

'It's such a rare thing, it's strange to have':

The Impact of anti-NMDAR encephalitis

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1. Thesis abstract

This thesis was completed by Della Nicolle for the degree of Doctor of Clinical Psychology at Cardiff University. The thesis is a systematic review and an interpretative phenomenological analysis investigating the impact of anti-NMDAR on cognitive functioning and identity respectively. This thesis was submitted on the 26th May 2017 and is comprised of a thesis abstract followed by three papers. Paper one has been prepared for submission to *Archives of Clinical Neuropsychology* and paper two for submission to *Psychology & Health*.

Paper one presents a systematic review of current published neuropsychological case studies and series with people with a diagnosis of anti-NMDAR encephalitis. The review was conducted to investigate the emerging cognitive profile for people diagnosed with anti-NMDAR encephalitis. It assessed the quality of these studies using a quality assessment tool created for the purpose of the study. The neuropsychological results were synthesised and the results discussed narratively. A review revealed difficulties with memory, particularly verbal memory, executive functioning and attention/processing speed.

Paper two is an interpretative phenomenological analysis of women with a diagnosis of anti-NMDAR encephalitis. The aim of this study was to explore the experience of women diagnosed with anti-NMDAR encephalitis and the phenomenon of identity change. Using a semi-structured interview the women were interviewed about their experience of having the illness, with a focus on impact on identity. These interviews were analysed for themes using the IPA method and four superordinate themes were discussed with direct quotes. Four superordinate themes were revealed '*Re-finding the 'normal' self*'; '*A 'special' identity*'; '*Evolving from the illness*' and '*Revised roles*'. Analysis revealed themes common to many

severe physical illnesses such as, not feeling oneself and post-traumatic growth. However, themes emerged specific to anti-NMDAR such as feeling abnormal due to the rarity of the disease and its psychiatric symptoms, feeling viewed as special and concerns around fertility and motherhood.

Paper three is a Commentary on the former two studies. This paper offers critical appraisal and reflection on the research process, the strengths and limitations of the papers and line of enquiry, as well as implications for further research, clinical practice and personal/professional development, and finally proposals for dissemination.

The term 'patients' will be used within the systematic review because of its common usage in the target journals, however, it is recognised that its origins are from the medical perspective and other terms that are more person-centred could also be chosen.

2. Systematic Review

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A systematic review of the neuropsychological sequelae of people diagnosed with anti-NMDAR encephalitis in the acute and chronic phases



2.1 Abstract

A systematic review was conducted to investigate the emerging cognitive profile for people diagnosed with anti-NMDAR encephalitis. Ten papers met the review criteria including five neuropsychological case studies and five case series; three of the ten studies used matched controls. The cognitive functioning of 54 patients (46 female: 8 male) was studied. A range of neuropsychological test batteries were used across the studies, administered between one to four times. Paper quality assessment was undertaken and outcomes summarised. Neuropsychological results during the acute phase (≤ 12 months) and chronic phase (>12 months) were extracted. A narrative review of the papers' findings revealed difficulties with memory, particularly delayed verbal memory, and executive functioning. This may be consistent with the role of NMDA receptors in the limbic system, specifically the hippocampus, which are thought to be essential to aspects of learning and memory. To date, there is a paucity of high quality neuropsychological and psychological research concerning the impact of anti-NMDAR encephalitis on cognitive function and psychosocial well-being, both of adults and particularly of those under 18 years. Significant limitations of the literature reviewed include lack of attention to pre-morbid functioning, insufficient rationale for neuropsychological battery choice, use of samples of convenience and limited translation of neuropsychological findings into rehabilitation.

Keywords: *anti-nmdar; encephalitis; autoimmune; neuropsychology; cognitive; functioning*

2.2 Introduction

Anti N-methyl-D-aspartate receptor encephalitis (anti-NMDAR) is a rare form of autoimmune encephalitis, officially categorised and named only in 2007 (Dalmau et al., 2007). It is an acute and often severe illness caused by the body's antibodies attacking, predominantly, the NR1 subunit of the NMDA receptors in the brain (Dalmau et al., 2008). It is often associated with a teratoma tumour, frequently ovarian in women and possibly testicular in men (Irani et al., 2010). However, there are an increasing number of cases reported with no identifiable tumour (Lim et al., 2014). The California Encephalitis Project (CEP), studying the epidemiology of encephalitis, found 65% of anti-NMDAR cases occurred in patients aged 18 or younger, with women significantly more affected than men (Gable et al., 2012). The illness typically initiates with prodromal influenza or viral type symptoms, such as headache, fever and nausea (Dalmau et al., 2011). Symptoms such as delusional thinking, mood disturbances and aggression then frequently develop (Kayser et al., 2013). These symptoms mean that 77% of patients first present for assessment by a psychiatrist (Kuppuswamy, Takala, & Sola, 2014) and that there is a risk of anti-NMDAR going undiagnosed, (Lennox, Coles, & Vincent, 2012) or resulting in a protracted time to diagnosis. This is significant given that quicker diagnosis and treatment is thought to improve prognosis (Kuppuswamy, Takala & Sola, 2014; Byrne et al., 2014).

Following the initial phase, most patients proceed into a period of alternating between catatonia and agitation with symptoms such as decreased levels of consciousness, hypoventilation, autonomic instability and oro-lingual-facial dyskinesias (involuntary repetitive movements of the mouth and face) (Dalmau et al., 2011a; Iizuka & Sakai, 2008; Titulaer et al., 2013). Loughan et al., (2016) report that in around 50% of anti-NMDAR cases, MRI scans of the brain have been normal (Dalmau et al., 2011; Maneta & Garcia, 2014) and any abnormalities found are usually small/transient despite the severity and duration of symptoms (Dalmau et al., 2011). Dalmau et al., (2011) reported that single photon emission

topography (SPECT) results have been variable, with some studies finding variable multifocal cortical and subcortical abnormalities, which change during the course of the disease (Llorens et al., 2010), and other studies finding no abnormalities (Iizuka & Sakai, 2008). Therefore, confirmation of the clinical diagnosis is typically determined via positive identification of NMDA antibodies in the cerebrospinal fluid and/or serum (Gresa-Arribas et al., 2014; Barry et al., 2015). For all patients, management of anti-NMDAR consists of first-line immunotherapy, including corticosteroids, intravenous immunoglobulins or plasma exchange (Dalmau et al., 2011; Chen et al., 2016). Teratomas are resected if identified (Irani et al., 2010). Some patients, such as those with a delayed diagnosis, will go on to have second-line immunotherapy, such as Rituximab (Dalmau et al., 2011).

Incidence and prevalence rates of anti-NMDAR encephalitis have yet to be established. However, research so far suggests that most patients recover fully medically or have mild sequelae, although a minority die or remain severely disabled (Dalmau et al., 2008). In a longitudinal study of 501 patients, Titulaer et al., (2013) found that 81% had a favourable outcome and 9.5% of patients had died after a median follow-up of 24 months. Three independent factors were predictive of good outcome: the rapid commencement of immunotherapy; tumour resection if needed; and less severe symptoms (i.e. not needing intensive care unit support). Titulaer et al., (2012) found 12% of their patients relapsed within 24 months, particularly when there was no associated tumour or undetected/recurrent tumours. However, the authors also found relapses were less frequent when patients received second-line immunotherapy (Titulaer et al., 2013).

With regards cognitive function, amnesia during the initial stages is often reported (Leypoldt et al., 2012; Titulaer et al., 2013). Dalmau et al., (2008) stated that, in their study of 100 patients with anti-NMDAR (91 women; mean age 23 years), 23 presented with short-term memory loss. Language is also affected, with a reduction of verbal output, some echolalia

(often together with echopraxia), and in some cases mutism (Dalmau et al., 2011). However, clinicians suggest memory difficulties and other neurocognitive abnormalities can be overlooked due to the dominance of psychiatric symptoms (Parfene et al., 2016) and speech difficulties, which interfere with the assessment of memory (Dalmau et al., 2008; Dalmau et al., 2011). Memory deficits are said to be consistent with the distribution and function of NMDARs in the brain, which are required for long-term potentiation in the hippocampus, thought to be the centre for learning and memory (McKeon et al., 2016; Rezvani, 2006). Research into the long-term neurophysiological and structural consequences of anti-NMDAR is still lacking given the relative infancy of the disease categorisation. Most research has been undertaken by Finke et al., (2012; 2013; 2016). Using resting state fMRI, Finke et al., (2013) found significantly reduced bilateral functional connectivity between the hippocampus and the anterior default mode network (aDMN). This was shown to be correlated with individual memory performance, despite normal routine clinical MRI and grey matter morphology. The DMN is found to be more active in resting, internally focused tasks and researchers suggest it is involved in episodic memory processing and imagination (Finke et al., 2013). These findings are consistent with the knowledge that the CA1 region of the hippocampus has the highest density of NMDARs in the brain (Finke et al., 2013). Whilst neuroimaging results are important in understanding the neurophysiological and structural impacts of anti-NMDAR, neuropsychological studies are needed to establish a cognitive profile and understand the impact of any cognitive difficulties on functioning and wellbeing.

Although this research is starting to emerge, a systematic review of neuropsychological studies of anti-NMDAR has not yet been completed. The aim of this study is to systematically investigate current literature on neuropsychological sequelae, to evaluate its quality and to attempt to establish a cognitive profile for this clinical population, both in the acute (≤ 12 months) and chronic (>12 months) phases.

2.3 Method

In this review of the literature, a systematic approach was adopted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance (Moher et al., 2009). The following search string was used: anti-NMDAR OR Anti-N-Methyl-D-Aspartate AND encephalitis AND Neuropsycholog* OR cogniti*. Appropriate studies were identified using PsycINFO, MEDLINE, Scopus and Web of Science. The search was limited to the English language. Given that anti-NMDAR was only officially categorised in 2007, the period of 2007 to March 2017 was searched, accepting articles and reviews. Studies of children (under age 18, based on a typical UK research cut-off) were excluded, due to the specificities of neurodevelopmental level on cognitive functioning (Johnson, Blum, & Giedd, 2009).

The search was devised to identify papers where the search terms appeared in the title, abstract or keywords. The abstracts identified in each of the four databases were downloaded into a reference manager and duplicates automatically removed. Titles and abstracts were screened and relevant papers' full texts were downloaded. Reference sections were then hand searched for any further relevant papers. *Figure 1* shows the search process. Single case studies were included given the limited literature in this area.

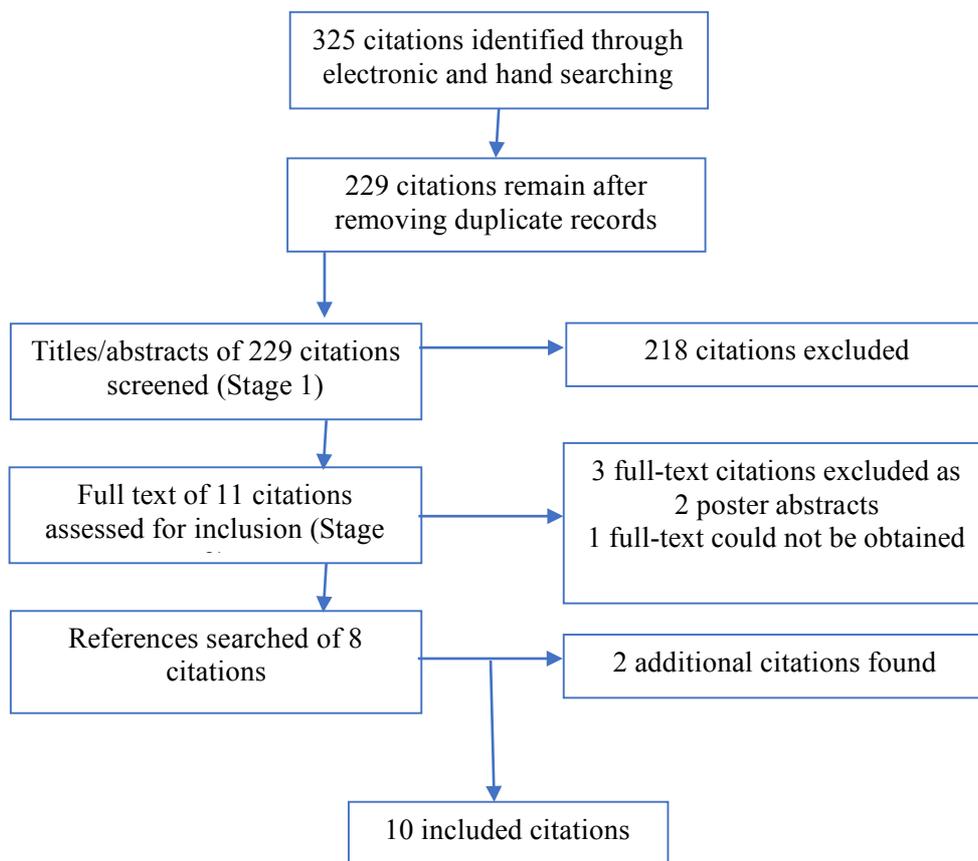


Figure 1: Overview of searching and screening process PRISMA (Moher et al., 2009)

2.3.1 An assessment of methodological quality

An examination of existing standardised quality appraisal checklists (Critical Appraisal Skills Programme (CASP, 2017); QUADAS-2 diagnostic study checklist (Whiting et al., 2011); Scottish Intercollegiate Guidelines Network (SIGN, 2017)) was carried out. It was concluded that they did not meet the specific requirements of this review of neuropsychological case studies/series. Therefore, a checklist was developed for the purpose of this review. This was based upon the foregoing existing checklists and guidance from: Evans (2010) on potential contra-indicators to neuropsychological testing validity; guidelines on psychometric testing (Psychologists Board New Zealand, 2015); information on single-case methodology in

neuropsychology (Crawford, 2017) and guidance on reporting of medical case studies (Cohen, 2006; Green & Johnson, 2006; McCarthy & Reilly, 2000). Each article was reviewed and given an overall score (possible maximum of 33; Appendix C) based upon which criteria were met. For ease of reference, articles are referred to as ‘Low’ (0-11), ‘Medium’ (12-22) or ‘High’ (23-33) quality, depending on their score. Given the small number of papers meeting the inclusion criteria, no articles were excluded on the basis of their score on the quality checklist, rather, this was used to critically appraise the quality of current literature and provide recommendations for future research. Two independent raters piloted the quality of the assessment tool, any differences in scoring were discussed and the tool’s wording changed accordingly. An independent rater then formally reviewed a total of five articles, which demonstrated high inter-rater reliability ($k=0.72$). All the scores were within the same category (Low, Medium, High), aside from Vahter et al., (2014), which the first author rated as ‘Low’ quality and the second rater as ‘Medium’ quality (one point difference).

2.3.2 Data extraction

Data were extracted from the articles by the first author and divided into acute (≤ 12 months), and chronic cognitive deficits, (> 12 months). This was in an attempt to establish a cognitive profile, firstly for the ‘acute’ neuropsychological phase of the illness i.e. from the onset of the symptoms (the period when most treatment is commenced and completed). Secondly, for the ‘chronic’ phase, for any cognitive difficulties remaining once treatment had ceased and which may affect patients’ resumption of day-to-day life. It should be noted there is currently little agreement as to the definition of ‘acute’ and ‘chronic’ periods and papers largely base this on medical and treatment criteria. McIvor & Moore (2007) refer to the acute stage as 4–6 weeks after symptom onset; post-acute stage as 2–6 months and the chronic stage as 6–13 months. However, time to treatment is under-reported across the ten articles: patients may not start

treatment until several months after symptom onset (Urakami, 2016); or it may be unknown (McKeon et al., 2017). Therefore, the ‘acute’ phase for the purpose of this neuropsychological review was defined as 0-12 months on the premise that if patients were still recovering from the systemic effects of the illness and if treatment was still being received, this would affect cognitive functioning. The terms chronic and acute were used as opposed to short and long-term to reduce confusion with short and long-term memory references.

2.4 Results

2.4.1 Search results and characteristics of studies

The search and screening process identified ten eligible articles, including five case studies (one single case study, four with multiple) and five case series (four with a single case and one with multiple; Appendix A). Three studies had matched controls and all patients’ neuropsychological test results were compared to normative samples. The data was derived from 54 patients diagnosed with anti-NMDAR from eight different countries. The time of neuropsychological testing since diagnosis varied considerably from eight days to 6.5 years (Appendix A). Seven articles described time since disease/symptom onset, one described time since diagnosis and one reported time since treatment completion. Five of the studies carried out neuropsychological testing with patients who had medical treatment only, four with those who had treatment and rehabilitation and one with a patient who had no treatment or rehabilitation. Eight articles were rated as ‘Medium’ quality, one ‘High’ quality and one ‘Low’ quality (Appendix E). Consistent with the current evidence on epidemiology of anti-NMDAR (Titular et al., 2012), there were more female participants than males (46F:8M).

The articles varied in their methodology, for example, with different patients tested at different times in their recovery, variability in the numbers of patients tested and presence or

absence of a control group (Appendix A). Additionally, many different neuropsychological tests were used to measure cognitive functioning across studies (Appendix F). Therefore, comparison of the articles was difficult and data-synthesis was not appropriate. As such, a narrative synthesis of the results was undertaken. The main results are presented under different cognitive domains, based on Lezak (2012) and the DSM-5 approach to classifying neurocognitive disorders (Sachdev et al., 2014). Five of the studies were case series, four of which assessed patients both during the acute and chronic phases, and as such the relevant results are discussed in the acute and chronic sections (Martin-Monzon et al., 2012; Vahter et al., 2014; Urakami, 2016; McIvor & Moore, 2017). Bach (2014) reported three case studies, but only the two patients assessed with formal neuropsychological testing, within the first twelve months, were included in the ≤ 12 month analysis. The patient assessed at 30 months did not undergo formal neuropsychological testing; data reported derives from behavioural observations and clinical judgement.

2.4.2 Synthesis results

The results of the synthesis are presented below; however, it should be stressed that the results are based on relatively small numbers of cases, particularly in the acute phase. The number of patients who were found to have cognitive difficulties for the cognitive domain are indicated alongside the relevant references (for example, **N=13**). Reflected in the quality assessment tool, a common methodological limitation of the case studies and series was inadequate reporting of the procedure of neuropsychological assessment and of patient demographics (Appendix E). For example, pre-morbid functioning was not assessed in half of the papers studied and as such any cognitive deficit found cannot be solely attributed to the effects of the illness. Therefore, the results below should be interpreted with caution, with close examination of both the number of patients included within each result summary and the quality assessment scores of the papers

included. Furthermore, there was a great deal of disparity with regards to how cognitive functions were classified and described by the articles. This is particularly evident for memory, which was subdivided differently by each of the articles. To present the results for memory, the most referred to memory subdivisions within the articles are summarised in each of the results sections.

2.4.3 Acute cognitive effects (≤ 12 months)

2.4.3.1 Description of articles

Seven of the ten articles included in this review assessed patients within the first 12 months from either diagnosis, symptom onset or at the start of rehabilitation, and are discussed below (Martin-Monzon, Trujillo-Pozo and Romeron, 2012; Marcos-Arribas, Almonacid & Dolado, 2013; Vahter et al., 2014; Bach, 2014; Loughan et al., 2016; Urakami, 2016; McIvor and Moore, 2017). A total of thirteen participants were assessed across the seven articles. The mean age of the patients was 28.7 (range: 19 to 47 years), with a higher ratio of female patients (10F: 3M). All but one article (Loughan et al., 2016) conducted case series where patients were assessed at two or more time points within the first 12 months. The case series or studies were judged as 'Medium' quality, except Vahter et al., (2014), which was of 'Low' quality and Loughan et al., (2016) which was 'High' quality, both largely due to the level of detail provided in the participant background section of the quality measure.

2.4.3.2 Memory

Memory was tested in all seven of the articles (**N=13**) with each study reporting some form of memory difficulty.

2.4.3.2.1 *Working/Short-term memory.* Working/short-term memory difficulties were specifically noted in three articles (Bach, 2014; McIvor & Moore, 2017; Urakami, 2016; N=9), with McIvor and Moore (2017) and Urakami (2016) reporting working memory deficits persisting at 12 months following treatment and treatment with rehabilitation respectively.

2.4.3.2.2 *Episodic recall.* Immediate recall difficulties were reported in four of the studies (Marcos-Arribas et al., 2013; Martin-Monzon et al., 2012; McIvor & Moore, 2017; Vahter et al., 2014; N=4) and delayed recall difficulties were reported in six articles (Bach, 2014; Loughan et al., 2016; Marcos-Arribas et al., 2013; Martin-Monzon et al., 2012; McIvor & Moore, 2017; Vahter et al., 2014; N=7). Visual memory difficulties were cited in four of the articles (Marcos-Arribas et al., 2013; Martin-Monzon et al., 2012; McIvor & Moore, 2017; Urakami, 2016; N=9) and verbal memory difficulties reported in all seven articles (Bach, 2014; Loughan et al., 2016; Marcos-Arribas et al., 2013; Martin-Monzon et al., 2012; Vahter et al., 2014; McIvor & Moore, 2017; Urakami, 2016; N=13).

McIvor and Moore (2017) reported deterioration in immediate recall, with their untreated patient's immediate memory score at six months dropping from the average to the low average range at 12 months. Within this, immediate verbal memory was within the low average range and significantly lower than predicted, however, immediate visual memory remained within the average range. The patient's overall delayed recall index score was not significantly improved at 12 months. Delayed visual memory in particular had not significantly improved from six to 12 months. Marcos-Arribas et al., (2013) reported significant immediate and delayed verbal and visual recall difficulties in the first few days of the patient presenting in hospital. However, investigation of the raw scores suggests that at four weeks all recall difficulties were resolved, although statistical significance was not reported. Vahter et al., (2014) found severe impairments in immediate verbal recall at day eight of the onset of the

illness, but at eight months and 12 months these had returned to 'normal'. Delayed verbal memory showed improvement in one subtest (Logical Memory II), however, other delayed verbal memory tests (Buschke) indicated moderate to severe difficulties, with Vahter et al., (2014) concluding that (delayed) verbal memory was the most impaired function at eight and 12 months. The patient's immediate and delayed visuospatial memory remained 'normal' throughout testing. Martin-Monzon's et al., (2012) patient had immediate recall difficulties at six months that were largely consistent at 12 months. Immediate visual recall showed no improvement by 12 months, with the patient scoring zero both times. Verbal recall deteriorated at 12 months, however it was unclear whether this was for immediate recall only or an average of both immediate and delayed recall, as only one score is reported. Loughan et al., (2016) reported 'lowered delayed' verbal and visual recall scores in their patient when tested at six months. One of Bach's (2014) patients displayed difficulties in delayed verbal memory six months after symptom onset, however, no serial assessments were carried out. Urakami (2016) found that group level verbal and visual memory difficulties found at six months had shown significant improvement after 12 months of treatment and rehabilitation, and had improved in relation to patients with herpes simplex encephalitis.

2.4.3.5 Executive functioning

Deficits in executive functioning were reported in four of the seven articles (Martin-Monzon et al., 2012; Vahter et al., 2014; Bach, 2014; Loughan et al., 2016; **N=5**). Bach (2014), Loughan et al., (2016) and Martin-Monzon et al., (2012) reported deficits in executive functions, such as planning, organisation, reasoning, problem solving, set shifting and maintenance and category fluency at six months, with some difficulties remaining in Martin Monzon's et al., (2012) patient at 12 months. However, no statistical analyses were performed on the latter. Bach (2014) reported that one patient's executive difficulties were sufficiently pronounced to

have an impact on her reintegration into education and on her future career. However, whilst Vahter et al., (2014) reported deficits in some tests of executive functioning at day eight, ranging from severe to mild, these appeared to return to the 'normal' range by eight months after onset. McIvor and Moore (2017) reported that their untreated participant had some difficulty when switching was introduced to the Trail Making Test, however overall they found his performance remained largely static and was not strongly suggestive of underlying executive dysfunction. Marcos-Arribas et al., (2012) also tested for executive function but reported normal scores in these tasks.

2.4.3.6 Attention and Processing Speed

Six of the seven articles reported difficulties with attention and processing speed (Martin-Monzon et al., 2012; Marcos-Arribas et al., 2013; Vahter et al., 2014; Bach, 2014; Loughan et al., 2016; Urakami, 2016; **N=12**), however, the majority reported mild to moderate levels of dysfunction that resolved at or before 12 months, across a range of attentional processes: selective and prolonged (Martin-Monzon et al., 2012); sustained (Loughan et al., 2016); and information processing tasks (Vahter et al., 2014; Loughan et al., 2016; Marcos-Arribas et al., 2013; Urakami, 2016). McIvor and Moore (2017) did not report any specific attentional difficulties in their patient and Urakami (2016) concluded patients with anti-NMDAR also showed significant improvement in attentional function within 12 months, in comparison to patients with herpes simplex encephalitis.

2.4.3.7 Language

Three articles found evidence of expressive and receptive language impairment (Vahter et al., 2014; Bach, 2014; Loughan et al., 2016; **N=4**). However, language impairment was often not formally tested and had improved in all three cases after three to six months of treatment.

Vahter et al., (2014) reported that one month after the disease onset, their patient developed progressive sensorimotor aphasia. However, three months after the first symptoms the aphasia had reportedly subsided. Bach (2014) qualitatively reported their patient had limited comprehension and no verbal words in the acute stage of illness. However, this improved throughout rehabilitation with only subtle deficits in language remaining. Loughan et al., (2016) reported language impairment in the acute phase, for which their patient received speech therapy. By the time of neuropsychological assessment six months post-diagnosis, his language appeared to have improved, with intact receptive language, and only mild word finding difficulties persisting.

2.4.3.8 Visuospatial abilities

Only one article reported impairment in visuospatial ability specifically (Martin-Monzon et al., 2012; N=1). Martin-Monzon et al., (2012) reported that their patient had difficulty, at both six and 12 months testing, with specific visuospatial skills such as cube analysis, position discrimination and number location. However, elementary visual perception (e.g. shape detection) and more elaborate functions (recognition of degraded stimuli, object identification) were undisturbed.

2.4.3.9 Social cognition

Social cognition was only investigated in one of the eight articles (Bach, 2014; N=2). The author used a 10-item questionnaire to assess patients' ability to understand other people's mental states and general cognition. Both individual patient and informant versions were given to two of the three cases studied in this article. Bach (2014) reported that one patient's score indicated she had newly acquired difficulties in empathising, tactfulness and ability to sympathise, together with reduced insight into these difficulties. Another patient reported new

difficulties recognising that she said things that upset others, understanding jokes, showing sympathy and being tactful. Informant scores corroborated this, however, no formal social cognitive tasks were administered.

2.4.4 Chronic cognitive effects (>12 months)

2.4.4.1 Description of cases

Six out of the ten articles presented in this review assessed patients a minimum of one year since disease onset/diagnosis (range 1–6.5 years; Finke et al., 2012; Martin-Monzon et al., 2012; Finke et al., 2013; Vahter et al., 2014; McKeon et al., 2016; McIvor & Moore, 2017). A total of 43 patients were studied across the six articles, mean age 27.6 (the approximate range was 16-44, however, two papers only reported the mean). Again, there were more female patients than male (37F:6M). All the papers were ‘Medium’ quality, except Vahter et al., (2014), which was scored as a ‘Low’ quality paper.

2.4.4.2 Memory

Memory difficulties persisting after the acute 12-month period were reported in all six articles (**N=43**).

2.4.4.2.1 Working/Short-term memory. Working and short-term memory difficulties were cited in five of the studies (Finke et al., 2012; Finke et al., 2013; Martin-Monzon et al., 2012; McKeon et al., 2016; McIvor & Moore, 2017; **N=42**). Finke et al., (2012), in their study of nine patients tested at a median of 43 months after disease onset, found significant impairments in working memory in four of the participants, in the routine neuropsychological assessment of working memory. The authors also administered an additional battery of short-term memory

(STM) tasks (delayed match-to-sample tasks), which they claim have been previously validated in patients with hippocampal damage (Braun et al., 2008; Finke et al., 2008). Patients were required to remember the colour, location or the association of colour and location of visual stimuli across delays of 900 or 5000 ms. They found that five patients had delay-dependent deficits in some aspect of this battery. However, they reported that three of these patients performed normally in the routine neuropsychological assessment of STM memory. Finke et al., (2013) also reported that their participants (N=24) showed substantial deficits in working memory at a median of 35 months after disease onset. Furthermore, McKeon et al., (2016) found the scores of their anti-NMDAR patient group fell significantly below (medium to large effect sizes) the control group in working memory. Martin-Monzon et al., (2012) report improvements in memory tasks at the 72-month follow-up. However, examination of the patient's raw scores suggests some residual impairment in working memory (on subtests of the WAIS-III). McIvor and Moore (2017) found their untreated patient's visual working memory remained largely unchanged from six to 30 months, staying in the low average range. However, his visual working memory score was largely impacted by his spatial addition score, which was significantly lower than predicted.

2.4.4.2.2 Episodic recall. Immediate recall difficulties were found in four of the six articles (Finke et al., 2012; Finke et al., 2013; McKeon et al., 2016; Martin-Monzon et al., 2012 **N=41**) and delayed recall difficulties in five articles (Finke et al., 2012; Finke et al., 2013; Martin-Monzon et al., 2012; McKeon et al., 2017; Vahter et al., 2014; **N=42**). Verbal memory difficulties were also reported in five of the articles (Finke et al., 2012; Finke et al., 2013; McIvor & Moore, 2017; McKeon et al., 2017; Vahter et al., 2014; **N=42**) and visual memory difficulties reported in two articles (Finke et al., 2012; Martin-Monzon et al., 2012; **N=10**).

McKeon et al., (2016) found that the scores of the anti-NMDAR patient group fell significantly below the control group in tests of verbal immediate and delayed recall, but not immediate or delayed visual recall. Similarly, Finke et al., (2013) also observed significant impairments in immediate and delayed verbal recall, but not visual, across 24 participants. Finke et al., (2012) reported significantly impaired immediate and delayed verbal recall in two of their nine patients and significantly impaired immediate and delayed visual recall in one patient. Vahter et al., (2014) found that 20 months after disease onset there remained a mild deficit in verbal delayed memory. They concluded that the most impaired function at long-term follow-up was delayed verbal memory, however, significance levels were not reported. McIvor and Moore (2017) reported that their untreated patient's verbal memory index at 30 months was comparable to his score at 12 months and so was not deemed to be a statistically significant change. However, his immediate and delayed verbal memory scores were in the average range. Martin-Monzon's (2012) single case study showed persistent immediate and delayed visual recall difficulties six years after disease onset, whilst verbal memory showed improvement. However, it is unclear whether the scores reflected clinically significant change. Furthermore, again, verbal memory was not divided into immediate and delayed recall so it is unknown if one was preferentially improved. Finke et al., (2012) found that in their specific STM battery, five patients had deficits in either STM of locations and/or colour-location associations, suggesting difficulties with immediate visual memory.

2.4.4.5 Executive functioning

Executive functioning difficulties were reported in five of the six articles (Finke et al., 2012; Finke et al., 2013; Martin-Monzon et al., 2012; McKeon et al., 2016; McIvor & Moore, 2017; N=42), with difficulties such as reasoning, rule finding, set shifting and set maintenance,

category fluency visuospatial planning/organisation and problem solving. Finke et al., (2012) found persistent impairments in executive functioning in five/nine patients. Finke et al., (2013) reported substantial group deficits in executive functions (N=24), although this appeared to be based only on performance in the STROOP test. Nonetheless, of the 24 patients, five did subjectively report executive functioning difficulties. McKeon et al., (2016) found the anti-NMDAR patients' group performance was significantly below matched controls for some aspects of executive functioning (visuospatial planning/organisation and problem solving) but not others (abstraction, response inhibition, flexibility and verbal fluency). They reported that aspects of executive functioning were amongst the most severely affected abilities at the individual level, but profiles ranged from 'normal' to 'extensive dysfunction'. Martin-Monzon et al.,'s (2012) patient showed some improvement in certain tests of executive functioning at 72 months post-initial onset, however, it is unclear whether these scores fell within 'normal' ranges. Vahter et al., (2014) found their patient's test scores in executive functioning remained in the normal range at 20 months. McIvor & Moore (2017) found some increased variability in individual tasks performance for executive functioning at 30 months, compared to six months. However, as before, they concluded his results were not strongly suggestive of underlying executive dysfunction.

2.4.4.6 Attention and Processing Speed

Attention and processing speed difficulties were reported in two of the articles (Finke et al., 2012; McKeon et al., 2016; N=16). Finke et al., (2012) observed impairments in attention in four of their nine patients, with one of these four patients also subjectively reporting attention difficulties. McKeon et al., (2016) found medium to large effect size differences between the anti-NMDAR patients and the control group for both sustained and divided attention and

information processing speed. Seven out of 24 patients in the study by Finke et al., (2013) subjectively reported difficulties with attention. However, the authors reported neuropsychological tests showed intact attention.

2.4.4.7 Language

Language was investigated in three of the six articles for long-term follow up (Martin-Monzon et al., 2012; Finke et al., 2013; McKeon et al., 2016; **N=32**) but no deficits were found. McKeon et al., (2016) reported that expressive language (Vocabulary, Graded Naming Test, spontaneous speech) was comparable between the anti-NMDAR group and matched controls. Finke et al., (2013) and Martin et al., (2012) both reported that testing revealed language was intact in their patients.

2.4.4.7 Visuospatial abilities

Visuospatial difficulties were reported in one of the six articles (McKeon et al., 2016; **N=7**) and tested in an additional three articles but no impairments were found (Martin-Monzon et al., 2012; Finke et al., 2013; Vahter et al., 2014; **N=32**). McKeon et al., (2016) tested for visuospatial organisation via the Rey figure copy and found a significant difference between the anti-NMDAR patients and matched controls.

2.4.4.8 Social Cognition

Only one article tested for social cognition (McKeon et al., 2016; **N=7**), with this being the main aim of the study. McKeon et al., (2016) administered the Mind in the Eyes Test, Advanced Test of Malingering (ToM), the Social Situations Test and the Emotion Attribution Task to seven patients with anti-NMDAR and compared their scores to matched controls. They found significant differences between the groups on using mental-state information to make

sense of social situations and judge the severity of interpersonal violations. Subjectively four out of the seven participants reported social withdrawal and one patient specifically reported occasional misinterpretation of social situations. McKeon et al., (2016) report that subjective social dysfunction experienced by patients can correspond to deficits in social cognition tasks and that anti-NMDAR may adversely affect the ability to decode and adaptively use mental-state information. However, the authors recognised their small sample size and that they ran many statistical comparisons. Therefore, they suggest the results should be interpreted cautiously.

2.5 Discussion

2.5.1 Acute cognitive effects (≤ 12 months)

Memory was the cognitive domain most tested, with all seven articles citing significant difficulties with some aspect of memory in their patients. Delayed verbal memory was the most commonly reported memory difficulty in all seven articles. Immediate and visual memory were the next most cited difficulties in four articles. Working/short-term memory difficulties were only reported in three of the articles. Attentional and processing speed difficulties were highly reported, in six of the seven articles, however these difficulties appeared to largely resolve across the first 12 months since disease onset/diagnosis. Four of the seven articles cited some form of executive dysfunction, such as difficulties problem solving, rule finding and set shifting. Language impairments were found in three articles, with word finding and verbal fluency being the most frequently evidenced deficits. Visuospatial difficulties were found in only two of the studies. Social cognition was the least explored cognitive domain with only

one of the articles examining social cognition. However, formal neuropsychological testing was not used.

2.5.2 Chronic cognitive effects (>12 months)

Memory was, again, one of the cognitive domains most affected in the chronic phase. Persistent memory difficulties of some form were reported in all six articles. Delayed verbal memory was also the most commonly discussed deficit in the chronic phase, reported in five articles. Working/short-term memory difficulties were the second most commonly reported difficulty, present in five of the articles. Immediate recall difficulties were reported in four of the articles and visual memory difficulties in only two articles. Executive dysfunction was a frequently reported deficit in the chronic phase, reported in five of the six articles. However, again, these differed greatly between patients, both within studies and between studies, with difficulties from problem solving to response inhibition and varying from mild to severe. Attention/processing speed difficulties were reported in only two of the articles. Visuospatial difficulties were only reported in one article and language difficulties were not found in any of the current articles. Social cognition was again the least explored cognitive domain, with only one article assessing social cognition and finding impairment. However, they did use formal neuropsychological testing, albeit on a small case sample.

2.5.3 Summary of findings

Memory was the cognitive domain most affected by anti-NMDAR in these studies, with all articles citing some form of memory difficulty. Deficit in memory is consistent with knowledge that NMDA receptors are highly concentrated in the limbic system, particularly the hippocampus, and are essential to aspects of learning and memory (Kruse et al., 2014; Lo et

al., 2010). Although NMDARs are thought to reactivate after immunological recovery has taken place, it is thought not possible for the grey and white matter to be increased (Martin-Monzon et al., 2012). This was reported by Finke et al., (2016), who found evidence for long-standing reduced microstructural integrity of both hippocampi, relative to controls. They reported that disease severity and duration predicted the extent of hippocampal damage, which then correlated with memory performance. They also found volumes of the left hippocampal formation correlated with verbal memory performance, which is in line with the theorised specificity of the left hippocampus for verbal stimuli and consistent with the findings of delayed verbal memory difficulties in all the current ten articles.

Executive functioning difficulties were reported in eight of the ten articles overall. However, results for the executive functioning tasks were variable, with deficits found across a variety of different tests, and patient's scores ranging from normal to severe. This is perhaps not surprising given that 'executive function' is an umbrella term that overarches a wide range of quite divergent skills and functions (Elliott, 2003). Nonetheless, these findings may be accounted for by Finke et al., (2013) who found reduced functional connectivity between the hippocampus bilaterally and the aDMN. The DMN includes the medial prefrontal cortex, which is associated with executive functions and working memory (Finke et al., 2013).

The findings of this adult population appear to be slightly varied from paediatric and adolescent cases, which seem diverse within themselves. Iadisernia et al., (2012) found deficits in attention, executive functioning, verbal fluency, and rapid naming in two paediatric patients. Poloni et al., (2010) also reported attention difficulties, together with deficits in working memory in one paediatric patient. Gitiaux et al., (2013) reported that three of the six children tested at follow up (median duration of 12 months; range 10 months to 5 years) received special education due to persistent semantic memory deficit (word retrieval difficulties) and visual episodic and working memory impairment. Matricardi et al., (2016) found over half of their

paediatric patients (total of 11) had residual deficits indicating frontal lobe dysfunction after, at least, a one year follow-up. Overall, investigation of neuropsychological sequelae in paediatric cases is extremely limited, indicating a need for more larger scale studies.

2.5.4 Limitations

This systematic review provides a summary of cognitive difficulties commonly reported in ten neuropsychological case studies/series. However, the results should be interpreted with caution given the large number of extraneous variables present. The articles differed greatly, with disparities in for example, whether patients received neurorehabilitation and which tests were used (Appendix F). Furthermore, the severity of the illness, for example whether there was intensive care treatment, is not indexed or reported consistently, nor are details of the treatments and when they were commenced and completed. Impact of the treatments, such as corticosteroids and Rituximab should also be taken into consideration as these can cause side effects such as fatigue, flu-like symptoms and pain (Buchman, 2001; Ikeguchi et al., 2012; Cancer Research UK, 2015; Mayo Clinic, 2017), all of which could negatively impact patient's test scores (Lezak, 2004 p. 125). Of particular note is the protracted use of corticosteroids, which have been implicated in cognitive difficulties referred to as a 'steroid dementia' (Brown, 2009; Keenan et al., 1996; Sacks & Shulman, 2005; Wolkowitz, Lupien, Bigler, Levin, & Canick, 2004; Wolkowitz, Lupien, & Bigler, 2007).

There remains a scarcity of research in this area, particularly high quality research. Most studies in this review were of 'Medium' quality. Reporting of the cases was not strong, with a significant lack of reporting of important neuropsychological variables such as, pre-morbid intellectual functioning, psychiatric history and any existing acquired brain injury (ABI; Lezak et al., 2004; Hebben & Milberg, 2009). For example, pre-morbid functioning was

not estimated in half of the papers studied and even when it was assessed it was often not appropriately compared to the IQ score at the time of testing. This is despite analysis of the raw scores indicating there was not a statistical difference between the two (Finke et al., 2012; 13; McKeon et al., 2017). Without sufficient background information, it cannot be confirmed whether any cognitive difficulties found represent the direct impact of anti-NMDAR on cognitive functioning. Furthermore, often participants acted as their own control, with repeated testing, but sufficient discussion was not given to a host of other possible extraneous variables. For example, whether there were practice effects, how the participant presented on that day, whether the same test conditions were in place each time, and whether the same person administered the battery each time. If test scores did differ across administrations, it would be difficult to attribute this entirely to a change in cognitive functioning.

The reporting of the scores was typically weak, often with a mixture of raw scores and index scores within the same articles' results section, and little discussion of whether a change in scores across administrations reflected clinically significant change (for example, Martin-Monzon et al., 2012). Half of the studies were single case studies or series and so only offer limited insight into how cognitive difficulties may present in people with anti-NMDAR. The chronic cognitive deficits discussed in this study have increased generalisability due to the larger case studies included (Finke et al., 2012; Finke et al., 2013; McKeon et al., 2016; **N=40**) and so provide greater evidence of the chronic cognitive effects of anti-NMDAR. This is promising given that chronic effects of anti-NMDAR are arguably more pertinent to investigate due to their potential impact on important aspects of day-to-day functioning, such as return to work.

Despite the potential for cognitive functioning to impact day-to-day functioning, this remained largely unexamined in the current papers. Furthermore, the meaning the individuals then ascribed to their level of participation, and overall quality of life (QoL), remained equally

unexamined. The latter is important to assess given the mixed findings in other neurological conditions of the impact of cognitive functioning on QoL (Baumstarck-Barrau et al., 2011; Benedict et al., 2005; Dijkers, 2004; Glanz et al., 2010; Goretti et al., 2010; Ponsford et al., 2008; Siponkoski et al., 2013; Tate et al., 2005). In a study of 109 encephalitis survivors Ramanuj et al., (2014) found that a poor Glasgow Outcome Score was the most strongly associated with a poor Health Related QoL (HRQoL). Further, that less than half of participants who made a ‘good’ recovery reported a HRQoL equivalent to the general population (Ramanuj et al., 2014). This suggests that the impact of encephalitis had adverse effects on many survivors’ QoL. However, these patients did not undergo neuropsychological testing, so the direct impact of cognitive functioning on QoL cannot be discussed. In the current reviewed articles, subjective complaints were only stated in five of the ten papers, and were usually reported in table form or only briefly in the main body. Furthermore, only Bach (2014) administered a formal measure, finding significant increases in satisfaction at follow-up on the QOLIBRI-OS (von Steinbuechel et al., 2012).

Psychological wellbeing was also only explored in four of the ten articles. This is significant given that if individuals perceive themselves to have cognitive difficulties, and feel they impact on their participation in their usual day-to-day life, this would likely cause anxiety and interact with the person’s ability to engage meaningfully in neuropsychological assessment (Lezak, 2004 p. 127). Researchers who did assess psychological wellbeing largely administered either the Hospital Anxiety and Depression Scale (Snaith, 2003) or the Beck Anxiety and Depression Inventories (Beck 1990; 1996). Only two articles (Bach, 2014; McKeon et al., 2016) discussed the impact of mood on functioning and QoL, either in the results section or discussion. Specific psychosocial difficulties such as the individual’s reconstruction of their identity (Charmaz, 1983; 2000), were also not explored in these articles, or any other articles on anti-NMDAR encephalitis to date.

A specific battery of cognitive assessments has not yet been devised to screen for cognitive deficits in anti-NMDAR (Bornstein, 1990). As discussed, whilst there were overlaps between tests used across the studies, there was disparity between the cognitive domains tested and which tests were used to examine performance in these domains (Appendix F). Instead a ‘scattergun’ approach appears to have been used, often with an extensive neuropsychological battery administered to see if any impairments can be detected. However, this approach can lead to Type I errors (Schatz et al., 2005). An exception to this was Finke et al., (2012) who reported that they conducted a neuropsychological assessment using memory tasks they claimed had previously been shown sensitive to hippocampal dysfunction.

Ecological validity of the neuropsychological assessments used was also not discussed, which is important given most tests used were not specifically designed to predict real-life functioning, such as the ability to live independently or return to work (Chaytor & Schmitter-Edgecombe, 2003; Sbordone, 2001). In these tests, the real-world context is removed and can be completed with few distractions, giving an artificial performance. As such the verisimilitude and veridicality approaches should be considered in future research (Spooner & Pachana, 2006).

Selection bias was evident across articles as patients typically recruited to the studies were opportunistically sampled from referrals to neurology or neuropsychology departments. Participants may have been chosen if their presentation was particularly unique (Barić, Andrijašević, & Beydoun, 2013; Rison, 2013; Rison, Shepphird, & Beydoun, 2016; Wong, 2008), which may skew the cognitive profile detected for this population.

2.5.5 Suggestions for theory and further research

There is an overall lack of research into the neuropsychological sequelae of anti-NMDAR encephalitis and larger case studies are warranted to develop a more robust cognitive profile

for this population. Chronic cognitive deficits have been found in seven articles, with two studies reporting difficulties up to six and a half years after onset (Martin-Monzon et al., 2012; Finke et al., 2013). Therefore, longitudinal neuropsychological testing would be recommended.

Professional consensus on a neuropsychological battery, grounded in neuropsychological theory, is needed to reduce the number of extraneous variables and provide replicability and generalisability. In their case series of three adolescents, Hinkle et al., (2016) concluded with the recommendation that batteries that formally assess memory, executive functioning, as well as language and attention, may be the most sensitive in identifying the common cognitive sequelae in anti-NMDAR. However, further professional opinion is needed regarding an appropriate battery.

Larger scale research projects would also help reduce selection bias and extraneous variables and would enable a more scientific approach to developing a cognitive profile for this population, rather than opportunistic sampling. Furthermore, careful consideration should be given to the utility and ethics of performing neuropsychological tests in clinical settings and how these results are fed back to patients (BPS, 2009; Monden, Gentry, & Cox, 2016).

A small number of studies (N=5) have begun investigating the benefits of neurorehabilitation, however, further larger scale studies are needed for the anti-NMDAR group. Gracey, Evans and Malley (2009) propose a Y-shaped model for rehabilitation in ABI, which identifies key discrepancies, such as between pre-injury and current self, and suggests how these could be targeted in rehabilitation. A model such as the Y-Shaped could be a useful tool for application with people with an ABI as a result of anti-NMDAR.

Anti-NMDAR is a relatively newly categorised illness (Dalmau et al., 2007) and as such so far there has been a focus on the medical understanding of the illness, with increasing drive towards neuropsychological understanding. However, taking into consideration the biopsychosocial approach, there is a need for understanding the psychological and social

factors associated with the illness, as well as the biomedical, and the interactions between all three (Gracey, Evans & Malley, 2009). Understanding the impact of this illness on QoL is crucial if health care professionals aim to provide person-centred care and improve the wellbeing of people diagnosed with anti-NMDAR. As such, there needs to be a focus on the personal meaning of the illness for the individual (Gracey, Evans & Malley, 2009).

2.5.6 Conclusions

A systematic review of the current literature suggests that the neuropsychological sequelae for anti-NMDAR encephalitis can include memory impairments, particularly delayed verbal memory; executive dysfunction and attentional/processing speed difficulties in the acute phase. However, further high quality studies are needed in this area to form a more substantial cognitive profile for this population. Psychological studies into this client group are so far absent and as such studies investigating patient experience of the illness and its impact on quality of life should be undertaken in the first instance.

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Appendix A: Table of study characteristics

Study	Setting	Participant information	Treatment/Rehabilitation as stated by the articles	Study or Series and Time points assessed (post symptom onset/diagnosis)	Domains assessed (as reported by articles)	Cognitive domains deficit found	Quality rating
<i>Finke et al., (2012)</i>	Participants recruited from the Department of Neurology, University Hospital, Germany	Participants: Eight female, 1 male (mean age 28.4 years, range 21–44 years) Matched controls: 12 healthy subjects without a history of neurological or psychiatric disorders who were matched for sex, age and	Five patients received first-line (immunotherapies including corticosteroids, intravenous immunoglobulin or both) during first 3 months of the disease, three patients received immunotherapy later in course of disease and one did not receive immunotherapy. One patient received second-line immunotherapy with methotrexate for 5 years. Two patients, ovarian teratomas were found and removed surgically. No rehabilitation.	Case study Median 43 months after disease onset. Range 23-69 months.	Perceptual organisation; attention; processing speed; verbal and non-verbal short-term memory; working memory, verbal and non- verbal episodic memory; executive functioning; general intellectual abilities	Working memory, episodic memory, delay-dependent deficits in STM tasks; executive functioning; attention	18 Medium

		educational level					
<i>Martin-Monzon et al., (2012)</i>	Patient sent for neuropsychological testing following admission to the Department of Neurology, at the Virgen del Rocío Hospital (Seville)	One female (aged 35)	Treatment with steroids, intravenous immunoglobulins, azathioprine, plasma exchange and cyclophosphamide. 4 relapses despite of adequate treatment. Neurorehabilitation over a period of 6 years.	Case series. Tested at 6, 12, 72 months after disease onset.	Orientation; general cognitive functions; verbal and figural short- and long-term memory; frontal executive functions; language; visuospatial cognition; motor skills	STM, anterograde, declarative memory; executive functioning; attention; visuooperative	16 Medium
<i>Finke et al., (2013)</i>	Patients were recruited in Germany and Austria between July 2011 and July 2012 and were referred to the outpatient clinic of the Department of Neurology of Charite Universit, Berlin for further counseling and treatment.	Participants: 21 females, 3 males (mean age 27.9 years) Matched controls: 21 females, 3 males (mean age 28.0 years).	Immunotherapy reported, not specified. No rehabilitation. Neuropsychological battery completed after the acute phase.	Case study. Mean 33 months (median 35 months, range 9-72 months). Calculated by the first author from the reported time between first symptoms and imaging. Working on the assumption neuropsychological testing would have been performed	Verbal memory; non-verbal short-term memory; working memory; verbal and non-verbal episodic memory; executive functioning; premorbid intelligence quotient; general intellectual abilities	Working memory, verbal LTM; executive functioning	14 Medium

				around the same time. Finke et al., reported “Twenty-four patients with anti-NMDAR encephalitis after the acute stage of the disease were studied”			
<i>Marcos-Arribas et al., (2013)</i>	Patient sent for neuropsychological testing following admission to the Neurology Department, Hospital Clínico San Carlos, Madrid, Spain	One female (aged 24)	Neuropsychological battery completed on admission. The patient underwent surgery within 7 days since admission and the diagnosis of mature ovarian teratoma was confirmed by pathology studies. Then nine alternate days sessions of plasmapheresis were then started. After one month the neuropsychological battery was repeated. No rehabilitation.	Case series: Tested at symptom onset & 1 month from symptom onset	Short-term memory; working memory; attention; semantic and episodic memories, visuospatial, praxical, thinking and language functions.	Short term verbal & visual memory; retrograde amnesia of 2 months; attention	14 Medium

<i>Vahter et al., (2014)</i>	Patient sent for neuropsychological testing following admission to the Department of Neurology, West-Tallinn Central Hospital, Estonia.	One female (aged 29)	Immunotherapy with plasma exchange, intravenous IgG, followed later by cyclophosphamide. Neuropsychological testing throughout acute period. No rehabilitation.	Case series. Tested 4 times at symptom onset, 8 months, 12 months, 20 months after symptom onset	Verbal memory; visuospatial memory; logical memory; executive functioning; information processing speed; verbal fluency; visuoconstructive abilities	Long term verbal memory; executive functioning; attention; language; visuoconstructive	11 Low
<i>Bach (2014)</i>	Participants referred to the Specialist Acquired Brain Injury Unit Outreach Team (community rehabilitation team), London.	Two female participants (aged 24 and 23)	Surgery (one patient) plasma exchange and course of intravenous immunoglobulin. Outreach Team for further management and rehabilitation.	Case study. Tested approximately 6 months after symptom onset. Determined from the narrative description of the cases.	Verbal memory; working memory; immediate memory; delayed memory; perceptual organisation; verbal fluency; attention; executive functioning; processing speed	Memory (long term verbal memory), working memory, STM; executive functioning; attention; language; social cognition	13 Medium
<i>Loughan et al., (2016)</i>	Participant referred for neuropsychological evaluation, Department of Neurology, USA	One male participant (aged 42)	Plasmapheresis, IV steroids, Rituximab, Cyclophosphamide. Inpatient rehabilitation for two months. Neuropsychological testing completed once	Case study. Tested 6 months post diagnosis	Working memory; verbal fluency; global ability; attention; effort; executive functioning; verbal comprehension; perceptual	Verbal memory; executive functioning; attention; processing speed; language	24 High

			discharged.		reasoning; verbal memory; visual memory; immediate memory; delayed memory		
<i>McKeon et al., (2016)</i>	Participants recruited via Queensland-based physicians to Neuropsychology Research Unit, Australia	Participants: 6 females, 1 male (mean age, 26.4 years; range, 16–37 years) Matched controls: 10 females, 4 males (mean age, 25.8 years; range, 16–38 years) without significant psychiatric or neurological histories	Four patients (P2, P3, P6, P7) received immunotherapy within a month of symptom onset, and had not relapsed. The remaining three patients (P1, P4, P5) had lengthy psychiatric histories and comparatively poorer response to immunotherapy. No rehabilitation.	Case study. Tested: Mean 19 months (median 22.5 months; range 7-41 months). Calculated by the first author from estimated time between treatment completion & neuropsychological assessment and mean 23 months (median 20 months, range 4-35 months). As calculated from estimated time between treatment initiation & current assessment. 3 patients had treatment ongoing	Episodic memory; semantic memory; language; auditory short term memory; working memory; attention; processing speed; executive functioning	Verbal & visual episodic memory, verbal STM, working memory; executive functioning; attention; processing speed; visuospatial organisation; social cognition	20 Medium

				at time of testing due to residual symptoms.			
<i>Urakami (2016)</i>	Participants undergoing rehabilitation at the National Rehabilitation Center for Persons with Disabilities, Japan	One male, five female participants (mean age 33.3 years; range 20 to 47 years)	Corticosteroids, intravenous immunotherapy (IVIg) and appropriate ovarian teratoma removal. Rehabilitation of 6 months approximately. Neuropsychological testing both before and after neurorehabilitation.	Case series. Tested twice. Mean 6 months after onset of symptoms (calculated by the first author from Table 1) and after rehabilitation (interval between start & end of rehab=mean 184.8 days).	Attention, verbal and non-verbal short-term and working memory, executive functioning; general intellectual abilities	Working memory, verbal memory, visual memory; attention; processing speed	14 Medium
<i>McIvor & Moore (2017)</i>	Participant referred to Department of Clinical Neuropsychology, The Walton Centre NHS Foundation Trust, Liverpool	One male participant (aged 19)	No treatment or rehabilitation. Spontaneous recovery assessed.	Case series. An untreated case tested three times over 30 months.	Delayed memory; immediate memory, visual memory; visual working memory; auditory memory; executive functioning; pre-morbid functioning	STM, auditory memory, delayed memory	19 Medium

Appendix B: Instruction sheet for quality assessment tool

Quality Assessment Tool for Neuropsychological Case Studies/Series (QATNCSS)

Instruction sheet

Accompaniments to this sheet:

- a) Quality assessment tool
 - b) Scoring grid to enable you to record the scores for each paper against the criteria.
-

Eligibility criteria for papers:

- 1. Original research papers for inclusion into a systematic review
- 2. Study design must be either a single/multiple neuropsychological case study or series

Method:

Scoring the studies:

- 1. Read through the research paper carefully

2. There are 26 quality criteria in the tool
3. Read each of the criteria and score from 0, 1, 2 or 3 (depending on the question) to obtain each score.
4. This will result in a score out of a maximum of 33
5. There are interpretations for the criteria at the end of this document

Heuristics for overall quality:

0-11 = low quality

12-22 = medium quality

23-33 = high quality

Scoring instructions:

Basic information

A. Participant information

This is based on whether the information is or is not present. For multiple cases this information should be presented for all participants

B. Diagnosis of anti-NMDAR

Score two if the authors give details about how the diagnosis was given

C. Number of cases studied

Score zero if one case is studied, one if more than one participant is studied and two if more than 10 participants are studied.

D. Time since diagnosis/initial onset

Time since diagnosis needs to be stated for all participants. This needs to be clearly stated either in the main body or table form and not left to the reader to extrapolate the time since diagnosis from additional background information.

E. Treatment e.g. Rituximab

This should be clearly stated for each participant.

F. Current medication

This should be clearly stated for each participant.

G. Psychoactive medication at time of testing (e.g. anti-psychotic, anti-depressant, steroid, opiate)

This should be clearly stated for each participant.

Participant background information

H. Previous psychiatric disorder

This should be clearly stated for each patient. This should be separate from discussion of the psychiatric symptoms that may have presented in the initial stages of the illness.

I. Learning disability

This should be clearly stated for each participant.

J. Congenital or previous neurological conditions, including brain injury, epilepsy

There should be discussion of whether there was any other illness or injury that may have caused acquired brain injury to the participant and if so relevant details given. This should be discussed in respect of all participants.

K. Current level of pain

Pain should be discussed, such as any, side effects of current treatments/medications (for example, Rituximab or corticosteroids) known to cause pain in some instances; pain from surgery (for example, tumour resection) or any pain from another cause not related to anti-NMDAR.

L. Educational attainment

This should be mentioned either participant by participant or in reference to matching with a control group, for example 'all participants were matched for educational level'. This is to ensure that educational attainment was considered by the researchers with regards impact on scores and tests that are compared to a normative sample.

M. Substance/alcohol misuse

This should be clearly stated for each participant.

N. Participant/Informant perspective on cognitive functioning

There should be either the participant's or an informant's perspective on the participants cognitive functioning discussed qualitatively. A higher score is not given if both perspective is given, as an informant may not have been present/available.

O. Level of distress e.g. depression or anxiety

Score one if details are given regarding the participant's qualitative views on their mood, or if an appropriate scale is used, such as the HADS. Score two if both are stated. This should be separate from the discussion around their psychiatric symptoms and mood during the acute phase. It should only relate to current mood.

Neuropsychological testing procedure

P. Compared to a control group

Score one if the participant group are compared to a control group in any form. However, qualitatively it should be noted whether these groups were adequately matched on factors such as age, sex, educational level.

Q. Pre-morbid test of intelligence

Scores for all participants on a validated test such as the TOPF should be clearly stated.

R. Effort test

Scores for all participants on a validated test such as the TOMM should be clearly stated.

S. Full test battery completed, covering main cognitive domains (perception; attention; memory and learning; executive function; and language)

No points should be given if an abbreviated test is administered such as the RBANS. One point should be given if only some cognitive domains are tested such as memory alone. Score two if more than one cognitive domain is tested. Note qualitatively whether adequate justification has been given to choice of tests.

T. Repeated testing

Score one if the battery is repeated more than once; score two if it is administered more than twice.

U. Replicable detail

The exact tests used and the procedure of the testing should be clearly stated in the methods section and/or in relevant tables. Any researcher should be able to easily replicate administration of the assessment on other cases.

V. Neuropsychological tools used specific to the language and culture of the participants

All tests will be assumed to be administered in the appropriate first language of the participant, unless stated otherwise.

W. Practise effects considered

This refers to practise effects both within the same neuropsychological battery, for example when multiple tests assessing the same cognitive domain are administered, and/or practise of the same tests over repeated testing.

Recovery reported:

X. Qualitatively

Score one if either the participant, informant or clinicians qualitative view of recovery is reported. A score of three is not offered if all three views are discussed as an informant may not have been available.

Y. Quantitatively

Score one if any appropriate quantitative measures have been administered to measure recovery, such as the FIM/FAM, to all participants.

Z. Neuropsychological assessment informed an intervention/recommendations

Score one if an intervention/s were either recommended or put into place, such as a neurorehabilitation programme. Or if recommendations for clinical practice are suggested.

Appendix C: Quality Assessment Tool for Neuropsychological Case Studies/Series (QATNCSS)

Basic information

A. Participant information

0 = Not reported

1 = Age and gender reported

B. Diagnosis of anti-NMDAR

0 = Not stated

1 = Stated

2 = Stated and means of diagnosis given e.g. CSF/serum testing

C. Number of cases studied

0 = 1

1 = > 1

2 = > 10

D. Time since diagnosis/initial onset

0 = Not reported

1 = Reported

E. Treatment e.g. Rituximab

0 = Not specified

1 = Specified

F. Current medication

0 = Not reported

1 = Reported

G. Psychoactive medication at time of testing (*e.g. anti-psychotic, anti-depressant, steroid, opiate*)

0 = Not reported

1 = Reported

Participant background information

H. Previous psychiatric disorder

0 = Not reported

1 = Reported

I. Learning disability

0 = Not reported

1 = Reported

J. Congenital or previous neurological conditions, including brain injury, epilepsy

0 = Not reported

1 = Reported

K. Current level of pain

0 = Not reported

1 = Reported

L. Educational attainment

0 = Not reported

1 = Reported

M. Substance/alcohol misuse

0 = Not reported

1 = Reported

N. Patient/Informant perspective on cognitive functioning

0 = Not reported

1 = Reported

O. Level of distress e.g. depression or anxiety

0 = Not assessed

1 = Assessed qualitatively

2 = Assessed using self-rating scales

3 = Assessed both, qualitatively and self-rating scales

Neuropsychological testing procedure

P. Compared to a control group

0 = No

1 = Yes

Q. Pre-morbid test of intelligence

0 = No

1 = Yes

R. Effort test

0 = Not administered

1 = Yes, standardised measure used (e.g. TOMM)

S. Neuropsychological battery covering main cognitive domains (perception; attention; memory and learning; executive function; and language)

0 = No, only abbreviated/screen test used

1 = Only one domain tested

2 = >1 domain tested

T. Repeated testing

0 = No repeat reported

1 = Repeated once more

2 = Repeated twice or more

U. Replicable detail

0 = Could not easily replicate

1 = Easily replicable

V. Neuropsychological tools used specific to the language and culture of the participants

0 = No

1 = Yes

W. Practise effects considered

0 = No

1 = Yes

Recovery reported:

X. Qualitatively

0 = *No*

1 = *Yes*, Participants' perspective on recovery

1 = *Yes*, Responsible clinician's perspective of recovery

1 = *Yes*, Informant's perspective on recovery

2 = *Yes*, a combination of the above

Y. Quantitatively

0 = *No*

1 = *Yes*, appropriate scales administered (such as QoL measure, FIM/FAM scores, modified Rankin Scale)

Z. Neuropsychological assessment informed an intervention/recommendations

0 = *No*

1 = *Yes*

<i>Appendix D: QATNCSS scoring table with second raters scores</i>		Study number									
QATNCSS criteria item	1	2	3- Finke 13	4	5-Marcos	6- Martin	7	8- McKeon	9	10- Vahter	
A	Participant information		1		1	1		1		1	
B	Diagnosis of anti-NMDAR		2		2	1		2		2	
C	Number of cases studied		2		1	1		2		0	
D	Time since diagnosis/initial onset		1		1	1		0		1	
E	Treatment e.g. Rituximab		1		1	1		1		1	
F	Current medication		0		1	0		0		0	
G	Psychoactive medication at time of testing		0		0	0		0		0	
H	Previous psychiatric disorder		0		0	0		1		0	
I	Learning disability		0		0	0		0		0	
J	Congenital or previous neurological conditions		0		1	0		1		0	
K	Current level of pain		0		0	0		0		0	
L	Educational attainment		0		1	1		0		1	
M	Substance/alcohol misuse		0		1	1		0		0	

N	Patient/Informant perspective on cognitive functioning			0		0		0		0
O	Level of distress e.g. depression or anxiety			0		0		0		2
P	Compared to a control group			1		0		0		1
Q	Pre-morbid test of intelligence			1		0		0		1
R	Effort test			1		0		0		1
S	Neuropsychological battery covering main cognitive domains			2		2		2		2
T	Repeated testing			0		1		1		0
U	Replicable detail			1		1		1		1
V	Neuropsychological tools used specific to the language and culture of the participants			0		0		0		0
W	Practise effects considered			1		1		0		1
X	Recovery reported-Qualitatively			0		1		0		1
Y	Recovery reported- Quantitatively			0		0		0		1
Z	Neuropsychological assessment informed an intervention			0		0		1		0
Total				14 Med		16 Med		12 Med		19 High

Study	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	TOTAL
<i>Finke et al., (2012)</i>	1	2	2	1	1	0	0	0	0	1	0	0	0	1	2	1	1	1	2	0	1	0	1	1	0	0	18 Med
<i>Martin-Monzon et al., (2012)</i>	1	2	0	1	1	1	0	1	0	1	0	1	1	0	0	0	0	2	2	1	0	0	0	1	0	0	16 Med
<i>Finke et al., (2013)</i>	1	2	2	1	0	0	0	0	0	0	1	0	0	0	0	1	1	1	2	0	0	0	1	1	0	0	14 Med
<i>Marcos-Arribas et al., (2013)</i>	1	2	0	1	1	1	1	1	0	1	0	0	1	0	0	0	0	1	1	1	0	0	0	1	0	0	14 Med
<i>Vahter et al., (2014)</i>	1	2	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	1	2	0	0	0	0	2	0	0	11 Low
<i>Bach (2014)</i>	1	1	1	1	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	1	0	1	1	1	1	13 Med
<i>Loughan et al., (2016)</i>	1	2	0	1	1	1	1	1	0	1	1	1	1	1	3	0	1	1	2	0	1	0	1	1	0	1	24 High

<i>McKeon et al., (2016)</i>	1	2	2	1	1	1	0	0	0	1	0	0	0	1	3	1	1	1	2	0	1	0	0	1	1	0	21 Med
<i>Urakami (2016)</i>	1	2	2	1	1	0	0	0	0	0	0	0	0	0	1	0	0	2	1	1	0	0	1	0	1	14 Med	
<i>McIvor & Moore (2017)</i>	1	2	0	1	1	1	1	0	0	1	0	0	0	1	0	0	1	0	2	2	1	0	1	1	0	0	19 Med

<i>Appendix F: Table of tests used by each study</i>			
Cognitive function	Tests used	Cognitive function	Tests used
<i>Verbal memory</i>		<i>Attention & Processing Speed</i>	
<i>Loughan et al., (2012)</i>	RBANS: List learning & Recall Story Memory & Recall	<i>Loughan et al., (2012)</i>	TMT: Part A & B
<i>Finke et al., (2012)</i>	RAVLT	<i>Finke et al., (2012)</i>	TAP
<i>Martin-Monzon et al., (2012)</i>	WMS III: Logical Memory Selective Reminding test	<i>Martin-Monzon et al., (2012)</i>	TMT: Part A WAIS-III: Digit Symbol-Coding
<i>Finke et al., (2013)</i>	RAVLT	<i>Finke et al., (2013)</i>	None named
<i>Marcos-Arribas et al., (2013)</i>	WMS-III: Logical Memory I & II Verbal Paired Associates I & II Word Pairs I & II Letter-Number Sequencing	<i>Marcos-Arribas et al., (2013)</i>	WAIS-III: Digit Symbol-Coding
<i>Bach (2014)</i>	WMS-IV:	<i>Bach (2014)</i>	TMT:

	Logical Memory I		Part A & B
<i>Vahter et al., (2014)</i>	WMS?: Verbal memory (assume all subtests) Buschke selective verbal memory, controlled long-term retrieval, long-term storage & later recall	<i>Vahter et al., (2014)</i>	TMT: Part A & B
<i>McKeon et al., (2016)</i>	WMS IV: Logical Memory I & II Verbal Paired Associates I & II	<i>McKeon et al., (2016)</i>	Digit Span Forwards Visual Scanning Time Letter Sequencing Time Number Sequencing Time Motor Speed Time Colour Naming Time Word Reading Time PRP Paradigm SART
<i>Urakami (2016)</i>	WMS-R (assume all verbal memory subtests)	<i>Urakami (2016)</i>	WAIS-III: Coding Symbol search
<i>McIvor & Moore (2017)</i>	WMS IV: Logical Memory I & II Verbal Paired Associates I & II	<i>McIvor & Moore (2017)</i>	None
Cognitive function	Tests used	Cognitive function	Tests used
<i>Visual memory</i>		<i>Executive function</i>	

<i>Finke et al., (2012)</i>	ROCFT: Copy, Delayed & Recall	<i>Finke et al., (2012)</i>	BADS Stroop Test Tower of London
<i>Loughan et al., (2012)</i>	RBANS: Figure Copy & Recall	<i>Loughan et al., (2012)</i>	D-KEFS
<i>Martin-Monzon et al., (2012)</i>	ROCFT: Immediate & Delayed recall WAIS-III: Design Immediate recall & Delayed recall	<i>Martin-Monzon et al., (2012)</i>	WAIS-III Matrix Reasoning TMT: Part B Stroop Colours and words Verbal fluency Wisconsin Categories
<i>Marcos-Arribas et al., (2013)</i>	ROCFT: Immediate & Delayed recall	<i>Marcos-Arribas et al., (2013)</i>	None
<i>Finke et al., (2013)</i>	None	<i>Finke et al., (2013)</i>	Stroop test Computerised go=no-go test Semantic fluency
<i>Bach (2014)</i>	None	<i>Bach (2014)</i>	BADS: Rule Shift Action program Key search Temporal Judgement Zoo map

			Modified six elements
<i>Vahter et al., (2014)</i>	Visual Spatial Memory: Immediate & Delayed recall	<i>Vahter et al., (2014)</i>	Clock drawing
<i>McKeon et al., (2016)</i>	ROCFT: Immediate, Delayed & Recall	<i>McKeon et al., (2016)</i>	D-KEFS: TMT Tower Test Verbal Fluency Proverbs Test Inhibition Test (Stroop Test) Inhibition/ Switching Test Hayling Test
<i>Urakami (2016)</i>	WMS-R: Visual memory (assume all subtests)	<i>Urakami (2016)</i>	None
<i>McIvor & Moore (2017)</i>	WMS-IV: Visual reproduction I & II	<i>McIvor & Moore (2017)</i>	D-KEFS: TMT Verbal Fluency Test
Cognitive function	Tests used	Cognitive function	Tests used
<i>Working memory</i>		<i>Visuospatial ability</i>	
<i>Loughan et al., (2012)</i>	WAIS-IV: Digit Span	<i>Loughan et al., (2012)</i>	WAIS-IV: Block design RBANS: Figure Copy

	Arithmetic		
<i>Finke et al., (2012)</i>	WAIS-IV: Digit Span Block Span	<i>Finke et al., (2012)</i>	ROCFT: Copy
<i>Martin-Monzon et al., (2012)</i>	WAIS-III: Digit Symbol Coding Digit Span backwards Letter Number Sequencing Arithmetic	<i>Martin-Monzon et al., (2012)</i>	Benton Visual Form Discrimination Test WAIS-III: Picture Completion
<i>Marcos-Arribas et al., (2013)</i>	WMS-III: Letter-Number Sequencing WAIS-III: Digit span	<i>Marcos-Arribas et al., (2013)</i>	ROCFT: Copy
<i>Finke et al., (2013)</i>	(WAIS?): Digit span backwards	<i>Finke et al., (2013)</i>	ROCFT: Copy
<i>Bach (2014)</i>	WAIS-IV: Digit Span	<i>Bach (2014)</i>	None
<i>Vahter et al., (2014)</i>	None	<i>Vahter et al., (2014)</i>	Clock drawing
<i>McKeon et al., (2016)</i>	WAIS-IV: Digit Span	<i>McKeon et al., (2016)</i>	ROCFT: Copy
<i>Urakami (2016)</i>	WAIS-III & WMS-R (assume digit span, arithmetic, symbol & spatial span)	<i>Urakami (2016)</i>	WAIS-III (assume block design)

<i>McIvor & Moore (2017)</i>		WMS-IV: VWMI- Spatial Addition & Spatial Span	<i>McIvor & Moore (2017)</i>	None
Cognitive function		Tests used		
Social Cognition				
<i>Bach (2014)</i>		No tests; A 10 item questionnaire to assess ability to understand other's mental states and general social cognition		
<i>McKeon et al., (2016)</i>	Mind in the Eyes Test Advanced ToM Test Social Situations Test Emotion Attribution Task			

WMS-R/III/IV (Wechsler Memory Scale Revised/Third/Fourth Edition); WAIS III/IV (Wechsler Adult Intelligence Scale Third/Fourth Edition); TMT (Trail Making Test); ROCFT (Rey-Osterrieth Complex Figure Test); RAVLT (Rey Auditory Verbal Learning Test); RBANS (Repeatable Battery for the Assessment of Neuropsychological Status); DT-VMI (Beery-Buktenica Developmental Test of Visual-Motor Integration); DTVP (Beery-Buktenica Developmental Test of Visual Perception); DKEFS (Delis-Kaplan Executive Function System); TOL (Tower of London test); BADS (Behavioural Assessment of the Dysexecutive Syndrome); TAP (Test battery for the assessment of attention)

3. Empirical paper

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Impact on identity: An interpretative phenomenological analysis of women diagnosed with anti-NMDAR encephalitis



3.1 Abstract

The aim of this study was to explore the experience of women diagnosed with anti-NMDAR encephalitis and the phenomenon of identity change. Eight women were interviewed; transcriptions were analysed with interpretative phenomenological analysis (IPA). Four superordinate themes were revealed *'Re-finding the 'normal' self'*; *'A special identity'*; *'Evolving from the illness'* and *'Roles and identity'*. Analysis revealed themes common to many severe physical illnesses such as not feeling oneself whilst unwell and moral and personal growth. However, themes emerged specific to anti-NMDAR such as feeling abnormal due to the rarity of the disease and its psychiatric symptoms, feeling viewed as special and concerns around fertility and motherhood. This study represents the first psychological study into anti-NMDAR encephalitis, and it is hoped will provide an initial base from which to build further research.

Keywords: *anti-nmdar; encephalitis; autoimmune; identity; experience; psychiatric*

3.2 Introduction

Anti N-methyl-D-aspartate receptor encephalitis (anti-NMDAR) is a rare form of autoimmune encephalitis, first officially categorised and named in 2007 (Dalmau et al., 2007). Psychiatric symptoms can be a large feature of the illness, with 77% of patients first assessed by a psychiatrist (Kuppuswamy, Takala, & Sola, 2014). However, whilst there are personal accounts of people's experience of anti-NMDAR in the public domain, to date, there are no psychological studies investigating how people experience the illness and specifically its impact on identity.

Anti-NMDAR is acute and often severe, caused by the body's antibodies attacking the NMDA receptors in the brain (Dalmau et al., 2008). It has been found to be more common in young women, however its incidence and prevalence rates are yet to be fully established (Dalmau et al., 2011). Onset is often insidious with prodromic, flu/viral-like, symptoms, giving way to psychiatric symptoms, such as anxiety, mania, and paranoia (Dalmau et al., 2011). This is often followed by seizures, decreased level of consciousness, abnormal movements (such as orofacial/limb dyskinesias) and autonomic instability. All patients are treated with first-line immunotherapy, including corticosteroids, intravenous immunoglobulins or plasma exchange (Dalmau et al., 2011; Chen et al., 2016). Some patients, such as those with delayed diagnosis, will go on to receive second-line immunotherapy, such as Rituximab (Dalmau et al., 2011). Most patients fully recover or have mild medical sequelae, however some die or remain severely disabled (Dalmau et al., 2008; Titulaer et al., 2013). Tumour removal, if present, early diagnosis and treatment have been found to lead to better cognitive outcome (Finke et al., 2012).

There is a paucity of literature regarding cognitive difficulties associated with anti-NMDAR. However, the number of neuropsychological/neurological case studies/series

published is gradually increasing, particularly within the adult population (for example, McKeon et al., 2016) but less so in the child/adolescent populations.

Whilst there is increasing medical understanding of the pathology of anti-NMDAR and its prognosis and treatment, less has been examined regarding the beliefs people with anti-NMDAR hold about this form of encephalitis. To date, insights into such health beliefs have come indirectly from anecdotal accounts (Brain On Fire: My Month of Madness, Calahan, 2013), with limited discussion in the neuropsychological case studies/series (Bach, 2015; McKeon et al., 2016).

Research investigating the psychological impact of other illnesses/conditions is well established, with identity being a prominent theme (Arroll & Howard, 2013; Medved & Brockmeier, 2008; Musser, Wilkinson, Gilbert, & Bokhour, 2015; Roger, Wetzel, Hutchinson, Packer, & Versnel, 2014). Research suggests illnesses are often associated with loss of self and reconstruction of a new self; changing life roles and contemplation of a new future; loss of self-worth and post-traumatic growth (Arroll & Howard, 2013; Goodman et al., 2005; Gracey et al., 2008; Muenchberger, Kendall, & Neal, 2008; Preston, Ballinger, & Gallagher, 2014). Charmaz (1983) was one of the first researchers to describe a loss of self in people with chronic illnesses, who she asserts witness their former selves “crumbling away”. This is purported to be due to an inability to hold onto previously valued roles in life (Charmaz, 2000) and can also relate to experiencing stigma and shame around the illness (Arroll & Howard, 2013; Charmaz, 1983, 2000). Bury (1982) conceptualised chronic illness as a ‘biographical disruption’ whereby an unwell person’s world is interrupted by the illness and everything they thought was certain about the world/their life is called into question. This is more recently conceptualised as a challenge to the assumptive world and related to illness intrusiveness (Devins, 2010). Nochi (1998) investigated identity in ten people who had sustained traumatic brain injury and found they experienced loss of self, for example, when comparing their present status with many

aspects of their past lives. Conversely, in another qualitative study of people who have suffered neurotrauma, Medved and Brockmeier (2008) asserted that participants emphasised an unbroken connection between their pre-and post-morbid lives. Faircloth et al., (2004), in a study with stroke survivors, also argued that biographical disruption is not the same for all people suffering with a chronic illness. They propose that people may give different meaning to the experience and ‘bracket off’ the effects of the stroke/chronic illness to maintain their sense of self pre-and post-stroke. The authors termed this ‘biographical flow’, other researchers have found several emergent strategies that enables this ‘flow’, such as humour and cognitive reframing (Roger et al., 2014). However, others take an intermediate stance, asserting that to suggest the self remains either completely lost or stable is too simplistic (Gelech & Desjardin, 2011). Gelech and Desjardin (2011) found, in their qualitative study of four participants with ABI, that loss and negative change were fused with features of growth, stability and transcendence.

Understanding the health beliefs of people diagnosed with anti-NMDAR is important for supporting both self-management and reconstruction or re-establishment of identity. Currently there are no studies primarily investigating this area. Therefore, the aim of this study was to explore the experience of women diagnosed with anti-NMDAR encephalitis and the phenomenon of identity change; whether anti-NMDAR is viewed by women as a disruption that has altered their sense of self, whether the self remains wholly intact or if there has been changes on facets of the self.

3.3 Method

3.3.1 Methodology selection

Interpretative Phenomenological Analysis (IPA) is a qualitative method with a focus on understanding the individual's experience. It has been widely applied within health psychology to further understand individual experience of illness (Brocki & Wearden, 2007; Biggerstaff & Thompson, 2008; Smith, 2011). IPA was chosen due to the lack of psychological research in anti-NMDAR encephalitis. The first author's perspective being that capturing individual illness representations and processes affecting identity would be a good basis from which to build further psychological research in this area. Furthermore, given that it provides a platform from which to hear individual voices, IPA is arguably in line with the drive within the National Health Service to acknowledge the service-user voice (Brocki & Wearden, 2007).

3.3.2 Participant sampling

A total of eight, international female participants (age range approximately 21-35) with a diagnosis of anti-NMDAR encephalitis were recruited (Table 1). Most recruitment (N=5) took place via a poster advertised on the Encephalitis Society, Research Currently Recruiting webpage. The remainder of the participants were recruited via snowballing (N=3). The inclusion criteria were women between the ages of 18 and 65 with a diagnosis of anti-NMDAR. Interested parties, who met these inclusion criteria, were invited to contact the lead author via email for more information. Information and consent forms were then emailed to the participants and interested parties completed and emailed them back to the researcher. Of all participants who expressed an initial interest, 42.11% were interviewed. An interview time was mutually agreed, due to the sample being largely international and time and budget constraints, face-to-face interviews were not feasible. Consequently, all interviews took place via Skype,

aside from one telephone interview when the participant did not have access to Skype. Guidance on using Skype for qualitative interviews was followed (Hanna, 2012; Seitz, 2016). Each interview lasted 60-90 minutes; the participants did not receive monetary compensation. Due to potential acquired brain injury (ABI) from the encephalitis, capacity to consent to participate, and for the interview to be recorded, was sought at the start of each interview, by assessing the participant's understanding of the study and revisiting the details of the consent form. All participants were deemed to have capacity by the lead author at the time of the interview, in keeping with the terms of the Mental Capacity Act (2005).

3.3.3 Ethics and Procedure

Ethical approval was obtained from Cardiff university ethics board (EC.15.10.13.4209). Pseudonyms are used throughout and all identifiable information has been removed. A semi-structured interview schedule (Appendix M) was created using guidelines from Smith, Flowers and Larkin (2009). A funnelling technique was employed, beginning with the set open questions. Reflection and summarising were used to clarify some of the participants' viewpoints and experiences. The Common-sense Model of Illness Representation (Weinman, Petrie, Moss-Morris, & Horne, 1996) was used to help structure the schedule; to gain an overall understanding of the participants' representations of the illness and its perceived impact on identity.

Pseudonym	Age	Ethnicity	Employment status	Disability	Time since diagnosis
Rachel	26-30	Caucasian	Part time	Yes- cognitive	>5 years
Jane	26-30	Asian	Unemployed	No	1-11 months
Natalie	31-35	Caucasian	Unemployed	No	>5 years
Laura	26-30	Caucasian	Part time	Yes- cognitive	>8 years
Sarah	26-30	Caucasian	Full time	No	>6 years
Katie	21-25	Caucasian	Part time	Yes- combination	>8 years
Bridget	31-35	Caucasian	Full time	Yes- combination	>3 years
Holly	31-35	Caucasian	Part time	Yes- combination	>2 years

TABLE 1: Demographics *Combination disability includes physical, cognitive, sensory, difficulties processing information, social, behaviour and emotional difficulties*

3.3.4 Analysis

The eight transcripts were analysed for common themes, using guidelines for IPA (Smith, Flowers & Larkin, 2009). The transcripts were read multiple times and exploratory comments noted for each transcript, focussing on descriptive, linguistic and conceptual details (Smith, Flowers & Larkin, 2009). Emergent themes for each transcript were identified by the first author from the exploratory comments and grouped together into separate word documents

for each transcript. Numbers were placed next to emergent themes that appeared to correspond to one another. Once the corresponding numbers were grouped a ‘working subordinate theme’ title was assigned to each number. This was repeated for each transcript. All ‘working subordinate themes’ across transcripts were analysed and refined into final the subordinate themes, via an iterative process of re-examination and discussion between co-authors (Appendices N-R). Four superordinate themes were created from the eight subordinate themes using the processes of subsumption and abstraction; polarisation was also considered (Smith, Flowers & Larkin, 2009). Subordinate themes identified appeared in at least half of the participants’ transcripts, in keeping with guidance from Smith, Flowers & Larkin (2009). Rigour and quality of analysis was ensured via triangulation, transparency and bracketing (Yardley, 1997). The respondent verification technique was also used (Appendix O). Transparency was achieved by documenting this process of analysis and providing direct quotations within the results section to evidence the themes for the reader (Street et al., 2016).

3.4 Results

Four Superordinate themes were identified from the coded transcripts and all addressed re-finding and re-constructing identity: *‘Re-finding the normal self’*; *‘Special self’*; *‘The evolving self’* and *‘Revised roles’*.

3.4.1 Re-finding the ‘normal’ self: ‘I’m kind of starting to getting back to normal’

Many of the participants disclosed feeling compromised whilst they were unwell. Holly encapsulated this whilst discussing others’ perceptions of her illness:

it was all invisible but I was really struggling still and I I was still very compromised as a person and I wasn't back to myself at all you know. (Holly)

Instead of describing her immune system as compromised, Holly describes being 'compromised as a person' extending the medical use of the word to encompass her entire identity. In common with each interview, Holly asserts that she 'wasn't herself', as though the 'self' had somehow disintegrated through the process of becoming unwell. When asked whether she viewed herself as an unwell person now, Holly judged this in terms of the immunologist's question as to whether she can do everything that she wants every day:

And in that regard I really can and that's definitely true in the last maybe three years, the first three years of my recovery were really difficult and then the the fourth and the fifth year you could see changes, you could see myself re-emerging but um in the last the last three years of my life has been pretty per like perfect. (Holly)

Holly highlighted a 're-emerging' process and suggested her real 'self' had been obscured by the illness. She also mentioned 're-emerging' in the same line as 'perfect', suggesting she thinks her life would be perfect if she was back to being herself before the illness. Most of the participants discussed 'normality' throughout the interview and only felt more 'normal' once they were more recovered.

*I was a good communicator and I got along with people and I was a good worker, a good daughter, a good friend and but the illness just kind of changed, the period of time that I can remember, the illness changed that but I'm **kind of** starting to getting back to normal (Jane)*

Here Jane repeats the word 'good' in reference to her former self and frames the illness as something that stopped her being 'good', suggesting you cannot be unwell and 'good' simultaneously.

All participants described a difficult route to diagnosis and there was an overall sense that they viewed themselves as ‘abnormal’ because the illness was rare and the cause unknown. This is encapsulated by a short quote from Laura when discussing the causes of the disease:

Yeah but it's such a rare thing it's strange to have you know (Laura)

Additionally, all the participants gave the impression that they felt there is a socially acceptable level of illness, which they surpassed, and made them appear unusual:

I was in intensive care I think for a little while and then yeah I went into the..., sort of ward, and then went up to the the normal ward as well [Laughs] (Sarah)

Sarah’s reference to one ward as normal suggests that intensive care is not normal and that being critically unwell is out of the ordinary. Whilst few people acquire illnesses that cause them to require specialist intervention in critical care, Sarah appeared embarrassed and ashamed by needing to access this level of care.

The participants all also discussed the diversity and uniqueness of the disease process, which also seemed to feed into their view of themselves as ‘abnormal’ when unwell:

as far as my friends go, my family wasn't [pauses] they didn't let them come to the hospital a lot or until later on just because of how crazy the disease is and they didn't know how I was going to act so they weren't really allowing people to come visit me until later on (Jane)

This extract suggests almost a level of detachment, as though Jane cannot recognise herself in her odd and unpredictable behavior. A great deal of the feeling of abnormality specifically seemed to stem from the experience of psychotic symptoms:

Those aren't normal things for like I guess at least my culture (Natalie)

Five participants discussed their experience of psychiatric symptoms, most women had been received treatment on a psychiatric ward either prior to or after diagnosis, and appeared to attempt to distance themselves from a mental health narrative:

Yeah see I was one of the lucky ones, many people with NMDA they present with psychosis first. I I to be honest I don't I feel like, my mum would agree, I don't see psychosis as a major part of my journey (Natalie)

These quotes suggested evidence that the women recognised the potential stigma of mental health difficulties as part of their illness. Furthermore, three participants seemed to need to actively normalise their illness by directly comparing it to a disease process that is perhaps more socially acceptable. As evidenced by Sarah when discussing attributions about the potential causes of the disease:

Yeah, I don't mind, I think everyone does it, it's a bit like if someone has cancer, and they think like this must be something I've done as it's such a terrible thing why do I deserve this sort of thing? (Sarah)

Therefore, despite anti-NMDAR being a medically recognised and diagnosed illness with a protracted immunological/neurological recovery period, participants seemed to be striving for legitimisation. This could be related to the disease being unknown in the lay population meaning the women frequently felt pressure to explain the illness to others. For example, when Laura is discussing needing to explain her word finding difficulties to others:

why I'm doing it so that's one thing like um you need people to know that the reason why you're um [pauses] oh I can't think of the word now umm you know just looking for words and stuff you want to say oh the reason why, just not that you're a bit crazy and can't think of things

3.4.2 A 'special' identity: 'He always called me his star patient'

Five participants discussed how they were identified as their doctor's 'special', 'star' or 'best' patient:

I still send him emails and he still keeps up with me and he was like if you ever think you're relapsing head straight out here and we'll get you in immediately so he always called me his, what do you call it, his star patient, because he absolutely loved me and every time I mean there for, for the last four years we were out there every probably 6 weeks (Bridget)

This extract demonstrates a very strong and positive doctor-patient relationship, which Bridget portrayed as very important for her recovery. Some people with anti-NMDAR can make a rapid recovery and their doctor's role in their treatment is crucial. The underlying reason for being termed a 'star' patient could be due to the often quite dramatic recovery a person with anti-NMDAR can make. An individual can progress from an induced coma to being almost recovered within a few months. It could be that this recovery time gives the doctors a sense of achievement and fulfilment, which is not always possible with other neurological/immunological cases, as identified by Jane:

And all the care they're putting into me and all you know they often, they'd consider me one of their best patients like they they often say their aim is to get everyone as well as I am (Jane)

These five women also spoke about the time and effort their doctors expended, feeling like they chose to go over and above their duty of care, which could have contributed to feeling viewed as 'special':

I think my my story is kind of special because just the way my doctor ended up going to this conference and talking to the leading doctor who who named this and then finding out (Sarah)

It was not just in relation to the medical profession that the participants referenced this 'specialness', they also discussed being treated favourably by friends and family, being allowed to 'get away with more':

Yeah I think there's a lot less expectations of me than say my siblings for example, or someone I went to school with, like people don't, don't necessarily treat me differently, but like [pause] I don't think if I hadn't had the brain injury my parents would be so happy with me living at home but then because I have it's kind of just like [pause] they don't mind as much? (Natalie)

This extract suggests that Natalie is happy to be viewed in some way as 'special' as it releases her from typical Western society restrictions of needing to be independent.

By receiving special treatment and by the nature of the disease being rare, it seems that on one level the women came to view themselves as 'unique' and perhaps 'special'. However, combined with this 'unique' and 'special' identity was also the feeling of being 'compromised' by the illness.

Yeah I mean yeah I think being sick or you know is so much part of my identity now like you know you know like I never like, the interesting thing about brain injury I think over a lot of different illnesses is and I say this all the time like you spend your whole life becoming somebody becoming whoever you're becoming and then like literally overnight that's all challenged and compromised (Bridget)

One particular way in which the participants described feeling compromised was in thinking they were less cognitively able, specifically regarding persistent word finding difficulties. Three participants also had concern over their weight and appearance, due to steroid use and all the participants disclosed lack of self-esteem and confidence. This feeling is elaborated by Bridget:

I think after a brain injury you really feel less than for a long time afterwards like particularly you know cognitively you're compromised you don't feel as smart, you don't feel as quick you don't feel as... you know there's a lot of things you don't feel (Bridget)

Bridget seems to be describing feeling ‘less than’ she was before the illness but possibly also feeling ‘less than’ others. She could also be describing some emotional numbing during the recovery process, or of consciously trying to detach from the new identity that she is forming.

It appears that the women held two views of themselves, simultaneously feeling both ‘special’ and ‘compromised’. ‘Specialness’ seemed to relate to being ‘unique’ and a ‘good’ patient who recovered well, whilst ‘compromised’ seemed to be more closely related to their true beliefs about their own self-worth and abilities.

3.4.3 Evolving from the illness: ‘I’m a much stronger person now’

Five participants described the experience of having had anti-NMDAR as associated with opportunities for growth. The interviews were interspersed with a sense of acceptance and gratitude for the increased insight and development the experience had given them. Five participants used the words ‘strong’, ‘strength’ and ‘fighter’ to describe themselves now. They felt that having survived the encephalitis made them a more resilient and overall ‘stronger’ person. The way in which the participants described becoming stronger differed slightly but was exemplified by Katie who felt that she had become a mentally stronger person, in that she no longer worried about things to the extent that she did before. Overall she felt that her mental health had improved as her anxiety levels had decreased:

*Well since I was young I was diagnosed with an anxiety disorder and so I lived with that for a long time really severely and um after being diagnosed and treated I I have very little anxiety and I’m a lot more secure I just feel a lot more **confident** than I ever did, I just find this kind of [pause] people just think I’m better overall I guess than I was before. I was very insecure with just myself and being alone and things like that but I’ve found now I’m a lot **stronger** (Katie)*

It appears Katie has developed a greater sense of her own resilience. The words she uses to describe how she feels about herself give a sense of perpetuity ‘*secure, confident, stronger*’, and seem to have released her from worrying about the smaller difficulties in life:

Yeah maybe I don't worry as much about about things like I used to (Katie)

Four participants showed pride in their recovery, Sarah exemplifies this:

Well I became like more positive in a way, it's more like I survived from this that I can do anything and other people are like yeah I can't do this because it's too hard, it's like, I will say, that's nothing, if I can survive from this, you can do that (Sarah)

She suggests that, due to the severity of the illness and the unpleasant treatments for anti-NMDAR, she has survived something largely incomparable to other life experiences, and that this has given her a mental strength somewhat over and above other people. Not all the participants felt the illness had made them stronger, one participant felt the opposite:

umm yeah ...you know I, I don't know I think I think as myself as a little bit more [laughs] fragile than I used to be in some ways you know (Bridget)

Although, in context, her perceived fragility appeared more in relation to her physical stamina, as opposed to the mental strength described by the other participants. As shown when discussing a charity 5km run she had committed to:

I wanna try it and I wanna feel like I've given it an effort without them assuming it's something I can't handle but at the same time if I can't handle it [laughs] I want them, my family, to understand that (Bridget)

Bridget seems to be evidencing resilience; she is pushing herself to do something at the limits of her stamina and is somewhat fearful at the prospect of this. However, she is determined to push herself and appears to feel confident in the knowledge that she will be supported and understood by her family.

Another way in which all the participants felt they had grown was in compassion towards others. They spoke about having greater understanding of other people's suffering, having experienced their own. The participants spoke about ways in which they had tried to 'give back' to other people diagnosed with anti-NMDAR, wanting to prevent others going through what they experienced:

Yeah I would say that and just not letting it be this you know bad thing that happened to me but turning it into something good for other people at least so that you know there're less people or maybe someone out there wouldn't have to go through the same thing or wouldn't have to go through it alone you know (Rachel)

Aside from the altruism of wanting to help others, there was also a sense of trying to find 'meaning', i.e. a reason for why they became unwell. The conclusion being that it was so they could then help others:

Um yeah I mean well I mean I I'm not allowed some people would say it's [pauses] had a positive impact on their life, I don't think I would go that far but I feel like for me I've been able to you know with this thing like a really rare disease I sort of felt like there's a reason I'm surviving these things and I need to turn a negative into a positive, for me that's the only way to sort of make sense of it (Laura)

This extract captures that, even if the positives were not immediately obvious, there appeared a deep need to create something positive from the illness, most tangibly perhaps through helping others.

2.4.4 Revised roles: 'I've just felt really inspired to write my own path'

The subject of life roles was consistent across all the transcripts. All of the participants focused on a change in their role in life with regards to their career or education. The women felt the illness had greatly impacted their planned career paths, either because of extended treatment

interfered with studying or availability for work, or because they now do not feel they have the same level of intelligence or energy to pursue their planned careers. Despite this, most of the participants appeared to re-frame this, describing feeling freed from obligation or not under the same social pressure to focus on their career. Instead they felt more able to focus on what they believed made them happy and on living more in the present rather than the future. This sentiment is summarised very clearly in a statement by Rachel:

the fatigue obviously means that I probably wouldn't be able to have a high job like I wanted to but then in other ways that's good because it's made me not worry about that sort of thing anymore and I tend to enjoy life more (Rachel)

Rachel's emphasis is on moving away from the drive to have a 'high job'; whilst for other participants the sense of freedom and re-prioritisation was more about the shift to a different career:

So I struggled a lot in the past three years thinking about where I wanted to go you know I went back to that idea of teaching and should I work with kids that way but in the bottom of my heart I knew it's not really what I wanted... in the last while I've just felt really inspired to write my own path whatever that may be but I would really like to start building a career (Natalie)

Natalie's use of words 'write my own path' implies she thinks that she now has greater control of her choices. Whereas before she might have felt that her life was on a particular trajectory, she felt liberated to reconsider her values and pursue choices that might build a career aligned with what she 'really wants'.

Four participants discussed the impact of anti-NMDAR on parenting and commented on its effects on their families or parenting plans. Two participants already had children when they became ill and one saw no long-term effects on parenting associated with the anti-NMDAR:

No not at all that's that's what's strange, no I've just, no I've just got on with everything but I've had my youngest since I had it last time and obviously I wasn't with them the time I was in hospital and when I came out I was just back to normal you know, cooking and getting them ready and stuff so really it hasn't it hasn't affected me like that, my lifestyle really, in that sense (Bridget)

Whereas, one mother spoke about the long-term impact on her relationship with her daughter:

Yeah that was probably the hardest part of my recovery was my daughter because when I got out of the hospital I still wasn't well and I was looking after her and I had a lot of resentment towards her I was very jealous of my husband with anybody and I had a lot of resentment towards my daughter and I, we, kind of our bond was broken and I am actually, we're still, we're going to counselling my daughter and I trying to, uhum so still trying to work on it, it's been a it's been that's been the hardest part about the sickness. (Holly)

Holly uses the term 'broken' in the extract, suggesting she feels there was a complete rupture in the relationship. For the other three women, there was concern about starting a family in the future and the long-term effects of anti-NMDAR and its treatment may have on fertility. For example, Natalie discussing taking Rituximab:

And I'm on it every like wha... what like is it going to affect me long term, in ten or fifteen years will I be suffering from something as a result of my them, my Rituximab and then again the daily immunosuppressants like they're grand I don't mind them, they don't affect me at the moment but if I were ever to plan to plan a family like er I'd have to come off them, they'd be toxic to anything like that. So there are things in the future that I'll just have to deal with when I come to them. (Natalie)

This extract shows how the illness can cause women to re-evaluate their future roles, with an emphasis on motherhood and the anxiety of wondering whether it will be possible to have children and take on a mothering role.

3.5 Discussion

The aim of this study was to explore the experience of women diagnosed with anti-NMDAR encephalitis and the phenomenon of identity change. The themes revealed that the rarity and unfamiliarity of the disease appeared to affect the women's views of themselves as 'normal'. How actively they were being treated and medically monitored appeared to influence how recovered and 'normal' they perceived themselves. This is consistent with research suggesting diagnosis of diseases can lead individuals to feel different or abnormal (Roger et al., 2014; Dickson et al., 2008) and to experience stigma (Charmaz, 2000). Particular to anti-NMDAR, was the presence of psychiatric symptoms appeared to exacerbate this feeling of abnormality. All but one of the women experienced a delay in receiving a diagnosis, partly as their presenting symptoms were attributed to mental health difficulties and most participants had spent time in a psychiatric ward initially. Varma and Sapra (2015) assert that psychiatrists need to keep a high level of vigilance with regards anti-NMDAR, particularly when patients are only partially or non-responsive to antipsychotics. They go on to argue this is most crucial when younger women present with acute onset neurobehavioural symptoms citing pre-existing stressors, because their diagnosis could potentially be missed or delayed. During the interviews, it was evident participants were keen to distance themselves from this mental health narrative but sanguine about acknowledging the neurological and immunological impact of the disease. This perhaps reflects research that has found individuals diagnosed with psychiatric disorders often report experiencing stigmatisation (Corrigan, Watson, & Barr, 2006; Dinos et al., 2004).

Three of the women made direct comparisons between anti-NMDAR and cancer during their interviews. They contrasted the rarity and lack of understanding of their ‘strange’ illness and its treatment with the perceived legitimacy of common, long-term physical health conditions such as cancer. Making this link might be primed perhaps, given that one of the main treatments for anti-NMDAR is Rituximab, which is also used to treat certain types of cancer (Cancer Research, UK, 2015).

Another theme revealed that most of the women felt they were viewed as ‘special’ by both health professionals and family/friends. This was due to being called ‘special’, ‘star’ or ‘best’ patients by their physician or, by having ‘special’ treatment at home, i.e. being allowed to behave in ways they felt they could not have in the past. Health professionals may treat individuals with anti-NMDAR in this way because the differential diagnostic process is specialist and because, given it is life threatening, clinicians promoting recovery take pride in how some people with anti-NMDAR return to full health under their treatment. Participants reported friends and family would have often witnessed them being critically ill, so displayed a sense of relief and gratitude when they achieved recovery, thus playing a part in treating them as ‘special’. However, the women also reported low self-esteem, largely due to word finding difficulties, suggesting that the women held dual beliefs about themselves, as both special but also simultaneously compromised. It is possible that the ‘specialness’ did not relate to their beliefs about themselves and their own self-worth, as they had little control over fighting their illness, which largely required an intensive biomedical approach. Instead feeling ‘special’ appeared to be more related to having developed this ‘unique’ illness and having surviving it, despite feeling they had no power over this. The influence of others on identity reconstruction is consistent with existing qualitative data investigating identity in chronic illnesses (Arroll & Howard, 2013; Atkin et al., 2010; Karnilowicz, 2011; Gelech & Desjardin, 2011). Researchers assert social relationships can influence how individuals with a chronic illness view themselves

and can either be nurturing or damaging to their own sense of self (Karnilowicz, 2011; Mathieson & Stam, 1995). In a study exploring psychological ownership and identity in chronic illness, Karnilowicz (2011) argued that to gain control over an illness, individual's must take some ownership. However, often this role is taken over by a loved one or medical professional, which can be problematic. They assert healthcare professionals need to be aware of this and allow individuals to take psychological ownership (Karnilowicz, 2011).

Impact on identity was not found to always be a negative process, with the women frequently reporting personal growth. Many of the women thought they were mentally stronger following the illness and better able to face life's adversities. They also felt they had greater compassion and empathy and were more willing to help others. This growth could be contextualised within the post-traumatic growth (PTG) literature, which has found PTG following severe physical illness and psychosis, with themes such as development of personal strength (Dunkley & Bates, 2015), reappraisal of life and priorities (Hefferon, 2009) and greater appreciation of life (Silva et al., 2011). This study also revealed impact on identity in relation to the roles the women felt they could hold in life following the illness, a finding consistent with the work of Charmaz (2000). Firstly, with regards their careers; overall it seemed the women had either shifted away from seeing themselves as 'career women' and were more focused on other elements of life, or were keen to ensure that their job was rewarding. This impact on career role has been found in other chronic illness studies. In a postal survey of 308 people with chronic illness, Bhatti et al., (2014) found major life-changing decisions (MLCDs) related to employment were found in 34% of patients, with some common decisions being career plan abandonment or going into part-time employment. Although there was a sense of loss with regards this, largely the impact on career appeared to link with the theme around PTG, with most of the women positively changing their career plans due to a shift in life priorities.

Another subordinate theme within 'Revised roles was the impact on the mothering role. Some of the women began to question whether they would be able to adopt a role as a mother in the future due to the uncertainty around the long-term effects of the illness and its treatment, on both fertility (Abdul-Rahman et al., 2016; Sanmaneechai, Song, Nevadunsky, Moshé, & Overby, 2013) and their health (Titulaer et al., 2013). One of the women worried about her role as a mother to her child after being discharged home. She felt she was still not 'herself' and that this affected her ability to parent her child. Another woman was concerned about their ability to conceive a healthy child in the future or had decided not to factor motherhood into their future at all, due to fears around their future health. This is also consistent with the findings of Bhatti et al., (2014) who found 24.3% of their participants made MLCs with regards motherhood, for example deciding not to have children or delaying plans to have children. This was due to concerns, for example, about looking after their health and baby's health simultaneously and long-term treatment.

The themes generated in this study suggest that the identity of the women interviewed was impacted in several ways following development of anti-NMDAR encephalitis. The majority of the women felt their identity was altered whilst they were unwell in that they viewed themselves as 'abnormal'. However, they discussed feeling more 'themselves' once they were more recovered immunologically and neurologically. The women also discussed a 'special' identity as a result of the illness, but this was coupled with a feeling of being 'compromised' by the long-term effects of the illness, such as cognitive difficulties. Many of the women also saw themselves as more empathic and mentally stronger. Change in life roles was also discussed, which appeared to alter the way in which the women viewed their identity. The themes therefore suggest that, consistent with some existing literature, there is a degree of biographical flow (Faircloth et al., 2014), with some of the women emphasising a re-emergence of their previous identities once the more severe symptoms of the illness had receded. This is

consistent with the research by Gelech and Desjardins (2011) that suggests whilst people do experience some loss of self post-illness/injury, there is also endurance and stability of self, combined with moral growth and transcendence. However, given the many other ways in which the women discussed that their identity had altered, it seems that there was a large degree of biographical disruption (Bury, 1982). The women were beginning to form new identities post-illness, based on the ways in which they felt they had altered, grown, and their change in life roles.

3.5.1 Critical evaluation

As is consistent with using the IPA method, this study focused on a homogenous sample of participants and as such the findings are not intended to be generalised. Instead they represent the experience of a small population of women with anti-NMDAR. This allowed for a deeper exploration of the women's experiences, and examination of psychological convergence and divergence within the group (Smith, Flowers & Larkin, 2009). However, it is recognised that, whilst the participants reported feeling comfortable discussing their experiences, the richness of the data could have been affected by use of Skype (Cater, 2011).

Sampling bias may have been present via the process of recruitment from an online research page, which may have led to people with particular characteristics/motivations being sampled, for example those more familiar with using the internet and possibly those seeking out/giving social support via online communities (Nambisan, 2011). These factors could therefore have affected the narratives of the participants and the themes derived.

3.5.2 Areas for future research and clinical implications

All the participants were at different perceived milestones in terms of their recovery, therefore a longitudinal study could track participant's views on identity at different stages of recovery or re-uptake of roles.

Researchers in acquired brain injury (ABI) have found that PTG increases with time since ABI (Gangstad, Norman, & Barton, 2009; Powell, Ekin-Wood, & Collin, 2007). A longitudinal study could also investigate whether PTG is experienced after anti-NMDAR and what mediates this, for instance, time since onset. Despite participants describing feeling viewed as ‘special’, all disclosed lacking self-esteem and feeling ‘compromised’. One clinical implication would be to investigate psychological wellbeing in this client group and offer some form of psychological support. Mindfulness-based techniques (MBT) have been investigated in other illnesses (cancer, HIV, chronic fatigue) with significant improvements found in measures such as, anxiety and fatigue and overall fostering of PTG (Garland, Carlson, Cook, Lansdell, & Speca, 2007; Milam, 2004; Surawy, Roberts, & Silver, 2005). A randomised control trial, comparing treatment as usual with MBT on a population of people with anti-NMDAR could be beneficial to see if this intervention is acceptable and helpful.

One theme that arose was regarding motherhood and fertility and, given this illness is more prevalent in women, this could be an important avenue for future research, particularly because resection of ovarian teratomas and use of Rituximab have been associated with fertility risks (Dalmau et al., 2008; Irani et al., 2010; Cancer Research UK, 2015). Exploring views on fertility and pregnancy would be important for this population and could go on to inform both the health information available to this population and how health professionals sensitively communicate this information (Bach, 2014). Patient counselling around infertility should also be integrated into standard care (Bach, 2014). Given the women’s discussions around family/motherhood, future research could also investigate the impact on families, particularly the relationship between mother-child.

One of the themes revealed the women felt they were viewed as ‘special’ by health care professionals. This bears consideration, given the potential cognitive difficulties in this population, which could give rise to vulnerability. Furthermore, patients might also feel

pressurised into presenting themselves as 'recovered' in order to be the 'best' when they might actually be suffering cognitive, psychological or behavioural difficulties. Thus, missing the chance for detection of these difficulties/potential relapses, and not receiving the therapeutic intervention they might need to maximise recovery and functioning. Therefore, whilst establishing a strong doctor-patient relationship is important, caution would be recommended for inter-professional communication and use of 'best' patient labels.

3.5.3 Conclusions

To conclude, this study has presented the experience of the impact on identity in eight women diagnosed with anti-NMDAR. It is the first piece of psychological research into anti-NMDAR and provides an exploration of how being diagnosed with a newly categorised and rare illness can affect an individual's identity. It offers insight into psychological factors both common to survival of many severe physical illnesses, such as not feeling oneself whilst unwell and moral and personal growth, but has also revealed factors particular to anti-NMDAR encephalitis. These include, feeling abnormal due to the novelty/rarity of the disease and the presence of psychiatric symptoms and feeling viewed as 'special'; and experiencing uncertainty around the long-term impact on fertility and parenting. It is hoped that this study will prompt further psychological research into anti-NMDAR, to provide increased insight into how this illness and its treatments are experienced by those diagnosed, and ultimately give further recommendations for professionals working with this population.

3.6 References

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3.7 Appendices

Appendix G: Ethical approval confirmation email

psychethics

Reply all |

Tue 10/11/2015, 11:58

Della Nicolle;

+1 more

Inbox

You forwarded this message on 13/11/2015 14:04

Dear Della,

The Chair of the Ethics Committee has considered your revised postgraduate project proposal: Experience of recovery: An interpretative phenomenological study of people who have been diagnosed with anti-nmda encephalitis (EC.15.10.13.4209R).

The project has been approved on the following condition:

- It should be made clear on the materials when the data will be anonymised – when any possibility of being able to link the data to the individual will be removed.

Please note that if any further changes are made to the above project then you must notify the Ethics Committee.

Best wishes,

Natalie

School of Psychology Research Ethics Committee

Cardiff University
Tower Building
70 Park Place
Cardiff
CF10 3AT

Tel: +44(0)29 208 70360

Email: psychethics@cardiff.ac.uk

<http://psych.cf.ac.uk/aboutus/ethics.html>

Prifysgol Caerdydd
Adeilad y Tŵr
70 Plas y Parc
Caerdydd
CF10 3AT

Ffôn: +44(0)29 208 70360

E-bost: psychethics@caerdydd.ac.uk

Appendix H: Email confirming permission to recruit via the Encephalitis Society website

From: Ava Easton <Ava@Encephalitis.info<mailto:Ava@Encephalitis.info>>
Sent: 25 September 2015 09:04
To: Della Nicolle
Subject: RE: Research proposal anti-nmdar encephalitis

Hi Della

We would be keen to support your project and help you recruit through our membership even as a primary source?

I just need your proposal and evidence of ethical approval in the first instance. And we would be delighted to help you disseminate findings.

We are a global organisation with a substantial UK membership as you might imagine.

Happy to help. Just let me know what you need.

You might be interested to attend our forthcoming annual encephalitis seminar in London on 7/12 where some of the top research in the country and top profs specialising in the condition will be presenting and networking. Let me know. In the future it might be a useful environment in which to present your findings.

Become a member which is free and takes 2 minutes online <http://www.encephalitis.info/get-involved/membership-online/professional-membership/> and you will be kept in touch with our research and professional work. You are also welcome to visit us anytime.

Let me know your further thoughts.

Kind regards
Ava Easton
Chief Executive

Email: NicolleD@cardiff.ac.uk

Phone: +44 (0)29 208 70582

This project has been reviewed and was ethically approved by The Cardiff School of Psychology Ethics Committee on the 10/10/2015.

Deadline: 01/12/2017



Study Information



Dear,

My name is Della Nicolle and I am a trainee clinical psychologist based at Cardiff University, Wales. I am in the process of completing my large-scale research project for the third and final year of my clinical psychology doctorate. I am interested in understanding the lived experience of women diagnosed with anti-nmdar encephalitis, by interviewing people who have the diagnosis.

This letter describes my study. Please read this to help you decide whether you would like to take part by being interviewed. If you like you can contact me to discuss it further. Then, if you would like to be interviewed I will ask you to sign and return the consent form, which I will post or email to you. Once this is signed and received, I can then either drive to your home, if it is within commutable distance from Cardiff, or I can call you via Skype. Alternatively, we can pay for your travel expenses for you to come to Cardiff University, if it is within commutable distance from Cardiff.

This project has been reviewed and ethically approved by The Cardiff School of Psychology Ethics Committee.

What is this study about?

I am interested in women's experiences of having a diagnosis of, and living with, anti-nmdar encephalitis.

Why have I been invited to take part?

I am inviting women between the ages of 18 and 65 with a diagnosis of anti-nmdar encephalitis within the last nine years i.e. since official recognition of the disease in 2007.

Do I have to take part?

No, you do not have to take part. It is completely up to you.

If you decide to take part, you can still change your mind at any time and withdraw from the interview and study without having to give a reason.

What happens if I do not take part?

Nothing will happen if you decide not to take part, or if you withdraw from the study. You will not lose the support of any support groups or services that you may be using.

What is involved if I do take part?

You and I will arrange a time to discuss your experiences of anti-nmdar encephalitis. This will take place in either a room at Cardiff University, your house or via Skype, wherever is mutually convenient.

We might talk for up to an hour, but we can go on for longer if you would like, or talk for less time. With your permission, I will record our conversation so that I can type it up afterwards.

Confidentiality and anonymity

The audio recordings of the interviews will be deleted once they have been transcribed.

All information that is collected about you during the course of the study will be kept strictly confidential. This means that in the write-up of the study, your name and any information that could be used to identify you will be removed or changed.

The only circumstance in which we may pass on your details to another professional would be if you either tell us that you are planning on harming yourself or somebody else, or if you give us serious reason to believe that you intend to commit a crime. This is to keep you and others safe. If this happens, we will talk to you first before talking to anyone else and hopefully together we can decide on a course of action. I am working under the supervision of Dr

Jennifer Moses and, if I remain concerned about you, I will also contact her for advice and to assist in deciding on any action.

Are there any disadvantages to taking part?

We do not think that there are any disadvantages to taking part in this study. However, some of your experiences of the illness might have caused you distress and be upsetting to talk about. It is up to you whether you talk about upsetting experiences. If you do find the interview distressing, you can contact Dr Jennifer Moses, Consultant Clinical Psychologist on 02920 870582 for further support or the Encephalitis Society, Website: www.encephalitis.info Email: mail@encephalitis.info.

Are there any benefits to taking part?

We hope that you will find the conversation interesting and even useful, as you will be encouraged to think about your unique strengths and how you have coped with having anti-nmdar encephalitis. The information you provide and the general findings from the study could help to make services better for people with anti-nmdar encephalitis and increase public awareness of the disease.

What will happen to the results of the research study?

Once I have completed all of the interviews I will write up my findings in a thesis that will be submitted to my university. In the future I may decide to shorten the write up and submit for publication in a scientific journal or present it as a poster. Both the thesis and journal will be able to be accessed by yourselves and other members of the public, but all information will be anonymised and you will not be identifiable.

What if there is a problem?

If you experience a problem or have concerns related to the study please do not hesitate to contact me, or either of my supervisors. If you would like to make a formal complaint, you can contact the Cardiff School of Psychology Ethics- Email: psychethics@cardiff.ac.uk, Telephone: +44 (0)29 2087 0360

I appreciate you taking the time to read this letter. If you have any questions or concerns please contact me, or the study supervisors listed below.

Contacts

If you have any questions about this letter please contact me:

Della Nicolle

Trainee Clinical Psychologist

Telephone: + 44 (0)29 208 70582

E-mail: NicolleD@cardiff.ac.uk

Alternatively, you can speak to my academic supervisor, Dr. Jennifer Moses, who is a Consultant clinical psychologist at Rookwood Hospital, Cardiff and the Academic Director of the Cardiff University Clinical Psychology Doctorate on: Email: Jenny.Moses@wales.nhs.uk, Telephone: +44 (0)29 208 70582.

If you would like to participate in this study then please call Della Nicolle on the number above to discuss this further. Alternatively, email Della Nicolle with your contact number

Many thanks for your time,

Della Nicolle

Trainee clinical psychologist



CONSENT FORM

Study Number: EC.15.10.13.4209R

Study Location: DClinPsych Programme, Cardiff University, Tower Building, 70 Park Place, Cardiff, CF10 3AT

Participant Identification Number for this trial:

Title of Project: Impact on identity: An interpretative phenomenological study of women who have been diagnosed with anti-nmdar encephalitis

Name of Researcher: Della Nicolle

Please initial box

- I confirm that I have read the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
- I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason.
- I understand that I can refuse to answer any question I am asked without giving any reason.
- I agree for the interview to be recorded and then typed-up. I understand that the recording will be kept in a safe place and then destroyed once it has been typed up.

- I understand that once the interview is typed-up, any information I provide that can be used to identify me, for example, my name, will be changed so that I cannot be identified.
- I understand that everything I say in the interview will remain confidential. A relevant professional will only be told about me if in the interview I say that I am thinking or planning to harm myself or someone else or commit suicide or a crime.
- I give permission for anonymised parts of the interview to be included in the thesis and in academic articles, posters and conferences.
- I understand that the anonymised transcripts may be used to support other research in the future, and may be shared anonymously with other researchers.
- I understand that where possible my GP will be notified that I am taking part in the study so that they can better support me if I need support following the interview.
- I agree to take part in the above study.

 Name of Participant Date Signature

Della Nicolle _____
 Name of Person Date Signature
 taking consent

Appendix L: Demographics form



DEMOGRAPHICS FORM

Please do not write your name on this form. It will be stored separately from your consent form and interview transcripts and will not be linked with your other information in any way. This information just allows us to provide an accurate description of the sample of participants.

For the following questions, please check just one response that you think most accurately describes you, and please leave the others blank.

Gender:

- Male Female Transgender

Age:

- 18-20
- 21-25
- 26-30
- 31-35
- 36-40
- 41-45
- 46-50
- 51-55
- 56-60
- 61-65

Ethnicity:

- White British
- Irish
- Gypsy or Irish Traveller
- Other White
- White and Black Caribbean
- White and Black African
- White and Asian
- Other Dual/Mixed Heritage
- Indian
- Pakistani
- Bangladeshi

- Chinese
- Other Asian
- African
- Caribbean
- Other Black
- American Indian/Alaska Native
- Native Hawaiian/Other Pacific Islander
- Arab
- Any other ethnic group

Current employment status:

- Employed full time
- Employed part time
- Volunteering
- Not currently in education/employment/volunteering
- In education/learning
- Self-employed
- Retired
- A combination of the above

Do you consider yourself to have a disability?

- No
- Yes - I have a physical disability
- Yes - I have a sensory disability
- Yes - I have difficulties processing information
- Yes - I have social, behavioral, or emotional difficulties
- Yes - A combination of the above

Approximate time since diagnosis: (≥ equal to or more than)

- 1 month - 11 months
- ≥ 1 year
- ≥ 2 years
- ≥ 3 years
- ≥ 4 years
- ≥ 5 years
- ≥ 6 years
- ≥ 7 years
- ≥ 8 years
- ≥ 9 years

Thank you very much for completing this questionnaire

Appendix M: Interview schedule

LSRP Interview Schedule

Research question: What is the impact on identity of women diagnosed with anti-NMDAR encephalitis?

Second (theory driven) question: To what extent does the common-sense model of illness help us to understand women's experience of anti-NMDAR encephalitis and its impact on their identity?

Impact

1. Can you tell me about the role anti-NMDAR has in your life at the moment?
Prompt: Do you feel unwell at the moment? How do you cope?
2. Can you tell me about if and how you think your life has changed since having anti-NMDAR?
Prompt: For example, the people who are important to you.
3. Has having anti-NMDAR changed your plans for the future, and if so how?
Prompt: Life goals such as relationships, career. Then: How do you feel about this?

Explanation for cause

4. Sometimes people go think about why they might have developed a particular illness, do you have any ideas around why you think you in particular developed anti-NMDAR?
Prompt: Doing a particular activity? Eating a particular diet?
5. What do you think other people believe is the cause of your anti-nmdar?
Prompt: Family, health professionals

Controllability/Timeline

6. Do you view yourself as being an 'ill' person *now* and how has this changed over time?

Prompt: Did you ever view yourself as an ill person? Do you now?

7. What or who do you think has been instrumental in controlling your illness?

Prompt: For example, health professionals, family, a particular treatment.

Identity

8. **Before** you developed anti-NMDAR how did you feel about yourself?

Prompt: For example your abilities, qualities as a person, self-image.

9. How do you think others viewed you **before** the diagnosis?

Prompt: For example how would they define your personality?

10. Has anti-NMDAR changed the way you view yourself now, in what way?

Prompt: Has it affected for example your confidence, your personality, your priorities in life?

11. Do you think having this condition has changed the way others view you now?

Prompt: Do others treat you differently now? Family/friends/mental health professionals?

Conclusions and Reflections on the Interview

Thank you for taking part in the interview, how did you find it?

Is there anything else you would like to add?

Appendix N: Example of an annotated script

Exploratory Comments	<p>. hasn't sort of talked through himself and also just the practicalities of the impact on the business, things like that? #00:21:17-0#</p> <p>. . respondent: exactly #00:21:17-0#</p> <p>. . interviewer: Ok, has having anti-nmdar changed your long term plans for the future do you think? #00:21:27-7#</p> <p>. . respondent: Yea I think, before I got sick I was studying theology and um like my hope was to be a teacher and uh I continued my degree after <u>after my year out</u> but my confidence was really affected at the time and I just couldn't and my dream of being a teacher or <u>whatever is was</u> at the time sort of strayed #00:21:58-9#</p> <p>. . interviewer: Yea #00:22:00-1#</p> <p>. . respondent: Yes but like I I always valued kind of you know</p>	Emergent Themes
Describes illness almost as a choice 'year out'		
Minimising of her previous dream- perhaps as feels she would no longer be able to achieve this?		Denial to protect self
Describes illness almost as a gift, insight it's given her		Change of career plans Illness as a gift

Exploratory Comments

Why mention cancer?
More understandable
illness or socially
acceptable?

kind of talking with people and being with people you and I think my perspective at the time and everything I'd been through and everything erm like the life experience I had been offered through this experience I kind of you know I thought this would be a great opportunity for me to come into a role where I'm kind of available for somebody you know like cancer.

Emergent Themes

Striving for legitimisation

Appendix O: Example of coding for themes with numbers on each transcript

Emergent themes Transcript 1

Working subordinate themes:

- 1- Strength
- 2- Old self as superior
- 3- Low self-esteem
- 4- Loss of role/impact on life trajectory
- 5- Relationship with Dr/illness (medicalization/special)
- 6- Compassion/empathy

Living with uncertainty

Blaming of oneself 3

Denial (of loss & considering cause)

Medical skepticism

Jealousy towards those recovered

Depersonalising

Comparisons to other illnesses

Questioning why

Impact across life 4

Physical & Emotional impact

Developmental disruption/regression 4 5

Loss of intelligence 3

Loss of professional career 4

Sense of freedom 1

Criticism of past self 2

Transitions/growing up 4 5

Finding inner strength 1

Selfishness/selflessness 6

Idealising of former self 2

Self-esteem 3

Mental health

Personality change 2

Impact on relationships

Loss of friends

Acknowledgment of struggles

Historical mental health difficulties

Reversion to old self 2

People not understanding

Feeling overprotected 5

Frustration

Anger at illness

Having no one to blame

Fear of judgment 3

Rejection of sick role 2

Loss of identity 2

Medicalisation 5

Relearning skills

Loss/misplacement of social skills 3

Gaining independence

Expert patient

Steroids

Impact of medication

Relationship with doctor 5

Dependency on others

Embarrassment at disability 3

Difficulty coping

Physical versus emotional support

Relief at being alive

Appendix P: Refining subordinate themes, creating Superordinate themes and finding complementary quotes

Working subordinate themes Transcript 1:

- Increased mental strength
- Old self as superior
- Low self-esteem
- Loss of role/impact on life trajectory
- Relationship with health care professionals/illness (medicalisation/special)
- Compassion/empathy

Working subordinate themes Transcript 2:

- Increased mental strength
- Compromised
- Psychotic symptoms
- Loss of career
- Best patient

Working subordinate themes Transcript 3:

- Low self-esteem
- Career
- Increased mental strength
- Feeling special
- Compassion/empathy
- Motherhood

Working subordinate themes Transcript 4:

- Increased mental strength
- Psychotic symptoms
- Re-emerging
- Education
- Relationship with Dr

Working subordinate themes Transcript 5:

- Comparison to other illnesses
- Re-emerging
- Low self-esteem
- Impact on life trajectory
- Treated as special by family
- Compassion/empathy

Working subordinate themes Transcript 6:

- Old self as superior

- Feeling less than
- Impact on career
- Treatment by family and friends
- Compassion/empathy

Working subordinate themes Transcript 7:

- Old self as superior
- Low self-esteem
- Severity of illness
- Motherhood
- Treatment by healthcare professionals
- Helping others/giving back

Working subordinate themes Transcript 8:

- Increased mental strength
- Severity of symptoms
- Re-emerging
- Cognitive difficulties (feeling compromised)
- Impact on motherhood
- Helping others/giving back

Subordinate themes revised:

Re-emerging
 Factors pertaining to abnormality
 Feeling Special
 Feeling compromised
 Increased mental strength
 Increased compassion and empathy
 Change in career/education
 Impact on motherhood

Superordinate themes:

Superordinate theme 1= Re-emerging

Superordinate theme 2 –Feeling ‘special’

Superordinate theme 3= Evolving from the illness

Superordinate theme 4= Revised roles

Refining of theme titles:

Re-finding the 'normal' self: 'I'm kind of starting to getting back to normal' (Transcript 4; 359)

A 'special' identity: 'He always called me his star patient' (Transcript 5; 167)

Evolving from the illness: 'I'm a much stronger person now' (Transcript 6; 395)

Revised roles: 'I've just felt really inspired to write my own path' (Transcript 3; 222)

Appendix Q: Emergent themes lifted from each transcript

Transcript 1

Sense of freedom 1

Selfishness/selflessness 1

Strength 1

Transcript 2

Illness improving the self 1

Improved mental health 1

Strength 1

Greater clarity 1

Transcript 3

Prioritizing of wellbeing 1

Change in life perspective/prioritization 1

Strengthening of relationships 1

Greater self-care 1

Positives of illness 1

Transcript 5

Living in the present 1

Emotional liberation 1

Happiness with life now 1

Thankful for recovery 1

Increased respect for self 1

Transcript 6

Stronger person 1

Self as a fighter 1

Appendix R: Frequency of subordinate themes within transcripts (including line numbers)

Subordinate Theme	Rachel	Jane	Natalie	Laura	Sarah	Katie	Bridget	Holly
<i>Re-emerging from the illness</i>		121; 337; 341	206; 495; 644	347; 359	276	50		19; 429
<i>Factors pertaining to 'abnormality' (psychosis, rarity, severity)</i>		313	443; 449	19; 315	38;			573
<i>Feeling 'special'</i>	48; 76; 141;161; 363; 385	181	507; 538		162;		209;213	
<i>Feeling 'compromised'</i>	44	63	69; 145; 589; 644			34; 272; 303	377	3; 293; 358
<i>Feeling stronger</i>	332	1; 267		255; 395	19; 383; 387; 415; 435	133;		
<i>Increased compassion and empathy</i>	68		672	167;	423	84;		
<i>Change in career/education</i>	44; 48;	96; 100	210; 214	143; 171; 407	85; 89; 104	341; 113	357; 377	
<i>Impact on motherhood</i>			522		7		488; 492	271; 274

Appendix S: Respondent verification

A summary of the super and subordinate themes was emailed to the participants for their opinion on the derived themes, whether they felt they resonated with their personal experience and whether they felt the concepts would be useful for the community. Half of the participants responded verifying that the themes resonated with their perspective and welcoming the findings as providing legitimacy for them in voicing their experience.

Sarah:

“I've just got a chance to read your analysis and I have to say it really speaks to me and I feel it captures my journey in a very wholesome way. In many ways this is the first time I have read an academic piece that focuses on the inner/emotional journey of people who have survived this illness. For me, that was the first part of the recovery process that I had any control over and the part that really emphasised to me what it takes for me to be "normal" again. I appreciate the point of view you have captured with your research and feel that it will contribute greatly to people understanding this condition more.

I can only thank you again!”

Rachel:

“Thanks for sending me your draft. It sums everything up well and I think the topics covered are very relevant and are able to reflect individual's experiences. It was interesting to know

that others have really gone through the same experience and have felt the exact same, in some cases.”

Bridget:

“Thank you! It is awesome! Thank you also for bringing light to this ugly disease! If you ever need anything else, please let me know”

Appendix T: Researcher's Position Statement

This position statement outlines the potential influences on the researcher, it was developed via the process of reflexive bracketing (Ahern, 1999).

The researcher writes from the position of a single, twenty-eight-year old British middle-class trainee clinical psychologist. The researcher's aim is to gain a doctorate in clinical psychology and possibly have the work published. With regards the power hierarchy, the researcher sits below the thesis supervisors (qualified clinical psychologists). The researcher potentially sits above the participants given their qualifications and the position of being an interviewer. The researcher only had one experience of working with this client group, whilst working as an assistant psychologist within a neuropsychology department. Once the neuropsychological assessment had been conducted and the results fed back to the patient, the patient revealed that they did not find the process very helpful for their wellbeing. This was because it highlighted to them their cognitive weaknesses and how much 'intelligence' they felt they had lost since having had the illness. This perspective led the researcher to consider the utility of neuropsychological assessments, as well as the overall cognitive profile of this population. It was this initial exposure that led to an interest in the illness and subsequent reading of the book *Brain on Fire: My month of madness* (Cahalan, 2013). This revealed to the researcher how novel the illness is and the potentially difficult road to diagnosis and treatment. As well as the perceived unpleasantness of the initial psychiatric symptoms. Combined, this motivated the researcher to investigate this population.

The researcher recognises that given their previous experience in a neuropsychological

department, there is a tendency to over focus on the cognitive difficulties an individual might have and the impact of these on their wellbeing and identity. The researcher has also worked on a six-month placement in a recovery and rehabilitation unit for people with severe and enduring mental health difficulties, predominantly schizophrenia, and has an interest in psychotic experiences. Therefore, this also may be an area the researcher is drawn to in the analyses. The group of participants will be working age females, like the researcher, and so it must be considered that the researcher may at times draw parallels between herself and the participants. This will need to be reflected on throughout the interviews and analyses.

Appendix U: Extract from Reflexive Diary

10th September

I have my fifth interview booked in for this evening. The participant is in another country and so I will be staying up late to do the interview via Skype. I need to be aware that my tiredness may make me rush the interview and potentially make more assumptions. I have completed the demographics sheet with the participant and know that she is quite young and had anti-NMDAR whilst she was a teenager. I need to not make assumptions about how this may have affected her cognitive and social development, for example her scholastic attainment and ability to build peer friendships. I know I have an interest in neuropsychology, and also neurology, so must not let this dictate the direction of the interview.

11th September

I think that my interest in the illness generally, it's trajectory, how it is treated, what the side effects are and long term effects, are affecting my follow-up questions and potentially becoming more medical, in order to satisfy my own curiosity. I need to be aware of this when I go into the next interview and analyse the data.

19th September

I have just conducted my sixth interview and I think I am summarising and reflecting too much, as I would in a clinical psychology assessment. I think that next time I should allow for more

silences so that the true phenomena can come to light, as opposed to trying so much to put the participant at ease and let them know that I empathise with what they've been through.

1st October

I have my seventh interview tonight and I need to remember not to go into the interview as a clinical psychologist trying to elicit therapeutic change, but rather as a researcher trying to explore the phenomena of the illness for this particular group of women. The participant tonight was very informal and chatty over their email when arranging this interview, therefore I need to be mindful of maintaining boundaries and a level of professionalism whilst building therapeutic rapport. It will be important to try to strike this balance.

2nd October

I think I managed to keep a professional boundary in the interview last night and think it was a successful interview with a lot of rich data, as the participants spoke at length for 90 minutes and was very self-reflective, to a level I was not expecting for someone who does not reflect as part of their profession. This just goes to show that you should try not to have preconceptions about what a person will speak about. I am feeling so grateful for the time these women are taking to email me, send the consent forms back etc. and to do the interviews, particularly as they are not being paid. At the end of the interviews the majority of participants are thanking me for conducting this research, which they feel needs to be done. I find this a very humbling experience as I do not feel that I am doing anything particularly impactful at this stage, however, on reflection this study could have an impact for the community once it is written up and disseminated. On listening to the transcript back I notice that I double up my questions,

which means that the participant either gets a little confused or only answers one question. I need to stick to asking one question and pause, instead of qualifying it with another question, as this is making the data a bit messier perhaps?

13th October

The eighth participant was the only participant that was not Caucasian and was brought up in a non-Western culture. I felt during the interview that the cultural difference was quite apparent, particularly when the participant was discussing her families views on the psychiatric symptoms. She was explaining that they did not understand why she was behaving in the way that she was and that they thought she was very “weird”. This was made more difficult as her mum (who was the person who supported her most) does not speak very good English and so could not have the psychiatric symptoms qualified by the doctor. I felt quite shocked by this lack of understanding and empathy for the participant by their family and had sympathy for her. However, I was very mindful of reflecting on this (in my mind) during the interview and, whilst we discussed the impact of this on her, I made a conscious effort not to show any shock I felt at this or to ‘side’ with the participant. I also tried not to make any assumptions on the what the participant would be thinking and feeling or make predictions on how they would answer the rest of the questions based on their cultural background. I think I was successful, in as much as you can be perhaps, in bracketing off my opinions and preconceived ideas about collectivist culture.

20th October

This participant seemed to have difficulty discussing the psychiatric symptoms and was keen to move on from any line of questioning about this. I found this very interesting and perhaps stayed on this topic too much. I need to be mindful of my interest in psychosis and not lead the questioning in this direction/stay on this topic when the participant wants to move on. Also, I am aware that it may just be my perception that they did not want to be associated with psychiatric illness, when actually they may not have thought it was very relevant. I need to think about this some more when I listen to the transcript back and begin to transcribe, see if I can notice any nuances in the way they spoke about the psychiatric symptoms.

20st November

I met with Jenny Mercer today to show her my exploratory comments and emerging themes. She discussed with me different ways of beginning to cluster the themes. I am feeling a bit overwhelmed as there seems to be quite a lot of themes and not all of them related to identity, which is my research question. Jenny encouraged me to re-focus on what it is I am asking in the research question and to just disqualify anything else even if it is interesting data. I find this hard as I want to do justice to everything that the participants shared with me. However, this is something I need to do to keep the empirical study focused. I am trying to let the data speak for itself and not draw upon the literature I have carried out so far, for example on biographical flow and disruption. I do not think I am thinking about scientific theories very much when considering themes, as the data is so rich with the patients' experiences that they are more dominant in my mind.

28th November

Feeling overwhelmed again, I don't know whether this is just the nature of the research process, of trying to bring things together like pieces of a jigsaw puzzle. Or if, because I am listening to the interviews, I am somehow assimilating the feelings of the participants of feeling overwhelmed by their illness. I expect it is a combination of both. However, there are some very interesting and novel themes now emerging, which I am pleased with.

Appendix V: Email from participant regarding taking part in the study

Re: Debriefing sheet

XXX XXX <XXX.XXX@gmail.com>

Reply all |

Thu 07/07/2016, 16:07

Della Nicolle

Inbox

Flag for follow up.

Hi Della, absolute pleasure and thanks for lending your expertise to finding out more about ANMDARE. It was very easy to talk to you and that's such a gift. Thank you so much and best of luck with your study. I have contacted X in X for you too.

Kind regards,

X



Debriefing Sheet

Title of Project: Impact on identity: An interpretative phenomenological study of women who have been diagnosed with anti-nmdar encephalitis

Name of Researcher: Della Nicolle

Thank you

Many thanks for taking part in this study. We hope that you have found it interesting. Please feel free to ask the Researcher any questions you have about the interview and the research area.

What was the purpose of the study?

This study investigated women's experiences of having a diagnosis of anti-nmdar encephalitis, how you get by from day to day and cope. We were also interested in how you think your identity has changed since diagnosis. As you know, anti-NMDAR is a relatively new diagnosis, having gained official recognition in 2007, and as such there has been little research, particularly qualitative, about people's experience of this disease. We felt it was vital to begin to explore the individual experience of anti-NMDAR, in order for people's voices to be heard and to help improve services for people with anti-NMDAR encephalitis, whilst also increasing public awareness of the disease.

Please note that the data analysis can be very lengthy. The researcher may not be able to give you any feedback as to what was found until the middle of 2017. However, if you would like to be contacted in the future regarding the final write up of the study then please let the researcher know.

Are the procedure and results confidential?

The audio recording of your interview will be deleted once it has been transcribed. All information that is collected about you during the course of the study will be kept strictly confidential. This means that in the write-up of the study, your name and any information that could be used to identify you will be removed or changed.

What will happen to the results of the research study?

Where appropriate, the results of this study will be presented at medical and scientific conferences and published in journals. The results may also be disseminated by The Encephalitis Society via their website, newsletters and conferences. You will not be identified in any report, presentation or publication. The results of this study may also help us to design future research projects and future researchers may use your anonymised data.

What do I do if I am unhappy with the way I was treated?

In the first instance, you should contact the supervisor of the leader of the Research Project:

Dr Jennifer Moses Consultant Clinical Psychologist and Academic Director Cardiff University Email: Jenny.Moses@wales.nhs.uk Telephone: +44 (0)29 208 70582
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If you are still unhappy, you should contact the relevant Ethics Committee:

Psychology Ethics Committee Secretary
School of Psychology
Cardiff University
Tower Building
Park Place
Cardiff
CF10 3AT UK

Tel: 029 2087 4007
Fax: 029 2087 4858
Email: psychethics@cf.ac.uk

What if I have become distressed as a result of this study?

If you have found the interview distressing you can contact Dr Jennifer Moses, Consultant Clinical Psychologist on 02920 870582 for further support or the Encephalitis Society, Website: www.encephalitis.info Email: mail@encephalitis.info. Your doctor is also an important person to speak to if you are distressed and concerned about yours/others safety.

Who has reviewed the study?

This study has been reviewed and approved by the Cardiff University School of Psychology Ethics Committee.

Contact for Further Information

Della Nicolle
Trainee Clinical Psychologist
Telephone: + 44 (0)29 208 70582
E-mail: NicolleD@cardiff.ac.uk

We would just like to take this opportunity to say once again, many thanks for your participation in this study and all the very best for the future.

4. Commentary

A critical evaluation of the empirical paper and systematic review investigating the impact of anti-NMDAR encephalitis

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4.1 Abstract

This paper offers a critical appraisal with discussion of the strengths and limitations of the papers and their line of enquiry, as well as implications for further research and clinical practice. Ethics and diversity are considered for the empirical paper and personal and professional development is discussed overall, along with a reflection on the research process. The commentary is divided into, firstly, discussion of the systematic review and secondly the empirical paper. The two papers are considered together for the dissemination plan, to discuss their potential impact for the anti-NMDAR encephalitis community.

4.2 Commentary on the systematic review

4.2.1 Strengths and weaknesses of the present study

Given that there is such a paucity of research in this area it could be argued that a systematic review is premature, and this was considered extensively within supervision. Broad search terms (anti-NMDAR OR Anti-N-Methyl-D-Aspartate AND encephalitis AND Neuropsycholog* OR cogniti*) were used to try to capture any neuropsychological articles within this area. Despite this wide-ranging approach only four appropriate studies could be located (Bach, 2014; Finke et al., 2012; 2013; Marcos-Arribas et al., 2013) during the time allocated for searching for papers (May 2016 to December 2016). However, at the beginning of 2017, four newly published studies were found whilst undertaking a final searching (Loughan et al., 2016; McKeon et al., 2016; McIvor & Moore, 2017; Urakami, 2016) and a further two via hand searching of these references (Martin-Monzon et al., 2012; Vahter et al., 2014). Therefore, once ten papers were identified, this was deemed sufficient to begin to investigate the neuropsychological sequelae of anti-NMDAR. It is possible that the search terms were too broad and neuropsychological studies missed. However, a trial was conducted of different search terms, before applying the chosen string systematically across databases, and the former string captured more appropriate studies. A strength of the systematic review is that, to the best of the researcher's knowledge, this was the first attempt at synthesising neuropsychological data to try to draw together a cognitive profile for anti-NMDAR.

A quality assessment tool was created for this systematic review as a literature search revealed no existing tool to assess the quality of neuropsychological case studies and case series. A search of other systematic reviews of neuropsychological case studies/series revealed it was typical for a tool to be created for the purpose of their study (Mahan, Rous, & Adlam, 2017; O'Sullivan & Newman, 2014), highlighting the need for professional consensus on a

validated quality tool. The tool created for this review appeared to be successful ($k=0.72$) in capturing quality indices such as, whether the studies reported pertinent background information and described the procedure in replicable detail. However, it perhaps did not manage to weight the importance of completing a case series and assessing more than one patient. Therefore, single case studies such as Loughan et al., (2016) scored higher on the checklist, whereas other, larger scale, studies such as Finke et al., (2013) scored lower. This is despite the study by Finke et al., (2013) potentially having greater impact and generalisability. Furthermore, whilst scoring, some of the factors appeared more prone to subjectivity than others, for example determining whether the informant perspective on cognitive functioning was sought. In Loughan et al., (2016) there was a narrative report of the clinical interview “mild daily forgetfulness was noted”, however, it was unclear whether this was the clinician’s perspective, the informant’s or the participant’s. Consequently, at times the rater’s scores differed. Moreover, even though the tool identified weaker papers, these were not then excluded due to the lack of a psychometric basis on which to operate a cut-off. For instance, the Standard Quality Assessment Tool for Evaluating Primary Research Papers from a Variety of Fields (Kmet, Lee and Cook, 2004) has a cut-off of 50% and Ghannouchi, Speyer, Doma, Cordier and Verin (2016) have operated this cut off to exclude papers falling below 50% on Kmet et al’s (2004) scale. As such, further development of this tool would be recommended for any future portfolio research.

There could be a case for this review to have focussed more on the chronic phase of the illness, as opposed to both stages, for a more in depth analysis. As the systematic review discusses, it is likely that cognitive functioning would be different at the various stages of recovery, due to the systemic effects of the illness and factors such as side effects of medication (Buchman, 2001; Ikeguchi et al., 2012; Cancer Research UK, 2015; Mayo Clinic, 2017). Current theory is that the antibodies cause selective but reversible decrease in NMDAR surface

density and synaptic localisation, which then deregulates the glutamatergic pathways, and although NMDARs can be reactivated, some neuronal damage may remain (Martin-Monzon et al., 2012; Finke et al., 2016). Arguably, the most effective time to assess for a cognitive profile is once recovery is more established, for example after the 12-month period. This could then elucidate longstanding cognitive effects of anti-NMDAR itself. However, it was felt that understanding the neuropsychological sequelae of the acute phase could prove useful to neuropsychologists assessing patients within this period. It could help inform the support and management patients need at this time.

This current review focused on an adult population, using 18 years as a cut-off point, based on the general UK definition of an adult (GOV.UK, 2014). An adult population was chosen due to the specificities of neurodevelopment on cognitive functioning. Furthermore, currently there are fewer published paediatric studies and as yet there is not an established adult cognitive profile for anti-NMDAR. Therefore, this systematic review may provide a model for a similar review of research emergent from work on anti-NMDAR in the paediatric population. There are a number of neurological case/cohort studies and series that appear to combine adult and paediatric cases (Dalmau et al., 2007; Iizuka et al., 2010; Titulaer et al., 2013; Chen et al., 2016). McKeon et al., (2017) included patients that were 16 years of age. Therefore, it could be argued that 16 is a more appropriate cut-off for the adult population, given that young people are deemed to have capacity to consent to treatment from age 16 (Care Quality Commission, 2015). However, 21 up to 30 years could also be argued to be a more appropriate cut-off for an adult population due to increasing neuroscientific evidence that synaptic pruning continues well into adulthood, particularly in the frontal lobes (Johnson et al., 2009). Furthermore, differences in child and adult presentations of anti-NMDAR have been reported (Florance et al., 2009; Dalmau et al., 2011; Zhang et al., 2017). Considering the epidemiology of anti-

NMDAR and the neuro-developmental psychology of adolescence, 18 was chosen as an appropriate compromise.

Examination of the impact of the timeliness of immunosuppressive treatment on cognitive outcome was beyond the scope of this systematic review, particularly given that this information was not explicitly provided in at least four of the articles. However, researchers did report significantly better cognitive outcome in patients with early immunotherapy in comparison with patients with delayed treatment (Finke et al., 2012; Urakami, 2016). This finding has been more recently replicated in children (Matricardi et al., 2016).

4.1.2 Limitations of the articles and line of enquiry

As discussed in the systematic review, whilst a cognitive profile appears to be emerging from current neuropsychological studies, there remains a scarcity of research in this area, particularly high quality research. Reporting of the cases was typically weak, with insufficient detail given to pertinent neuropsychological variables such as premorbid intellectual functioning, psychiatric history and any existing acquired brain injury (Lezak, 2012; Hebben & Milberg, 2009). Without full reporting of historical information, the association between cognitive difficulties and anti-NMDAR remains uncertain and subject to question. Furthermore, often participants were acting as their own control, but sufficient discussion was not given to replicable detail. Therefore, if a change in score is found, it cannot be solely attributable to the effects of the illness.

Additionally, a specific battery of cognitive assessments has not yet been devised to screen for cognitive deficits in anti-NMDAR (Bornstein, 1990). Whilst there were overlaps between tests used across the studies, there remains disparity between the cognitive domains tested and which tests are used to examine performance in these domains (Appendix F). A

‘scattergun’ approach appears to have been used, which could have led to Type I errors (Schatz et al., 2005).

As mentioned in the systematic review, it is also important to consider the ecological validity of neuropsychological assessments; most tests currently used were not specifically designed to predict real-life functioning, such as the ability to live independently or return to work (Chaytor & Schmitter-Edgecombe, 2003; Sbordone, 2001). In many tests, the real-world context is absent and so the tests can be completed with little distraction, which can give an artificial performance. One approach utilised to address ecological validity is the verisimilitude approach, whereby tests attempt to emulate the cognitive demands of day-to-day life (Spooner & Pachana, 2006). Such tests include The Test of Everyday Attention (TEA; Robertson et al., 1996), the Behavioral Assessment of the Dysexecutive Syndrome (BADS; Wilson et al., 1996), the Rivermead Behavioral Memory Test (RBMT; Wilson, Cockburn, & Baddeley, 1985), and the Cambridge Test of Prospective Memory (CAMPRMPT; Wilson et al., 2004). A second approach to consider ecological validity is veridicality; statistical analyses are used to assess the relationship between performance on traditional neuropsychological tests, (such as, Wechsler Memory Scales—Fourth Edition, 1997) and measures of everyday functioning (such as, employment status, clinician's ratings, behavioral observations) (Spooner & Pachana, 2006). These approaches have both been used to assess ecological validity of neuropsychological tests in people with a traumatic brain injury (Cuberos-Urbano et al., 2013; Odhuba, Broek, & Johns, 2005). Whilst some neuropsychological tests may not have been designed to predict how people would live day-to-day, Jung (2017) argues they have advantages. Typically, they have standardised norms, which allows for group comparisons, and they more directly assess cognitive performance than other injury/severity related assessments, such as the Glasgow Coma Scale or location of a lesion (Jung, 2017). Furthermore, they can be completed in conjunction with imaging techniques to give greater evidence for cognitive

impairment and whether this relates to functioning (Martin-Monzon et al., 2012). For example, using resting state fMRI, Finke et al., (2013) found significantly reduced functional connectivity between the anterior hippocampus and the anterior default mode network, which correlated with individual memory performance on a neuropsychological test battery in 24 participants. More recently, Finke et al., (2016) found reduced volumes of hippocampal input and output structures and impaired microstructural integrity, which strongly correlated with memory performance in 40 patients with anti-NMDAR. Considering these studies, there is an argument for the pairing of neuropsychological testing and brain imaging to track the pathology of the illness (Finke et al., 2012). Harvey (2012) asserts serial neuropsychological assessment alone will likely be a cheaper way of tracking cognitive functioning, rather than repeated scanning. Furthermore, there is an argument that imaging techniques for assessing cognitive functioning in brain injury patients are not always reliable (Bigler, 2001). Bigler (2001) claims brain lesions are not always detected via traditional MRI scans and that absence of detectable abnormalities does not always mean there is an absence of functional abnormality. However, Lees-Haley et al., (2003) argue not to assume cognitive dysfunction without evidence, also not to underestimate psychological explanations for any cognitive effects that are observed, such as effort, response bias and compensation-related contexts, which were largely not addressed in the current studies. Therefore, arguably neuropsychological testing can help elucidate cognitive impairment, particularly when combined with a comprehensive clinical interview, effort tests and clinical observation (BPS, 2009). Importantly, when ecological validity is addressed, neuropsychological testing can help inform clinicians regarding a person's day-to-day functioning and assist in informing neurorehabilitation plans (Bach, 2014; Bradley, 2015; Loughan et al., 2016; Martin-Monzon et al., 2012; Urakami, 2016). Finke et al., (2012) assert that neuropsychological testing can help to monitor the illness activity after the acute stage and

track the “precise characterisation” of any cognitive difficulties, which would be important for “appropriate neuropsychological rehabilitation”.

As discussed in the systematic review there was little examination of the interaction between cognitive functioning, QoL and psychological wellbeing across the neuropsychological studies. Only Bach (2014) administered a formal QoL measure (QOLIBRI-OS; von Steinbuechel et al., 2012), finding significant increases in satisfaction at follow-up. Psychological wellbeing (such as levels of anxiety and/or depression) was explored in four of the ten articles (Bach, 2014; Finke et al., 2012; Loughan et al., 2016; McIvor & Moore, 2017; McKeon et al., 2016). Researchers who did assess psychological wellbeing largely administered either the Hospital Anxiety and Depression Scale (Snaith, 2003) or the Beck Anxiety and Depression Inventories (Beck 1990;1996). One of Bach’s (2014) patients showed a significant increase in anxiety from baseline to six-month follow-up (HADS score 9 to 15) and McKeon et al., (2016) found a significant difference between control and anti-NMDAR patient anxiety scores, the latter of which were just within ‘caseness’ i.e. clinical levels of depression/anxiety. However, it is not possible to draw conclusions on patients’ level of distress based on this limited set of research outcomes. Both depression and anxiety would be important to consider in future studies; understanding people’s level of distress is crucial if appropriate psychological support is to be offered. Furthermore, with regards neuropsychological testing, distress can impact an individual’s ability to fully concentrate on the cognitive tasks at hand, due to either a heightened arousal system and/or their mind understandably being preoccupied with psychological stress (Lezak, 2004 p. 127). Only the latter two articles (Bach, 2014; McKeon et al., 2016) discussed the impact of mood on day-to-day functioning. Specific psychosocial difficulties such as the impact on identity (Charmaz, 1983; 2000), were also not explored in these articles, which gave rise to the focus of the empirical study.

A further consideration is the studies' aims and their utility. As these are the first neuropsychological studies investigating anti-NMDAR, largely their aim was to report on neuropsychological sequelae (Finke et al., 12; 13; Loughan et al., 2016; Marcos-Arribas et al., 2012; McIvor & Moore, 2017; Vahter et al., 2014). However, four of the studies did aim to elucidate effective rehabilitation methods for this population (Bach, 2014; Loughan et al., 2016; Martin-Monzon et al., 2012; Urakami, 2016). Nevertheless, none of the studies reported on the patients' understanding or views on being tested, nor how it benefited them as individuals, with regards person-centred care (NHS Wales, 2017). Therefore, whilst the studies were beneficial to furthering understanding of the illness, there is a need for questions around the ethics of conducting, sometimes quite lengthy, neuropsychological batteries (Wong, 2006). Attention should be paid to the third BPS ethical principle of 'Responsibility', within the Code of Ethics and Conduct (British Psychological Society, 2009), which cites "Avoid harming clients, but take into account that the interests of different clients may conflict".

4.1.3 Suggestions for further research

Overall there is a lack of research into the cognitive difficulties associated with anti-NMDAR encephalitis, larger case studies are needed to help develop a stronger evidence-based cognitive profile for this group. Persistent cognitive deficits have been found in seven articles, with two studies reporting difficulties up to six years after onset (Martin-Monzon et al., 2012; Finke et al., 2013). As such, longitudinal neuropsychological testing would be recommended for this population, taking into consideration the ethics of extensive and repeated testing (BPS, 2009).

As discussed, a small number of studies (N=5) have begun investigating the benefits of neurorehabilitation for this population, however, further studies are also needed to confirm evidence-based strategies for people with anti-NMDAR. Lessons learned in other neuropsychological rehabilitation programmes may be applicable (Gracey, Evans & Malley,

2009; Holleman, Vink, Nijland, & Schmand, 2016; Rohling, Faust, Beverly, & Demakis, 2009) but currently rehabilitation is not able to be guided by evidence-based practice in anti-NMDAR.

The area where research is significantly lacking is investigation of the patient's experience of their cognitive difficulties. Future studies should aim to contextualise the neuropsychological results with clinical observation, informant report and patient self-report, in conjunction with administration of tools such as the FIM and FAM and QOLIBRI-OS. Understanding the cognitive profile of an illness is arguably only beneficial if health care professionals also understand how any impairments impact on people's daily functioning, how this impairment is perceived by individuals and therefore how it affects their overall QoL and mental health (Dijkers, 2004). The experience of people with anti-NMDAR goes beyond the examination of their neuropsychological impairments, and investigation of the process of role re-uptake, vocational rehabilitation, peer support, or parenting in the presence of cognitive difficulties is crucial to determine, however this has not yet begun for this group.

Other avenues for future research could focus on the delay in diagnosis and the initial treatment for psychiatric symptoms. These could potentially be areas where there is particular psychological impact given the literature base in chronic fatigue syndrome around deligitimisation (Dickson, Knussen, & Flowers, 2007; Ware, 1992) and stigma in psychiatric disorders (Corrigan, 2004; Corrigan, Watson, & Barr, 2006; Dinos et al., 2004). Furthermore, these were both themes highlighted within the empirical paper.

Research into the child and adolescent population, and the impact of anti-NMDAR on neurodevelopmental functioning, is even more lacking, and as such would be an important research area. As has been explored in other chronic childhood illnesses, such as viral encephalitis, exploration into the impact on the young person's education, family systems and

social development would be pertinent (Hooper, Williams, Sarah, & Chua, 2007; Starza-Smith, Talbot, & Grant, 2007; Wiseman, 1996).

4.2.4 Implications for clinical practice

This systematic review could serve as a useful tool to clinical neuropsychologists who have not previously been referred someone with anti-NMDAR. The review will allow them to quickly access a preliminary cognitive profile of 54 patients in order to make a more informed choice on selection of tests for the neuropsychological test battery.

It is important to consider that all the participants in the empirical paper discussed a loss of confidence in their intelligence post-illness. Therefore, one clinical practice implication would be for professionals to be particularly mindful of this vulnerability whilst undertaking neuropsychological tests. Careful consideration should be given to the utility of performing neuropsychological tests and how the results are fed back to patients (Monden et al., 2016).

As previously discussed by other researchers, clinicians are potentially at risk of misdiagnosing anti-NMDAR as a psychiatric disorder given the common psychiatric symptoms at onset (Dalmau et al., 2011). The participant studied in the Loughan et al., (2016) paper was initially misdiagnosed and treated for an anxiety disorder, the medication of which exacerbated his psychotic symptoms, with later suicidal ideation. In addition, significantly better cognitive outcome has been found in patients with early immunotherapy in comparison with patients with delayed treatment, in both adults and children (Finke et al., 2012; Matricardi et al., 2016). Both these factors highlight the importance of early diagnosis, from a psychological and neuropsychological perspective, which could be achieved via thorough history taking and an awareness of comorbid neurological symptoms (Loughan et al., 2016).

Neurorehabilitation recommendations, based on the current study's findings are not possible due to lack of reporting on the techniques. However, Bach (2014) and Martin-Monzon et al., 2012 suggest that a variety of models may be beneficial to people presenting with cognitive deficits and emotional distress, such as multimodal consolidation techniques, stimulus valence for encoding, behavioural learning paradigms, and use of compensatory strategies (for example, diaries, checklists, smartphone alerts, visual cuing). As well as psychoeducation to improve health literacy and adjustment around acquired brain injury and psychological therapies (for example, CBT, systemic family therapy) (Bach, 2014). Gracey, Evans and Malley (2009) propose a Y-shaped model for rehabilitation in ABI, which could be suitable for this population, and integrates research from psychosocial adjustment, awareness and well-being following brain injury.

Once researchers have gained greater understanding of the perceived impact of cognitive difficulties, both practical and emotional, it can aid health care professionals in offering appropriate, person-centred care (NHS Wales, 2017). It could also influence guidelines and policy maker's recommendations for the care of people with anti-NMDAR.

4.3 Commentary on the Empirical Paper

4.3.1 Choice of research topic

Anti-NMDAR encephalitis is unique in its biopsychosocial presentation because, it differs from other forms of encephalitis in its auto-immune genesis, there is a risk of it being misdiagnosed as a psychiatric condition, and in the recency of its ‘discovery’, meaning people affected have sought to raise awareness of it in the media (‘My Brain on Fire’; Cahalan, 2013). Although there is growing interest in anti-NMDAR, medical research into the illness is still in its relative infancy (Chen et al., 2016; Dalmau et al., 2007, 2011; Finke et al., 2012; Gresa-Arribas et al., 2014; Iizuka & Sakai, 2008; Kayser et al., 2013; Kuppuswamy et al., 2014b; Titulaer et al., 2013) and how to improve its diagnosis and management medically remains the subject of debate, with the rarity of the condition making a systematic approach to trialing treatments difficult (Zhang et al., 2017). Similarly, there are few studies providing evidence on which to base prognosis or rehabilitation. Neuropsychological studies into this illness are just starting to address the question of its impact on cognitive functioning (Iizuka et al., 2010; Iadisernia et al., 2012; Finke et al., 2013; Bach, 2014; Loughan, Allen, Perna, & Malkin, 2016; Matricardi et al., 2016; McKeon et al., 2016; Urakami, 2016; McIvor & Moore, 2017; Hinkle et al., 2017). However, as people affected by anti-NMDAR seek to find a way to live with its long-term consequences, and clinicians seek ways to support them, there is little beyond anecdote and case series to guide them. There have been no previous studies to the author’s knowledge that have used either a qualitative or a quantitative method to explore the lived experience of anti-NMDAR encephalitis.

Impact on identity is a well-researched topic within psychological literature on other chronic and traumatic physical health conditions, such as chronic fatigue syndrome and acquired brain injury, other auto-immune conditions, such as multiple sclerosis, and severe mental illness (Arroll & Howard, 2013; Bury, 1982; Charmaz, 1983; Faircloth et al., 2004;

Gelech & Desjardins, 2011; Karnilowicz, 2011; Medved & Brockmeier, 2008; Musser et al., 2015; Roger et al., 2014; Yanos, Roe, & Lysaker, 2010). Furthermore, identity was a topic that a member of the Encephalitis Society thought important for exploration, when consulted on their opinion regarding the direction of the empirical study. Therefore, identity was chosen as a suitable research topic for introductory psychological research within anti-NMDAR.

A qualitative approach was deemed appropriate to describe the experience in the words of those affected, before seeking to quantify the experience of the group as a whole or, to attempt to test theories that might be applicable. A quantitative approach was considered; however, this approach is typically of value if the aim is, for example, to test theories or broad explanations and apply these results to many people (Creswell, 2012). However, given the reasons above, the aim was to explore the perceptions of individuals, which lends itself to a qualitative approach. It is hoped that beginning with rich data will avoid pre-judgements about how people experience this illness and stimulate exploration into new areas, such as the findings regarding ‘specialness’. Furthermore, understanding people’s experience of an illness can further understanding of their health-related choices and treatment adherence (Munhall, 1994).

Interpretative Phenomenological Analysis (IPA) was chosen as a methodology due to its focus on the experience of individuals, providing an inductive approach, in contrast to the more typical ‘top-down’ health psychology approach, which is deductive and derivative (Reid, Flowers & Larkin, 2005). Grounded theory (GT) was considered as it is a popular qualitative method (Charmaz, 2014), furthermore, Creswell (2012) asserts that GT can generate a theory when there is not an existing theory that addresses the identified problem or the participant population. Therefore, GT could arguably have been a viable qualitative model for the empirical study. However, Creswell (2012) also suggests that GT is used when a broad theory or explanation of a process is needed; given there is no pre-existing psychological literature

into anti-NMDAR the authors concluded that developing a theory may be premature, and what may be more pertinent is an initial exploration of the lived experience of the illness. Discourse analysis (Starks, Brown & Trinidad, 2007) was also considered but dismissed, as IPA similarly includes examination of the use of language and discourse (Larkin, Smith & Flowers, 2009), but with an overall examination of phenomena. Finally, thematic analysis was considered, Braun & Clarke (2006) assert that thematic analysis is a qualitative method in and of itself, and that other methods such as IPA can be constrained by their theoretical underpinnings. However, Pringle et al., (2011) argue that theoretical underpinnings can add both purpose and depth to the exploration. Brocki & Wearden (2007) suggest that IPA aims to go further than a 'standard thematic analysis' by using direct quotes and metaphors to root the analysis directly in participant's words. Furthermore, Hefferon and Gil-Rodriguez (2011) discuss that when IPA is poorly carried out and remains broadly descriptive, with little interpretation, then the data lacks depth and "demonstrates little difference to a standard thematic analysis". Therefore, suggesting that IPA provides something above analysis for themes, and therefore why IPA was finally chosen as a qualitative model. Pringle, McLafferty & Hendry (2011) suggest this approach appears to be in keeping with the current National Health Service efforts to consider service-user perspectives and provide person-centred care (Five year forward view, NHS 2014). IPA is thought to allow "more room for creativity and freedom" than other qualitative approaches, which Pringle, McLafferty and Hendry (2011) state may be pertinent for unusual groups or situations, where "beliefs and expectations may be 'outside the perceptual field' of healthcare professionals" (Biggerstaff & Thompson, 2008). Overall, in a systematic review of IPA studies, Brocki and Wearden (2007) concluded that IPA can be a useful research tool within health psychology. However, it is important to acknowledge certain assumptions of the model, for example the interpretations are bound by a participant's ability to sufficiently articulate their thoughts and experiences (Brocki and Wearden, 2007). Capacity was judged as

being present in all the participants by the researcher, however, as discussed patients did report difficulties with word finding. As such, it is possible that these difficulties impeded some of their ability to fully articulate the depth of their experience.

4.3.2 Methodological decisions

IPA typically focuses on a fairly homogenous sample (Smith, Flowers & Larkin, 2009), working on the premise that it is important to recruit a closely defined group for whom the research question will be significant. The participants in the empirical paper were already closely defined given that the illness is rare, however, it was decided that the sample would be further homogenised via recruitment of adult women. This decision was taken due to findings that there are significantly more women affected by the illness than men and children (Titulaer et al., 2013), which would aid recruitment.

It was decided that eight participants would be recruited to the study, based on advice by Turpin et al., (1997) that between six to eight participants is appropriate for an IPA study for a clinical psychology trainee. This sample size is also recommended by Smith, Flower and Larkin (2009).

The empirical study used a semi-structured interview (Appendix M), designed by the author using guidelines from Smith, Flowers and Larkin (2009). The interview was co-constructed with the member of the Encephalitis Society, who gave their opinion via a Skype interview on types of questions they thought would be important to explore, given their experiences. A draft of the semi-structured interview was then sent to the member for their comments, and relevant changes made. Semi-structured interviews are the most common form of data collection for IPA (Reid, Flowers & Larkin, 2005). They are deemed to be a flexible data collection tool, as they allow for modification of the questions based on the participant's responses and exploration of interesting and important topics by the interviewer (Smith, 2008).

This contrasts with questionnaires or a structured interview, which purposefully limits what a participant can discuss and is therefore arguably less likely to uncover novel phenomena or their complexity (Smith, 2008). The semi-structured interview was framed with regard to the domains of the Common-Sense Model of Illness Representation (CSM) (Leventhal, Meyer & Nerenz, 1980; Weinman, Petrie, Moss-Morris, & Horne, 1996). Health psychology is concerned with understanding the factors that influence a person's management of their illness and identifying targets for intervention (Petrie et al., 1996). The CSM hypothesises that people create mental representations of their illness based on concrete and abstract information available to them, to make sense of the illness and its impact (Hagger & Ordell, 2003). Understanding individuals' health representations can help predict coping behaviours and outcomes. As such, this model was chosen to help elicit an overall understanding of women with anti-NMDAR's illness representations and their impact on identity. However, it should be noted that using a model to help structure the semi-structured interview is not advised by the IPA model (Smith, Flowers & Larkin, 2009) and could be viewed as superfluous or even as a barrier to being a flexible data collection tool, i.e. too structured to allow fluidity of patients' responses. This should be taken into consideration for any portfolio studies arising from this study. However, from the researcher's perspective, using the model did not seem to affect the flow of the interviews and provided a good guide from which to form broad and relevant interview questions.

Smith, Flowers and Larkin (2009) recommended using between six to ten interview questions with prompts, which would establish the area of interest without dictating the flow of narrative. The semi-structured interview contained eleven questions, with a focus on identity, co-constructed with the member of the Encephalitis Society. This amount of questions could be a potential limitation of the study. Hefferon and Gil-Rodriguez (2011), in an article on the method of IPA for The Psychologist, assert that students tend to produce semi-structured

schedules that are too long and detailed. They argue that this is restrictive and that producing a schedule with shorter, general questions helps to ensure that the researcher does not impose their understanding of the phenomenon on the participant's narrative. However, it should be noted that not all the questions were asked in every interview, the first author was guided by the participants and remained on topic with the participant, as opposed to halting the flow of narrative to ask another question. This seemed to allow for collection of data that was 'interviewee focussed'. Frequently the questions from the semi-structured interview had already been covered by the participant and did not need to be asked. The questions around identity were asked later in the interview. This was in line with Smith, Flowers & Larkin's (2009) opinion that this topic will likely be easier talked about once other topics have been discussed and a rapport has been built, which the researcher thought was appropriate and seemed to then fit well within the interviews.

The procedural steps for IPA analysis outlined by Smith, Flowers & Larkin (2009) were loosely followed. This was in line with the authors opinion that IPA is non-prescriptive and the steps should be adaptable given the research situation. Giorgi (2000) also asserts that IPA should not be followed in prescribed stages. Participants were recruited via an online research page through the Encephalitis Society website. Therefore, the findings will be partially defined by those participants who were willing to be involved (Smith, 2008).

Approximately only 500 cases of anti-NMDAR have so far been reported in studies (Barry, Byrne, Barrett, Murphy & Cotter, 2015). As such, recruitment of this group could have been very challenging. This was managed via flexibility with the interview technique, allowing use of Voice over Internet Protocol (VoIP) technologies, in this instance Skype. Other researchers such as Cater (2011) have found building a therapeutic rapport via Skype challenging. However, Deakin and Wakefield (2013) found rapport building was quicker via Skype and only more difficult when the participant was particularly reserved. To overcome the

latter they exchanged a series of emails to establish connection with participants over time (Deakin & Wakefield, 2013). Due to the nature of setting up the interviews, sending information and consent forms and arranging convenient times for interview, a series of emails were exchanged between the researcher and interviewees in the empirical study. Therefore, the researcher felt that some rapport was already established before the interview. Furthermore, it is possible that some participants felt more able to speak freely whilst in their own chosen environment. Additionally, both interviewer and interviewee were able to maintain their own personal space. All of which may have created greater opportunity for gathering richer data (DiCicco-Bloom & Crabtree, 2006; Seitz, 2015). Iacono, Symonds and Brown (2016) concluded, in their discussion on Skype as a tool for qualitative research, that whilst VoIP mediated interviews cannot completely replace face-to-face interviews, they are a viable and effective alternative, particularly when there is a large geographical range, as there was in this current study. Overall, use of VoIP was not deemed by this study's researcher to be an impediment to developing rapport, this is evidenced by most participants voluntarily emailing after the interview to thank the researcher for taking up this study, and sharing that they felt it easy to talk to them about their experiences (Appendix R).

4.3.3 Bracketing

The researcher's role and potential biases/influence in development and conducting of the study was considered using reflexive bracketing. This was achieved by taking into consideration the three areas of presupposition outlined by Ashworth (1996) and Ahern's (1999) ten tips for bracketing. Smith, Flowers and Larkin (2009) suggest that you may want to widen your knowledge with a literature review once you have chosen a topic. By doing so one is therefore assimilating scientific knowledge. The first area Ashworth (1999) suggests bracketing is scientific theories, knowledge and explanations "the life-world is to be studied in

its own terms, irrespective of any connection with external “variables” that science alleges”. Given that there is not any psychological research into anti-NMDAR to date, there were not any specific theories found in relation to the illness. However, there were several theories and hypotheses for other chronic and traumatic illnesses/injuries that were examined, such as ‘biographical flow/disruption’ (Bury, 1982, 1991; Gelech & Desjardins, 2011; Medved & Brockmeier, 2008; Roger et al., 2014). As scientific theory was examined, this knowledge therefore needed to be bracketed, both throughout the interview and interpretation stages. This was achieved by keeping a reflexive diary (Finlay, 2008; Appendix Q) and regular supervision. Ashworth (1996) asserted that ‘the life-world’ should not be attempted to be explained with regards the causes from ‘objective reality’. Whilst there were questions referring to perceived cause in the semi-structured interview, their aim was to open the possibility of exploring philosophical and/or spiritual beliefs, as well as any potential feelings of personal responsibility around developing the illness. The aim was not to try to uncover the facts around the cause of the illness. However, sometimes the participants answered these questions with regards the scientific cause, which led onto a mutual discussion of this. As such it must be recognised that this may have gone against Ashworth’s first presupposition. Ashworth’s (1999) second area to bracket was around the researcher adopting no position on the correctness or falsity of the claims that are implicitly made by the research participants. Again, this was explored via the reflexive journal (Finlay, 2008) and supervision. It was felt that this was largely achieved, with the researcher remaining accepting of the participant’s perceived experiences. The third area (Ashworth, 1999) focused on bracketing the personal views and experiences of the researcher; this was attempted by writing a position statement (Appendix P). Whilst this identified personal feelings and preconceptions, it is arguably impossible to be completely objective (Schutz, 1994) and the themes formed are largely a subjective experience (Smith, Flowers & Larkin, 2009). It cannot be overlooked that the women interviewed were broadly the same age,

ethnicity and educational level as the researcher. This could have influenced the saliency of certain themes to the researcher, for example impact on motherhood and career, as they are common subjects for this life stage (Baltes, 1987). The researcher's demographics may also have influenced the topics that the participants felt comfortable to discuss and possibly thought the researcher may have been able to empathise with. In this sense, the themes may have been co-constructed between the participants and researcher. This was discussed in depth via supervision and there was careful examination of the transcripts to ensure these themes were discussed frequently.

4.3.4 Limitations of the line of enquiry

IPA is an idiographic approach, the results of which are not intended to be generalised (Smith, Flowers & Larkin, 2009), therefore the results of this study are limited to the homogenised group from which they have been developed. Therefore, this approach could be criticised for having limited impact (Anderson, 2010). However, Smith, Flowers and Larkin (2009) suggest that if the analysis is detailed and transparent, and related to previous literature then it is possible to have 'theoretical transferability' (rather than 'empirical generalisability'). It may be possible for the reader to use their existing professional and experiential knowledge to assess the findings, and possibly combine with claims from quantitative studies, to help "illuminate the universal" (Hefferon & Gil-Rodriguez, 2011). Smith, Flowers & Larkin (2009) argue that the aim of IPA is to "ensure that the account produced is a credible one, not the only credible one". Furthermore, Smith (2008) discuss that with cumulative studies, conducted with other groups, more general claims may be possible.

4.3.5 Future research and clinical implications

The current study provides insight into how anti-NMDAR is experienced by patients, with emphasis on the impact on identity. This study extends the evidence base for the impact on identity from chronic and traumatic health conditions. It suggests that there can be both biographical disruption (Bury, 1982), whereby the individual feels their sense of self has been lost, but also biographical flow, where facets of the self remain consistent (Faircloth et al., 2004). This understanding of identity is crucial if healthcare professionals aim to provide person-centred care (NHS Wales, 2017) and help patients with self-management. Unless professionals understand the meanings people attribute to their illness, they cannot help to alter health behaviours and lifestyles (Munhall, 1994) via adequate psychoeducation and support. For example, one patient in this study discussed how she did not like to inform her doctor when she thought she was having a relapse as she did not want to go back onto steroids, of which one of the side effects was weight gain.

Respondent: But I suppose for me as soon as I tell anyone that I'm ill, I know what the consequences are, so, I don't like it? if that makes sense? So I tend to leave it

Munhall (1994) asserts that only by maintaining an open and adaptable approach can we truly reach, hear and understand participants' experiences, particularly those who may need the most support.

The empirical study is preliminary in nature and therefore also highlights several possibilities for future research. Both clinical implications and research opportunities will now be discussed under the four superordinate themes.

'Re-finding the 'normal' self

All the participants were at different perceived milestones at different time points in terms of their recovery (for example, leaving hospital, completing rehabilitation, stopping medications).

Therefore, a longitudinal study could track participant's views on identity at different stages of recovery or re-uptake of roles, particularly given that the participants described feeling "odd", "compromised" and "abnormal" whilst they were acutely unwell.

Most of the women had received psychiatric care before being diagnosed with anti-NMDAR, and this association appears to have increased their feeling of 'abnormality'. Researchers assert that psychiatrists need to be aware of misdiagnosis of this client group and should maintain a high-level of suspicion when patients are only partially/non-responsive to antipsychotics (Varma & Sapra, 2015). This is particularly important to consider given that mental health difficulties are often diagnosed more in women, for example, unipolar depression is currently reported as nearly twice as common in women (WHO, 2017). However, Norman (2003) suggests sex differences in rates of depression may be to do with culturally defined differences in factors such as gender differences in help seeking, coping styles and/or life stress, as opposed to biological factors. The age range of women in this study was 21-35 years, with most of the women diagnosed some years previously, presenting a young population of women. Recent reports/surveys in England have found young women to be the highest-risk group for diagnosis of common mental health disorders, self-harm, PTSD and bipolar disorder (Lessof et al., 2016; McManus et al., 2016). Therefore, whilst the novelty and rarity of the disease will likely play a large role in the delay in diagnosing anti-NMDAR, potential bias towards viewing women's symptoms as mental health related, cannot be overlooked and it may be beneficial for clinicians to have awareness of this.

'Evolving from the illness'

As discussed in the empirical study, researchers in ABI have found that PTG increases with time since ABI (Collicutt, McGrath & Linley, 2006; Gangstad et al., 2009; Powell et al., 2007). As such, a longitudinal study could investigate whether PTG is experienced after anti-NMDAR

and if time since onset is a significant correlate. Furthermore, Silva et al., (2011) found people were more likely to experience PTG if they perceived greater functional consequences of their ABI. Therefore, a future avenue of research could investigate whether relapse and an increased treatment length are more likely to lead to subjective beliefs about change post-injury that are aligned with PTG, such as re-evaluation of life goals (Devine, Reed-Knight, Loiselle, Fenton, & Blount, 2010; Grace, Kinsella, Muldoon, & Fortune, 2015; Mehrabi, Hajian, Simbar, Houshyari, & Zayeri, 2015). Outcome measures could also be administered such as, the posttraumatic growth inventory (Tedeschi & Calhoun, 1996), the Hospital Anxiety and Depression Scale (Snaith, 2003), the Beck Anxiety and Depression Inventories (Beck 1990; 1996) and tracked over time, along with qualitative interview, to investigate the psychological impact of anti-NMDAR.

'Roles and identity'

One theme that was revealed centred around motherhood and fertility and, given women are currently more likely to be diagnosed, this would be an important avenue for future research, as highlighted in the empirical study. Dalmau et al., (2008) found diagnosis of anti-NMDAR was associated with ovarian teratomas in 59% cases (100 participants, 91 women). However, Irani et al., (2010) reported only 26% cases had associated ovarian tumours (9 of 34 cases). Nonetheless, if a tumour is detected/suspected an oophorectomy is conducted, which can pose a risk to fertility (Abdul-Rahman et al., 2016; Bach, 2014). Additionally, treatments such as Rituximab, one of the more common second-line treatments (Dalmau et al., 2011) has been linked with loss of fertility (Cancer Research UK, 2017). The US Federal Drug Administration (FDA, 2017) asserts there are no adequate, well-controlled studies in humans for Rituximab with regards risk to pregnant women. They also suggest that the potential benefits may outweigh the potential risk but strongly advise avoiding pregnancy 12 months after its last

administration (FDA, 2017). In a case study of three patients, Ojeda-Urbe et al., (2013) found no significant adverse effects or complications were observed during the pregnancy of three women given Rituximab for varying autoimmune diseases (not anti-NMDAR), and all three patients delivered healthy newborns. However, they do suggest that there is low level risk to the foetus, which could be outweighed by the benefit to the mother. Nevertheless, there appears to be limited research into this area and the health information available is arguably confusing for the lay public. It suggests reduced fertility without adequate explanation of why, and highlights some small risk to unborn babies, which is likely to be salient to women aiming to start a family. Exploring views on fertility and pregnancy would be important for this population, research could help shape the health information available to people with anti-NMDAR and assist health professionals in how to sensitively deliver this information (Bach, 2014). Bach (2014) recommends that patient counselling regarding infertility should be “integrated into standard guidelines of best practice” and routinely offered to this patient group.

‘A special identity’

One of the themes in the empirical study revealed the women felt viewed as ‘special’ by healthcare professionals. This bears consideration, particularly given the potential cognitive difficulties in this population (Martin-Monzon et al., 2012; Finke et al., 2012; 2013; Marcos-Arribas et al., 2013; Vahter et al., 2014; Bach, 2014; Urakami 2016; Loughan et al., 2016; McKeon et al., 2016; McIvor & Moore, 2017), which could give rise to vulnerability. Whilst it was extremely positive to hear of the strong relationships between participants and their physicians, one clinical implication could be to urge caution with use of ‘best’ patient labels. Miscommunication might be particularly impactful whilst the individuals are still trying to re-establish their identity during the recovery process (Karnilowicz, 2011).

Despite participants often describing being thought of and labeled by healthcare professionals as ‘special’, they all also discussed low self-esteem and confidence, and rarely attributed their recovery to their own efforts. Therefore, one clinical implication would be to offer some form of psychological support to this client group, which promotes internal locus of control for health outcomes. Mindfulness-based techniques (MBT) have been investigated in other populations with significant improvements found in measures such as, anxiety and fatigue and overall fostering of PTG (Garland et al., 2007; Milam, 2004; Surawy et al., 2005). MBT could therefore be a successful treatment option for people with anti-NMDAR. A randomised control trial, comparing treatment as usual with MBT on a population of people with anti-NMDAR could be beneficial to see if this intervention is acceptable and helpful. It is recognised that this could be difficult given the rarity of the disease, however, studies with larger numbers of participants have been achieved (Finke et al., 2013).

4.3.6 Ethics and Diversity

Capacity to consent was considered extensively before recruitment of participants, due to the potential for participants to have cognitive difficulties (Finke et al., 2012; McIvor & Moore, 2017). Assessing capacity to consent was discussed in detail on the university ethics application (Appendix G), in line with the Mental Capacity Act (2005). Ethical considerations were also considered due to the sensitive nature of the topics being discussed in the interview. The interviewer used their professional judgement as to whether the interview was becoming too distressing to the participant and if they felt it was, checked how the participant was feeling and whether they were ok to continue and, if necessary, changed the topic. Only on one occasion did one of the participants become distressed; she explained that she felt her emotions were more labile since having the illness. The participant did not seem particularly concerned about becoming tearful and naturally let her feelings run their course before moving on from

the topic. This process required minimal input from the interviewer aside from a naturally empathic approach. None of the participants contacted the researchers (as was offered via the Debriefing form) with concerns regarding emotional distress. This does not guarantee there was not residual emotional distress. However, it was the researcher's opinion that none of the participants required further emotional support as a result of having taken part in the interview.

Power imbalance during the interview process was also considered, as the researcher was aware that the interviewees often viewed them as a professional with, potentially, "organisational and institutional power" (Das, 2010). However, the power appeared well balanced from the researcher's perspective, due to the anxieties the researcher had regarding recruitment numbers for the study and ensuring that rich data was collected (Karnieli-Miller, Strier, & Pessach, 2009). This would then have come across in their communication style with the participants. The researcher was aware of the potential for power imbalance and so endeavoured to create an open and equal stance in the interviews, which seemed to be effective given the feedback from participants (Appendix R).

Diversity and culture were also considered throughout the research process. The sample were predominantly white, middle class women from Western countries and educated to, at least, college level. The similarity of the participants was in keeping with recruitment of a homogenised sample, as recommended for IPA (Smith, Flowers & Larkin, 2009). There was only one participant whose first language was not English. During the interview, some of the questions were rephrased and some additional prompting given, to aid the participant's understanding. An interpreter was not offered to conduct the interview in the participant's first language, however this could have been considered (BPS, 2008). This may have allowed the participant to express themselves more fluidly and articulately. Language is crucial to bear in mind given that it is often tied to identity (Joseph, 2004). However, researchers have asserted that phenomenological studies, which involve translating transcripts, are not amenable to cross-

language designs generally as they require exact focus on “how participants use language to describe their experiences and language is a part of the identity of the person experiencing the phenomenon, translation disrupts the fluid process from inception through dissemination of studying the participants’ use of language to describe the experience of the phenomenon” (Squires, 2009; p.279). Therefore, not ensuring that all participants’ first language was English may be a limitation of the study. There did appear to be some salient themes around cultural norms within the participant’s transcript:

respondent: Even I came back home, I was diagnosed, I was all acting all weird, like I was saying I’m hearing things, someone’s telling me something, like those things and she was like oh you’re creepy

interviewer: Okay

respondent: Those aren’t normal things for like I guess at least my culture

There were also cultural and societal nuances across the other interviews, for example when discussing the impact of the illness on their lives, for some participants the financial impact was great due to lack of free healthcare in their country and differences in sickness pay:

respondent: Umm [pauses] no I mean everyone it really affects every aspect of your life you know, I know that there’s you know a financial concern too for some people and it’s not that I don’t have that, it’s just my dad did a really good job of stockpiling umm [pauses] disability and stuff for me when I was out so I was okay, and my job I still had my job which was like the biggest miracle of all

Interestingly, despite these cultural differences, many of the themes remained consistent across cultures. Nonetheless, culture and language were important diverse factors to consider whilst the author was undertaking the interviews and conducting the analysis.

4.4 Dissemination

Permission was sought at the end of each interview to save the participants' email addresses on an encrypted word file so they could be contacted with copies of the completed studies. All the participants gave their consent to keep their email address and as such will be emailed final drafts of the papers. It is hoped these studies will further legitimise patient experience and act as a platform for voicing their experience, as was suggested by the participants in the respondent verification. The studies may then be further disseminated by the participants sharing them with their wider networks. Both the studies will also be submitted to the Encephalitis Society and will be featured in their newsletter and on their website. Relevant conferences such as the Science Conference and Encephalitis Society conferences will also be explored, to give an oral or poster presentation of the studies. The researcher will also present the studies at the fortnightly Neurosciences meeting within their local health board.

Wide reaching dissemination is important given that anti-NMDAR is a rare illness, but is being diagnosed internationally. There are many health professionals who will not yet have heard of or encountered the illness. However, it is crucial to raise awareness given that the illness, when not treated, can be fatal or have long-term effects (Titulaer et al., 2013). More widespread knowledge of the early stages of anti-NMDAR, such as psychiatric and prodromal symptoms, could help health care professionals query and potentially identify the illness earlier, which could lead to a better outcome (Finke et al., 2013). Approximately 77% of patients diagnosed with anti-NMDAR were first assessed by a psychiatrist (Kuppuswamy, Takala & Sola, 2014). Therefore, there is increasing literature discussing the need for psychiatrists to have increased awareness of anti-NMDAR and to maintain suspicion for the illness. Particularly when there is no history of psychiatric illness (Barry et al., 2011; Ryan et al., 2013) or when patients are only partially or non-respondent to antipsychotic medications (Varma & Sapra, 2015). Varma and Sapra (2015) also highlight increased vigilance is needed

when treating young women, where the illness may be overlooked when in the background of a stressor. Chapman and Vause (2011) highlight that psychiatrists can encounter patients with anti-NMDAR in a range of settings such as inpatient units, consultation-liaison services and outpatient offices. Therefore, they should have some understanding of the clinical characteristics, differential diagnosis, treatments and unique management of dilemmas of this condition (Chapman & Vause, 2011). Varma and Sapra (2015) urge that an interdisciplinary approach, including psychiatrists, neurologists, paediatricians, gynaecologists, oncologists and immunologists, is needed for timely identification and treatment. It is therefore hoped that these studies will be added to the growing literature for anti-NMDAR and help to raise awareness of the illness both in the health profession and lay public. Publishing the empirical study and systematic review in different journals should raise awareness in different spheres.

4.5 Personal and professional skills and values

Undertaking this research has overall improved my knowledge base of anti-NMDAR and other chronic and traumatic illnesses and the role clinical psychology takes with regards research and intervention. It has also strengthened my knowledge of systematic reviews, interpretative phenomenological analysis and the literature around identity and illness. The process has developed my competence in the use of critical appraisal of neuropsychological research and its methods, and provided me with insight into the importance for clinicians to reflect on their communication strategies with those in recovery from a rare and traumatic illness. The latter of which will influence the way in which I will work clinically in the future. It has also been an exercise in being a reflective scientist-practitioner and has provided me with strong research skills that can be transferred into my qualified role.

4.6 Reflections on the research process

I was keen to develop a research project that would make a genuine and impactful contribution to a service user population and so undertook to create a project myself that I felt could achieve this. I had an existing interest in anti-NMDAR from having carried out a neuropsychological assessment with a patient with anti-NMDAR whilst an assistant psychologist within a neuropsychology outpatient clinic. I then went onto read the book *Brain on Fire: My week of Madness* (Susannah Calahan), which furthered my interest, largely due to the initial presenting psychiatric symptoms and the possible acute and chronic cognitive difficulties, both of which appeared to be important topics for involvement of clinical psychology. Creating my own research question was an interesting and rewarding experience and generated a feeling of being an autonomous researcher. I also feel this allowed me to develop the full breadth of research skills, from the initial stages of identifying an area of research need, to the process of being submission ready. However, this also meant that I was involved in every aspect of the decision-making process from the initial to final stages, which proved demanding at times. As there is no current psychological research in this area, it meant that the direction of the study was largely limitless. Therefore, whilst creating a research project was exciting, it was also at times overwhelming and I used supervision with both of my tutors to refine my ideas and create a definite direction for the research. This was not one discussion but rather involved constant self-reflection and discussions with my supervisors. This ensured that I remained on track with the set research questions and did not get diverted by other ideas that arose, particularly during the literature search and in the analyses.

Another challenge that arose during the research process was balancing the workload of the research project with working on other assignments, working on placement and keeping a good work-life balance. Overall, I feel I was able to maintain a good balance due to organisation of research days and setting very strict boundaries regarding only doing the

appropriate work/activities in the appropriate setting. This process clearly highlighted to me the challenges that can arise when endeavouring to carry out a piece of research as a qualified clinical psychologist. However, it also showed me the fulfillment that can be achieved in creating a piece of work you feel may be of benefit to a specific population. Additionally, it allowed me to begin to practice the skills needed in balancing different work demands.

I was conscious when developing the empirical study that the process of conducting the interviews could be emotionally taxing for me personally, with the women discussing the emotional impact of the illness. Whilst I was very engaged in the women's experiences and felt empathy for their situation, I feel my skills as a trainee clinical psychologist, and experience prior to training, prepared me well for managing the themes that arose during the interviews. I did not feel distressed following the interviews and could manage the participants' occasional distress, with them not reporting any additional distress from participating in the research as discussed. I found the interview process enjoyable, I was interested to hear of the women's experiences, particularly of the growth that they felt from having had the illness. I also felt proud to be making some small contribution to the understanding of the illness and its impact and in increasing awareness.

I did not have any prior experience of conducting a systematic review and did not have extensive knowledge of how to conduct one. Therefore, entering this process was intimidating, however, I was keen to build expertise in this area, which I felt was lacking.

There were very limited studies into neuropsychological sequelae of anti-NMDAR overall, but particularly up until January 2017. Therefore, there was a taxing period where I was unsure whether a systematic review in this area would be possible and as such several different avenues were explored. This uncertainty created a high level of stress and I used self-care and supervision to work through these difficulties. This experience served as a useful lesson in the practicalities of conducting research.

Overall, I found the research process genuinely intellectually stimulating and rewarding, despite the challenges that arose. I was pleased I could see my research topic achieved and am hopeful that it will be the start of a portfolio of research into this interesting area of autoimmune diseases.

4.7 References

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