The experiences of Sleep, Mood and Dissociation in Non-Epileptic Seizures.

Saafi Mousa

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THE STATEMENT OF INTEGRITY

The candidate confirms that the work submitted is her own and that appropriate credit has been given where reference has been made to the work of others.

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ABSTRACT

Introduction: Non-epileptic seizures (NES) refer to seizures and involuntary movements that look like epilepsy but are of unclear aetiology. It has been suggested that a range of psychological factors are important in the development of NES. Recent research has suggested impaired sleep might be a maintaining factor for NES, with some suggesting that sleep may influence seizures via its influence on dissociation. Understanding sleep in NES is important because if poor sleep is a key feature of NES, then treatments, such as CBT-I, that readily improve sleep in physical and mental health problems, may be worthy of trial in NES. I aimed to explore whether those with NES experienced more subjective or objective impaired sleep, whether this was linked to next day functioning, and if possible, to the occurrence of seizures.

Methods: A control group ($N = 20$) and a NES sample (N=17) completed baseline questionnaires on sleep, dissociation, anxiety and depression and provided demographic information. Then for 6 consecutive nights wore an Actiwatch activity monitor and completed a daily sleep diary and daily measures of mood and dissociation. The NES sample was also asked to provide seizure frequency details at baseline and daily throughout the study period.

Results: Analysis using independent sample t-tests and multi-level modelling suggests that those in the NES group report subjectively and experience objectively poorer sleep. No sleep variables from the preceding night's sleep affected next day mood and dissociation or next day seizure frequency. However, the sample was underpowered for this analysis.

Conclusion: Preliminary outcomes show that impaired sleep (both objective and subjective) is a feature of NES and that this could have clinical implications. However, future research with larger samples is required to explore whether sleep might directly influence seizure occurrence, dissociation and mood.

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Chapter 1. Literature Review

1.1 Non-epileptic seizures (NES)

In 1878, Professor of Physiology, Arthur Gamgee, published an account in which he depicts a case by French neurologist Jean-Martin Charcot, demonstrating what he called “Hystero-Epilepsy". In this account, he describes symptoms, specifically seizures, that mimic those of epilepsy but were acquired due to mental distress as opposed to neurological or organic causes. Gamgee’s account was the first published work on what is now commonly known as Non-Epileptic Seizures (NES) and Non-Epileptic Attach Disorder (NEAD). While there is currently no agreed term to describe NES, they have previously also been known as pseudo-seizures, hysterical seizures, psychogenic seizures, dissociative convulsions and seizures and are now classified in the DMS-5 and ICD-10 as a form of conversion disorder. The development of the understanding of NES can be indicated by the terms employed to describe this, which initially adopted a stance in which these seizures were "pseudo", suggesting that these seizures were not "real" and were perhaps "put on" by individuals. This then moved to the understanding of NES in the context of mental distress and as a result of "hysteria", which despite having multiple unclear definitions, eventually became synonymous with the physical expression of severe emotional pain (Whitlock, 1967). Similarly, a more recent understanding of NES is that it is a set of movements and sensations, similar to those in epilepsy, believed to be caused by psychological factors (Lesser, 1996).

The most recent developments in theorising the aetiology of NES perhaps take a more biopsychosocial view on NES, and take a more monist perspective on mind and body (Brown and Reuber, 2016) Indeed, it has further been said that NES "*straddle the continuum of neurology to psychiatry, and their presentation blurs the margins of these two disciplines"* (LaFrance, 2012, p.177).

The main feature of NES is its similar symptomology to epilepsy; in fact, it has been suggested that NES accounts for 15-30% of presentations in epilepsy services (Bodde et al., 2009). It is thought that currently, there are 15,000 people in the UK living with NES (NEAD, 2019); however, difficulties in identifying NES indicate that this figure is likely to be higher. Moreover, it is thought that around 2 to 33 in 100,000 are likely to be affected by NES (Benbadis & Hauser, 2000), suggesting that the first figure is a considerable underestimation, further indicating the lack of a solid understanding of NES. It is thought that NES is more likely to be developed by women and figures suggest that 60- 75% of NES sufferers are women (O'Sullivan, 2007; McKenzie, Russell, Pelosi & Duncan, 2010).

There is an acknowledgement that NES comes with considerable costs to sufferers, their carers and our health systems (LaFrance & Benbadis 2006; Smith, 2014; Fitzsimmon, Page & Aram, 2017; Karakis et al., 2014). This suggests that there is a real need for a better understanding of the development and maintenance of this condition. For this thesis, I have chosen to use the term NES to refer to both NES and NEAD and to adopt an open position concerning the possible causes of NES.

It is both that which is similar, and that which differs that distinguishes NES from Epileptic Seizures (ES). It is crucial to be able to differentiate between NES and ES as incorrect diagnoses are inappropriate, ineffective, expensive and impact significantly on the lives of patients with NES (Krumholz, 1999). Much of the research in NES is in comparison to ES, often in an attempt to emphasise the psychological or somatic nature of NES, as well as how seizures are subjectively experienced in these two seizure conditions. Individuals with NES report more frequent and disabling seizures than those with epilepsy (Barry et al., 1998). Additionally, individuals with NES also report significantly worse quality of life and mood problems (Szaflarski et al., 2003) and perceive their health status to be poorer (Al Marzooqi, Baker, Reilly & Salmon, 2004) than individuals with ES. Furthermore, it is likely that individuals with NES feel less supported or not believed by health professionals as it was found that many clinicians perceive these individuals to be able to control their seizures (Iriarte, Parra, Urrestarazu & Kuyk, 2003).

Many attempts have been made to distinguish between the physical characteristics between NES and ES. Gröppel, Kapitany & Baumgartner (2000) analysed EEG videos of 27 patients and identified three clusters of NES; clonic and hypermotor movements, trembling of the upper and lower extremities and falling on the floor as the only symptom. This supports other studies that have distinguished between NES and have found that patients with motor manifestations of NES had a history of sexual and physical abuse, compared to those with limp or unresponsive presentations (Abubakr, Kablinger & Caldito, 2003). Other studies further

investigating NES characteristics have suggested that ictal eye closure captured on EEG video was a reliable differentiator between NES and epilepsy (Chung, Gerber & Kirlin, 2006). However, it was later found that this was only able to accurately identify 64% of the cases with NES (Syed et al., 2008). Furthermore, research suggests that those with NES are less likely to present with increased heart rate during seizures when compares to ES (Oliveira, Gondim, Hogan & Rola 2007). It has been found that an increase in heart rate of 30% or more, almost always successfully distinguished ES from NES (Opherk & Hirsch, 2002). Despite efforts, there are currently no clear set of characteristics or symptoms that can concretely and accurately distinguish NES from ES from observation only.

1.2 Development of NES

The term NES clearly describes that the seizures are not epileptic but is not informative about the nature or development of these seizures. The development of NES has been debated at length, and I would argue, has a significant impact on if and how diagnoses of NES are made, as well as how health professionals engage with individuals with NES. The majority of current literature maintains the position that NES is likely caused by psychological factors and research commonly prefaces NES with the word “psychogenic” (PNES). However, psychological factors are a relatively all-compassing term and can include experiences of trauma, mental health conditions, interpersonal problems, attachment, alexithymia, family dysfunction and stressful life circumstances. Furthermore, all these factors are known to interact, further complicating the observation of cause-and-effect in NES. In this first section

of the thesis we will describe research on psychological factors implicated in NES.

1.2.1 Trauma

One of the most researched possible causes or contributors to NES is trauma. Trauma is described as *"the unique individual experience of an event or of enduring conditions in which the individual's ability to integrate his or her emotional experience is overwhelmed (i.e. his or her ability to stay present, understand what is happening, integrate the feelings, and make sense of the experience), or the individual experiences (subjectively) a threat to life, bodily integrity, or sanity* (Pearlman & Saakvitne, 1995, p. 60). There is extensive literature on the impact of emotional trauma on our bodies and physical health, however none as influential as the Adverse Childhood Experiences (ACE) studies. In these large-scale studies, they found that traumatic childhood experiences were significant predictors of health risk behaviours and development of poor physical health, including obesity, cancer and cardiovascular diseases (Felitti et al., 1998; Anda et al., 2006), even in the absence of PTSD (Sledjeski, Speisman & Dierker, 2008). In line with this, much of the research in NES suggests that emotional trauma contributes to the development of NES (Kuyk et al., 1999). A review of 17 studies observing the link between NES and traumatic experiences found that 44-100% of participants with NES reported at least one traumatic experience. Furthermore, the population that presents with NES are more likely than those with epilepsy to report multiple or ongoing traumatic experiences, which are thought to be key in predicting the development of NES (Rosenberg et al., 2000), in particular, abuse and neglect are implicated (Proença et al., 2011).

Additionally, abusive childhood experiences are not unique to NES, and many with ES have had such experiences too. However, childhood psychological abuse in NES was found to be a notable difference when comparing the groups and was thought to be mediated by family dysfunction (Salmon, Al-Marzooqi, Baker & Reilly, 2003). A further study investigating the predisposing, precipitating and perpetuating factors of NES found primarily trauma, closely followed by bereavement and family dysfunction to be significant predisposing and precipitating factors (Reuber, 2007). Effectively, it has been argued, in line with some early psychological thinking on the matter, that research into trauma in NES is suggestive of a model in which NES is a physical communication of that which could not be or was not allowed to be expressed verbally (Quinn, Schofield & Middleton, 2010). This supports findings in which those living with NES have rated their family as particularly dysfunctional concerning communication (Krawetz et al., 2001).

Although it is widely accepted that there is a high prevalence of trauma in individuals with NES (Brown & Reuber, 2016b) and that trauma can even predict the development of somatic symptoms (Sansone, Pole, Dakroub & Butler, 2006), the majority of people who have experienced trauma do not develop NES. Furthermore, a systemic review of the psychological aspects of NES by Brown & Reuber (2016a), suggests that the extensive research into trauma in NES does so retrospectively, over-represents women, often have small sample and effect sizes and are usually conducted in comparison to ES instead of other mental health difficulties. The authors further indicate that these studies lack standardised clinical interviews,

possibly because those with NES are more likely to present in neurology services rather than psychiatric services. This suggests that while trauma could be a factor in the development of NES, a better understanding is required to distinguish between those who do develop NES and those who do not.

There is some evidence to suggest that the development of NES is perhaps linked to the processes that change as a result of the trauma as opposed to the traumatic experiences themselves. For example, research suggests that those with NES were more likely to adopt less effective emotional coping styles such as avoidance and were less likely to engage in task-orientated coping techniques such as problem-solving (Myers, Fleming, Lancman, Perrine & Lancman, 2013). Additionally, experiences of interpersonal trauma, such as physical, emotional and sexual abuse, can significantly impact on the way individuals perceive and process information and threat (Buckley, Blanchard & Neill, 2000). Moreover, Bakvis and colleagues (2009) conducted a study using pictorial Stroop Task with 19 individuals with NES and a control group of 20. While this was a relatively small sample, they found that the participants with NES, who self-reported sexual abuse, indicated significantly more hypervigilance than the control group. These findings suggest that a critical difference between those who have experienced trauma and further go on to develop NES may lie in how their perception and processing of threat is affected.

Whereas the majority of research in trauma in NES focuses on interpersonal and developmental trauma, there is evidence that other traumas such as the consequences of war, political unrest, torture, poverty and natural disasters are equally likely to

contribute to the development of NES (Moreno & Peel, 2004; Mateen, 2010). Although such traumas may be less likely to occur in developing countries, they're often witnessed in refugees and migrants who access care in the western world. In Germany, in the height of the political unrest that led to the wave of refugee resettlement in Europe, they found that that 20% of refugees attending emergency services presented with NES, which is likely to have occurred from trauma such as forced displacement rather than cultural differences (Brinckmann, van Noort, Leithner & Ploner, 2018).

It may be interesting to note that the majority of research in NES in migrant, refugees and other race, ethnic or cultural differentiations consistently use the term pseudo-seizures when referring to NES. This is despite the call to avoid this term due to the negative implications the word "pseudo" has on both those living with and those treating NES (O'Hanlon, Liston & Delanty, N. (2012). It could be thought that such research conducted in Western countries, could be mirroring how NES is conceptualised in other ethnic and cultural communities. Nonetheless, it raises further questions about possible systemic and internalised biases in how clinicians and researchers perceive the occurrence of NES in non-Western communities.

1.2.3. Mental Health Difficulties

There is extensive literature that suggests that those with NES experience higher levels of mental health difficulties such as anxiety and depression (Prueter, Schultz-Venrath & Rimpau, 2002), low self-esteem (Dimaro et al., 2015), post-traumatic

stress disorder (PTSD) (Fiszman, Alves-Leon, Nunes, Isabella & Figueira, 2004) and dissociative disorders (D'Alessio et al., 2006). Individuals with NES have even been found to experience higher levels of anxiety, low mood and hostility when compared to those with other somatoform or functional symptoms (Mökleby, Blomhoff, Malt, Dahlström, Tauböll & Gjerstad, 2002). There is even some evidence to suggest that the combination of depressive and dissociative symptoms can predict the development of NES (Mazza et al., 2009), particularly if there has been a previous experience of physical or sexual abuse (Scioli-Salter et al., 2016). While it is suggested that half of those living with NES have psychological comorbidities (Seneviratne, Briggs, Lowenstern & D'Souza, 2011), mental health difficulties are often considered a response to traumatic and stressful experiences and it is difficult to distinguish between whether mental health difficulties precede the development of NES, co-exist as comorbidities or develop as a result of living with NES. Additionally, individuals with NES are less likely than those with ES to consider psychological factors important in the context of their conditions (Stone, Binzer & Sharpe, 2004) and may, therefore, fail to report such experiences.

It is difficult to establish precisely how mental health difficulties can lead to the development of NES and perhaps the key to understanding this is to look beyond these difficulties into the processes that maintain them. For example, while it has continuously been reported that those living with NES experience more emotional disorders, there is little understanding about what differentiates between those living with emotional disorders who develop NES and those who do not. In recent years, however, some research has focused on the underlying, transdiagnostic processes of

emotional disorders such as the implicit and explicit mechanisms of such experiences. For example, Dimaro and colleagues (2014) found no differences between the levels of implicit and explicit cognitions of anxiety reported by those with NES and those with ES. However, they did find that those with NES showed more discrepancies between implicit and explicit measures of anxiety, fitting the current understanding of the NES profile in that these individuals may experience emotions as overwhelming and out of their control (Novakova, Howlett, Baker & Reuber, 2015). This is likely to lead to those with NES employing coping strategies such as avoidance to escape emotions experienced as overwhelming (Goldstein & Mellers, 2006; Frances, Baker & Appleton, 1999). In turn, avoidance has been found to correlate with self-reported seizure frequency in NES (Dimaro et al., 2014), suggesting that the maladaptive cycle of NES is possibly maintained by avoidance.

1.2.4. Interpersonal Processes & Attachment

Similarly to trauma and mental health difficulties, interpersonal difficulties or diagnoses of personality disorders have been linked to the development and maintenance of NES. The prevalence of interpersonal problems in those living with NES range from 10% to 86% and are likely to contribute to the difficulties in the diagnosis and management of NES (Lacey, Cook & Salzberg, 2007). There is some further evidence that diagnoses of personality disorders were significantly more present in those with NES when compared to ES and that this is a better predictor of NES development than any other mental health difficulty (Direk, Kulaksizoglu, Alpay & Gurses, 2012). This likely to be linked to the interpersonal and development experiences of trauma in those with or able to meet the criteria of

personality disorders (Silk, Lee & Hill, 1995). These traumatic experiences thought to lead to interpersonal difficulties are particularly damaging when they occur during childhood (Herman, Perry & Van der Kolk, 1989; Johnson, Cohen, Brown, Smailes & Bernstein, 1999; Grover et al., 2007). While it is not unusual for those with ES to have experienced interpersonal difficulties as a result of childhood traumas (Harden et al., 2009), the nature of these traumas may have further implications for the development of NES. For example, in a study that found a history of sexual abuse in both NES and ES groups, the NES group were much more likely to have had a closer relationship with their perpetrator (Alper, Devinsky, Perrine, Vazquez, B., & Luciano, 1993). It is, therefore, perhaps unsurprising that those with NES present with that is considered maladaptive personality traits (Reuber, Pukrop, Bauer, Derfuss & Elger, 2004).

In an attempt to better understand the underlying mechanisms of NES, research has sought to identify how these link to specific clusters of personality disorders as set out by the DMS5 and ICD10. While different diagnoses and processes of personality disorders have been linked to somatoform conditions such as NES (Bornstein & Gold, 2008), the majority of this research supports that those with NES are most likely to present with a borderline process (Hovorka, Nežádal, Herman, Němcová & Bajaček, 2007). Some research into interpersonal processes and NES has moved away from diagnoses of personality disorders and focused on traits instead. For example, it is not unusual to find features of somatisation in those living with NES; however, it has been suggested that the combination of traits of somatisation and externalisation are particularly relevant to the development and maintenance of NES

(Bodde et al., 2011; Testa & Brandt, 2010). Those with NES are often also perceived to have traits such as care-seeking through sick roles. Contrary to these perceptions; however, Testa & Brandt (2010) found that there was no difference in the implicit attitudes and beliefs towards illness when comparing their NES group to healthy controls. Similarly, other research has focused on the perceptions of childhood experiences in those with both NES and borderline processes and found that these individuals were more likely to recall lack of parental warmth and regular parental rejection (Binzer, Stone & Sharpe, 2004). The evidence outlined above makes a good case for the consideration of interpersonal difficulties in the treatment of NES (Cragar, Berry, Schmitt & Fakhoury, 2005).

Interpersonal difficulties have been extensively linked to attachment, the symptom of the first, often in line with features of the latter (Adshead & Sarkar, 2012). Attachment styles could be used to predict the development of interpersonal difficulties as it was found that those with secure attachments are less likely to develop such problems (Meyer, Pilkonis, Proietti, Heape & Egan, 2001). Bartholomew & Horowitz (1991) best explain adult attachments using their four category-model, which defines the types of attachment as the following:

- **Secure:** High self-worth, comfortable with autonomy, and forming close relationships.
- **Preoccupied:** Sense of self-worth dependent on approval and acceptance of others.

- **Dismissing:** Overt high self-worth, denial of distress and importance of relationships.
- **Fearful:** Negative self-view, distrust of others, high distress and apprehension of close relationships.

A secure attachment infers that while growing up, an individual had caregivers that were emotionally available and able to regulate their own as well as the child's emotions (Sable, 2008). Insecure attachments, however, suggest that such emotional availability was lacking and are linked to experiences of childhood adversity including poor support and low self-esteem, which in turn mediate future mental health difficulties (Bifulco, Moran, Ball & Lillie, 2002). It therefore stands to reason that attachment styles would be an important field to explore in the development of NES.

A recent study found that while there was comparatively little difference between the attachment styles of those with NES and ES, that the attachment of the first is much more likely to be linked to mental health difficulties when compared to those with latter (Green, Norman & Reuber, 2017). Other studies focusing on specific attachment styles suggest that in particular, fearful-avoidant attachment styles prominent in those with NES (Holman, Kirkby, Duncan & Brown, 2008; Lally, Spence, McCusker, Craig & Morrow, 2010; Reis & Grenyer, 2004). That being said, attachment styles are linked to a range of mental health difficulties, traumatic experiences and maladaptive coping techniques, indicating the problem in examining the direct link between attachment and NES.

1.2.4 Alexithymia

The inability to recognise, describe and express emotions and emotional experiences is also known as alexithymia (Sifneos, 1973) and a common suggestion about NES and other functional symptoms is that it develops out of the lack or inability to express emotional experiences (Reuber, House, Pukrop, Bauer & Elger, 2003; Quinn, Schofield & Middleton, 2010). Moreover, the term conversion disorders indicate that these are conditions in which psychological distress is converted to or manifests as physical symptoms. This is not a new concept, in fact, Freud first used to term conversion disorder precisely to describe such a process in which that which was too painful to be acknowledged or felt consciously, would present itself unconsciously through the body (Blitzstein, 2008). This psychodynamic conceptualisation of NES further suggests that this happens through the development of defensives such as denial and repression (Jawad et al., 1995).

It is, therefore, unsurprising that the relationship between alexithymia and NES has warranted research. There are conflicting findings for the prevalence of alexithymia in NES; a small study comparing alexithymia in NES with those with epilepsy and a control group found that 90.5 % individuals with NES met the criteria for alexithymia (Bewley, Murphy, Mallows & Baker, 2005). Others, however, have found this prevalence to be much lower (25.5%), but suggest that the alexithymia alongside other emotional regulation difficulties could be used to distinguish between types of NES, which in turn could guide treatment (Brown et al., 2013). Additional research has found alexithymia to be particularly important in self-reported measure of seizure severity (Urbanek, Harvey, McGowan & Agrawal,

2014), further suggesting that an inability to express emotional experiences, may lead to higher prevalence of somatisation. That being said, it is thought that alexithymia found in those with NES was likely to be a result of trauma, further providing evidence for the link between trauma and NES (Myers, Matzner, Lancman, Merrine & Lancman, 2013). Nevertheless, alexithymia is not unique to somatoform conditions and has been considered a predisposing factor in a variety of mental health difficulties, including eating disorders and substance misuse (Salminen, Saarijärvi & Äärelä, 1995). Furthermore, the inability to recognise and express emotional stimuli is often an aspect of common mental health difficulties, making it difficult to distinguish whether alexithymia is a preceding or a separate co-occurring factor (Berthoz, Consoli, Perez-Diaz & Jouvent, 1999).

1.2.6 Family Dysfunction

Family dysfunction has been linked to the many variables discussed in this literature review and is known to be a feature in depression, (Miller et al., 1992); attachment difficulties (Shaw & Vondra, 1993); interpersonal difficulties (Carr & Francis, 2009) and alexithymia (Mallinckrodt, King & Coble, 1998). Moreover, many indicators of family dysfunction such as neglect, and interfamily sexual abuse are considered also considered to be traumatic experiences in their own right. The complexity of traumatic experiences in the context of family dysfunction may be particularly important when considering how distress is expressed and is likely to lead to the "unspeakableness", which in turn provides an explanation for how somatisation may develop (Salmon et al., 2003).

However, “unspeakable dilemmas” may also contribute to the development and maintenance of family dysfunction (Betts & Boden, 1992). A study analysing taped clinical interview of 14 adolescents and adults with NES and their families found that in 13 out of the 14 interviews, there appeared to be evidence of a “unspeakable dilemma” (Griffith, Polles & Griffith 1998). The authors further found this dilemma was most likely to be concerned with person with NES or their direct family member, that the person with NES was the most silent in these interviews and that they had managed to effectively conceal their distress from their families by way of suppression.

This might explain why people with NES are more likely to perceive their families as not committed or as unsupportive to each other when compared to control and ES groups (Moore, Baker, McDade, Chadwick & Brown, 1994). These authors also report that NES participants were more likely to perceive their families of being less concerned with ethical or moral values. Furthermore, family stressors such as illness within the family and having a carer’s role has been found to an important maintenance factor for NES (Reuber, 2007). It could therefore be further theorised that the somatisation of psychological distress that arises from having a carer's role, may be a critical factor in the maintenance of seizure occurrence for individuals with NES.

1.2.7 Stressful life circumstances

There is some evidence that individuals with NES are much more likely to have experienced ongoing stressful life events throughout childhood and as an adult when

compared to both the general public and those living with ES (Tojek, Lumley, Barkley, Mahr & Thomas, 2000). The same study found that as those with NES were more likely to receive a diagnosis in adulthood and have a family member with ES and that this could have contributed to the development of NES as a way to cope. Similarly, an earlier study suggested that NES could be seen as a pattern learned to cope with stressful experiences (Ramani, Quesney, Olson & Gumnit, 1980).

However, there is an alternative argument, suggesting that those with NES consider their general ongoing lives more stressful when compared to both the general population and those living with epilepsy (Frances, Baker & Appleton, 1999). Effectively, it is argued that those with NES do not objectively experience more severe stressors, but rather that they experience these stressors as more distressing and are less able to adopt helpful coping strategies (Testa, Krauss, Lesser & Brandt, 2012). That being said, individuals with NES are less likely to report stressful life experiences (Stone, Binzer & Sharpe, 2004), which could be explained by findings that those with NES are much more likely to adopt avoidant coping styles in stressful situations (Goldstein & Meller, 2006) and when faced with social threats (Bakvis, Spinhoven, Zitman & Roelofs, 2011). Perhaps it could be said that stressful experiences in which expression of this could be deemed particularly difficult, such as family dysfunction, could lead to the expression of distress in another way, i.e. somatisation. Furthermore, it has been suggested that individuals with NES adopt an external locus of control in the context of their health (Goldstein, Drew, Mellers, Mitchell-O'Malley & Oakley, 2000), further indicating that factors perceived as controllable, such as stress, could be challenging to accept. Finally, the under-

reporting of stressors may also imply resistance to psychological or circumstantial explanations of what is experienced as a physical condition and be linked to a desire for physical symptoms to be taken more seriously by health professionals.

1.2.6 Non-psychogenic explanations

So far we have concentrated on psychogenic or psycho-social explanations for NES and associated variables. However, NES are considered a medically unexplained symptom (Weiland et al., 2012) and therefore, an emphasis has been placed on psychological factors in the development and maintenance of NES, often overshadowing other possible causes. While it is theorised that the development of NES does not develop in the same neurological manner that can be observed in ES, this does not exclude other non-psychogenic contributions to the development of NES. It has been found that 24-32% of individuals with NES reported a history of a brain injury prior to developing this condition (Barry et al., 1998; Westbrook, Devinsky & Geocadin, 1998). There have also been cases in which individuals with NES have been found to present with some abnormalities in-between seizures during EGG screenings (de Timary et al., 2002). Further findings suggest that organic brain disorder markers are not uncommon in NES (Reuber, Fernandez, Helmstaedter, Qurishi & Elger, 2002; Ding et al., 2013; Arthuis, Micoulaud-Franchi, Bartolomei, McGonigal & Guedj, 2015).

Other neurodevelopment factors such as intellectual disability (ID) continue to receive little interest in NES research, despite indications that occurrence of 20-30%

of ID in NES is comparable with to that of ES (Kanemoto, Goji, Tadokoro, Kato & Oshima, 2017). However, ID in ES has been researched at length, including prevalence (McGrother et al., 2006), the impact of living with this dual diagnosis (Bowley & Kerr, 2000) and gene expressions (Lemke et al., 2014). Furthermore, there is limited research into the neuropsychological profiles of those living with NES, but findings suggest that whilst women with NES do not meet the criteria for ID, their neuropsychological outcomes suggested working memory and attention impaired when compared to those with ES (Strutt, Hill, Scott, Uber-Zak & Fogel, 2011). Other studies however, that have found that a poor working memory in those with NES was likely to be linked reported incidents of abuse (Williamson, Holsman, Chaytor, Miller & Drane, 2012). Additionally, I have been unable to find any studies specific to the occurrence of NES in those living with autism, despite there being much research into the co-occurrence of ES in autism (Gillberg, 1991; Canitano, 2007; Tuchman, Cuccaro & Alessandri, 2010). While this is likely to be a reflection of a lack of a congruent understanding of NES both in clinics and in research, it indicates an important gap in the literature.

Non-neurological physical conditions have also been linked to NES; for example, asthma and gastro-oesophageal reflux disease were both found to be predictors of NES (Elliott & Charyton, 2014). That being said, physical conditions themselves could be psychogenic (De Wet, Mellers, Gardner & Toone, 2003). Additionally, if adverse childhood experiences are thought to predisposition individuals to the development of physical conditions (Felitti et al., 1998; Anda et al., 2006), then the link between physical conditions and NES tells us little about cause-and-effect.

Furthermore, many people with neurological and other physical conditions also experience mood and functioning impairments, yet unlike with NES, little attention is paid to whether such impairments preceded the development of these conditions. This may indicate that healthcare continues to hold a dualistic view off wellbeing in which we appear to value physical conditions more as their measurability enable us to view it as more accurate.

It is worth noting that there are many neurological symptoms and conditions of which we have little knowledge about how they are caused and the factors that contribute to their development. However, none have received as much attention as NES in discounting it as a neurological condition. While there may be many reasons why there is such an interest in how NES develops, such as the ability to distinguish this from ES, it is clear that psychogenic explanations for this condition are favoured, despite the lack of clear cause-and-effect evidence. Disbelief from health professionals in patient's ability to control NES (Iriarte et al., 2003) may also contribute to the lack of willingness to investigate non-psychogenic pathways to the development of NES. Nonetheless, this raises questions about the possibility of neurological or organic causes of NES that have either received little interest or have been discounted.

1.2.7. Biopsychosocial explanations

One of the most researched aspects of NES is in relation to dissociation, which is described as a complex psychophysiological process that changes the way

individuals experience their self, their ability to access their memories and knowledge, and how they might behave (Putnam, 1994). The International Classification of Diseases (ICD-10)1 defines dissociation as *". . . a partial or complete loss of the normal integration between memories of the past, awareness of identity and immediate sensations, and control of body movements*" (p 151). Firstly, a distinction must be made between dissociation as a state or a symptom and dissociative disorders (DID). The DMS-5 (2013) and ICD-10 (2016) list the following dissociative disorders:

- Dissociative identity disorder (DID)
- Dissociative amnesia including Dissociative Fugue
- Depersonalisation/Derealisation Disorder
- Other Specified Dissociative Disorder
- Unspecified Dissociative Disorder

Furthermore, Dissociative Disorders of Movement or Sensation come under Functional Neurological Symptom Disorders (FND) section in the DSM 5, while the ICD-10 lists it alongside the other dissociative disorders (Black & Grant, 2014; World Health Organisation, 2014). Dissociation is identified by ruling out epilepsy and other organic or neurological conditions (DSM-IV, 1994).

There are five core symptoms that dissociative disorders are based on; amnesia, depersonalisation, derealisation, identify confusion and identify alternation (Steinberg, 1995). For this literature review, we're interested in dissociative

symptoms and dissociation as a state, in particular amnesia, depersonalisation and derealisation. This is because our study aims to look at whether there is a relationship between sleep and dissociation in the context of seizure frequency, rather than investigating the occurrence of DID in seizure disorders.

Dissociation has been extensively and significantly linked mood impairment, psychiatric diagnosis and to the prevalence of traumatic experiences (Coons, Bowman, Pellow & Schneider, 1989: Banyard, Williams & Siegel, 2001). However, there is some suggestion that traumatic experiences on their own do not predict dissociation unless this occurs alongside experiences of post-traumatic stress and emotional dysregulation (Briere, 2006). Other theories have linked dissociation to proneness to fantasies, suggestibility of memories and cognitive failures such as distractibility (Giesbrecht, Lynn, Lilienfeld & Merckelbach, 2008). In this context, dissociation appears to be linked more to unusual sleep experiences such as nightmares and vivid dreaming rather than impaired sleep (Koffel & Watson, 2009). Van der Kloet, Merckelbach, Giesbrecht & Lynn (2012) reviewed the literature on the relationship between sleep and dissociation and argued that dissociation emerges from disturbed sleep. They propose that dissociation is caused by sensitive sleep-wake cycles, in which dream-like activity mediates memory failure, which in turn increases dissociative experiences. They further propose that improved sleep can reduce experiences of dissociative symptoms.

1.2.8. Dissociation in NES

Dissociation is considered to be essential to the process of NES (Williams et al., 1993). Moreover, NES are often described as dissociative seizures both in research and clinically (Wood, McDaniel & Burchfiel, 1998; Meller, 2005). Van der Kruijs and colleagues (2011) conducted a neuroimaging study, in which they found that both NES and dissociation implicated parts of the brain responsible for voluntary muscle movement (precentral sulcus) and emotion regulation, visceral sensory perception and self-awareness (insula). They further found that subjective measures of levels of dissociation collaborated these findings and that those with NES experienced more dissociation when compared to a healthy control group.

However, conceptualising NES as dissociative seizures would suggest that dissociation is a process exclusively found in NES, therefore not accounting for the findings that dissociation has also been extensively linked with ES (Alper et al., 1997) and other organic conditions (Good, 1993). Furthermore, the other terms describing NES are also indicative of causation, of which there is yet to be a clear understanding of. Therefore, it may be more appropriate to use the term NES in research investigation dissociation across the seizure disorders. Furthermore, there is some evidence that although dissociation is a mechanism in both NES and epilepsy, different kinds of dissociative experiences are involved in different seizures. Alper and colleagues (1997) used the Dissociative Experience Scale (DES) to investigate the difference in dissociation between NES and epilepsy. The DES categorises dissociative experiences into the following six domains; depersonalisation, derealisation, amnesia, gaps in awareness, absorption, and imaginative involvement

(Bernstein & Putnam, 1986). They found that those with NES experienced dissociation in the form of depersonalisation and derealisation, whereas those with epilepsy experienced dissociation in the form of amnesia, but that both groups experienced much more dissociation than the non-clinical population. Interestingly, depersonalisation and derealisation are also the dissociative aspects most likely to be implicated in the development of depression and panic (Soffer-Dudek, 2014). If it was possible to distinguish between the dissociation experiences in NES when compared to that of epilepsy, this could be a useful tool in the 'positive' diagnosis of NES rather than ruling out known neurological conditions.

1.3 Diagnosis of NES

Appropriate and correct diagnosis of NES is important so that individuals are not wrongly treated for epilepsy and has been found to drastically reduce A&E attendance and hospital admissions (Razvi, Mulhern & Duncan, 2012). Diagnosis is further essential so that if there are underlying psychological difficulties, that these can be addressed (Reuber & Elger, 2003). Particularly as it has been suggested that individuals with NES present with significantly more interpersonal problems (Galimberti et al., 2003); decreased mood and quality of life (Szaflarski et al., 2003) and sleep disturbances (Graham & Kyle, 2017) than those with epilepsy. However, diagnosis is not straightforward as NES is not identified using theory, but rather by ruling out physical conditions and causes (Brown & Reuber, 2016). As it is thought that NES may be considered an individual's attempt to express psychological distress in the form of unexplained medical symptoms (Reuber, House, Pukrop,

Bauer & Elger, 2003), diagnosis is also likely to include some exploration of current or historical psychological distress.

Diagnosis of NES is made by process of elimination in which other neurological causes and conditions are ruled out, alongside other symptoms unique to (ES), such as tongue biting and incontinence (de Timary et al., 2002). The use of ECGs to diagnose NES is both expensive and uncommon, and differential techniques are required to identify NES accurately. However, a review assessing the likelihood of diagnosis via means of "*demographic and medical history variables, seizure semiology, provocative testing, prolactin levels, single photon emission computed tomography, psychological testing, and neuropsychological testing*" has found these means may only be useful as an additional tool to ECG (Cragar et al., 2002). The practice of diagnosing NES is further complicated by how clinicians and patients experience the communication of this diagnosis. It takes years for a correct diagnosis of NES to be made, and many patients have been incorrectly initially diagnosed with epilepsy and treated inappropriately with anti-epileptic medication (Reuber et al., 2002).

As there is significant research to indicate that different types of traumas might be essential in the development of NES, it is vital to think about an individual's life history when suspecting NES (Brown & Trimble, 2000). However, most patients with NES see neurologists when presenting with seizures that they may believe to be epileptic and professionals without a psychological background may not be best placed to inquire about traumatic experiences if they lack the skills to contain

responses to talking about trauma. Additionally, once a diagnosis of NES has been given, clinicians, often neurologists, then have to navigate sharing what is considered to be a psychological diagnosis with patients who present with physical symptoms and may have already been misdiagnosed with a medical condition. This may then be experienced by patients as not being believed to have "real" seizures, which for some mimicked the experience of not being believed when disclosing abuse as children, suggesting that if not conducted carefully, diagnosis could be experienced as traumatising (Prigatano, Stonnington & Fisher, 2002)

Thomson and colleagues (2009) interviewed patients who had recently been diagnosed with NES and found the emotional impact of the diagnosis to range from relief to anger. They found that patients who experienced relief reported that this was because their condition was now known and that their seizures were not as a result of something more sinister. Patients who experienced anger reported feeling irate at previous misdiagnoses as well as at the individuals responsible for their traumatic experiences, as their NES diagnosis was communicated by explaining NES as a possible response to trauma. Furthermore, reactions to the communication of diagnosis of NES is considered to indicate prognosis, as it has been suggested that maintenance of seizure occurrence following diagnosis was linked to reactions of confusion or anger, while a reduction of seizure occurrence was linked to reactions of relief (Carton, Thompson & Duncan, 2003).

When using a protocol that included a detailed verbal and written information about NES, at the 3-month follow-up, 14% of patients reported that they were seizure-free

and 63% reported that their seizure-frequency reduced by >50% (Hall-Patch et al., 2009). However, individuals with NES continue to be confused about their diagnosis and its relevance to their experiences of the condition (Green, Payne & Barnitt, 2004). Similarly, hospital admissions remain high in the NES population, even when NES was considered to be resolved (Ettinger, Devinsky, Weisbrot, Ramakrishna & Goyal, 1999). Ongoing somatisation of emotional difficulties in the absence of seizures is a further indication that treatment needs to go beyond seizure reduction.

1.4. Treatment of NES

Currently, there is no agreed standard treatment of NES as we lack in-depth knowledge as well as data from powered-RCTs (Smith, 2014). A survey of 130 health professionals who work with NES in the UK, 93% cited psychological intervention as their treatment of choice (Mayor, Smith & Reuber, 2011). Similarly, psychological interventions have received the most empirical interest. The highest quality study to date was a pilot RCT comparing CBT with and without standardised medical care (SMC) (*N*=33) with SMC alone (*N*=31) with findings that suggested that CBT together with SMC was most effective in reducing seizures (Goldstein et al., 2010). Indeed, other methodologically limited, smaller or uncontrolled studies suggest that psychotherapies could be helpful. Kuyk and colleagues (2008) investigated an open inpatient treatment for NES, which consisted of individual psychotherapy, psychomotor and creative therapy, family therapy and participation in group therapies for seven months. They found that seizure frequency decreased significantly, followed by improved measures of mood, dissociation and ability to cope. Further evidence for psychological treatment has found that 12-session CBT

treatment was effective in complete seizure cessation by the last session in 11 out of 17 participants that completed the treatment (LaFrance et al., 2009). Other studies have shown that psychodynamic therapy has lasting improvements as at an average follow-up period of 42 months found 25.5% of participants were seizure-free, and a further 40.4% reported >50% improvement in seizures. (Mayor, Howlett, Grünewald, & Reuber, 2010).

There is also some limited, but promising research suggesting the potential for the inclusion of EDMR in the psychological treatment of NES (Kelley & Benbadis, 2007). Additionally, it was also suggested that a brief 4-session psychoeducation was could be effective in seizure cessation in some individuals with NES (Wiseman, Mousa, Howlett & Reuber, 2016). Nonetheless, it is worth noting that because individuals with NES seek treatment for physical symptoms as opposed to psychological difficulties, they may not be agreeable to psychological interventions. There is also a lack of guidance in terms of what NES treatment and whether this needs to be directed at seizure reduction or at the suspected underlying experiences and emotions that may have contributed to the development of NES.

1.5. Sleep

Since Aristotle first developed his ideas on sleep and dreams some 2000 years ago (Gallop, 1990), the function of sleep has continued to be investigated and theorised and is considered to be a complex process that we have yet to fully understand (Barbera, 2008). That being said, it is clear that sleep is thought of as the gateway to

good health (Alvarez & Ayas, 2004) while poor sleep is associated with impaired health (Gallicchio & Kalesan, 2009). Although the amount of sleep is an essential factor, it has also been argued that the quality of sleep is better related to overall wellbeing rather than how long someone has slept (Pilcher, Ginter & Sadowsky, 1997). Furthermore, individuals who felt satisfied with the sleep they experienced also reported better overall wellbeing and quality of life (Jean-Louis, Kripke & Ancoli-Israel, 2000), however, we are unable to draw causal conclusions from these results.

Considering how much of an impact impaired wellbeing and reduced quality of life can have on day-to-day functioning, improvement of sleep should be imperative. While sleep deprivation has been known to impact on cognitive and motor functioning significantly, it was found that perhaps the most significant impact was on mood (Pilcher & Huffcutt, 1996). Sleep deprivation impairs an individual's ability to regulate their emotions and leads to an increase in negative cognitive bias while reducing the ability to concentrate on non-negative events and experiences (Gobin et al., 2015). This implies that the lack of sleep can reduce people's abilities to cope as they may be unable to use coping strategies such as distraction if they are prone to concentrate on negative events and experiences.

Additionally, a systematic review found that sleep deprivation did not only lead to decreased ability to express emotions but also impaired the ability to recognise emotions in others, crucial for creating and maintaining social interactions (Beattie et al., 2015). It is important to consider that this might mean that impaired sleep

could be a factor in interpersonal conflicts and relationship difficulties. Sleep deprivation is not only known to be a factor in the development of mental health difficulties, but there is also evidence that sleep deprivation continues to be a factor in the maintenance of mental health difficulties (Wehr, Sack & Rosenthal, 1987). Furthermore, impaired sleep impacts our ability to make any decision (Harrison & Horne, 2000), which has a wide-ranging impact on daily functioning.

Sleep difficulties have been extensively investigated in chronic health conditions (Davidson et al., 2002; Russell, Wearden, Fairclough, Emsley & Kyle, 2016), mental health difficulties (Tsuno, Besset & Ritchie, 2005; Lamarche & De Koninck, 2007) and substance misuse (Stein & Friedmann, 2006; Brower & Perron,2010). While there has been a considerable amount of research into the impact of impaired sleep, much of this is based on subjective measures. It is well known that individuals who consider themselves to have impaired sleep, report less sleep subjectively than is captured by objective measures such as actigraphy (Van De Berg et al., 2008). However, if individuals perceive their sleep to have been disturbed, or in some way unsatisfying, this could also be a factor for incorrect subjective measures of sleep. Given this, studies investigating sleep should do so using both subjective and objective measures such as Actigraphy; the data produced by activity monitors, often worn on the wrists or waist, which measure movement and estimate sleep for periods with little or no movement.

While a considerable amount of research is focused on whether sleep is affected by chronic conditions, there is some evidence to suggest the opposite too. For example,

it was found that impaired sleep may contribute to the development of conditions such as Type 2 Diabetes (Kawakami, Takatsuka & Shimizu, 2004; Cappuccio et al., 2010a), particularly as impaired sleep impacts on the metabolic processes in a way that makes individuals vulnerable to the development of Type 2 Diabetes (Knutson et al., 2007). In a systematic review about the link between sleep and mortality, it was found that long durations of sleep were predictors of death in the prospective population, in the same way, that short durations of sleep might be (Cappuccio et al., 2010b).

Impaired sleep can be caused by factors that interrupt the circadian rhythm that manages our body clock in terms of sleep and wakefulness throughout the day (Cole & Richards, 2007). A commonly occurring factor in circadian rhythm disruption is perceived stress (Treharne et al., 2007). Particularly stress associated with events or expectations of the following day, which has been shown to lead to a shorter period of sleep, as well as fragmented sleep (Âkerstedt, 2006). There is some indication that this is especially the case for individuals with a reduced ability to cope with or manage their stress, which would suggest that learning coping or management skills may lead to improved sleep (Sadeh, Keinan & Daon, 2004). This implies that health conditions, including emotional and cognitive difficulties, may impact on sleep through stress. Furthermore, impaired sleep in itself can increase cortisol levels the following day, alongside a reduced resilience to deal with stress (Leproult, Copinschi, Buxton & Van Cauter 2007). This is suggestive of a cycle in which stress is a contributor to impaired sleep, a consequence of sleep impairment and a maintenance process in impaired sleep.

Much of the research in sleep focused on impaired sleep in the context of sleep deprivation and disturbances, however, it is important to note that excessive sleep has also been known to impact on overall wellbeing (Ohayon, Reynolds & Dauvilliers, 2013; Jennum, Ibsen, Avlund, & Kjellberg, 2014). Additionally, excessive sleep has been extensively linked to diagnoses of mood disorders and severe emotional distress (Billiard, Molenc, Aldaz, Ondze, Besset, 1994; Soehner, Kaplan & Harvey, 2013). In fact, Hypersomnia is noted alongside Insomnia in the DSM5 under Sleep-Wake Disorders, further indicating that excessive sleep may be linked to impaired functioning. That being said however, Hypersomnia has been used inconsistently by research to describe excessiveness of various sleep domains and there is some discussion around whether Hypersomnia should be further distinguished between how long people spend in bed and how long they are actually asleep (Kaplan & Harvey, 2009).

1.5.1 Sleep Treatment

The NICE Guidelines (2015) recommends sleep hygiene, hypnotic medication and cognitive and behavioural interventions for short-term and long-term insomnia. Sleep hygiene in this context refers to advice about lifestyle changes such as exercise, the limitation of caffeine intake and fixed times for sleep. Whilst there is little support for the effectiveness of sleep hygiene on by itself, it's considered an important part of tackling insomnia (Falloon, Arroll, Elley & Fernando, 2011). Instead, Cognitive Behavioural Therapy for Insomnia (CBT-I) appears to be the most effective and well-researched intervention for insomnia. CBT-I consists of 5 features; sleep hygiene, stimulus control, sleep restriction, cognitive restructuring,

and relaxation training (Morin & Benca, 2012) and can be effectively delivered as self-help on paper and electronically (Rybarczyk, Mack, Harris & Stepanski, 2011).CBT-I has been found to improve sleep in individuals with insomnia (Okajima, Komada & Inoue, 2011), individuals with both insomnia and psychiatric comorbidities (Taylor & Pruiksma, 2014) and those with chronic conditions such as cancer (Fleming, Randell, Harvey & Espie, 2014). There is also evidence of improved mood and quality of life when CBT-I is used to treat disturbed sleep in neuropsychiatric and chronic conditions (Hingray, Biberon, El-Hage & de Toffol 2016). Furthermore, CBT-I has been found to significantly improve experiences of pain intensity and catastrophising, fatigue when treating fibromyalgia (Lami et al., 2016), a condition characterised by high levels of somatisation (Wolfe & Hawley, 1998).

1.5.2 Sleep in NES

Sleep in NES is an understudied field (Pavlova, Allen & Dworetzky, 2015) despite evidence that those experiencing seizures suffer from disturbed sleep (Bazil, 2003). If ES are known to be linked to impaired sleep and the improvement of sleep known to impact favourable on seizure control (van Golde, Gutter & de Weerd, 2011), it stands to reason that this may be applied to NES. Indeed, for psychogenic explanation of NES, poor sleep could be a cause of the emotion regulation difficulties that appear in NES or could reflect the impact of traumatic experiences interfering with sleep, like with PTSD. Given the key role of sleep in all possible explanations of NES (see Figure 1 that shows the theoretical role of sleep in extreme

psychogenic and biological explanations of NES), several research groups have begun to research sleep in NES.

Bazil, Legros & Kenny (2003) conducted a small comparison study of sleep between epilepsy (*N*=10) and NES (*N*=8) and found that sleep was experienced comparatively in both groups. They did, however, find that participants with NES had significantly more REM sleep, similar to those with mood disorders, and theorise that this may have been mediated by comorbidities of depression in the NES group. If this is true, then it could be further hypothesised that interventions that are known to improve sleep disturbances in those with depression, such as CBT-I (Manber et al., 2008), may prove useful in treating impaired sleep in NES.

Graham & Kyle (2017) measured sleep and functional impairment in a clinical sample (*N*=20) alongside an online sample (*N*=205) with FND. They found that impaired sleep was a key feature in functional impairment the following day and that this was independent of depression despite previous suggestions that poor sleep in NES is mediated by depression (Bazil, Legros & Kenny, 2003). Sleep in NES appears to have gathered more interest in the two years since our research idea was first developed and current literature acknowledges that sleep complaints are a significant problem for those living with NES (Erickson et al., 2019). Recently a study measuring objective experiences of sleep in individuals with NES and epilepsy using Polysomnography (PSG) found that both groups experience similar sleeping patterns, in particular, late onset of sleep, but that those with NES presented with more period limb movement throughout their sleep (Popkirov, Stone & Derry,

2018). Another recent study showed that those with NES were more likely to subjective experience greater sleep latency when compared to those with NES (Latreille, Dworetzky, Baslet & Pavlova, 2019). However, this same research team reported in an earlier paper than generally those with NES were more likely to report more severe sleep disturbances subjectively (Latreille, Baslet, Sarkis, Pavlova & Dworetzky, 2018). That being said, Latreille and colleagues (2018) note that 46% of their NES participants carried a diagnosis of a sleep disorder, compared to 30% in the epilepsy group. They further also noted significantly more use of anti-depressants in the NES group, which are likely to contribute to disturbed sleep (Wilson & Argyropoulos, 2005).

1.6. Summary of Literature Review

To summarise our literature review, research in NES suggests that a wide range of variables can contribute to the development and maintenance of the condition. Much of the research has focused on how trauma, mental health conditions, interpersonal problems, attachment, alexithymia, family dysfunction and stressful life circumstances are linked to NES. However, there is limited literature that has aimed to pull this research together to provide a coherent and biopsychosocial understanding of the factors involved in NES.

One such attempt is a systemic review by Brown & Reuber (2016), in which they gathered theorised variables of the development of NES and categorised this into four models of process; NES as a dissociative phenomenon, NES as serving a psychological function, NES as a hard-wired response, NES as learned behaviour

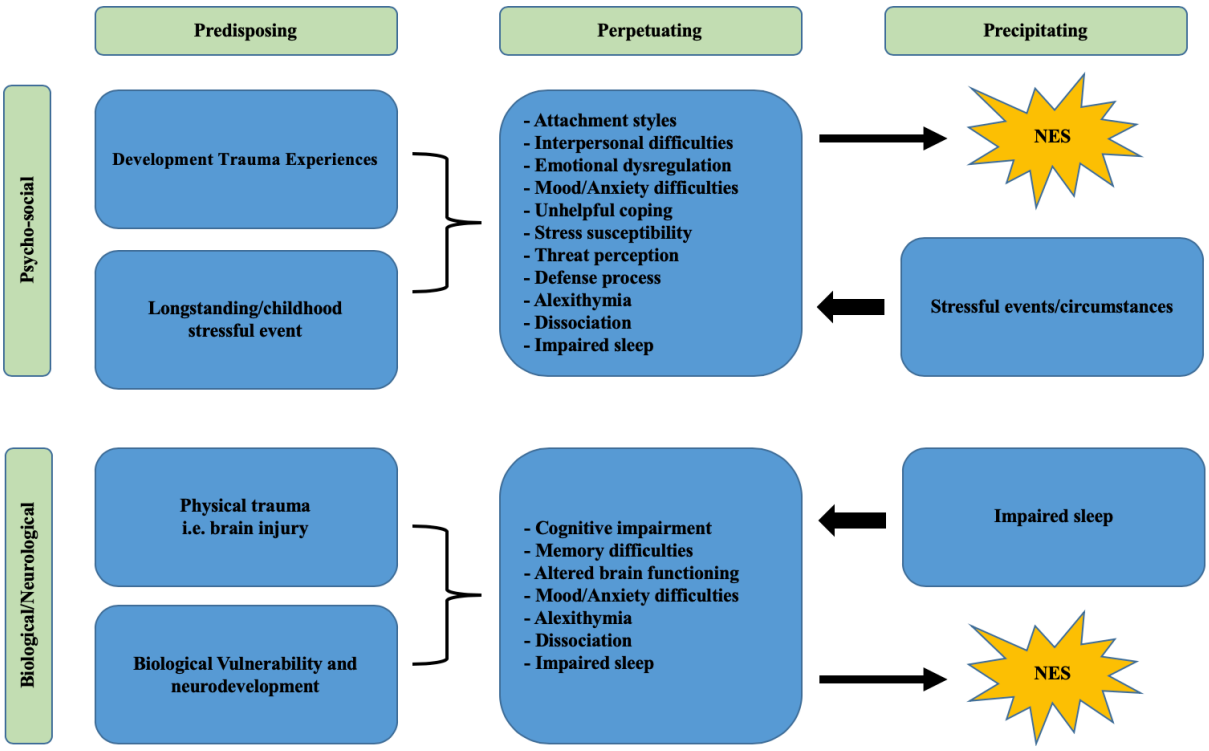
and NES as a possible consequence of impaired cognitive function. This model suggests that all the variables mentioned above could be considered as potential biopsychosocial pathways for the development of NES. Furthermore, the authors acknowledge that the variables contributed to each of these models may overlap and that this is not an exhaustive list of known causations, but rather an attempt to categorise and review the most commonly researched ideas. However, as suggested in this literature review at several points, the variables thought to be important in the development of NES do not occur in isolation and are known to interact with each other.

Chapter 2. Rationale

To demonstrate that impaired sleep could be considered a common factor irrespective of how the development of NES is theorised, we have deliberately adopted a dualistic approach in reviewing the research in NES, which is depicted in Figure 1. We hope that this will show that because impaired sleep has been linked extensively to all the suspected caused of NES, that sleep is likely to be an important factor in NES, irrespective of the model used to explain its development.

Sleep appears to be clinically meaningful and found to be related to functional impairment and mood and sleep interventions such as CBT-I have been found to be effective in improving sleep, mood and quality of life in neuropsychiatric and chronic conditions (Hingray et al., 2016). The extensive research in the relationship between epilepsy and sleep further implies that identifying and addressing sleep difficulties in epilepsy, could reduce seizure frequency (Malow, 2004; Accardo & Malow, 2015). This would indicate that it would be useful to investigate if sleep impacts on seizure frequency and if so, it stands to reason that a sleep intervention could possibly be tested to reduce seizure frequency in NES too. Furthermore, there are currently no agreed standard treatments for NES (Martlew et al., 2007; Smith, 2014). If sleep appears to be an important factor in NES then, as CBT-I has been found to effectively improve sleep (Manber et al., 2014), a next step would be to trial this intervention as a means to improve outcomes in NES.

Figure 1. Proposed Summary Model for Variable Interaction by Graham, 2019



2.1 Current understanding of Sleep in NES

During the time in which this project was designed, research into sleep in NES had been limited to only two published studies. One, a cross-sectional study measuring subjective sleep (Graham & Kyle, 2017) and the other, a very small cross-sectional study (Bazil, Legros & Kenny, 2003) with no information on how sleep impacts on other clinically important factors in NES, such as dissociation, mood or seizures. Since then, four more papers have been published looking at sleep in NES. Two of these were cross-sectional, trait level questionnaire studies that found that people with NES subjectively report poorer sleep disturbances (Latreille et al., 2018; Erickson et al., 2019). One used PSG and showed that people with NES have greater

period limb movement than people with epilepsy (Popkirov, Stone & Derry, 2018). The final study used subjective and objective measures of sleep comparing NES and ES samples and suggest that both groups have similar sleep structure but that those with NES were more likely to subjective report poorer sleep (Latreille et al., 2019).

Our study therefore aimed to address the gaps in these recent studies in sleep in NES. Firstly, it is important to measure both subjective and objective measures of sleep in NES as it is important to know whether sleep disturbances experienced are as a result of a sleep misperception. Moreover, subjective measures alone are unable to tell us anything about the characterisation of sleep in NES and studies that have included both subjective and objectives of sleep did not control for known sleep disorders ((Latreille et al., 2019). Secondly, current studies of sleep in NES have compared this sample to those with epilepsy, failing to account for well documented understanding of disturbed sleep as a feature of epilepsy (Derry & Duncan, 2013). Our study has therefore used both subjective and objective measures of sleep, compared a NES sample to a control sample and sought to exclude participants with known sleep problems and epilepsy.

Furthermore, research suggests that poor sleep is linked to increased dissociation and impaired mood (van Heugten-van der Kloet, Giesbrecht, & Merckelbach, 2015), which have both been found to be an important part of the process of seizures in NES (Hingray et al., 2016). It is therefore unsurprising that recent studies in sleep in NES have hypothesised that dissociation may be a key factor in impaired sleep in this condition and suggest that further studies should focus on investigating the link

between sleep, dissociation and NES (Graham & Kyle, 2017; Popkirov et al., 2018). We therefore wanted to also explore whether sleep affected next day dissociation, mood and seizures as previous studies have not addressed these issues.

2.2. Research Aim & Objectives

To characterise sleep in NES, in terms of daily sleep behaviours, subjective and objectively measured sleep (see Figure 2).

2.2.1. Objectives

1. To assess whether people with NES appear to experience subjectively or objectively measured worse sleep than people without NES.

   We hypothesise people with NES will experience subjectively and objectively greater sleep impairment. We also hypothesise that those with NES will report a greater misperception between subjectively and objectively measured sleep.

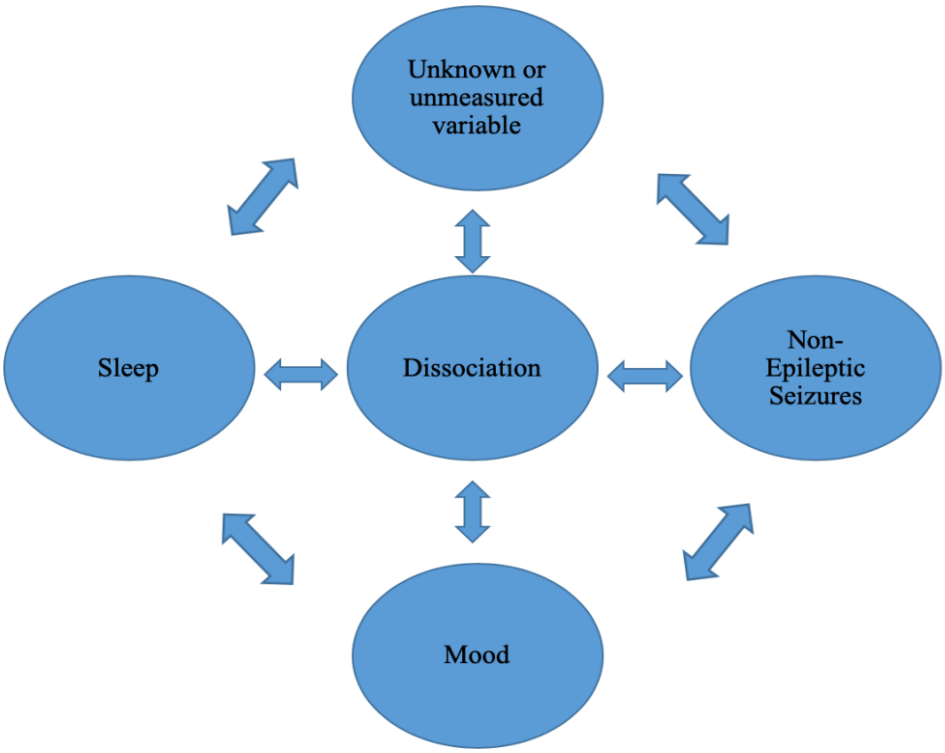
2. To prospectively investigate whether subjectively or objectively poorer sleep leads to higher levels of dissociation and lower mood on the next day.

   We hypothesise that impaired sleep the preceding night will lead to poorer functioning the following day for both our NES and our control samples.

3. If possible, to assess whether seizures occur more often on days following poor sleep, as opposed to days following better sleep in people with NES.

   We hypothesise that people with NES who experience impaired sleep the preceding night will have more seizures the following day.

Figure 2. Proposed Sleep, Mood, Dissociation & Seizure Model



Chapter 3. Methods

3.1 Design

This was a prospective, comparison study of subjectively and objectively measured daily sleep variables in a cohort of people with NES and a control group without seizure disorders. We have chosen this design in order to meet the current gap in research while attempting to account for the limitations acknowledged by other studies.

3.2. Sample

Clinical Sample

For this study, we aimed to recruit individuals with a formal diagnosis of NES or NEAD from NHS services at the Leeds Teaching Trust, Sheffield Teaching Trust and Mid York Trust. To minimise the chances of recruiting individuals who may experience epileptic seizures but for whatever reason have not received a diagnosis of epilepsy, we only recruited individuals whose formal diagnosis had been made by a neurologist (see Table 1). Additionally, for more accurate sleep outcome measures, we excluded anyone with a known sleep disorder or chronic sleep problems.

Individuals with dual diagnoses of NES and ES were excluded in this study as it is not always possible to distinguish between the different seizures. This would further not have allowed us to observe any possible links between sleep and the occurrence of non-epileptic seizures. We further excluded anyone reporting a risk of significant self-harm or suicidality as sensitive questions may be harmful or increase risks.

Table 1. NES Sample Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Diagnosis of NES or NEAD made by a neurologist	Dual Diagnosis of NES/NEAD and Epilepsy
Under the treatment of a recruitment centre	Individuals with known sleep disorders.
Able to wear an Actiwatch for a week	Inability to speak and/or read English
Between 18 and 70 years of age	Reporting risk of self-harm or suicide
Able to complete questionnaires either on paper or electronically	Any physical or intellectual disability that would hinder their ability to give consent or to participate

Control Sample

The participants for the control group were recruited from non-NHS settings, namely the University of Leeds participant database. This database consists mainly of University staff and students and other local volunteers who have chosen to be part of the pool of research volunteers. Similar to our clinical sample, we excluded participants with known sleep disorders or chronic sleep problems and anyone who reported risk to themselves (see Table 2).

Table 2. Control Sample Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Able to wear an Actiwatch for a week	Diagnosis of any seizure or sleep disorders
Between 18 and 70 years of age	Inability to speak and/or read English
Able to complete questionnaires either on paper or electronically	Reporting risk of self-harm or suicide
	Any physical or intellectual disability that would hinder their ability to give consent or to participate

3.3 Sample Size

We aimed to recruit *N*=25 individuals with NES and *N*=25 individuals without seizure disorders for our control group. Based on effect sizes from previously published research (Graham & Kyle, 2017), this sample size would allow us to investigate medium to large differences in sleep outcomes between those with NES and those without. The sample size further enabled us to investigate medium to large correlations between outcomes within our NES group.

3.4. Materials

Data was collected in two stages and included several questionnaires recording sleep, mood, and dissociation, as well as recorded objective sleep parameters. In the first stage, participants completed a one-off battery of questionnaires, and in the second, they completed short daily measures and diaries. The measures and equipment used in this study are described below.

3.4.1. Baseline Measures

Demographic information

Participants were asked for their gender, age, ethnic background, the status of employment, whether they experienced seizures, and how many they experienced in an average month. This provided some basic background of our participants without compromising their anonymity.

Pittsburgh Sleep Quality Index (PSQI)

The PSQI (Buysse et al., 1999) is the most widely used psychometric measure of the quality of sleep (Lee, 2016). It has been used in studies for a variety of physical and mental health conditions and has been widely translated for cross-cultural use (Smith & Wegener, 2003). The PSQI measures sleep over a month and includes items assessing sleep efficiency, perceived sleep quality and daily disturbances (Cole et al., 2006). The PSQI consists of 19 items answered in both free text and four frequency options;

- Not during the past month (scored as 0)
- Less than once a week (scored as 1)
- Once or twice a week (scored as 2)
- Three or more times a week (scored as 3)

The PSQI measures sleep over seven domains; sleep latency (SL), total sleep time (TST), wakefulness after onset of sleep (WASO), sleep efficacy (SE), sleep disturbances (awakenings) and day-time functioning.

Dissociative Experience Scale-II (DES-II)

The DES-II (Carlson & Putnam, 1993) is an updated version of the DES (Bernstein & Putnam, 1986) and is a trait measure of dissociation rather than a state measure. It contains 28 questions about dissociative experiences measured on a scale of 0 to 100% and contains three sub-scales: amnesia, depersonalisation/derealisation and absorption. Essentially, the DES-II is the same as the DES but has a simplified scoring procedure and provides the average DES scores for a range of psychiatric conditions for comparison purposes. The DES-II further distinguishes between low and high scores by using a score of 30 or above to indicate high levels of dissociation.

Generalised Anxiety Disorder 7 (GAD7)

The GAD7 (Spitzer, Kroenke, Williams, & Löwe, 2006) is a questionnaire measuring the severity of anxiety. The GAD7 is widely used in outpatient and therapy services. The scale asks about symptoms that may have occurred in the last two weeks and consists of 7 questions that can be answered using four levels of frequencies:

- Not at all (score of 0)
- Several days (score of 1)

- More than half the days (score of 2)
- Nearly every day (score of 3)

The GAD7 is scored by adding up all of the scores and using the total scores as an indication of the level of anxiety individuals report. A total score of 5 suggests low levels of anxiety, a total score of 10 suggests moderate anxiety and a score of 15 and above indicates severe anxiety. When using the threshold of a total score of 10, the GAD7 has been found to have an 89% sensitivity of detecting anxiety (Kroenke et al., 2007).

The Patient Health Questionnaire 9 (PHQ 9)

The PHQ-9 (Kroenke, Spitzer & Williams, 2001) is used to monitor the severity of depressive symptoms. The PHQ-9 is widely used in outpatient and therapy services as well as in medical services to assess depression alongside physical conditions. The scale consists of 9 questions which are derived from the DSM-IV criteria of depression; however, the scale is not used as a diagnostic instrument. Like the GAD7, the PHQ-9 asks about symptoms in the past two weeks using four levels of frequencies;

- Not at all (score of 0)
- Several days (score of 1)
- More than half the days (score of 2)
- Nearly every day (score of 3)

The PHQ-9 is scored by adding up all of the scores and using the total scores as an indication of how much depressive symptoms individuals report. The cut-off scores for mild, moderate and severe are the same as they are for the GAD7. Furthermore, when using the threshold of a total score of 10 or above, the PHQ-9 has been found to have an 88% sensitivity of detecting depression (Kroenke, Spitzer & Williams, 2001).

Seizure frequency

Participants with NES were also asked to report the number of seizures they experienced over the past month.

The initial battery of questionnaires was collected and stored on Online Surveys (previously Bristol Online Surveys). This data is anonymous, and Online Surveys automatically assigned each participant a number, which was then be used to link data with the actigraphy and daily measures completed by each participant. This data was linked to demographic information, but these did not contain any identifiable or personal data.

3.4.2. Daily Measures

Actigraphy

The gold standard objective measure of sleep is PSG, which measures several physiological processes in order to get detailed results about sleep experiences. PSG is often used to diagnose sleep disorders but is expensive to use and difficult to

access. It has, therefore, been suggested that actigraphy measures such as the Actiwatch might be the next best objective measure of sleep for research purposes (Lee, 2016). The Actiwatch is a wrist-worn activity monitor that measures levels of activity, wakefulness and sleep by continuously capturing the level of movement and body position to indicate physical activity and waking and sleep cycles. While the Actiwatch does not provide details on sleep stages, it is considered a valid and useful tool in the measurement of objective total sleep time and the wakefulness after the onset of sleep in clinical populations (Marino et al., 2013). For this study, we used the ActiGraph wGT3X-BT Actiwatch. The data collected from the Actiwatch was stored on the software provided by the makers of Actiwatch, Actigraph. This software is called ActiLife (version 6), which is used to both store and analyse the data collected from the Actiwatch. Actigraph will not have access to any of the data collected, stored and analysed on their software during this study.

Consensus Sleep Diary (CSD)

The CSD was developed by insomnia experts and service users (Carney et al., 2012) in an attempt to create a standardised sleep diary. It is a standardised dairy that collects data on time gone to bed, the onset of sleep, total sleep time, sleep disturbed, total time awake due to disturbances, wakefulness after sleep and perceived quality of sleep. It further notes activities such as naps during the day, the number of caffeinated drinks and medication. The CSD has previously been used alongside the PSQI and actigraphy (Landry, Best & Liu-Ambrose, 2015) and was found to correlate effectively with actigraphy (Grandner et al., 2006). Finally, the CSD tracks sleep over a week, matching the period we are collecting daily measures for.

Daily measure of Dissociation

To our knowledge, there are currently no short, daily scales that measure dissociation. We, therefore, developed a short measure using relevant items from existing measures. We used four items from the State Scale of Dissociation (SSD) developed by Krüger & Mace in 2002. This 56-item scale measures states of depersonalisation, derealisation, identity, confusion, identity alteration, amnesia and hypermnesia and was validated against the Dissociation Experience Scale (Bernstein & Putnam, 1986). The items are measured from "*Not at all*" to "*Very much so*". Based on clinical experiences, we selected two depersonalisation and two derealisation items with good face validity and changed the wording to measure the state of dissociation daily as opposed to momentarily:

- "Today, things around me seemed unreal or dreamlike."
- "Things around me looked different today, from the way they usually do."
- "Today, my body has felt vague, indefinite, strange."
- "Today, my body seemed disconnected from my thoughts, my feelings, myself"

Daily measure of Mood

The international short-form measure for positive and negative affect (I-PANAS-SF, Thomson, 2007) measures daily mood. It consists of 10 items, measuring across five negative affects (upset, hostile, ashamed, nervous and afraid) and five positive affects (alert, inspired, determined, attentive and active). The measure asks, "Thinking about yourself and how you normally feel, to what extent do you

generally feel [item],” on a 5-point scale from “never” to “always”. The I-PANAS-SF has been used as a daily measure of mood (Brogan & Hevey, 2013) and modified to ask, “indicate to what extent you felt this way during the day today”, on a 10-point scale from “very little” to “very much” (Lacaille, Sadikaj, Nishioka, Flanders & Knäuper, 2015). For continuity between the daily measures in our study, the wording of the first point-scale to was changed to “not at all” and the last point-scale to “very much so”.

Daily Seizure Record

NES participants were asked to note the number of seizures they have experienced that day.

The data collected from the daily scale for dissociation and mood, as well as the frequency of seizures experiences, were stored and managed using the SPSS programme. This database is anonymous, and participants are distinguished by the participants' number allocated to them by Online Surveys when they first partake.

3.5. Study procedure

3.5.1. NES Sample

All potential participants were approached by their clinicians in routine appointments. Clinicians informed potential participants about the study by giving suitable patients a letter of invitation and a participant’s information sheet. The letter of invitation informed potential participants that they could indicate their interest to

partake by informing their clinicians. After this, their names were passed on to me, and I contacted them within two weeks. I was in regular contact with the recruitment centres to be informed about potential participants. Once I was given the names and telephone numbers of individuals who expressed an interest in partaking, these were kept in the Study File at the recruitment centre.

Potential participants were contacted at least 24 hours after receiving the participant's information sheet. When interest in partaking was confirmed over the telephone, myself and potential participant agreed on a time and date to meet at the participant's local hospital. The I did not store this personal information, and all telephone calls were made from the admin offices of the site where the participant was approached. All participants were contacted within two weeks of receiving the participant's information sheet.

3.5.2. Control Sample

All our control participants were recruited from the University of Leeds's pool of volunteers' mailing list. A recruitment email was sent to the mailing list, outlining the study and how participants could contact the researcher to express an interest in participating. In an attempt to match the demographics of our prospective NES population, in the first instance, we sought out female participants over the age of 25, in line with the findings that NES was more likely to be diagnosed from the 20s onwards (Ettinger et al., 1999). To ensure that our sample would include a wide range of ages, including older adults, we also recruited from the University of Leeds's pool of older adults' panel for volunteer research participants over the age of

60. I was given access to this panel and contacted six individuals from this panel by email, one of whom agreed to take part.

3.5.3. Stage 1

The first stage of the study, the pre-participation meeting occurred in the participant's local health centre and lasted from 30 to 60 minutes per participant. I first sought to confirm the participant's interest in partaking and ensured that all participants understood what was being asked of them. I then confirmed with all participants that they met the inclusion criteria and whether any of the exclusion criteria applied to them. Participants were then asked to read the consent form and sign this to indicate their understanding of participation and their rights as a volunteer in this study.

Participants were then asked the completed the pre-participation battery of questionnaires (PSQI, GAD7, PHQ9, DES-II and demographic information). Most of the participants completed this electronically; however, some participants struggled to do so and requested to do this on paper instead. Upon completion of this, participants were talked through the second stage of this study, which they were to complete at home. I then set up the Actiwatch and demonstrated to participants how to use it. Participants were also shown the sleep diary and the dissociation and mood scale and given instructions on how to complete this over the next week. Participants were then offered a date and time to meet for a half an hour post-participation meeting. Finally, all participants were given my contact details as the CI in case they needed any support

3.5.4. Stage 2

During the second stage of this study, participants were asked to wear the Actiwatch continuously and only to remove this temporarily when they are taking a shower. Participants were also asked to complete a sleep diary upon waking and the dissociation and the mood scales before going to bed. Participants were further asked to note down the number of seizures they have experienced that day. Participants were encouraged to put reminders on their phone to complete their daily measures or to keep their folder next to their beds as a reminder to complete these. However, I did not keep a record of whether participants did either of these things.

3.5.6. Stage 3

In the final stage of the study, participants were asked to attend a half hour post-participation meeting in which they returned the Actiwatch and the completed diaries and questionnaires. All participants were asked about their experiences of taking part in the research and whether there were any difficulties or issues they encountered. I informed the participants that an anonymised summary of the overall results will be shared with each recruitment centre and that they would be able to request access to this from their healthcare teams. All participants were then thanked for their participation and reimbursed for their travel costs with a £25 Love to Shop Voucher as standardly offered by the University of Leeds.

3.6. Ethical Considerations

3.6.1. Ethical Approval

For this study, we sought ethical approval from both the HRA and NHS England

and the University of Leeds. We chose to seek ethical approval separately for our two groups as we anticipated that the ethical approval for our clinical sample might take some time and therefore intended to recruit our control sample while ethical approval was in process. Seeking approval separately enabled us to start the study before individual trust's approvals were in place, therefore avoiding a delay in the start of recruitment.

Ethical approval for this study was granted from the NHS Research Ethics Committee (**IRAS project number: 239312**) on 12th of September 2018 and from the Ethics committee at The School of Psychology at the University of Leeds (**PSC-431**) on the 18th of September 2018.

3.6.2. Risk Management

There was the possibility that some participants might have found it distressing to complete questionnaires about their mood, in particular, one of the questions on the PHQ-9 that asks about thoughts concerning self-harm and suicide. Participants were told at the start that while the content of their contact with me was confidential, that if they share anything that indicates a risk to themselves or others, that their healthcare team would be informed. Furthermore, these initial questionnaires were completed on a tablet in the presence of myself and care was taken to not include sensitive questions in the daily measures completed by participants in their homes.

For this study, we also produced a risk management plan if a significant risk to self or others was identified. In this, we outlined that we could take several possible

courses of action. For participants who were not currently under the care of a psychology or psychotherapy team, they would be signposted to their GP. For participants who indicate that they are at immediate risk of harm, local safeguarding leads would be contacted by myself for further guidance and advice. A copy of the risk protocol was kept in the Study File at all times.

3.6.3. Data protection & Confidentiality

Personal data, in particular, names and phone numbers were used to contact participants to set a date and time for the pre-participation meetings. This data was then recorded on a paper sheet which was kept in the Study File, in a locked drawer at the recruitment centre. This data was not collected for any other purposes than contact and was only accessed at the study site to make telephone contact with the participants. All signed consent forms were also kept in the Study File, and upon completion, these were scanned into a password protected secure drive on University computers and not linked to the data collected in any way. The paper copies of the consent forms were shredded. The University Information Protection Policy and the DClinPsychol Policy on Safeguarding Sensitive Data was followed.

3.7. Recruitment Barriers

Several barriers made the process of recruitment more challenging than initially expected. Firstly, due to loss off access to intended funding, our recruitment samples had to be reduced to *N*=20 in each group. Secondly, while ethical approval had been given by the HRA and NHS England, in September 2018, the individual trust

approvals took a further four months. Recruitment of the clinical sample, therefore, began in January 2019.

Thirdly, we did not account for a large number of individuals with NES, who also experienced a brain injury (Westbrook, Devinsky & Geocadin, 1998). As brain injuries are linked to sleep difficulties (Castriotta & Murthy, 2011) and memory difficulties (Smith, Okiyama, Thomas, Claussen & McIntosh, 1991), we decided that this would not give us an accurate reflection of sleep and have therefore decided not to include anyone with a history of brain injury in this study. However, in doing so, we limited the pool of potential participants. Similarly, I had failed to account for other physical and emotional difficulties that would not allow participants to complete the pre-participation meeting in half an hour. There were also times during recruitment in which participants experiences seizures, further increasing the time it took to complete the initial meetings.

Fourthly, many participants required hospital transport to attend hospital appointments and were unable to attend the research meetings without transport arrangements. As we were unable to meet these needs financially and to avoid any costs to the recruitment trusts, participants unable to attend these meetings were unfortunately not able to participate. Finally, many of the participants contacted expressed an interest to be seen either before or after their routine appointments such as therapy sessions. However, this was difficult to facilitate due to time and room access limitations.

3.8. Data Analysis

The data collected from the Actiwatch was processed using the ActiLife software, which establishes the levels of activity and sleep of the duration participants wear the Actiwatch. The ActiLife software requires information about time gone to bed and time out of bed from the sleep diary to produce Actigraphy output (see Appendix 8.4.1), which was then added to the data comprising sleep, dissociation, mood and seizure frequency outcomes and analysed using SPSS. We used independent sample T-Tests with Bonferroni Corrections to explore whether there is a difference in these measures between those with NES and the control group. We further planned to explore whether there is a relationship between the measures of sleep, dissociation, mood and seizure frequency by multi-level modelling. As SPSS is not considered the most effective software for multi-level modelling (Sommet & Morselli, 2017), we used R to explore whether seizure occurrence was linked to the impaired sleep the night before using a mixed effects logistic model. We also used a mixed linear effect model to assess whether next day dissociation and negative mood was affected by sleep the night before.

3.9 Max Hamilton Fund

I received £200 from the Max Hamilton Fund at the University of Leeds to supplement my research budget as I no longer had access to intended additional funding agreed to reimburse my participants. As we did not meet our planned sample number for the NES group, £75 of this money was returned to the Fund.

Chapter 4. Results

4.1 Sample Demographics

In total, 20 control participants and 17 NES participants completed the study. I initially recruited 27 NES participants, however, nine were unable to partake as either their physical or emotional wellbeing had deteriorated, and one participant did not attend. All 17 NES participants were recruited from the Sheffield Teaching Hospitals site. Both groups had similar age ranges and gender distributions. The ethnicity of the participants differed somewhat across the group as the control group included four participants that identified as black, Asian or of mixed heritage. In relation to the employment, only 33% of NES participants were employed full-time, compared to 70% of the control group. However, there were more people in the NES group that worked part-time (11.8%) when compared to those in the control group (5%; Table 1). Finally, 76.5% of our NES sample was either currently undergoing psychotherapy or had completed psychotherapy within a month of participation.

Table 3. Sample Demographics

	CONTROL (*N*=20)	**NES (*N*=17)**
MEAN AGE (STANDARD DEVIATION)	38.3 (11.9)	38.6 (16.2)
GENDER FEMALE (%)	75	76.5
ETHNICITY WHITE BRITISH (%)	75	94.1
EMPLOYMENT (FULL-TIME %)	70	35.3
(PART-TIME %)	5	11.8
(RETIRED %)	-	5.9

4.2 Baseline outcomes

Outcomes measured at baseline were compared using an independent sample t-test with a Bonferroni Correction of $p \leq 0.01$. This showed that there are significant differences between the groups on all measured trait properties; sleep, dissociation, anxiety and depression (see Table 3).

The PSQI is scored using a global score between 0 (no sleep difficulties) and 21 (severe sleep difficulties) without suggested cut-off points. On average, those in the NES group reported significantly poorer overall sleep; t (26.7) =6.8, $p \leq 0.001$ and with a large effect size, r = .80, when compared to the control group.

The DES-II scale used a cut-off point of 30 to distinguish between low and high levels of dissociation, with a suggestion that the average score for the general population is 5.4. Those in the NES group reported significantly higher levels of dissociation than those in the control group; t (20.2) = 4.7, $p \leq 0.001$ and represented a large effect size, r = .72. The results further show that both groups experience much higher dissociation than authors of the scale indicate as cut-off points for different psychiatric diagnoses.

The GAD7 cut-off points are 5 for mild, 10 for moderate and 15 for severe anxiety experienced. Our results show that the NES group scored an average between the moderate and severe anxiety whereas the control group, as expected scored below

the cut-off point for mild anxiety. The difference between the groups was statically significant; t (21.5) = 5.4, $p \leq 0.001$ and represented a large effect size, r = .76.

The PHQ-9 cut-off points are 5 for mild, 10 for moderate, 15 for moderately severe and 20 for severe depression. As shown in Table 2 the NES participants scored close to moderately severe depression whereas the control group scored below the cut-off point for mild depression. The difference between the groups was large and statistically significant; t (22.5) = 7.2, $p \leq 0.001$. Furthermore, the number of seizures experiences by the NES group ranged from 0 (less than 1 a month) to 150 seizures a month, with an average of 2.4 seizures a month.

Table 4. Mean & Standard Deviations of Baseline Outcomes

	CONTROL (*N*=20)	**NES (*N*=17)**	**DIFFERENCE**
PSQI	4.5 (2.8)	12.8 (4.4)	*p = 0.000 (r = 0.80)* **
DES-II	23.9 (20.3)	86.6 (51.5)	*p = 0.000 (r = 0.72)* **
GAD7	3.7 (2.9)	12.7 (6.4)	*p = 0.000 (r = 0.76)* **
PHQ-9	3.2 (3)	14.9 (6.1)	*p = 0.000 (r = 0.84)* **
SEIZURE FREQUENCY	-	21.4 (38.2)	

** $p \leq 0.001$

On the PSQI, the NES group reported getting significantly more sleep disturbances, less sleep, poorer quality sleep and worse daytime functioning than the control group., However, there did not appear to be a significant difference between the groups in the use of sleep medication (see Table 5).

Table 5. Baseline PSQI Sleep Components

	CONTROL (*N*=20)	**NES** (*N*=17)	**DIFFERENCE**
QUALITY	.65 (.59)	2 (.90)	*p =0.000 (r = .73)* **
LATENCY	.70 (1)	2.53 (80)	*p =0.000 (r = .72)* **
DURATION	.30 (.57)	2.13 (1.26)	*p =0.000 (r = .77)* **
EFFENCIENCY	55 (.76)	2.19 (1.11)	*p =0.000 (r = .71)* **
DISTURBANCE	1.21 (.54)	1.88 (.78)	*p =0.006 (r = .49)* *
MEDICATION	.10 (.45)	.47 (1)	*p =.175 (r = .29)*
DAY-TIME FUNCTION	1 (.65)	1.82 (.88)	*p =0.003 (r = .51)* *

* $p \leq 0.01$, ** $p \leq 0.001$

4.3 Objectives

4.3.1 To assess whether people with NES appear to experience subjectively or objectively measured worse sleep than people without NES.

Hypothesis 1: People with NES will report greater subjective sleep impairment

The averages of each group's subjective measures of sleep collected from the sleep diaries and were analysed using an independent samples t-test with Bonferroni

correction of $p = 0.01$. There were no significant differences in:

- Sleep Latency (SL) Time between trying to sleep and falling asleep.
- Sleep Efficiency (SE) The percentage of actual sleep out of the total time in bed.
- Total Time in Bed (TIB) Time between getting into bed and getting out of bed.
- Total Sleep Time (TST) Total time of actual sleep.
- Wakefulness After Onset of Sleep (WASO) Time spend awake after sleep onset
- The number of awakenings during sleep.

There was, however, a significant difference in Sleep Quality (SQ), which refers to the subjective perceptions of the overall quality of sleep and is measured on scaled scores of 0 (very good), 1 (good), 2 (fair), 3 (poor) and 4 (very poor). The NES group reported significantly poorer SQ than the control group; t (33.2) = - 4.2, $p \leq$ 0.001, with a large effect size of $r = .57$. The SQ was the only statically significant difference across all sleep domains between the two groups.

Hypothesis 2: People with NES will experience greater objective sleep impairment

Objective measures of sleep were collected by the Actiwatch and analysed using the ActiLife software. The Actiwatch must be used with a sleep diary as the software requires a time gone to bed and a time out of bed in order to compute the sleep properties. The software then produces an actigraphy output for each day and measured data for SL, SE, TST, WASO and Awakenings (see Appendix 8.4.1.).

This data was then further analysed using an independent samples t-tests, with a Bonferroni Correction of $p = 0.01$.

There were no significant differences between the two groups in objectively measures SL, TIB and TST. The NES group experienced significantly more WASO than the control group; t (23.5) = 3.7, $p \leq 0.001$ and represented a large effect size, $r = .60$. The NES participants experienced almost twice as much objectively measured WASO than the control group (see Table 6).

The NES group also experienced significantly less SE than the control group; t (24.9) = -3.7, $p \leq 0.001$ and represented a large effect size, $r = 60$. The PSQI suggests that SE below 85% indicates difficulties with sleep and our results show that both groups scored below this threshold with subjectively measured SE, however the control group this meet this threshold with objectively measured SE.

Furthermore, the NES group experienced significantly more awakenings during sleep when compared to the control group; t (34.6) = 3.8, $p \leq 0.001$, with a large effect size, $r = .51$.

Table 6. Subjective & Objective Outcomes of Daily Sleep

	SUB CONTROL (*N*=20)	**SUB NES** (*N*=17)	**SUB DIFFERENCE**	**OB CONTROL** (*N*=15)	**OB NES** (*N*=17)	**OB DIFFERENCE**
SL (MINS)	15. 3 (11.3)	51.3 (58.5)	*p =0.023 (r=.52)*	13.4 (10.2)	14.7 (23.3)	*p = 0.836 (r=.04)*
SE (%)	81.6 (9.9)	71.8 (14.7)	*p = 0.027 (r=.41)*	86.4 (4.4)	77.8 (8.4)	*p = 0.001 (r=.60)* **
TIB (MINS)	533.1 (53.4)	564.6 (114)	*p = 0.308 (r= .22)*	537.3 (61.7)	565.3 (112.3)	*p = 0.384 (r= .17)*
TST (MINS)	433.2 (57)	399.5 (105.6)	*p = 0.250 (r= .24)*	462.5 (47.9)	429 (59.2)	*p = 0.087 (r=.31)*
WASO (MINS)	99.9 (56.8)	165.1 (104.3)	*p = 0.030 (r= .43)*	61.4 (28.6)	121.6 (60.6)	*p = 0.001 (r= .60)* **
AWAKENINGS (FREQUENCY)	1.5 (.86)	2.7 (2.1)	*p = 0.042 (r=.43)*	11.8 (7.6)	21.2 (7.2)	*p = 0.000 (r=.55)* **
SQ (0-4)	1.3 (.72)	2.3 (.77)	*p = 0.000 (r=.57)* **	-	-	-

* $p \leq 0.01$, ** $p \leq 0.001$

Hypothesis 3: People with NES will show greater misperception of sleep

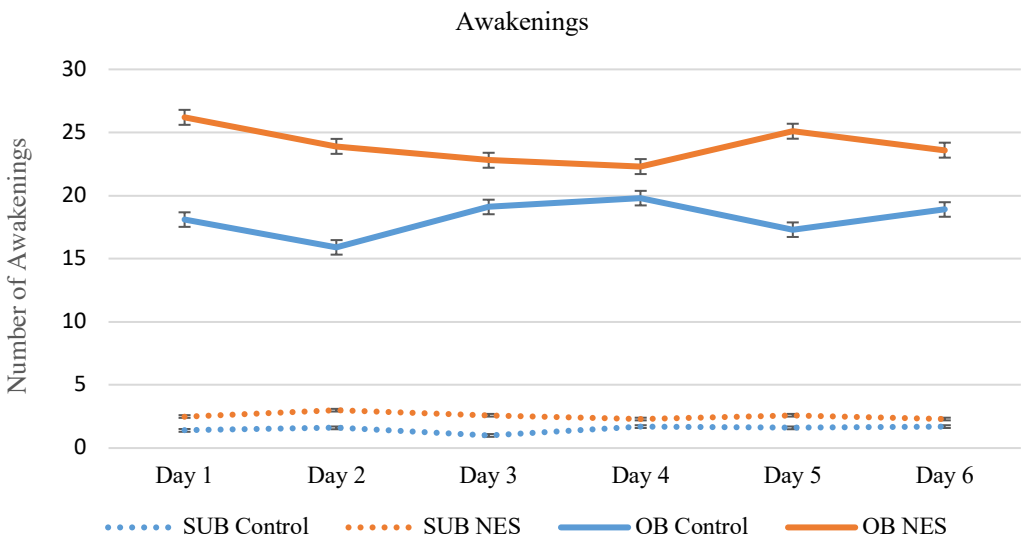
An independent samples t-test with a Bonferroni correction of $p = 0.01$ was conducted to assess a difference between the groups in the misperception, or the gap between their subjective and objective measures of sleep. The outcomes show that there were no significant differences between the two groups' misperception across all the sleep domains (see Table 7).

Table 7. The Misperception between Subjective & Objective Outcomes of Sleep

	CONTROL (*N*= 15)	NES (*N*=17)	DIFFERENCE
SL (MINS)	.10 (16.2)	36. 6 (66)	*p = 0.040 (r = .46)*
SE (%)	3.3 (8,6)	6 (14.5)	*p = 0.532 (r = .12)*
TIB (MINS)	.54 (4.1)	.68 (7.9)	*p = 0.953 (r = .01)*
TST (MINS)	18.3 (46.4)	29.4 (92.1)	*p = 0.664 (r = .08)*
WASO (MINS)	31.2 (46.4)	43.5 (85.6)	*p = 0.612 (r = .10)*
AWAKENINGS (FREQUENCY)	13.8 (5.2)	18.5 (5.9)	*p = 0.023 (r = .40)*

The results also show that both groups underestimated or under-reported the number of awakenings they experienced. In fact, both groups under-estimated their number of awakenings by 87.2% (see Figure 3).

Figure 3. Objective-Subjective Awakenings Misperception



4.3.2. To prospectively investigate whether subjectively or objectively poorer sleep leads to higher levels of dissociation and lower mood on the next day.

Hypothesis: Impaired sleep on preceding night, will lead to poorer next day mood and dissociation

Before I looked at the relationship between impaired sleep and functioning, I analysed the measures of mood and dissociation using an independent samples t-test with a Bonferroni correction of $p = 0.01$ (see Table 8). The results showed that the control group, on average experienced significantly more Positive Affect (PA) than the NES group; t (31.) = -2.9, $p \leq 0.01$ and represented a medium effect size of r = .46. Additionally, the NES group reported significantly more dissociation than the control group; t (18.8) = 6.9, $p \leq 0.001$ and represented a large effect size of r = .85. On average, the NES group experienced seizures daily (M = 1.1, SD = 1.7).

Table 8. Mood, Dissociation and Seizure Frequency outcomes.

	CONTROL (*N*=20)	**NES (*N*=17)**	**DIFFERENCE**
PA	28 (9.3)	18 (11.)	*p = 0.007 (r = .46)* *
NA	9.4 (4.3)	14.8 (9.4)	*p = 0.040 (r = .43)*
DISSOCIATION	1.2 (.48)	3.8 (1.5)	*p = 0.000 (r = .85)* **
SEIZURE FREQUENCY		1.1 (1.7)	

* $p \leq 0.01$, ** $p \leq 0.001$

As the results show that the NES sample presented with objectively poorer sleep across the sleep domains of SE, WASO and awakenings and reported higher levels of state dissociation, we aimed to further explore the relationships between sleep and next day dissociation. We fitted a mixed linear effect regression model to analyse the relationship between dissociation and preceding night's sleep, using the objective measures of SE, TST, WASO and awakenings. To select the most appropriate covariates, a LASSO regression model was fit to identify key variables, before refitting the model with no regularization (see Appendix 8.4.3.2). The resulting model found no strong association between SE and dissociation (*C*= 0.01; *CI* [-0.03, 0.05]; *p* = 0.573), between WASO and dissociation; (*C* = 0.0000684; *CI* [-0.005, 0.005]; *p* = 0.980) and between number of awakenings and dissociation (*C* = -0.03; *CI* [-0.068, 0.006]; *p* = 0.101).

The model did however show an association between having NES and experiencing dissociation; (*C* = 1.33; *CI* [0.52, 2.13]; *p* = 0.002) and that having dissociation on the preceding day was strongly associated with experiencing dissociation the following day; *(C*= 0.484; *CI* [0.283, 0.684]; *p* = 0.000). This model suggests that preceding night's sleep was not associated with next day dissociation. However, it does show that there is an association between having NES and next day dissociation and preceding day dissociation and next day dissociation. This suggests that those with NES were more likely to report high levels of dissociation. It also indicates that high levels of dissociation on the preceding day, was strongly associated with high levels of dissociation the next day.

Next, we fitted another mixed linear effect regression model to analyse the relationship between NA and preceding night's sleep, using the objective measures of SE, TST, WASO and awakenings (see Appendix 8.4.3.3). Like above, a LASSO regression model was fit to identify key variables before refitting the model with no regularization on the reduced set of variables. The regularisation strength was determined using a grid search aiming to minimize the Akaike Information Criterion (AIC). The resulting model found no strong association between we found no strong associations between TST and NA; (C = -0.0012543; CI [-0.0030, 0.0005]; p = 0.170). Following a LASSO analysis, the sleep variables of SE, WASO and awakenings were removed, suggesting no associations between these variables and NA. A Pearson Correlation was conducted afterwards to confirm that there were no detectable associations between the removed sleep variables and NA.

4.3.2. If possible, to assess whether seizures occur more often on days following poor sleep, as opposed to days following better sleep in people with NES

Hypothesis: Impaired sleep on preceding night, will lead to more seizures the next day

We fitted a multivariate mixed effects logistic regression model to analyse the relationship between seizures and preceding night's sleep, while controlling for dissociation and mood. The random effect is used to give individual patients unique intercepts which helps to control for the effect of any other patient characteristics effecting the outcome which were not collected within our data. Additionally, all continuous variables were normalised by the changing the means to 0 and the standard deviations to 1 before model fitting. To select the most appropriate

covariates, a LASSO regression model was fit to identify key variables, before refitting the model with no regularization on the reduced set of variables. The regularization strength was determined using a grid search aiming to minimize the AIC. The resulting model did not show any strong association between seizure frequency and WASO (OR = 1.65; CI [0.44, 6.23]; p = 0.460) and between seizure frequency and awakenings; (OR = 0.20; CI [0.98, 26.55]; p = 0.053) (see Appendix 8.4.3.2.).

Chapter 5. Discussion

I set out to assess whether people with NES appear to experience subjectively or objectively measured worse sleep than people without NES. I hypothesised that people with NES would experience subjectively and objectively greater sleep impairment and that they would report a greater misperception between subjectively and objectively measured sleep. I then explored whether preceding night's sleep would affect next day mood, dissociation and seizure frequency.

5.1. Do people with NES experience subjectively and objectively worse sleep?

5.1.1. Hypothesis: People with NES will report greater daily subjective sleep impairment

On average, the NES sample reported poorer outcomes on all sleep domains; however, this difference was only significant for SQ. This is in line with current findings from cross-sectional studies that those with functional symptoms such as NES are likely to report subjectively poor sleep (Graham & Kyle, 2017; Erickson et al., 2019). Moreover, it has been suggested that SQ is a better indicator of overall wellbeing than the actual amount of total sleep (Pilcher et al., 1997), which in turn is likely to be a reflection of the well-documented link between mood and sleep.

Furthermore, it has been found that mood, in particular depression is a better predictor of subjective SQ than PSG measured impaired sleep, even in the presence of sleep disorders such as Obstructive Sleep Apnoea (Wells, Day, Carney, Freedland & Duntley, 2004). This suggests that even though people with NES are thought to

perceive their difficulties as more disabling (Frances et al., 1999), that self-reported perception of sleep are equally important when exploring the impact of sleep on overall wellbeing. In fact, those who report a better SQ are also more likely to report their overall wellbeing and quality of life as better (Jean-Louis et al., 2000). Therefore, if we assume that subjective measures of sleep do not impact on functioning, we risk minimising sleep problems and in turn, might be less likely to offer interventions to improve sleep if sleep problems are not considered "real".

5.1.2. Hypothesis 2: People with NES will experience greater objective sleep impairment

The objective daily sleep outcomes showed that on average, those with NES experienced poorer sleep across all the sleep domains. These differences were significant, for three of the sleep domains in which the NES sample experienced more WASO and awakenings, and significantly less SE. This differs slightly from a similar study in which they found that those with NES did not experience objectively worse sleep on any other domain than SL (Latreille et al., 2019). That being said, this study compared the sleep in NES and epilepsy samples, and impaired sleep is a known feature in epilepsy (Derry & Duncan, 2013). Furthermore, high frequency of awakenings (Taylor, Lichstein, Durrence, Reidel & Bush, 2005) and poorer sleep efficiency as a result of excessive nocturnal wakefulness (Hein, Lanquart, Loas, Hubain & Linkowski, 2017) have previously been considered to characterise sleep problems in depression. This suggests that those with NES present with a similar sleep architecture those living with depression, as previously hypothesised (Bazil et al., 2003).

Furthermore, it is important to note that SE encompasses both WASO and awakenings as the overall variable indicating time not spend sleeping following the onset of sleep; therefore, WASO and awakenings are not independent of SE.

Theories into how people with NES perceive and process experiences generally imply that they were likely to over-estimate whether their sleep was impaired. However, our objectively measured sleep outcomes show that people with NES do spend more time awake after the onset of sleep and do experience a higher frequency of awakenings, therefore suggesting that those with NES do have actual poorer sleep. The number of objectively measured awakenings in the NES sample (21.2 ± 7.2) was comparable to a sample with co-occurring Obstructive Sleep Apnoea and Periodic Limb Movement Disorder (20 ± 20.26) (Kushina et al., 2001). This supports findings that people with NES experience more movement in their sleep (Popkirov, Stone & Derry, 2018) and may be experiencing disturbances comparable to those with diagnoses of sleep conditions.

Additionally, it is not uncommon for people with NES to report that they experience seizures during their sleep (Thacker et al., 1993; Duncan et al., 2004) and the higher frequency of awakenings or movements observed in our study may elude to nocturnal experiences of seizures. That being said, a study exploring nocturnal seizures in NES suggests that rather than seizures occurring in sleep, they appeared to occur in what is considered pseudo-sleep, i.e. may appear to be asleep but EEG measurement indicate evidence of wakefulness (Benbadis, Lancman, Wolf & Morris, 1997).

5.1.3. Hypothesis 3: People with NES will show greater misperception of sleep

I were particularly interested in whether there would be a difference between the two groups in the misperception of sleep, i.e. the gap between subjectively and objectively measured sleep. The results showed that on average, the NES group had a larger misperception across all measured sleep domains than the control group. However, none of these differences was significant. Interestingly, both groups under-estimated their number of awakenings by 87%, suggesting that both groups experienced more awakenings than they subjectively perceived.

It is important to note that while actigraphy has been considered the best objective measure of sleep in the absence of PSG (Lee, 2016) and suggested to be useful in the measurement of WASO and TST (Marino et al., 2013), it does in fact only measure movement and that it computes lack of movement as sleep. Additionally, actigraphy has been suggested to be less accurate when measuring sleep in samples with high levels of WASO (Paquet, Kawinska & Carrier, 2007), such as our NES sample. Furthermore, it has been previously found that actigraphy recorded awakenings were significantly more than self-reported awakenings (Lockley, Skene & Arendt 1999) and this is likely to be influenced by the differences between how awakenings are measured. For example, actigraphy awakenings are measured by movement as opposed to "being awake", whereas the participants are only able to report on awakenings while they were aware of being woken up. That being said, actigraphy awakenings are comparable to those measured by PSG (Lichstein et al., 2006) and therefore, perhaps a better indication of awakenings than the sleep diary. Furthermore, research may do well to further distinguish between movement while

sleeping and awakenings that include "being awake", to account for the large discrepancies between subjective and objectively measured awakenings.

Moreover, while I collected data on whether participants took medication specifically for sleep, I did not collect data on the use of anti-depressants, which are known to impact on sleep (Wilson & Argyropoulos, 2005). It is also important to acknowledge that the differences in sleep across seasons have been well-documented and findings suggest that we sleep more in the winter when compared to spring and summer (O'Connell, Griffiths, & Clemes, 2014). The control group was recruited between November and January and while the NES group was recruited between January and June and although the NES sample did not report less objective total sleep time, they did experience more sleep disturbances, which may have been influenced by seasonal impact on sleep.

5.2. Does subjectively or objectively measured impaired sleep lead to poorer functioning the following day?

5.2.1. Hypothesis: Impaired sleep on a preceding night, will lead to poorer next day mood and dissociation

Before exploring whether sleep had an impact on next day functioning, I first looked at the level of functioning, in this case, mood and dissociation, that was reported by the groups across the week. The results for the daily measures of mood and dissociation indicate that the control participants, on average, reported significantly more PA and significantly less dissociation than the NES sample. This is in line with

the baseline outcomes for mood and dissociation and therefore, as expected, suggests that trait properties of mood and dissociation can predict state mood and dissociation. These results support existing knowledge, as outlined above, that impaired mood (Mökleby et al., 2002; Prueter et al., 2002; Seneviratne et al., 2011) and higher levels of dissociation (Williams et al., 1993; Mazza et al., 2009; Van der Kruijs et al., 2011) are documented extensively in NES research.

To explore whether impaired sleep on a preceding night affects mood and dissociation on the following day, we fitted mixed-effects logistic regression using objective measures of SE, WASO and awakenings as the outcomes of these sleep domains suggested impaired sleep. We also added TST to account for whether this might also have an impact. We found no strong associations between these variables of sleep and dissociation and NA. This is likely to have been affected due to our sample being underpowered. Furthermore, following the LASSO analysis, all sleep variables apart from TST were removed for our NA model, we can, therefore, assume that there was no strong association between these measures of impaired sleep. This was further confirmed with a Pearson Correlation, which demonstrated no strong relationships between our variables of impaired sleep and NA.

Furthermore, as the LASSO analysis appeared to have successfully "pruned" out the variables with the least strength in association, we may have been underpowered in the length of the study rather than sample size. Nonetheless, causality between sleep and mood is known to be challenging to explore as mood has been found to predict future sleep problems, which in turn are likely to increase mood problems (Jansson-

Fröjmark & Lindblom, K. (2008). It has, therefore, been suggested that the relationship between sleep and mood should always be considered bi-directional (Alvaro, Roberts & Harris, 2013).

Furthermore, in line with current findings, we found that our NES sample experienced significantly more impaired sleep and significantly higher levels of dissociation across the study period (Giesbrecht & Merckelbach, 2004). However, we were unable to find a strong relationship between these variables. Instead, we found that NA on a preceding day was associated with less NA the day after, perhaps indicating a regression to the mean. We further found that levels of dissociation the preceding day were associated with dissociation the following day, suggesting that perhaps experiences of dissociation lasted longer than a day and instead were experienced for more extended periods. This was unexpected considering the research base showing an association between sleep and dissociation and findings that suggest that dissociation is worsened after impaired sleep (Van der Kloet et al., 2012).

That being said, our daily dissociation measure was not a standardised questionnaire as we were unable to find a state dissociation questionnaire that could be completed daily. Instead, based on clinical experience, we selected two depersonalisation and two derealisation items from the SSD (Krüger & Mace, 2002), which was validated against the DES. We chose not to include items that could be interpreted in several ways such as *"I am in a world of my own at the moment"* and those that could be influenced by many variables such as *"I am having difficulty taking in new*

information". We also avoided items that indicated experiences linked to DID such as *"Someone else is in control now"* and "*My inner voices are talking"*. However, it is possible that the daily dissociation outcomes might have been different had we chosen different items from the SSD. Furthermore, the daily dissociation outcomes from our control group show minimal experiences of dissociation, which is in contrast with the baseline outcomes of dissociation for the control participants.

5.3. Does impaired sleep on a preceding night, lead the more seizures the following day?

5.3.1. Hypothesis: Impaired sleep on a preceding night, will lead to more seizures the next day

In the NES sample, 15/17 participants regularly experienced at least one seizure a month and reported seizure frequency ranged from 1 to 34 seizures over six days. Our outcomes from the multivariate mixed-effects logistic regression model showed no strong associations between our objective measures of SE, WASO, TST and awakenings and seizure frequency. Nonetheless, there did appear to be a promising association between the number of awakenings in the preceding night and next day seizure frequency (OR = 0.20; CI [0.98, 26.55]; p = 0.053), suggesting that this association may have been stronger if our sample was not underpowered.

Nonetheless, mood and dissociation were controlled for mood in this model, which may have reduced the power of our sample and impacted whether any direct association could be identified between the sleep variables and seizure frequency.

Furthermore, as there is currently no research that addresses the direct link between sleep and seizure frequency, we are unable to draw any assumptions about this relationship. However, extensive research in the relationship between epilepsy and sleep does suggest that identifying and addressing sleep difficulties in epilepsy could reduce seizure frequency (Malow, 2004; Accardo & Malow, 2015). This indicates that the impact of sleep in seizures may be worth further exploration.

5.4 Sample demographics

The gender distribution in the NES participants (76.2 % females) are comparable the suggestive figures that 60-75% of NES sufferers are female (O'Sullivan, 2007; McKenzie, Russell, Pelosi & Duncan, 2010). This could be explained by the over-representation of women in traumatised populations, characterised by the high prevalence of gender-based violence and abuse, in the context of systemic oppression (Segalo, 2015). That being said, other research claims that women do not experience a higher prevalence of interpersonal traumatic experiences but rather that they appear to be twice as likely to be vulnerable in developing psychological difficulties following these experiences (Breslau, Chilcoat, Kessler, Peterson & Lucia, 1999).

Similarly, the mean age of the NES sample (38.6 ± 16.2) was comparable to that in a recent similar study looking into sleep in NES by Latreille and colleagues (2018) with a large (N=149) NES sample (38 ± 13.3). Moreover, in line with the majority of research in NES, many of the participants were of white ethnicity. However it is important to note that the majority of our clinical sample was recruited from a

psychotherapy service and people of ethnic minority groups are less likely to be referred to talking therapies (Rabiee & Smith, 2014), despite findings of high prevalence of NES in immigrants and refugees (Brickmann et al., 2018). Finally, many NES studies have found consistently that those in their samples reported low levels of employment and figures to suggest that less than half of those with NES are employed (Carton et al., 2003; Al Marzooqi et al., 2004; Karakis et al., 2014). In line with this, only 35.3% of the NES sample reported they were in full-time employment compared to 70% of the control sample. It is thoughts that unemployment in NES is linked to psychiatric comorbidity (McKenzie, Graham & Duncan, 2016) and may, therefore, continue to be a feature even when medically unexplained symptoms are accounted for.

5.5. Baseline Outcomes

5.5.1. Baseline Mood

The baseline mood outcomes suggest that the NES group report significantly more anxiety and depression and is in line with the current understanding that people with NES also experience anxiety and depression (Mökleby et al., 2002; Prueter et al., 2002; Seneviratne et al., 2011) and suggests our sample was comparable to other NES research samples. Nevertheless, like much of the research into mood in NES, our results are unable to show whether impaired mood precedes the development of NES or whether it develops as a result of living with NES.

However, 76.5% of our NES sample had either recently completed or was currently receiving a course of psychotherapy in a specialist NES Psychotherapy service,

which is likely to have influenced their mood outcomes. On the one hand, getting worse before “getting better” is a well-documented phenomenon in psychotherapy (Min & Yong, 2009; Joseph, Murphy & Regel, 2012; Owen et al., 2015) and this could have contributed to the high levels of anxiety and depression reported by our sample. On the other, there may also be the possibility that the mood outcomes in our study are "improved" and mood may even be more impaired in an NES population not accessing psychotherapy. Furthermore, I did not have access to the baseline mood outcomes for these participants collected routinely by the service and am, therefore, unable to draw any conclusions about the baseline mood outcomes in the NES sample. Additionally, our sample was too small to distinguish between the results of those in therapy and those who were not, without comprising participants’ anonymity.

In hindsight, I might have had a better understanding of mood in NES if I included measures to assess the transdiagnostic processes across impaired mood such as threat perception, unhelpful coping and likelihood to experience distress and emotions as more overwhelming. This might have told us more about the underlying processes that contributed to the development or maintenance of NES and might have better enabled us to theorise the psychological functioning of NES. However, our study was not conducted to understand the role of mood in NES; instead, it was specifically aimed at understanding sleep in NES and mood was measured to be able to account for this.

5.5.2. Baseline Dissociation

The baseline dissociation outcomes show that the NES group experienced significantly more trait dissociation than our control group as measured by the DES-II. This is in support of the extensive findings that dissociation is a crucial process in NES (Williams et al., 1993; Wood, McDaniel & Burchfiel, 1998; Meller, 2005). Surprisingly, while the control group's outcomes suggest that they experienced significantly less dissociation, their average scores (23.9 ± 20.3) are much higher than what the authors of the DES-II suggest is the average for the general population. The control sample scored higher than the suggested cut-off for eating disorders (15.8), schizophrenia (15.4) and BPD (19.2), (Coons et al., 1989), despite their mood outcomes suggesting that this group experienced relatively little mood difficulties.

One possible explanation might be that some of the items on the scale could be interpreted in more ways than one. For example, item 11 states *"Some people have the experience of looking in a mirror and not recognising themselves"*, and some people may interpret this in relation to their physical appearances having changed in some way rather than a depersonalisation experience in which they do not recognise themselves. Furthermore, I did not collect any information on the overall physical wellbeing of our samples, and as dissociation may also occur alongside organic and medical conditions (Good, 1993), it is possible that the control group's high levels of dissociation could be accounted for by unmeasured variables of physical health. That being said, these are assumptions, and I am not sure of the exact reasons behind our high dissociation scores for our the group.

On the one hand, the high dissociation outcomes in the control group, could suggest that dissociation alone may not be a factor in developing NES, on the other, as the NES participants' outcome was nearly four times as high as the control group, it could be hypothesised that unusually high experiences of dissociation are unique to NES. Furthermore, the NES mood outcomes was suggestive of moderate to moderately severe depression alongside high levels of dissociation, possibly indicating that there might be a relationship between dissociation and depression in NES, as previous suggested (Mazza et al., 2009). However, previous NES studies using the DES found that only 15.3% of their NES sample scored ≥30 (Reuber et al., 2003), compared to our sample in which 88% of NES participants scored ≥30.

Furthermore, our NES sample's average DES-II scores (86.6 ± 51.5) are considerably higher than Carlson & Putnam's (1993) cut-off points for Dissociative Disorder Not Otherwise Specified (36) and Dissociation Identity Disorder (48). This may indicate that our dissociation outcomes are not comparable to other similar studies and are perhaps influenced by the small sample size or unknown or unmeasured variables that have contributed to our results. Additionally, the DES was last updated in 1993, and while it is a widely used and well-recognised tool to indicate dissociation as a trait, it is possible that it does not capture our current understanding of dissociation which has continued to develop since.

5.5.3. Baseline Sleep

The baseline sleep outcomes indicate that NES participants in our study reported significantly more impaired sleep as captured by the PSQI global score. When

looking at the individual sleep domains separately; the NES group reported that it took them significantly longer to fall asleep, that their sleep was shorter and less efficient, that they experienced more sleep disturbances and that their daytime functioning was more impaired. The only sleep domain in which the two groups did not differ was whether participants had taken medication specifically to help them sleep in the past month. The results support the findings of recent NES research suggesting that this group of people are more likely to report impaired sleep (Latreille et al., 2018; Erickson et al., 2019).

A possible explanation for our sleep outcomes might be that people with NES are thought to have a reduced ability to cope with stress (Testa et al., 2012), which in turn has been linked with impaired sleep (Sadeh et al., 2004). Alternatively, as those with NES are thought to consider their overall health as poor (Al Marzooqi et al., 2004), it is likely that they also perceive their sleep to be more impaired than it is. However, these conceptualisations are based on assumptions that people with NES perceive their functioning to be more impaired as opposed to objectively experiencing poorer health. Furthermore, it is worth mentioning that anecdotally, the majority of NES participants verbalised that they found this questionnaire challenging to complete. In particular, they reported that they found it difficult to remember what their sleep was like and the nature of this questionnaire requires those completing it to estimate what their sleep has been like over the past month. It has been suggested before that those with NES might have difficulties with their working memory (Strutt et al., 2011) and may have contributed to the difficulties they experienced in completing this questionnaire.

5.6. Methodological considerations

5.6.1. Strengths

To our knowledge, this study was the first to attempt to observe whether objectively and subjectively measured sleep interactions with next day functioning in relation to mood, dissociation and seizure frequency. This study was able to show that people with NES are likely to experience significantly more impaired sleep and subjectively report worse sleep quality than the general public. These outcomes are clinically relevant and contributes to our knowledge about features of NES. Additionally, I excluded people with a dual diagnosis of NES and ES, anyone with a history of a brain injury and known sleep disorders and have therefore attempted to account for circumstances known to cause sleep disturbances.

Moreover, the results show that there were no significant differences in the misperception of sleep across the two groups despite suggestions that people with NES are likely to over-report their difficulties. The results were further able to characterise the objective sleep profile of NES to encompass poorer sleep efficiency caused by wakefulness throughout sleep and frequency of awakenings as opposed to sleep duration, similar to those with depression. Furthermore, we found an indication that there could be a relationship between the number of awakenings during the preceding night on seizure frequency the following day, a finding worth further exploration by studies with larger samples. Finally, our study was conducted at a time when sleep in NES had started to gain interest, therefore, hope it will contribute to the limited research in this field and act as a building block for future studies.

5.6.2. Limitations

Irrespective of the results showing statically significant differences in the experiences of sleep between the two groups, our samples were small, unequal and we were unable to seek additional data to make up for data lost due to errors. I had to reduce our sample sizes due to unforeseeable loss of funding and additionally, due to drop-outs we did not meet our NES sample size. Therefore, our reduced sample size may have meant that the multi-level modelling was underpowered and that I was unable to explore associations between sleep, mood and dissociation and seizure frequency.

Moreover, our NES group reported more dissociation and poorer mood when measured at baseline and when measured daily across six days. As dissociation and mood have extensively been linked to impaired sleep, this is likely to have influenced our subjective and objective sleep outcomes for our NES group. Similarly, our sleep outcomes may have also been influenced by factors I did not take into account such seasonal changes, whether participants were undergoing psychotherapy and the use of anti-depressants. Finally, while actigraphy is considered an effective way to collect objective sleep data, it is less effective than PSG when recording large amounts of WASO like those recorded in the NES sample in our study. Therefore, while this study adds to our understanding of sleep in NES, further research is required.

5.7. Clinical implication

There is an increasing interest in sleep within NES, and we hope that our outcomes contribute to this. Our results suggest that poor sleep is an objective and subjective problem in NES, rather than a misinterpretation of sleep experienced. We, therefore, hope it will encourage clinicians to inquire about sleep routinely. Given that sleep impairment is present and is an important indicator of overall wellbeing across populations, sleep interventions such as CBTI-I could be considered for those with NES who report impaired sleeping. Additionally, trails for CBTI-I to improve sleep in NES in order to improve overall wellbeing may now be warranted. However, our data was too underpowered to detect the impact of poor sleep in next day seizures; we are therefore unable to suggest whether sleep interventions will improve seizure severity in NES.

5.8. Research recommendation

This study shows promising outcomes indicating that sleep is an important factor in the experience of NES and suggests a profile for sleep impairment in NES of excessive nocturnal wakefulness and awakenings. However, the limitations with our study suggest that there are several aspects that future research may focus on to both expand this field of research and to address the limitations we came across. Firstly, I recommend that future studies further explore the experiences of sleep in NES using larger samples from an NES population in settings beyond psychotherapy services as this is likely to have impacted our outcomes. Secondly I suggest that if such research includes a control sample that that is data collected alongside the NES data to control for the impact of seasonal changes on sleep. Thirdly, future research

would well do adopt a longitudinal design in order to explore whether impaired sleep leads to poorer next day functioning and higher seizure frequency. Finally, as the research in this field grows, I hope that research will extend their focus into whether sleep interventions such as CBT-I might be useful in improving sleep and functioning in those with NES.

5.9. Conclusion

This prospective study exploring whether impaired sleep is a feature in NES demonstrates that those with NES are more likely to experience objectively poorer sleep efficiency, more extended periods of wakefulness and more awakenings. The outcomes further showed that those with NES did not have larger misperceptions of sleep than the control groups, as initially expected. Due to our small and underpowered sample, I was unable to show any associations between preceding night's objective measures of impaired sleep and next day mood, dissociation and seizure frequency. However, I did find an indication that preceding night's awakenings may be linked to seizure frequency the following day, which is worth exploring in future research.

Chapter 7. References

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Chapter 8. Appendix

8.1 HRA, School of Psychology Ethical Approval Letters
8.2 Study Documents
8.3 Study Material
8.4 Analysis Output

8.1 Approval Letters

8.1.1. HRA Approval Letter

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Miss Saafi Mousa
Psychologist in Clinical Training
Leeds Teaching Hospitals NHS Trust
St James's University Hospital
Beckett Street
Leeds
LS9 7TF

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

12 September 2018

Dear Miss Mousa

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**The experience of sleep, dissociation and mood in Non-Epileptic Seizures.**
IRAS project ID:	**239312**
REC reference:	**18/NE/0285**
Sponsor	**The University of Leeds**

I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?
The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Clare E Skinner
Tel: 01133434897
Email: governance-ethics@leeds.ac.uk

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

IRAS project ID	239312

Your IRAS project ID is **239312.** Please quote this on all correspondence.

Yours sincerely

Maeve Ip Groot Bluemink
Assessor

Email: hra.approval@nhs.net

Copy to: *NHS Research Ethics Officer, The University of Leeds – Sponsor Contact*
Mrs Anne Gowing, The Leeds Teaching Trust Hospitals – Lead R&D Contact

IRAS project ID	239312

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [1]		14 August 2018
HRA Schedule of Events	1 (HRA final)	11 September 2018
HRA Statement of Activities	1 (HRA final)	11 September 2018
IRAS Application Form [IRAS_Form_16082018]		16 August 2018
Letter from sponsor		14 August 2018
Letters of invitation to participant [LOI]	1	10 August 2018
Non-validated questionnaire [DMS Scale]	1	16 July 2018
Other [Clarification of Methodology and Design]	1	10 September 2018
Other [Trainee Clinical Psychology Information]	1	16 July 2018
Other [Research Panel Constitution]	1	16 July 2018
Other [GCP Certificate]	1	20 January 2018
Other [SoE Certificate]	1	04 May 2018
Other [Risk Protocol]	1	16 July 2018
Participant consent form [Consent Form]	1	16 July 2018
Participant information sheet (PIS) [Updated PIS]	2	04 September 2018
Research protocol or project proposal [Study Protocol]	1	16 July 2018
Sample diary card/patient card [Sleep Diary]		
Summary CV for Chief Investigator (CI) [CI CV]	1	16 July 2018
Summary CV for supervisor (student research) [Supervisor's CV (A Weighall)]	1	22 August 2018
Summary CV for supervisor (student research)		16 July 2018
Validated questionnaire [DES-II]	1	15 August 2018
Validated questionnaire [PSQI]		
Validated questionnaire [GAD7]		
Validated questionnaire [PHQ-9]		
Validated questionnaire [MATRICS Sleep Diary]		

IRAS project ID	239312

Summary of assessment

The following information provides assurance to you, the sponsor and the NHS in England and Wales that the study, as assessed for HRA and HCRW Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England and Wales to assist in assessing, arranging and confirming capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards?	Comments
1.1	IRAS application completed correctly	Yes	IRAS Form [A78] corrected to 'No', it is not expected that the research will lead to new IP.
2.1	Participant information/consent documents and consent process	Yes	Changes have been made to align the PIS with HRA & HCRW Approval standards.
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	A Statement of Activities has been submitted and it is intended for this to be used as the contract between the Sponsor and NHS sites.
4.2	Insurance/indemnity arrangements assessed	Yes	The Applicant confirmed that the Actiwatch devices will be on loan to the sites from the University of Leeds and are covered under the University's indemnity arrangements.
4.3	Financial arrangements assessed	Yes	No application for external funding has been made. There will be no financial provisions to the sites.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	The Applicant confirmed that the research team will not have access to any medical or care notes. Clinicians will only pass on names and phone numbers, if consent to do this has been received from potential participants.

Section	Assessment Criteria	Compliant with Standards?	Comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	REC Favourable Opinion was issued by the North East - Newcastle & North Tyneside 1 REC.
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
There is one type of participating NHS organisation; therefore, there is only one site type. The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence. If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS or on the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net, or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

IRAS project ID	239312

Principal Investigator Suitability

This confirms whether the sponsor's position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and Wales, and the minimum expectations for education, training and experience that PIs should meet (where applicable).

Local Collaborator (LCs) are expected for this type of study. The LCs have been identified as follows:

- Leeds Teaching Hospitals NHS Trust: Miss Saafi Mousa (CI – employed by site)
- Sheffield Teaching Hospitals NHS Foundation Trust: Professor Markus Reuber (Consultant Neurologist)
- Mid Yorkshire Hospitals NHS Trust: Dr Charlotte Baker (Consultant Neuropsychologist)

GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken.

Use of identifiable patient records held by an NHS organisation to identify potential participants without their prior consent should be undertaken by a member of the direct care team for the patient, so it would not normally be acceptable for this to be done by staff not employed by that organisation.

Where arrangements are not already in place, research staff not employed by the NHS host organisation undertaking any of the research activities listed in the research application would be expected to obtain a Letter of Access based on standard DBS checks and occupational health clearance.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.

The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Some participants may also be recruited outside the NHS and some activity may take place outside the NHS. HRA & HCRW Approval does not cover activity outside the NHS. Before recruiting or undertaking activity outside the NHS the research team must follow the procedures and governance arrangements of responsible organisations.

8.1.2. NHS to NHS Letter of Access

CONFIRMATION OF PRE-ENGAGEMENT CHECKS

Research Office
G11 Rowan House
Pinderfields Hospital
Wakefield
WF1 4DG

Re: Researcher's name: Saafi Mousa

Job title**: Trainee Clinical Psychologist**

Contract end-date**: 30th September, 2019**

Workplace and postal address:
Department of Clinical Psychology, Fielding House. St James's University Hospital, Beckett Street, Leeds, LS9 7TF

Electronic Staff Record number: **26192508**

As the representative of the NHS employer[1] of the above-named person, I can confirm that s/he is employed by this organisation. I understand that the responsibility for ensuring that the appropriate pre-engagement checks have been undertaken rests with us as the individual's substantive employer. I can confirm that the appropriate pre-engagement checks have been completed, commensurate with her/his job description and proposed research role in your NHS organisation, and in line with NHS employment checks standards

Name of employer's representative: Dr Jan Hughes

Job Title: Joint Programme Director

Workplace address:

Department of Clinical Psychology, Fielding House. St James's University Hospital, Beckett Street, Leeds, LS9 7TF

Tel: 0113 3432738

Email: j.hughes@leeds.ac.uk

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[1] For clinical academics, this would be a representative from their HEI employer

8.1.3. School of Psychology, University of Leeds Approval

From: Ethics <donotreply@leeds.ac.uk>
Date: 18 September 2018 at 11:28:25 BST
To: <H.Nash@leeds.ac.uk>
Subject: Your ethics application has been passed.
Reply-To: <donotreply@leeds.ac.uk>

Dear Hannah Nash,

Re your ethics application, The experiences of sleep, dissociation and mood in non-epileptic seizures., ethics reference number: **PSC-431.**

I am pleased to inform you that the above research application has been reviewed by the School of Psychology Research Ethics Committee and has been approved.

If the reviewers have left any comments they will appear below.

Primary reviewer comments (if applicable) Cristina Harney:

Secondary reviewer comments (if applicable) :

Please note that this approval only relates to the particular version of documentation supplied in this specific application (**ethics ref no: PSC-431**).

If you wish to make any amendments to the approved documentation, please note that all changes require ethical approval prior to implementation.

Please note: You are expected to keep a record of all your approved documentation, as well as documents such as sample consent forms, and other documents relating to the study. This should be kept in your study file, which should be readily available for audit purposes.

You will be given a two-week notice period if your project is to be audited. There is a checklist listing examples of documents to be kept which is available at http://ris.leeds.ac.uk/EthicsAudits.

Yours sincerely,

School of Psychology Research Ethics Committee

8.2 Study Documents

8.2.1. Letter of Invitation

Letter of Invitation

Dear Potential Participant,

You are being invited to take part in a study about sleep in non-epileptic seizures (NES);

"The experiences of sleep, dissociation and mood in non-epileptic seizures".

My name is Saafi Mousa and I am currently a Psychologist in Clinical Training at the University of Leeds. In order to complete my Clinical Psychology Doctorate Programme, all trainees are asked to complete a Thesis undertaking original clinically-important research. I am interested in sleep in NES.

Ethical approval for this study has been sought from the NHS Research Ethics Committee (IRAS project number: 239312).

Sometimes, people with NES report that they have difficulties sleeping and currently, we know little about the relationship between NES and sleep. Our study aims to investigate how people with NES sleep and whether this can affect how people feel the next day, in relation to seizures and mood. We hope our study will address the gap in our knowledge about NES and to use this knowledge to influence treatment options for people with NES.

If you decide to take part, we ask that you consent to your clinician passing on your name and phone number to the researcher. If you partake, we would ask you to attend a half an hour pre-participation meeting in which you will be asked to complete questionnaires about your experiences of sleep, mood and dissociation. After this meeting, we will ask you to wear an activity monitor on your wrist for a week and to complete a sleep diary in the mornings and a short mood and dissociation questionnaire in the evening. After this week, we will ask you to come back in to return the activity monitor and completed diaries and questionnaires.

Please read the included Participant's Information Sheet attached carefully. If you do not wish to take part, please return this letter and participation sheet to your clinician.

However, if you are interested in taking part, or if you would like to find out more about the study, you do not have to do anything at this stage. If you do not return this letter and participation sheet to your clinician, they will ask if they can give your name and phone number to the researcher working on the study. The researcher will then contact you within the next four weeks to discuss the study.

If you have any concerns about the study, please contact Dr Chris Graham, Clinical Psychologist and University Academic Fellow, or Mrs Clare Skinner, Head of Research Integrity and Governance:

Dr Chris Graham
C.D.Graham@leeds.ac.uk |
0113 3433910

Mrs Clare Skinner
Goverance-Ethics@leeds.ac.uk |
0113 3434897

8.2.2. Participant's Information Sheet

Participant Information Sheet

The experiences of Sleep, Dissociation and Mood in Non-Epileptic Seizures

You are being invited to take part in this research project. This sheet tells you about why we are doing this study and what it will involve. It's important that you understand the study before you decide to get involved.

Who will be doing this project?

Saafi Mousa, Trainee Clinical Psychologist at The University of Leeds will be doing this project. As part of the three-year training course all trainees are asked to complete a Thesis undertaking original research in order to complete the Clinical Psychology Doctorate Programme.

What is the purpose of the project?

There is little knowledge on what causes Non-Epileptic Seizures (NES), and currently there is no gold standard treatment for those with NES. Individuals with this condition often report sleep difficulties. However, to help us design future treatments we need more detailed knowledge about how people with NES experience sleep.

In this study, we want to know about what sleep is like for people with NES and how it affects next day feelings. We hope to address the gap in our knowledge about NES and to use this knowledge to influence treatment options for people with NES.

What will happen if I choose to take part?

This study will involve two meetings that will take no longer than 30 minutes and a 7-day period in which we will ask you wear an Actiwatch at home and complete daily questions.

You will be invited to a pre-participation meeting at your local hospital, where you usually meet with your healthcare team. In this meeting, Saafi will give you more information about the study. This meeting will give you the opportunity to talk through any questions or worries you might. You will then be asked to provide written consent to participate.

You will then be asked to complete questionnaires about your experiences of sleep, dissociation and mood.

After this, we will show you how to use an activity watch that we will give you, and how to complete the daily sleep and mood diaries. You will also be given contact details of the researcher should you want to contact them with any questions or queries you may have in your time as a participant.

You will be asked to meet again after 7 days to return the activity watch and the diaries you completed at home and to debrief about your participation in this study.

Do I have to take part?

No. You might decide that you don't want to take part– that's okay. Not taking part will not have any impact on the care you receive from your healthcare team.

What are the advantages and disadvantages of taking part?

There are no direct benefits of taking part of this study. However, as there is relatively little information on how to treat NES and we hope that understanding sleep in NES will inform future new treatments.

Taking part will take up some of your time. You will be asked to complete a sleep diary upon waking and a questionnaire asking about experiences of dissociation, mood and seizures at the end of the day. It may take you up to 10 minutes to complete these in the morning and up to 10 minutes in the evening. You will also be asked to wear an activity monitor on your wrists consistently for 7 days and you may find that this inconvenient.

What will happen to the results?

As part of training at The University of Leeds all Trainee Clinical Psychologists are required to write the results up in a written report. The information within the report might be used in other ways, for example at conferences, meetings, poster presentations and in academic journals. You won't be identified in any report or publication. We also hope to feedback the results to all the departments from which we have recruited.

Will my answers be kept confidential?

Yes. All the data collected from the questionnaires will be saved to a secure University server that can only be accessed by Saafi Mousa. The only time we would have to share information outside of your healthcare team is if we felt that your safety or another person's safety was at risk, but we would always try to talk to you about this first.

What if I change my mind?

Once you have completed the questionnaires, we are unable to withdraw your data as this is collected anonymously and is therefore not identifiable. If you decide to take part and change your mind afterwards you can contact the researcher and inform them of this.

What happens next?

You will be contacted by Saafi Mousa to see whether you are still interested in taking part of this study. If you decide that you would like to take part, Saafi will agree a date and time with you over the phone to come in for a pre-participation meeting at your local hospital.

If you have any concerns about the study, please contact my university supervisor, Dr Chris Graham or the Faculty Research Ethics and Governance Administrator:

Dr Chris Graham (Clinical Psychologist and Research Fellow at the University of Leeds) C.D.Graham@leeds.ac.uk | 0113 3433910

Faculty Research and Governance Administrator

FMUniethics@leeds.ac.uk | 0113 343 1642

Data Protection Information

The University of Leeds is the sponsor for this study based in the United Kingdom. We will be using information from you in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Leeds will keep identifiable information about you for 3 years after the study has finished.

Your rights to access change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information by contacting David Wardle, University Data Protection Officer on DPO@leeds.ac.uk.

What happens to the data collected from me in this study?

Your NHS organisation will collect information from you for this research study in accordance with our instructions. Your NHS organisation will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from the University of Leeds and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Your local NHS organisation will pass these details to the University of Leeds along with the information collected from you. The only people in the University of Leeds who will have access to information that identifies you will be people who need to contact you for data collection meetings if you have indicated that you are interested in taking part in this research. The people who analyse the information will not be able to identify your data and will not be able to find out your name, NHS number or contact details from the data collected.

Your local NHS organisation will keep identifiable information about you from this study for 3 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

The information collected for this study will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

8.2.3. Consent Form

Consent to take part in **The experiences of Sleep, Dissociation and Mood in Non-Epileptic Seizures**	Add your initials next to the statement if you agree
1. I confirm that I have read and understand the information sheet dated [16/07/2018] explaining the above research project.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without there being any negative.	
3. I give permission for members of the research team to have access to my anonymised responses.	
4. I understand that my name will not be linked with the research materials, and I will not be identified or identifiable in the report or reports that result from the research.	
5. I understand that partaking in this study will not in any way, influence the care I receive from my healthcare team at my local hospital.	
6. I agree for the data collected from me to be stored for up to 3 years after completion of project and used in relevant future research in an anonymised form.	
7. I understand that other genuine researchers will have access to this data only if they agree to preserve the confidentiality of the information as requested in this form.	
8. I understand that this consent form will be stored safely and not linked to any of the data collected from me in this study.	
9. I understand that I am agreeing to complete questionnaires about my wellbeing and some of these may be sensitive in nature.	
10. I agree that if I disclose intent to harm myself or another person that the researcher may inform my healthcare team or make a referral to the appropriate service.	
11. I have had the opportunity to ask questions about the project.	
12. I agree to take part in the above research project.	

Name of participant	
Participant's signature	
Date	
Name of lead researcher	
Signature	
Date	

8.3 Study Material

8.3.1. PSQI

PITTSBURGH SLEEP QUALITY INDEX (PSQI)

INSTRUCTIONS: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, when have you usually gone to bed at night?

   USUAL BED TIME _____

2. During the past month, how long (in minutes) has it usually take you to fall asleep each night?

   NUMBER OF MINUTES _____

3. During the past month, when have you usually gotten up in the morning?

   USUAL GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

   HOURS OF SLEEP PER NIGHT _____

INSTRUCTIONS: For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(a) ...cannot get to sleep within 30 minutes	☐	☐	☐	☐
(b) ...wake up in the middle of the night or early morning	☐	☐	☐	☐
(c) ...have to get up to use the bathroom	☐	☐	☐	☐
(d ...cannot breathe comfortably	☐	☐	☐	☐
(e) ...cough or snore loudly	☐	☐	☐	☐
(f) ...feel too cold	☐	☐	☐	☐
(g) ...feel too hot	☐	☐	☐	☐
(h) ...had bad dreams	☐	☐	☐	☐
(i) ...have pain	☐	☐	☐	☐

(j) Other reason(s), please describe

_____

_____

How often during the past month have you had trouble sleeping because of this?	☐	☐	☐	☐

PSQI Page 1

	Very good	Fairly good	Fairly bad	very bad
6. During the past month, how would you rate your sleep quality overall?	☐	☐	☐	☐

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?	☐	☐	☐	☐
8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?	☐	☐	☐	☐

	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐	☐	☐	☐

	No bed partner or roommate	Partner/ roommate in other room	Partner in same room, but not same bed	Partner in same bed
10. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐	☐	☐	☐

If you have a roommate or bed partner, ask him/her how often in the past month you have had...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
(a) ...loud snoring	☐	☐	☐	☐
(b) ...long pauses between breaths while asleep	☐	☐	☐	☐
(c) ...legs twitching or jerking while you sleep	☐	☐	☐	☐
(d) ...episodes of disorientation or confusion during sleep	☐	☐	☐	☐
(e) Other restlessness while you sleep; please describe	☐	☐	☐	☐

8.3.2 DES-II

Dissociative Experiences Scale - II

Instructions: This questionnaire asks about experiences that you may have in your daily life. We are interested in how often you have these experiences. It is important, however, that your answers show how often these experiences happen to you when you **are not** under the influence of alcohol or drugs. To answer the questions, please determine to what degree each experience described in the question applies to you, and circle the number to show what percentage of the time you have the experience.

For example: 0% (Never) 10 20 30 40 50 60 70 80 90 100% (Always)

There are 28 questions. These questions have been designed for adults. Adolescents should use a different version.

Disclaimer: This self-assessment tool is not a substitute for clinical diagnosis or advice.

1. Some people have the experience of driving or riding in a car or bus or subway and suddenly realizing that they don't remember what has happened during all or part of the trip. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

2. Some people find that sometimes they are listening to someone talk and they suddenly realize that they did not hear part or all of what was said. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

3. Some people have the experience of finding themselves in a place and have no idea how they got there. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

4. Some people have the experience of finding themselves dressed in clothes that they don't remember putting on. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

5. Some people have the experience of finding new things among their belongings that they do not remember buying. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

6. Some people sometimes find that they are approached by people that they do not know, who call them by another name or insist that they have met them before. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

7. Some people sometimes have the experience of feeling as though they are standing next to themselves or watching themselves do something and they actually see themselves as if they were looking at another person. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

8. Some people are told that they sometimes do not recognize friends of family members. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

9. Some people find that they have no memory for some important events in their lives (for example, a wedding or graduation). Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

10. Some people have the experience of being accused of lying when they do not think that they have lied. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

11. Some people have the experience of looking in a mirror and not recognizing themselves. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

12. Some people have the experience of feeling that other people, objects, and the world around them are not real. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

13. Some people have the experience of feeling that their body does not seem to belong to them. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

14. Some people have the experience of sometimes remembering a past event so vividly that they feel as if they were reliving that event. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

15. Some people have the experience of not being sure whether things that they remember happening really did happen or whether they just dreamed them. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

16. Some people have the experience of being in a familiar place but finding it strange and unfamiliar. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

17. Some people find that when they are watching television or a movie they become so absorbed in the story that they are unaware of other events happening around them. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

18. Some people find that they become so involved in a fantasy or daydream that it feels as though it were really happening to them. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

19. Some people find that they sometimes are able to ignore pain. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

20. Some people find that they sometimes sit staring off into space, thinking of nothing, and are not aware of the passage of time. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

21. Some people sometimes find that when they are alone they talk out loud to themselves. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

22. Some people find that in one situation they may act so differently compared with another situation that they feel almost as if they were two different people. Circle the number to show what percentage of the time this happens to you. 0% 10 20 30 40 50 60 70 80 90 100%

23. Some people sometimes find that in certain situations they are able to do things with amazing ease and spontaneity that would usually be difficult for them (for example, sports, work, social situations, etc.). Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

24. Some people sometimes find that they cannot remember whether they have done something or have just thought about doing that thing (for example, not knowing whether they have just mailed a letter or have just thought about mailing it). Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

25. Some people find evidence that they have done things that they do not remember doing. Circle the number to show what percentage of the time this happens to you. 0% 10 20 30 40 50 60 70 80 90 100%

26. Some people sometimes find writings, drawings, or notes among their belongings that they must have done but cannot remember doing. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

27. Some people sometimes find that they hear voices inside their head that tell them to do things or comment on things that they are doing. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

28. Some people sometimes feel as if they are looking at the world through a fog, so that people and objects appear far away or unclear. Circle the number to show what percentage of the time this happens to you.

0% 10 20 30 40 50 60 70 80 90 100%

Total:	**DES Score: ____** (Total divided by 28)

8.3.3. GAD-7

GAD-7 Anxiety

Over the last 2 weeks, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Column totals: ___ + ___ + ___ + ___

= Total Score _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

8.3.4. PHQ-9

PHQ-9 Depression

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
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	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
Column totals	___	+ ___	+ ____	+ ___

= *Total Score* _____

8.3.5. Sleep Diary

MATRICS Sleep Diary- Screening ID:__________

Today's date	Sample 4/5/11							
1. What time did you get into bed?	10:15 p.m							
2. What time did you try to go to sleep?	11:30 p.m							
3. How long did it take you to fall asleep?	55 min.							
4. How many times did you wake up, not counting your final awakening?	3 times							
5. In total, how long did these awakenings last?	1 hour 10 min.							
6. What time was your final awakening?	6:35 a.m.							
7. What time did you get out of bed for the day?	7:20 a.m							
8. How would you rate the quality of your sleep?	☐ Very poor ☑ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good	☐ Very poor ☐ Poor ☐ Fair ☐ Good ☐ Very good
9a. How many times did you nap or doze?	2 times							
9b. In total, how long did you nap or doze?	1 hour 10 min.							
10. Comments (if applicable)	I have a cold							

8.3.6. Daily Mood & Dissociation Scale

Daily Mood and Dissociate Measure

Day & Date: _____ **Time:** _____

This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. Indicate to what extent you felt this way **today**:

(**1** = Not at all **10** = Very much so)

Upset _____	Nervous _____
Hostile _____	Determined _____
Alert _____	Attentive _____
Ashamed _____	Afraid _____
Inspired _____	Active _____

The questions below contain phrases about experiences that you may or may not have **today.** For each statement, please tick the box corresponding to the intensity of your experience, as shown in this example:

Not at all ☐☐☐☐☐☑☐☐☐☐ **Very much so**

Today, things around me seemed unreal or dreamlike **Not at all** ☐☐☐☐☐☐☐☐☐☐ **Very much so**

Things around me looked different today from the way they usually do **Not at all** ☐☐☐☐☐☐☐☐☐☐ **Very much so**

Today my body has felt vague, indefinite, strange **Not at all** ☐☐☐☐☐☐☐☐☐☐ **Very much so**

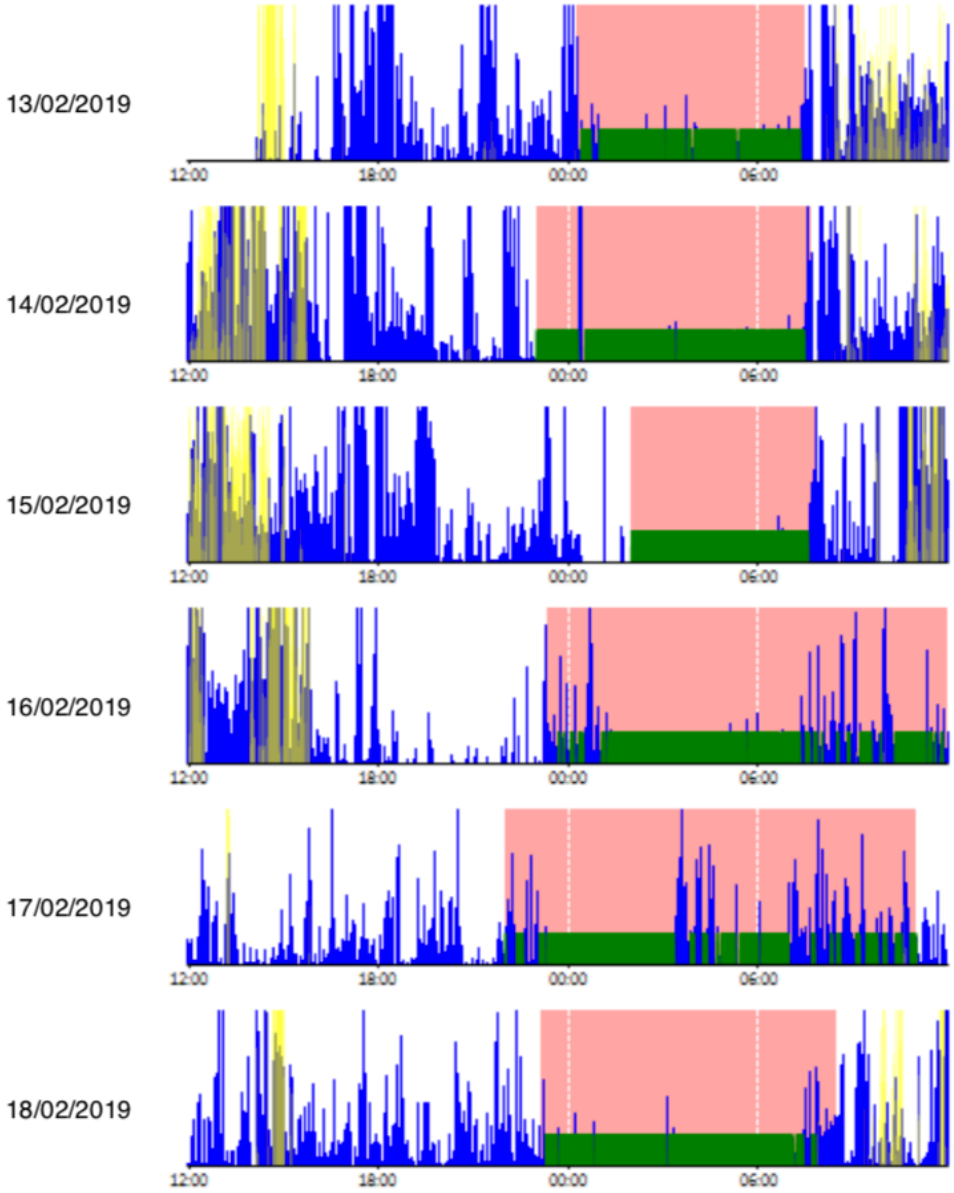
Today, my body seemed disconnected from my thoughts, my feelings, my self **Not at all** ☐☐☐☐☐☐☐☐☐☐ **Very much so**

If you have experienced any seizures today, please note down below how many you have had:

Number of seizures today _____

8.4. Analysis Output

8.4.1. Actigraphy Output



8.4.2. Actigraphy Analysis Output

Sleep Period Breakdown

Sleep Algorithm Used: Cole-Kripke

In Bed	Out Bed	Latency (min)	Efficiency	Total Time in Bed (min)	Total Sleep Time (TST) (min)	Wake After Sleep Onset (WASO)	# of Awakenings	Avg Awakening (min)
14/02/2019 00:15	14/02/2019 07:30	9	77.47%	435	337	89	35	2.54
14/02/2019 23:00	15/02/2019 07:40	0	86.35%	520	449	71	31	2.29
16/02/2019 02:00	16/02/2019 07:50	0	91.14%	350	319	31	14	2.21
16/02/2019 23:20	17/02/2019 12:00	22	59.74%	760	454	284	45	6.31
17/02/2019 22:00	18/02/2019 11:00	0	56.54%	780	441	339	37	9.16
18/02/2019 23:10	19/02/2019 08:30	8	80.89%	560	453	99	23	4.3
23:37	**09:05**	**6.5**	**75.35%**	**567.5**	**408.83**	**152.17**	**30.83**	**4.94**

8.4.3. Multi-Level Modelling Output

8.4.3.1. Impact of Sleep on Seizures

```
Call:
glmmLasso(fix = nxtday_seizures_bin ~ sleep_efficiency + sleep_time_norm +
    wake_time_norm + num_awakenings_norm + pos_mood + neg_mood +
    seizures_bin + total_diss, rnd = list(pid = ~1), data = subset,
    lambda = mylambda[which.min(mybic)], family = binomial(link = logit))


Fixed Effects:

Coefficients:
                    Estimate StdErr z.value p.value
(Intercept)         -1.40756     NA      NA      NA
sleep_efficiency     0.00000     NA      NA      NA
sleep_time_norm      0.00000     NA      NA      NA
wake_time_norm      -0.15438     NA      NA      NA
num_awakenings_norm -0.43875     NA      NA      NA
pos_mood             0.00000     NA      NA      NA
neg_mood             0.00000     NA      NA      NA
seizures_bin         1.04939     NA      NA      NA
total_diss           0.00000     NA      NA      NA

Random Effects:

StdDev:
          pid
pid 0.3647424
Generalized linear mixed model fit by maximum likelihood (Laplace
  Approximation) [glmerMod]
 Family: binomial  ( logit )
Formula: nxtday_seizures_bin ~ wake_time_norm + num_awakenings_norm +
    seizures_bin + (1 | pid)
   Data: as.data.frame(subset)

     AIC      BIC   logLik deviance df.resid
    86.2     97.8    -38.1     76.2       70

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.4257 -0.3633 -0.1523  0.4889  2.0117

Random effects:
 Groups Name        Variance Std.Dev.
 pid    (Intercept) 5.699    2.387
Number of obs: 75, groups:  pid, 16

Fixed effects:
                    Estimate Std. Error z value Pr(>|z|)
(Intercept)          -1.1308     0.8302  -1.362   0.1732
wake_time_norm        0.5012     0.6780   0.739   0.4598
num_awakenings_norm  -1.6294     0.8416  -1.936   0.0529 .
seizures_bin         -0.1993     1.1856  -0.168   0.8665
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr) wk_tm_ nm_wk_
wake_tm_nrm -0.154
nm_wknngs_n  0.233 -0.737
seizures_bn -0.202 -0.295  0.348
```

8.4.3.2. Impact of Sleep on Dissociation

```
Call:
glmmLasso(fix = nxtday_total_diss ~ c(nes) + sleep_efficiency +
    sleep_time + wake_time + num_awakenings + pos_mood + neg_mood +
    seizures_bin + total_diss, rnd = list(pid = ~1), data = subset,
    lambda = mylambda[which.min(mybic)])


Fixed Effects:

Coefficients:
                    Estimate StdErr z.value p.value
(Intercept)      -0.58692013     NA      NA      NA
c(nes)            1.26458220     NA      NA      NA
sleep_efficiency  0.00703217     NA      NA      NA
sleep_time       -0.00030813     NA      NA      NA
wake_time         0.00000000     NA      NA      NA
num_awakenings   -0.02411922     NA      NA      NA
pos_mood         -0.00699728     NA      NA      NA
neg_mood          0.01758620     NA      NA      NA
seizures_bin      0.31604925     NA      NA      NA
total_diss        0.47282414     NA      NA      NA

Random Effects:

StdDev:
          pid
pid 0.2545419
```

```
Linear mixed-effects model fit by REML
 Data: as.data.frame(subset)
       AIC    BIC    logLik
  607.9307 640.21 -292.9654

Random effects:
 Formula: ~1 | pid
        (Intercept) Residual
StdDev:   0.2331392 1.541699

Fixed effects: nxtday_total_diss ~ c(nes) + sleep_efficiency + sleep_time
+      num_awakenings + pos_mood + neg_mood + seizures_bin + total_diss
                     Value Std.Error  DF   t-value p-value
(Intercept)      -0.9079692 1.8968009 109 -0.478685  0.6331
c(nes)            1.3254765 0.3954273  30  3.352011  0.0022
sleep_efficiency  0.0100255 0.0177228 109  0.565680  0.5728
sleep_time       -0.0002845 0.0017408 109 -0.163442  0.8705
num_awakenings   -0.0255632 0.0175275 109 -1.458463  0.1476
pos_mood         -0.0068996 0.0121240 109 -0.569086  0.5705
neg_mood          0.0174123 0.0162424 109  1.072023  0.2861
seizures_bin      0.2868856 0.4159572 109  0.689700  0.4918
total_diss        0.4924786 0.1007758 109  4.886873  0.0000
 Correlation:
                 (Intr) c(nes) slp_ff slp_tm nm_wkn pos_md neg_md szrs_b
c(nes)           -0.538
sleep_efficiency -0.827  0.276
sleep_time       -0.189  0.175 -0.292
num_awakenings   -0.383 -0.158  0.563 -0.471
pos_mood         -0.276  0.141 -0.027  0.184 -0.013
neg_mood          0.013  0.056 -0.115  0.089 -0.134  0.020
seizures_bin      0.125 -0.227 -0.110  0.076  0.020 -0.012 -0.044
total_diss       -0.037 -0.354  0.022  0.017  0.078  0.251 -0.412 -0.324

Standardized Within-Group Residuals:
        Min          Q1         Med          Q3         Max
-3.54935869 -0.41401913 -0.08655344  0.18166982  3.41826658

Number of Observations: 148
Number of Groups: 32
```

8.4.3.3. Impact of Sleep on NA

```
Call:
glmmLasso(fix = change_neg_mood_norm ~ c(nes) + sleep_efficiency +
    sleep_time + wake_time + num_awakenings + pos_mood + neg_mood +
    seizures_bin + total_diss, rnd = list(pid = ~1), data = subset,
    lambda = mylambda[which.min(mybic)])


Fixed Effects:

Coefficients:
                   Estimate StdErr z.value p.value
(Intercept)       4.3608e-01     NA      NA      NA
c(nes)            3.5846e-02     NA      NA      NA
sleep_efficiency  0.0000e+00     NA      NA      NA
sleep_time       -7.4827e-05     NA      NA      NA
wake_time         0.0000e+00     NA      NA      NA
num_awakenings    0.0000e+00     NA      NA      NA
pos_mood         -4.3779e-04     NA      NA      NA
neg_mood         -3.6259e-02     NA      NA      NA
seizures_bin      0.0000e+00     NA      NA      NA
total_diss       -1.1633e-02     NA      NA      NA

Random Effects:

StdDev:
           pid
pid 0.07673674

Linear mixed-effects model fit by REML
 Data: subset
       AIC      BIC    logLik
  431.7638 455.4104 -207.8819

Random effects:
 Formula: ~1 | pid
        (Intercept)  Residual
StdDev:   0.4290569 0.8167547

Fixed effects: change_neg_mood_norm ~ c(nes) + sleep_time + pos_mood + neg
_mood +      total_diss
                Value Std.Error  DF   t-value p-value
(Intercept)  1.2576999 0.6646554 112  1.892259  0.0610
c(nes)       0.2805510 0.2395307  30  1.171253  0.2507
sleep_time  -0.0012543 0.0009080 112 -1.381314  0.1699
pos_mood    -0.0097857 0.0081842 112 -1.195674  0.2343
neg_mood    -0.0760892 0.0102863 112 -7.397148  0.0000
total_diss  -0.0136127 0.0565321 112 -0.240796  0.8102
 Correlation:
           (Intr) c(nes) slp_tm pos_md neg_md
c(nes)     -0.598
sleep_time -0.754  0.127
pos_mood   -0.534  0.148  0.167
neg_mood   -0.117  0.032  0.005  0.033
total_diss -0.084 -0.366  0.120  0.308 -0.447

Standardized Within-Group Residuals:
       Min         Q1        Med         Q3        Max
-3.2710158 -0.4726063 -0.1568389  0.2101136  3.7737950

Number of Observations: 148
Number of Groups: 32
```