (e.g. in the afternoon, Friday day time)?

_____

_____

Thank you for completing this demographic questionnaire.

Please now proceed to the other questionnaire pack.

The Emotional Processing Scale- 25 (EPS - 25)

Baker, R., Thomas, S., Thomas, P.W., Gower, P., Santonastaso, M., & Whittlesea, A. (2009). The Emotional Processing Scale: scale refinement and abridgement, Journal of Psychosomatic Research, 68 (1), 83-88.

Patient Health Questionnaire - 9 (PHQ - 9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

		Not at all	Several days	More than half the days	Nearly every day
1	Little interest of pleasure in doing things				
2	Feeling down, depressed, or hopeless				
3	Trouble falling or staying asleep, or sleeping too much				
4	Feeling tired of having little energy				
5	Poor appetite or overeating				
6	Feeling bad about yourself- or that you are a failure or have lets yourself or your family down				
7	Trouble concentrating on things, such as reading the newspaper or watching television				
8	Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual				
9	Thoughts that you would be better off dead or hurting yourself in some way				

Generalized Anxiety Disorder -7 (GAD - 7)

Over the last 2 weeks, how often have you been bothered by the following problems?

		Not at all	Several days	More than half the days	Nearly every day
1	Feeling nervous, anxious or on edge				
2	Not being able to stop or control worrying				
3	Worrying too much about different things				
4	Trouble relaxing				
5	Being so restless that it is hard to sit still				
6	Becoming easily annoyed or irritable				
7	Feeling afraid as if something awful might happen				

Patient Health Questionnaire – 15 (PHQ - 15)

During the past 4 weeks, how much have you been bothered by any of the following problems? Please tick as appropriate.

		Not bothered at all	Bothered a little	Bothered a lot
1	Stomach pain			
2	Back pain			
3	Pain in your arms, legs or joints (knees, hips etc.)			
4	Menstrual cramps (women only)			
5	Headaches			
6	Chest pains			
7	Dizziness			
8	Fainting spells			
9	Feeling your heart pound or race			
10	Shortness of breath			
11	Pain or problems during sexual intercourse			
12	Constipation, loose bowels or diarrhoea			
13	Nausea, gas or indigestion			
14	Feeling tired or having little energy			
15	Trouble sleeping			

PTSD Checklist for DSM - 5 (PCL - 5)

Instructions: Below is a list of problems that people sometimes have in response to a very stressful experience. Please read each problem carefully and then circle one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

	In the past month, how much were you bothered by:	**Not at all**	**A little bit**	**Moderately**	**Quite a bit**	**Extremely**
1	Repeated, disturbing, and unwanted memories of the stressful experience?					
2	Repeated, disturbing dreams of the stressful experience?					
3	Suddenly feeling or acting as if the stressful experien were actually happening again (as if you were actuall back there reliving it)?					
4	Feeling very upset when something reminded you of the stressful experience?					
5	Having strong physical reactions when something reminded you of the stressful experience (for exampl heart pounding, trouble breathing, sweating)?					
6	Avoiding memories, thoughts, or feelings related to th stressful experience?					
7	Avoiding external reminders of the stressful experien (for example, people, places, conversations, activities objects, or situations)?					
8	Trouble remembering important parts of the stressful experience?					
9	Having strong negative beliefs about yourself, other people, or the world (for example, having thoughts su as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)?					
10	Blaming yourself or someone for the stressful Experience or what happened after it?					
11	Having strong negative feelings such as fear, horror, guilt, or shame?					
12	Loss of interest in activities that you used to enjoy?					
13	Feeling distant or cut off from other people?					
14	Trouble experiencing positive feelings (for example, being unable to feel happiness or have loving feelings for people close to you)?					
15	Irritable behaviour, angry outbursts, or activing aggressively?					
16	Taking too many risks or doing things that could caus you harm?					
17	Being “superalert” or watchful or on guard?					
18	Feeling jumpy or easily startled?					
19	Having difficulty concentrating?					
20	Trouble falling or staying asleep?					

Emotion Regulation Questionnaire (ERQ)

Instructions and Items

We would like to ask you some questions about your emotional life, in particular, how you control (that is, regulate and manage) your emotions. The questions below involve two distinct aspects of your emotional life. One is your emotional experience, or what you feel like inside. The other is your emotional expression, or how you show your emotions in the way you talk, gesture, or behave. Although some of the following questions may seem similar to one another, they differ in important ways. For each item, please answer by marking on the scale where 1= strongly disagree and 7 = strongly agree.

1. When I want to feel more *positive* emotion (such as joy or amusement), I *change what I'm thinking about*.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

2. I keep my emotions to myself.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

3. When I want to feel less *negative* emotion (such as sadness or anger), I *change what I'm thinking about*.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

4. When I am feeling *positive* emotions, I am careful not to express them.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

5. When I'm faced with a stressful situation, I make myself *think about it* in a way that helps me stay calm.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

6. I control my emotions by *not expressing them*.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

7. When I want to feel more *positive* emotion, I *change the way I'm thinking* about the situation.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

8. I control my emotions by *changing the way I think* about the situation I'm in.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

9. When I am feeling *negative* emotions, I make sure not to express them.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

10. When I want to feel less *negative* emotion, I *change the way I'm thinking* about the situation.

1	2	3	4	5	6	7
Strongly disagree			Neutral			Strongly agree

Appendix 8

Expressive suppression study image disgust ratings

The images used in Chapter 4.3. had previously been validated in a student sample for a master's project (Walsh, 2012). The mean disgust ratings of images used in the passive (Table 26) and suppress condition (Table 27) were compared with an independent measures bootstrapped t-test. There was no significant difference between mean disgust ratings between conditions; $t(10) = -1.3$, $p = .90$, 95% CI [-5.03, 5.78].

Table 26 – Passive condition disgust ratings

Image name	**Mean Disgust valence**
1_Skin ulcer	71.25
89_Parasite	73.75
2_Rotten teeth	75.06
8_Herpes eye	74.13
90_Faeces	74.31
78_Maggoty foot	84.07
Mean (*SD*)	75.43 (4.23)

Table 27 - Suppress condition disgust ratings

Image name	**Mean Disgust valence**
19_Tongue tumour	75.45
86_Dog wound	79.14
80_Pus	66.92
83_Faeces	74.31
71_Scaley foot	77.19
6_Infected toenail	81.69
Mean (*SD*)	75.78 (5.07)