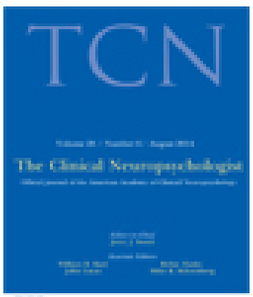

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Anti-N-Methyl-D-Aspartate Receptor Encephalitis: A Review and Neuropsychological Case Study

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Objective: Anti-*N*-Methyl-D-Aspartate Receptor (NMDAR) Encephalitis is an autoimmune-mediated encephalitis, which may be associated with a tumor, which occurs when antibodies bind central NMDA receptors. Although typically diagnosed in women, approximately 20% of cases have been males. Due to the challenges with identification, imaging, and diverse symptom presentation, this syndrome is often misdiagnosed. Accurate diagnosis may provide an opportunity for introduction of disease-modifying therapies, which may alter disease trajectory. Moreover, neuropsychology has yet to fully clarify the pattern of impairments expected with this disorder. *Methods*: This manuscript reviews a single case study of a 42-year-old male diagnosed with NMDAR encephalitis. Neuropsychological evaluation was completed subsequent to diagnosis, treatment, and rehabilitation. Ongoing patient complaints, approximately six months post diagnosis, included reduced sustained attention, poor word retrieval, and daily forgetfulness. Adaptive skills were improved following rehabilitation. *Results*: Direct testing revealed mildly impaired sustained attention, processing speed, oral word fluency, and executive functioning. All other cognitive domains were within estimated premorbid range, low average to average. *Conclusions*: Neuropsychological deficits were consistent with mild frontal brain dysfunction and continued recovery. This case illustrates the need for medical and psychological practitioners to understand NMDAR encephalitis, its symptom presentation, and related neuropsychological impact; particularly with the potential for misdiagnosis.

Keywords: Anti-*N*-Methyl-D-Aspartate Receptor Encephalitis; Cognition; Executive dysfunction; Autoimmune-mediated encephalitis.

INTRODUCTION

Limbic encephalitis (LE) is an autoimmune syndrome where the body produces antibodies against itself. Localized to the cerebral hemispheres—LE typically affects the medial temporal lobes (hippocampi & amygdalae) and orbitofrontal cortex (Wandinger, Saschenbrecker, Stoecker, & Dalmau, 2011). Deficits often result in short-term memory loss, complex partial seizures, and behavioral abnormalities including affective variations, hallucinations, disinhibition, and personality changes. Symptom onset begins rapidly with changes in mood and personality, worsening drastically over the course of a few days to weeks (Gultekin et al., 2000).

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Inflammatory cells are found within the cerebrospinal fluid (CSF), early in the disease course in patients with LE. Magnetic resonance imaging (MRI) results may be normal; yet at times hyperintensities can been seen on the T2-weighted or FLAIR images. Electroencephalogram (EEG) can also include focal or generalized slowing and occasional epileptiform activity, again, particularly in the temporal areas (de Beukelaar & Sillevis Smitt, 2006; Lawn, Westmoreland, Kiely, Lennon, & Vernino, 2003; Rees, 2004). However, diagnosis can be difficult as diagnostic markers are often lacking and/or can be similar to other cancer related complications including brain metastases, toxic or metabolic encephalopathies, infections, and or side-effects of cancer treatments (Gultekin et al., 2000). In fact, Gultekin et al. (2000) revealed that in their investigation of 50 patients with LE, only 54% had abnormal EEG readings, 56% had abnormal MRI findings, 60% had positive antibodies, and 80% had abnormal CSF findings. LE entities appear to be autoimmune mediated and represent potentially lethal syndromes. Immunosuppressive therapy and treatment of the underlying malignancy remains the main management.

NMDAR encephalitis

One LE to be identified recently is Anti-*N*-methyl-D-aspartate receptor encephalitis (NMDAR encephalitis). NMDAR encephalitis is a syndrome mediated by anti-NMDA-R autobodies. NMDA receptors are ligand-gated cation channels which are highly expressed in the forebrain, limbic system, and hypothalamus, and play a role in synaptic transmission and plasticity (Bliss & Collingridge, 1993; Chapman & Vause, 2011; Lau & Zukin, 2007; Yashiro & Philpot, 2008). In NMDAR encephalitis, antibodies cause a reduction in glutamate receptors (NMDA receptors & NMDA receptor clusters) on the cell surface of neurons in postsynaptic dendrites (Chapman & Vause, 2011; Wandinger et al., 2011). It is hypothesized that the cluster density of NMDA receptors on the post-synaptic neuron is reduced by NMDA antibodies subsequently, leading to inactivation of gamma-aminobutyric acid (GABA) ergic interneurons (Granerod et al., 2010; Kuppuswamy, Takala, & Sola, 2014; Maneta & Garcia, 2014; van de Riet & Schieveld, 2013). GABA-ergic dysregulation is thought to be a potential cause of catatonia and psychotic symptomology often seen in individuals with NMDAR encephalitis (Dalmau, Lancaster, Martinez-Hernandez, Rosenfeld, & Balice-Gordon, 2011; Maneta & Garcia, 2014). In addition, in the limbic system where a high density of NMDA receptors are located, synaptic density is lost (Florance et al., 2009) resulting in decreased function in the hippocampus and consequently causing the severe memory deficits (Dalmau et al., 2011; Fei & Tsein, 2009; Nakazawa et al., 2002; Tsien, Huerta, & Tonegawa, 1996).

Demographics

The prevalence of this autoimmune-mediated encephalitis is unknown, but reported cases are rapidly increasing, causing many researchers to believe that it may be more frequent than previously suspected (Granerod et al., 2010; Dalmau et al., 2011). Initially thought to exclusively occur in young females in association with an ovarian teratoma, it has now been identified in children and young adults, in either

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gender (Dalmau et al., 2011; Sansing et al., 2007; Maneta & Garcia, 2014; van de Riet & Schieveld, 2013), yet remains rare in the first decade of life (Armangue, Titulaer, Malaga, et al., 2013; Dalmau et al., 2011; Luca, Daengsuwan, Dalmau, et al., 2011; Zekeridou, Karantoni, Viaccoz, et al., 2015). Black females over age 18 may be more likely to have an underlying disease-associated tumor (Titulaer et al., 2013a). The mean age of diagnosis is 23 years, however, there have been many "late-onset" reported cases of patients over 80 years of age (Day, High, Cot, & Tang-Wai, 2011; Titulaer et al., 2013a; van de Riet & Schieveld, 2013).

Symptomology

Symptom presentation in children compared to adults is vastly different. Symptoms of NMDAR encephalitis in children are difficult to differentiate because they most often present as behavioral changes (Dalmau et al., 2011; Leypoldt, Gelderblom, Schöttle, Hoffmann, & Wandinger, 2013; Leypoldt et al., 2013). Initially, children begin having frequent seizures followed by behavior problems including inattention, temper tantrums, hyperactivity, or irritability. In addition, children can develop psychotic behaviors, mutism, or unresponsiveness. Because of this, many children go misdiagnosed during the initial stages of the disorder.

In adults, symptom presentation is separated into multiple phases: (a) prodromal phase, (b) psychotic/seizure phase, (c) unresponsive phase, and the (d) hyperkinetic phase. (Peery et al., 2012). In 70% of adults, the prodromal phase lasts approximately 5–14 days and includes subfebrile temperatures, malaise, headache, upper respiratory problems, nausea, fatigue, vomiting, and diarrhea. The following phases may vary in sequence, presentation, and severity. The psychotic/seizure phase is characterized by emotional/psychotic symptoms such as delusions, hyper-religiosity, hallucinations, depression, paranoia, and apathy. Insomnia is also a symptom in this stage. Sometimes catatonic symptoms (withdrawal, staring, posturing, and negativism), seizures (commonly generalized tonic-clonic), abnormal involuntary movements (especially involving the perioral masculature), autonomic instability, memory deficits, speech difficulties, anterograde amnesia, and attention deficits develop. When an individual progresses to this stage, hospitalization in an intensive care or psychiatric unit frequently precedes accurate medical diagnosis due to patients often being misdiagnosed as having schizophrenia, conversion disorder, or postpartum psychosis (Bergink et al., 2015; Dalmau et al., 2007, 2008; Finke et al., 2012; Maneta & Garcia, 2014; Nakazawa, 2012). In the unresponsive phase, patients often present to the emergency room if not already hospitalized due to their inability to follow verbal commands and appearance as being mute or akinetic. Lastly, the hyperkinetic phase is characterized by autonomic instability manifesting with hypo/hypertension, cardiac arrhythmia, hypoventilation, and hyper- or hypothermia. Dyskinesias, extrapyramidal signs, and stereotyped motor automatisms may also be noticed.

Diagnostic approach

Although there are many symptoms of this disease, the wide variations in clinical presentation and course of symptom development cause detection to be challenging.

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Identification of high titers of NMDA autoantibodies in an individual's CSF or serum is critical for diagnosis as abnormalities are reportedly present in up to 80% of patients and this percentage increases as the disease progresses (Gresa-Arribas, Titulaer, Torrents, et al., 2014; Maneta & Garcia, 2014). It should be noted that the sensitivity of CSF testing is higher than serum. Unfortunately, disease progression is rapid with severe disability, or death, usually occurring between three and five months of symptom onset (van de Riet & Schieveld, 2013).

In approximately 50% of the cases to date, MRI's of the brain have been normal (Dalmau et al., 2011; Maneta & Garcia, 2014), suggesting imaging may not be the most appropriate means for detection. If there is an abnormality found in these scans, they are usually small or transient (Dalmau et al., 2011). Although EEG readings are abnormal in most patients, they reveal non-specific, slow, and disorganized brain wave activity sometimes with electrographic seizures resulting in difficulty deducing diagnostic or treatment information. Although follow-up MRI's have typically remained normal or show minimal change (Dalmau et al., 2011), recent investigations by Finke and colleagues (2015) suggest long-term structural hippocampal damage and associated memory deficits. To date, neither brain biopsies nor autopsy findings provide diagnoses for NMDAR encephalitis post-mortem (Camdessanché et al., 2011; Dalmau et al., 2007, 2008; Tüzün et al., 2009). In LE, a tumor is detected in 20–70% of antibody-positive cases. More specifically, in NMDAR encephalitis studies, only 20–63% patients have been documented to have identifiable tumors (Dalmau et al., 2008; Irani et al., 2010) which may be involved in the disease pathogenesis in those cases (Dabner, McCluggage, Bundell, et al., 2012; Day, Laiq, Tang-Wai, & Munoz, 2014; Tüzün et al., 2009).

Treatment

NMDAR encephalitis has been found to have a better prognosis than most other encephalitides (Maneta & Garcia, 2014). However, prognosis is significantly improved with rapid diagnosis and prompt treatment (Titulaer et al., 2013b). Once diagnosis is confirmed, first line treatment involves the removal of a teratoma (if found), corticosteroids, and intravenous immunoglobulins or plasma exchange. If patients do not respond to these methods, second-line treatment often includes rituximab or cyclophosphamide (Dalmau et al., 2011; Kuppuswamy et al., 2014; Maneta & Garcia, 2014). In addition, electroconvulsive therapy has also been used to treat specific symptoms, such as catatonia. However, the effectiveness has been reported as variable (Kuppuswamy et al., 2014; Maneta & Garcia, 2014).

Recovery/cognitive impairments

With early detection, more than 75% of patients recover completely or have only mild sequelae (Dalmau et al., 2011; Finke et al., 2012; Kuppuswamy et al., 2014; Nakazawa et al., 2002; Wandinger et al., 2011). This high percentage of recovery is consistent with the hypothesis that this type of encephalitis involves synaptic modifications rather than neuronal cell death (Irani & Vincent, 2001). Finke and colleagues (2012, 2015) found that patients who received immunotherapy during the initial onset had a better cognitive outcome than those who received immunotherapy later. For

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example, they reported that of the 472 patients who underwent first-line immunotherapy or tumor referral, 251 (53%) improved within the first four weeks. Another 53% ($n = 125$) went on to receive better outcomes following second-line treatment immunotherapy. However, overall, up to 25% of cases reported across studies still result in severe disability or death (Dalmau et al., 2011; Finke et al., 2012; Titulaer et al., 2013b; van de Riet & Schieveld, 2013). Relapse is said to occur in approximately 12% of cases (Titulaer, et al., 2013b).

Of those who ultimately make a full recovery medically, approximately 85% continue to have cognitive and behavioral abnormalities upon hospital discharge, requiring supervision and rehabilitation (Dalmau et al., 2008). Long-term impairments are observed in the areas of attention, working memory, episodic memory, and executive functions. Despite the high rate of recovery, there are still cases in which the patient does not recover fully (Finke et al., 2012; Kuppuswamy et al., 2014). Titulaer et al. (2013b) found that some individuals needed up to 18 months to recover, where Leypoldt and colleagues (2013) presented a case which reportedly took three years of recovery to fully return to premorbid functioning status. Unfortunately, even years after treatment is complete for the disease, patients are often still recovering from persistent executive functioning and memory deficits (Dalmau et al., 2008; Finke et al., 2012, 2015; Irani et al., 2010).

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CASE BACKGROUND

Mr X

This case study examines the neuropsychological profile of a 42-year-old right-handed male (Mr X) following the diagnosis and treatment of NMDAR encephalitis. Mr X was referred for a neuropsychological evaluation approximately 6 months post diagnosis in order to assess the extent and nature of cognitive impairment and determine eligibility for return to work status.

Cognitive/psychosocial history

Prior to illness, Mr X reported intact cognition. Although significantly improved since rehabilitation, Mr X described continued impairments in attention, language, and memory. Per clinical interview, Mr X required cuing for sustained attention; however, his processing speed and divided attention had returned to baseline. Receptive language was intact; yet Mr X continued to demonstrate mild word finding difficultly and slurred speech during conversations. Mild daily forgetfulness was also noted. Long-term memory was reported as intact. Regarding current activities of daily living, Mr X reported independence with all activities of self-care. He began operating a motor vehicle short distances during the day without error. Mr X reported ability in managing his medication, schedule, and finances; however, his wife continued to perform these duties. She stated this was her preference, not a reflection of his ability.

Mr X had 12 years of education and was trained as a mechanic. He is married (8+ years) and has two biological children and two stepchildren. Mr X worked 40–50+ h weekly prior to illness. Job related duties included monitoring the operation

of machinery and mechanical equipment by completing preventive maintenance requirements and troubleshooting any malfunctions. He was the direct supervisor for the floor mechanics at the facility. He was not currently working at the time of this evaluation, yet he continued to receive speech, occupational, and physical therapy (6 h each/week). This occurred at his home residence.

Psychiatric history

Mr X denied a history of depression, anxiety, or anger. However, he noted increased frustration due to the inability to work. As coping strategies, Mr X performed household chores and exercised daily. He denied current suicidal or homicidal ideation, or hallucinations. Mr X reported a good support system of family and friends. Appetite and sleep regime were reported as intact. Current substance use was denied except for an occasional alcoholic beverage (1×/week).

Medical history

A timeline of Mr X's symptom trajectory is provided in Figure 1. Initial symptom onset included "nervousness, extreme anxiousness with panic attacks and insomnia." Following unsuccessful treatment with a benzodiazepine from an urgent care facility, Mr X presented multiple times at the local emergency room complaining of similar symptoms. He was treated for hypertension and hypokalemia. Following the initiation of lorazepam twice, intravenously, Mr X began to hear music and voices (inaudible to others). He was admitted to the Psychiatric department only to become increasingly agitated and paranoid. This led to him signing out against medical advice. Suicidal

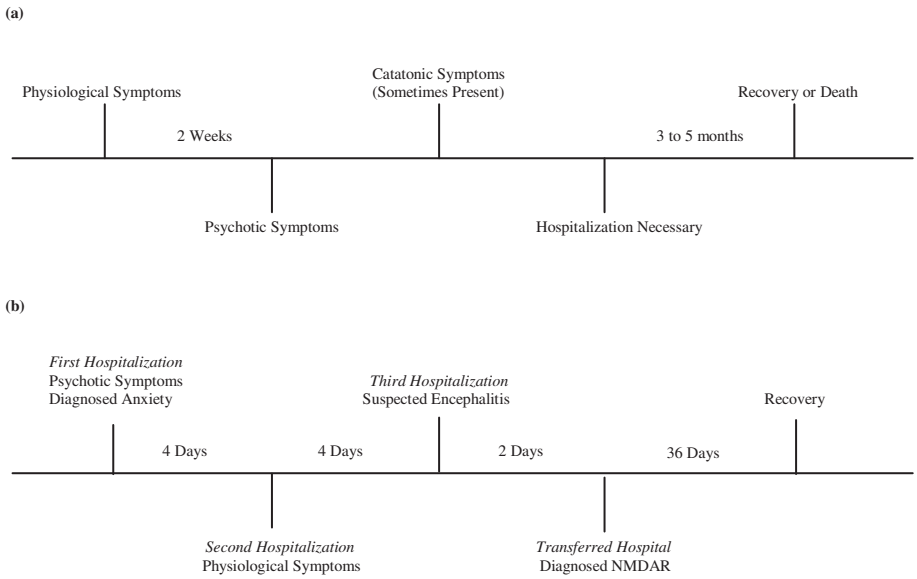

Figure 1. (a) NMDAR Encephalitis: Typical Trajectory of Symptom Presentation. (b) Mr. X's Trajectory of Symptom Presentation.

ideation ensued at this time. Mr X was admitted again and underwent two lumbar punctures. Initial lumbar puncture evidenced no infection; however, after fever onset, another lumbar puncture revealed an elevated white blood count (133/mm^3). Reports revealed continued episodes of altered mental status during this time. A diagnosis was inconclusive; therefore, Mr X was referred to another medical facility. Upon arrival Mr X went into respiratory distress resulting in intubation. After a third lumbar puncture, Anti-NMDA-R autoantibodies were discovered in Mr X's serum and CSF, finally leading to a diagnosis of NMDAR encephalitis. CT full-body imaging showed no evidence of mass to suggest tumor or neoplasm growth. Mr X was the first male at the facility to be diagnosed with NMDAR encephalitis.

Mr X underwent six rounds of plasmapheresis, a five-day course of IV steroids, four doses of rituximab, and two cycles of cyclophosphamide. Tracheostomy and PEG placement followed. He was decannulated one month later. CT scans revealed bilateral pulmonary emboli. He was anticoagulated with Heparin. Follow-up CT revealed no emboli present. He was also treated for Pseudomonas bacteremia with a course of IV Zosyn. Mr X was admitted to an inpatient rehabilitation center one month later for further medical management. During rehabilitation, he participated in various types of therapy including rehab nursing, nutrition, as well as psychological services. He received physical therapy to increase motor control; speech therapy for language impairment; and occupational therapy for cognitive support, to set goals, and increase ability to complete daily tasks. These therapies significantly reduced Mr X's frustration, per his wife. He participated in in-patient rehabilitation for two months.

At the time of the neuropsychological evaluation, Mr X denied pain, numbness, or tingling. He reported intact fine motor control, yet mild continued difficulty with his right foot ("foot drop.") He continues to exercise daily. He denied previous psychiatric

Table 1. Neuropsychological evaluation

Neuropsychological measure	References
Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV)	Wechsler (2008)
Advanced Clinical Solutions (ACS)	Wechsler (2009)
Wide Range Achievement Test—Fourth Edition (WRAT-4)	Wilkinson (2006)
Delis-Kaplan Executive Function System (D-KEFS)	Delis, Kaplan, and Kramer (2001)
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	Randolph, Tierney, Mohr, and Chase (1998)
Trail Making Test (TMT A & B)	Reitan and Wolfson (1993)
Grooved Pegboard	Reitan and Wolfson (1993)
Finger Tapping	Reitan and Wolfson (1993)
Grip Strength	Reitan and Wolfson (1993)
Wisconsin Card Sorting Test (WCST)	Heaton (2003)
Test of Memory Malingering (TOMM)	Tombaugh (1996)
Boston Naming Test (BNT)	Kaplan, Goodglass, and Weintraub (1983)
Conners' Continuous Performance Test (CPT)	Conners, Epstein, Angold, and Klaric (2003)
Adaptive Behavior Assessment System—2nd Edition (ABAS-II)	Harrison and Oakland (2003)
Beck Depression Inventory (BDI-II)	Beck, Steer, and Brown (1996)
Beck Anxiety inventory (BAI)	Beck and Steer (1990)
Personality Assessment Inventory (PAI)	Morey (1991)

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Table 2. Neuropsychological evaluation results

Measure	Index	Subtest	Standard score	Percentile
ACS		Test of premorbid functioning	85	16
WAIS-IV	VCI		89	23
		Vocabulary	85	16
		Similarities	95	37
		Information	90	25
	PRI		86	18
		Block design	85	16
		Matrix reasoning	100	50
		Visual puzzles	80	9
	WMI		89	23
		Digit span	85	16
		Arithmetic	95	37
	PSI		84	14
		Coding	95	37
		Symbol search	75	5
RBANS	Memory	List learning	80	9
		List recall		26–50
		Story memory	105	63
		Story recall	90	25
		Figure copy	115	84
DKEFS		Figure recall	85	16
	Verbal fluency			
		Letter fluency (time)	70	2
		Category fluency (time)	70	2
		Category switching (# correct)	80	9
WRAT-4				
TMT		Math computation	86	18
		Trail Making Test A	83	13
WCST		Trail Making Test B	95	37
		Total errors	<55	<1
		Perseverative responses	<55	<1
		Categories completed	0	<1
BNT			94	34
CPT-II		Omissions	65	94
(*t*-score)		Commissions	37	11
		Hit RT	88	99
		Variability	69	97
	Global Ability	Perseverations	46	37
ABAS-II		Conceptual	90	25
MOTOR		Social	89	23
		Practical	82	12
			96	39
	Finger tapping	Dominant	114	82
	Grooved	Non-dominant	108	70
		Dominant	93	32
	Grip strength	Non-dominant	87	19
		Dominant	83	13
		Non-dominant	88	21

(*continued*)

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Table 2. (Continued)

Measure	Index	Subtest	Standard score	Percentile
BDI-II (raw score)			1	Minimal
BAI (raw score)			3	Minimal

Note: ACS = Advanced Clinical Solutions; WAIS-IV = Wechsler Adult Intelligence Scale-Fourth Edition; VCI = Verbal Comprehension Index; PRI = Perceptual Reasoning Index; WMI = Working Memory Index; PSI = Processing Speed Index; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; D-KEFS = Delis-Kaplan Executive Function System; WRAT-4 = Wide Range Achievement Test-Fourth Edition; TMT A & B = Trail Making Test; WCST = Wisconsin Card Sorting Test; BNT = Boston Naming Test; CPT-II = Conners' Continuous Performance Test-2nd Edition; HIT RT = Hit Reaction Time; ABAS-II = Adaptive Behavior Assessment System-2nd Edition; BDI-II = Beck Depression Inventory; BAI = Beck Anxiety Inventory.

history and his developmental history appeared noncontributory. History of seizures, stroke, concussions, or other brain injuries were denied. Current medications included Nudexta, divalproex sodium, pravastatin cholesterol, potassium chloride, and lisinopril/HCTz.

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Neuropsychological evaluation

Evaluation procedures included administration and scoring with interpretation of comprehensive quantitative and qualitative measures (See Table 1). Neuropsychological test results are provided in Table 2. Mr X has what was presumed to be valid test data as there was no clear secondary gain for underperformance, passing score on the Test of Memory Malingering and Reliable Digit Span, and he had a valid Personality Assessment Inventory (PAI; INC = 49, INF = 59, NIM = 47, PIM = 59). Mr X demonstrated intact vision and hearing sufficient for testing. Mr X was not in acute pain or emotional distress and his test performance is considered an accurate reflection of his current level of functioning.

Mr X's premorbid functioning was estimated to be low average (SS = 85) or slightly higher. According to his test results, most of his cognitive functioning aligned with this low average (or above) performance including intact working memory, divided attention, word reading, object naming, receptive language, verbal comprehension, visual reasoning, mathematic computations, and immediate and delayed memory (with lowered delayed scores). Mr X's executive functioning presented as variable, ranging from average to impaired. Continued weaknesses were noted in Mr X's mildly impaired processing speed, sustained attention, and oral word fluency. Psychological testing revealed no evidence of psychopathology (PAI; DEP = 50, ANX = 42, MAN = 53, PAR = 55, & ARD = 59). No distinct pattern of lateralization was evident during cognitive or motoric measures. Neuropsychological deficits suggest frontal lobe deficits including attention, speed of thinking, fluency, and mild executive dysfunction. Recommendations following neuropsychological evaluation can be found in Table 3.

Table 3. Recommendations following neuropsychological evaluation

(1) *Employment*. It was recommended that Mr X be able to return to work with specified modifications
  (a) Initially be supervised, in which duties are modeled and then checked for accuracy before working independently
  (b) Begin working without the requirement of fast reaction time
  (c) Begin with a reduced schedule and work up to full-time employment
  (d) Utilize checklists or "to-do lists"
  (e) Frequent breaks should be implemented to proactively deter fatigue

(2) *Continued neurorehabilitation, as needed*. It was recommended that Mr X continue to receive rehabilitation services (specifically speech and language therapy) for processing speed and language fluency

(3) *Mood*. Mr X denied experiencing any significant psychological distress. However, it was recommended that if he begins to experience an increase in emotional symptoms after returning to work, that he participate in brief individual psychotherapy

(4) *Medication*. Given that there is no history of seizures, a stimulant was recommended to assist with his mildly impaired processing speed. It was noted and discussed that adding a stimulant may reduce his seizure threshold. All medication decisions were deferred to the prescribing physician

(5) *Neuropsychology follow-up*. If Mr X's mild cognitive weaknesses did not continue to improve, he was encouraged to return for a follow-up neuropsychological evaluation in six months

DISCUSSION

This manuscript sought to present the complex presentation of NMDAR encephalitis, its wide spectrum of symptoms and often misdiagnosis, and the neuropsychological profile of a 42-year-old right-handed male.

Consistent with reports from other published cases (Kayser & Dalmau, 2011), mild frontal lobe impairments were found including reduced sustained attention, processing speed, oral word fluency, and executive functioning. Although Mr X reported mild concern with memory, his evaluation results suggested intact recall of both short- and long-term information, though a weakness in list learning. Rather, this may be memory concerns secondary to his mild executive dysfunction and reduced word retrieval skills. It should be mentioned that during rehabilitation, Mr X participated in various types of therapy including rehab nursing, counseling, physical therapy, occupational therapy, and speech therapy. During this time, Mr X was focused on improving his performance status, along with his cognitive, physical, and psychological well-being. Improving attention, processing speed, memory, and language functioning were incorporated into these therapies, at times on a daily basis. It is assumed that these therapies significantly improved his cognitive performance by the time he was assessed in this neuropsychological evaluation (six months post diagnosis). Having a baseline and pre-rehabilitation evaluation would have been useful in monitoring Mr X's progress through his rehabilitation and continued treatment program.

Mr X reported at the onset of testing that his primary concern was to be cleared to return to work. As the lead industrial mechanic at his employment facility, prior to hospitalization, he was responsible for monitoring the operation of machinery and mechanical equipment by completing preventive maintenance requirements and troubleshooting any malfunctions. In addition, Mr X held a demanding 40–50+ h work week. Based on the assessment report, it was concluded that although Mr X did have some continued mild impairments; his ability to return to work was possible with some

minor adjustments (See Table 3) including initial supervision, memory compensatory strategies, and structure to compensate for mild attention and executive dysfunction. Again, rehabilitation assisted with his recovery by teaching effective compensatory skills and improved insight.

Clinicians involved in early diagnostic work-ups are at risk to misdiagnose NMDAR encephalitis as a psychiatric disorder because of early symptom presentation. Several times Mr X was misdiagnosed and treated as though he was suffering from a primary anxiety disorder. As a result, he was administered lorazepam, which he reports exacerbated his psychotic symptoms. Lorazepam is commonly used in the management of catatonia (due to all causes) and continues to be provided to individuals with NMDAR encephalitis in the ICU-setting who require sedation. Caution is warranted in the use of typical and atypical antipsychotic medications when used for the treatment of NMDAR encephalitis as they may exacerbate dystonic and/or catatonic symptoms (Maneta & Garcia, 2014). Further, Mr X experienced suicidal ideation, which may have been highly detrimental had he not been accurately diagnosed soon afterwards. The case of Mr X provides evidence of how important it is to recognize the link/trajectory between psychiatric symptoms and autoimmune-mediated LE, specifically NMDAR encephalitis. These evaluations necessitate a thorough history taking and an awareness of comorbid neurological symptoms.

Limitations

Limitations of this study include absence of specific lab data and imaging. Additionally, the medication regime including divalproex sodium may have contributed to the areas of cognitive weaknesses/impairment. Mild emotional distress, though not reported symptomatology, may have slightly impacted his performance; specifically his slow processing. Case studies, though potentially very informative, have limited generalizability. Research regarding NMDAR encephalitis remains relatively new and continues to be explored. Continued research and awareness is needed, specifically more neuropsychology research to examine the long-term cognitive impairments.

DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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