

CASE STUDY

Cognitive recovery from Encephalitis Lethargica

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Abstract

The cognitive profile and outcome of Encephalitis Lethargica has not been systematically described in the literature. Treatment has typically focused upon medical management. The first case report of a patient with Encephalitis Lethargica who underwent a systematic programme of cognitive rehabilitation is presented. Initial neuropsychological assessment conducted during her acute presentation indicated generalized cognitive dysfunction, including memory and executive function impairments. An outpatient cognitive rehabilitation programme addressed the development of awareness and the remediation of memory and executive function impairments. Repeat assessment indicated significant improvement in cognitive function. The components of her rehabilitation programme are discussed. She has been able to successfully return to her pre-morbid level of work responsibility within 8 months of her admission.

Keywords: *Encephalitis Lethargica, cognitive rehabilitation, recovery*

Introduction

In 1917, Von Economo described Encephalitis Lethargica, a disorder presenting with an influenza type illness and followed by sleep disorder, basal ganglia disturbance and neuropsychiatric sequelae [1]. His was the first observation of patients during what was to become an epidemic between 1916–1927. Since this time, the incidence of the disease has diminished and only sporadic cases have been reported in the literature. Encephalitis Lethargica has continued to be of interest due to the Parkinsonian-like disorder that appears in many of its survivors [2, 3]. The disease has also piqued interest as, until recently, it was not associated with any causative agent.

The acute phase of Encephalitis Lethargica begins with a prodrome of malaise, mild pharyngitis, headache and low-grade fever [4]. A great variety of symptoms then appear, depending on the localization of the virus within the brain. These include signs of basal ganglia involvement, oculogyric crises, ophthalmoplegia, obsessive compulsive behaviour, akinetic mutism, central respiratory irregularities

and somnolence and/or sleep inversion [5]. The cognitive profile associated with the acute presentation of Encephalitis Lethargica has not been systematically described. Rather, the focus has been on neuropsychiatric symptoms. Acutely, patients have been reported to develop psychosis [6, 7], depression or anxiety [8, 9]. Oblique references to cognitive function have been made, with reports of bradykinesia [6], disinhibition and hypersexuality [7, 9].

Improvement in the acute symptoms of Encephalitis Lethargica has been reported with administration of steroids [6], sedatives [8] and ECT [9]. Successful treatment of Encephalitis Lethargica with steroids led investigators to hypothesize that the disease was immune mediated. In an investigation of 20 patients with an Encephalitis Lethargica type syndrome, Dale et al. [10] found antibodies reactive to the basal ganglia. They proposed that antibodies induced after streptococcus infection cross-react with components of the basal ganglia to produce movement and psychiatric disorders. The similarity of their patients to Von Economo's historical descriptions suggests that

Encephalitis Lethargica is more prevalent than suggested by recent literature [11].

With respect to outcome, Von Economo noted a 40% mortality rate [1]. Post-mortem examination of Von Economo's patients revealed widespread microscopic inflammatory loci in the gray matter, with a predilection for the mid-brain, diencephalon and basal ganglia [1, 5]. A further 20% of Von Economo's patients had residual 'chronic invalidity' ([1], p. 1697). Twenty-six per cent were noted to have residual impairments, but were able to work, and only 14% of his patients made a complete recovery. Patients who initially make an apparent complete recovery have been reported to develop Parkinsonian features months or years later, in up to 80% of patients in some reports [2]. These features have been reported to occur in the absence of 'dementia' [4].

A range of cognitive outcomes following Encephalitis Lethargica has been described. Lishman [4] reports that adolescents tend to have residual changes in cognition and personality, including impulsivity, in the absence of intellectual changes. Howard and Lees [5] describe the neuropsychological functioning of two of four patients they reviewed. At 3 months, their first patient was reported to have 'the mental age of approximately 3 years' (p. 21). Follow-up of their third patient at 1 and 5 years post-illness indicated a severe level of impairment such that she required residential care. Kapadia and Grant [8] allude to cognitive function with the observation that their patient made a good physical recovery, but had a residual 10-month span of amnesia. No further information was provided. Finally, Blunt et al. [6] describe two patients. The first patient was noted to have profound cognitive deficits on discharge with bradyphrenia and bradykinesia. At 5- and 18-month review, she appeared to have no behavioural or cognitive problems. At discharge, a second patient was noted to have executive dysfunction, motor perseveration, apraxia and hesitant speech. Six-month review suggested apparent resolution of these difficulties with a normal Mini-Mental state examination. There appears to be no description of the treatment of the cognitive sequelae of Encephalitis Lethargica. However, rehabilitation of cognitive impairments as a result of Encephalitis Lethargica may fall under the rubric of treatment for post-encephalitic Parkinson's disease.

In this report, the case of a young woman with an Encephalitis Lethargica type syndrome is described. As noted above, the cognitive and behavioural sequelae of the disease are poorly documented, across both acute and chronic conditions. A detailed neuropsychological profile associated with the condition is, therefore, reported. Reports of treatment

have focused upon medical management. Although long-term cognitive and behavioural changes have been anecdotally described, there has been minimal documentation of the treatment of cognitive changes as a result of Encephalitis Lethargica. Thus, the cognitive rehabilitation programme that was developed to improve her cognitive function and assist with return to work is described.

Report of a case

AW is a 24-year-old, right-handed woman. She had completed 12 years of school and a degree in performing arts. At the time of her admission, she worked as a teacher's assistant in drama and also taught classes in special education and mathematics. At the time of her illness onset, AW was in the process of completing her training to qualify as a teacher. There was no prior medical history of note.

AW was initially admitted to a local psychiatric hospital following the rapid onset of confusion, paranoid delusions and agitation. After an expression of self-harm, she was compulsorily admitted into psychiatric care and treated with neuroleptic medication. Due to increasing drowsiness, after 6 days AW was transferred to the neurological unit of the district hospital. Upon admission, her Glasgow Coma Scale score was 14. She showed increased tone in all limbs and an ataxic gait. A CT brain scan did not indicate any abnormalities. Over the next few days, she became increasingly confused. She appeared to be in a catatonic state with rigidity, a psychological pillow and waxy flexibility. She experienced several episodes of very high temperatures and what appeared to be generalized seizures and myoclonic jerks. AW underwent extensive investigations that were all normal. Serial EEGs did not show any epileptiform abnormalities. A MRI brain scan was found to be normal. She screened as positive for anti-basal ganglia antibodies and was diagnosed with Encephalitis Lethargica. AW was then treated with steroids and began to make a slow improvement. At this time, she was referred for neuropsychological assessment to gauge her level of cognitive functioning and advise on rehabilitation, including return to work.

Initial assessment

Neuropsychological assessment was conducted ~6 weeks following admission. Pre-morbid function was estimated to have been in the average range as measured by the NART-R [12]. Results of the initial assessment are shown in Table I. Overall, the results indicated a moderate degree of generalized cognitive impairment. Executive skills were impaired, with poor performance on tests of concept formation,

Table I. Summary of neuropsychological test scores.

	Assessment 1	Assessment 2
<i>WAIS 3</i>		
Digit Span (ss)	8	12
Similarities (ss)	5	10
Picture Completion (ss)	5	13
Block Design (ss)	5	9
Matrix Reasoning (ss)	5	10
Digit Symbol (ss)	8	11
GNT (%ile)	10 (<5%)	25–50
Object Decision (5% cut-off)	10 (<5%)	19 (>5%)
RCFT delayed (%ile)	<1st	4th
<i>WMS 3</i>		
Word List Total (ss)	7	14
Word List Del Recall (ss)	9	9
Word List Del Recog (ss)	6	12
PAL immediate (ss)	5	7
PAL delayed (ss)	3	8
Faces immediate (ss)	3	15
Faces delayed (ss)	8	17
MCST	4	3
DKEFS Inhibition (ss)	10	12
DKEFS Inhib/Switch err (%)	1	8
Phonemic Fluency (ss)	13	19
Category Fluency (ss)	14	15

WAIS 3 = Wechsler Adult Intelligence Scale—3rd edition [13], GNT = Graded Naming Test [14], Object Decision from the Visual Object and Space Perception Battery [15], RCFT = Rey Complex Figure Test [16], WMS 3 = Wechsler Memory Scale—3rd edition [17], PAL = Paired Associate Learning, Del = Delayed, MCST = Modified Card Sorting Test [18], DKEFS = Delis-Kaplan Executive Function System [19], Inhib/Switch err = DKEFS inhibition/switching uncorrected errors, ss = scaled score, %ile = percentile % = cumulative percentile.

complex mental flexibility and verbal abstraction. Memory was poor, with impaired non-verbal recall and recognition and impaired verbal associate learning. Non-verbal intellectual abilities, visuoperception and naming were also impaired. However, auditory verbal short-term and working memory were intact. Speed of processing was satisfactory. Other aspects of memory and executive function were intact, with adequate verbal list learning, inhibition and fluency. On the basis of these assessment results, AW was offered outpatient cognitive rehabilitation to assist with her goal of return to work.

Treatment

AW stated that her primary goal was to return to work. She was, therefore, offered eight outpatient sessions, in addition to a review assessment. Each session addressed the development of awareness and management of memory and executive impairment. A summary of each treatment session is shown in Table II.

Impaired insight was suggested by the discrepancy between AW's subjective reports and those of her mother, in the context of impairments on

Table II. Summary of treatment sessions.

Session 1	Assessment of insight and mood. Interview with AW's mother.
Session 2	Education about illness and brain/behaviour relationships. Feedback of test results. Discussion of compensatory strategies. Introduction of memory diary.
Session 3	Review of memory diary. Administration of EBIQ and memory aids questionnaire. Reinforcement of compensatory strategies. Introduction of problem-solving framework.
Session 4	Review of memory diary. Discussion of compensatory strategies. Administration of DASS. Practise of problem-solving framework.
Session 5	Review of memory diary. Practise of problem-solving framework. Plan for graded return to work.
<i>Repeat neuropsychological assessment</i>	
Session 6	Feedback about repeat assessment. Reinforcement of memory aids and problem-solving framework. Plan for return to work.
Session 7	Review of return to work. Reinforcement of strategies.
Session 8	Review of return to work. Reinforcement of strategies. Discharged.

neuropsychological assessment. Whilst she denied changes, her mother noted a number of cognitive and behavioural difficulties post-discharge. Level of awareness was also measured by the European Brain Injury Questionnaire (EBIQ [20]). This is a self-report measure concerning the subjective experience of cognitive, emotional and social difficulties of people with brain injury. Although she did not endorse cognitive problems, there were mild symptoms of depression and anxiety. The Depression, Anxiety and Stress Scales (DASS [21]) were administered to further investigate these symptoms. However, the DASS did not indicate any significant endorsement of symptoms of depression, anxiety or stress.

Development of awareness was targeted via education about assessment results, the illness that she sustained and the potential impact of cognitive difficulties upon her return to work. AW also completed a diary between sessions to note the frequency of common memory problems in everyday life. This memory diary, based on Sunderland et al. [22], had the two-fold aim of increasing awareness of problems and gathering information about the functional impact of these problems. Her mother also filled in the diary for the first month. The contents of the memory diary were reviewed at the beginning of each session. Initially, AW noted a number of mild memory difficulties. Across subsequent sessions the reported memory difficulties decreased in frequency until no difficulties were endorsed. At this point, the diary was discontinued. During the final sessions,

AW was able to describe her cognitive changes without prompting, including strategies to manage residual and future problems.

As noted in Table I, the initial assessment indicated a degree of memory impairment. As awareness of mild functional memory difficulties increased, treatment sessions incorporated training in the use of compensatory memory strategies. A memory compensation questionnaire indicated that AW already used strategies such as Post It notes, a diary and her mobile phone. She also used routine to aid her memory as, for example, she always took her medication after her meals. External compensatory strategies built upon these techniques, which were reinforced across sessions within the context of her return to work. She was also given written information about memory strategies [23].

Given evidence of executive difficulties on neuropsychological assessment, it was decided to introduce a structured approach to problem-solving, as described by Evans [24]. This approach adopts a framework focusing on the solution of complete problems, with different stages in the process highlighted depending upon the individual's problems. The framework begins with identification and definition of the problem. Generation of solutions is then addressed, including a decision on the best solution for the problem. Steps to solve the problem, including strategies to apply, are then listed. Prompts for monitoring and evaluation of the plan are also included. The problem-solving framework and template were introduced under the guise of support for AW's return to work. Hypothetical and real life examples were practised across sessions. Particular attention was given to her ability to clarify and extract relevant information, to define a problem and her reasoning abilities. With practice, AW was able to work through the template independently.

Review assessment

With evidence of diminished everyday memory problems and good understanding of the problem-solving template, a repeat assessment and graded return to work was planned. The second assessment was conducted ~8 weeks after the initial testing. Results of the review assessment are shown in Table I. A significant degree of improvement was evident. Although there was a brief interval between assessments, the magnitude of improvement across tests suggest that this change is unlikely to be due to practice alone [25, 26]. Non-verbal intellectual abilities, naming and visuoperceptual skills had improved. Information processing remained satisfactory. Attention was investigated further with administration of the Test of Everyday Attention [27]. Results, as shown in Table III, indicated satisfactory

Table III. Performance on test of everyday attention.

	Assessment 1	Assessment 2
Map Search—1 minute (ss)	nt	10
Map Search—2 minutes (ss)	nt	8
Elevator Count	nt	7
Elevator Count Distract (ss)	nt	13
Vis Elevator—accuracy (ss)	nt	8
Vis Elevator—timing (ss)	nt	6–7
Tel Search (ss)	nt	12
Tel Search Counting (ss)	nt	13–17

Elevator Count Distract = elevator count with distraction, Vis Elevator = visual elevator, Tel Search = telephone search, Tel Search Counting = telephone search while counting, ss = scaled score, nt = not tested.

Table IV. Performance on behavioural assessment of dysexecutive syndrome.

	Assessment 1	Assessment 2
Overall score	nt	108
Rule Shift (ps)	nt	4
Action Program (ps)	nt	4
Key Search (ps)	nt	1
Temporal Judgement (ps)	nt	3
Zoo Map (ps)	nt	4
Modified Six Elements (ps)	nt	4

ps = profile score, nt = not tested.

visual search, sustained attention, working memory and divided attention. Memory function had improved, as verbal paired associate learning and non-verbal recognition memory were now satisfactory. Executive function was more thoroughly investigated with administration of the Behavioural Assessment of the Dysexecutive Syndrome [28]. AW performed well across tasks of mental flexibility, planning and judgement, as can be seen in Table IV. Inhibition and fluency also continued to be intact and verbal abstraction had improved. However, mild difficulties remained in concept formation and complex flexibility. Non-verbal recall also continued to be impaired.

AW was provided with feedback about her repeat assessment. Given evidence of mild residual impairment on non-verbal memory, external compensatory strategies were reinforced. These included the use of her diary, increased organization and time, written notes and routine. In light of her weak executive functions, the problem-solving framework was also reviewed, with particular emphasis on planning and systematically working through steps to solve a problem. A graded return to work as a trainee teacher was discussed. AW planned to reduce her workload to only teach drama. Initially, she aimed to observe a colleague's classes before teaching with supervision. At a review session following 2 weeks of work, AW stated that she had observed lessons for 5 days

and then taught three lessons with supervision. Compensatory strategies were reviewed to manage subjective complaints of fatigue, misplacing items and taking longer to get organized. A final review session was held after 4 weeks of full time work. AW stated that she had returned to her pre-morbid level of work responsibilities. Compensatory strategies to manage future difficulties were discussed, with AW independently volunteering techniques.

Discussion

For the first time, the cognitive profile and outcome of a case of Encephalitis Lethargica has been described in detail. Until now the cognitive profile and outcome of Encephalitis Lethargica have not been systematically described. AW was a 24-year-old female who presented with confusion, agitation and psychotic features. Her diagnosis was confirmed with the presence of anti-basal ganglia antibodies. She was then successfully treated with steroids and her clinical presentation began to improve. Initial neuropsychological assessment indicated impaired executive skills, memory and non-verbal intellectual abilities. Following outpatient cognitive rehabilitation, review assessment indicated significant improvement with only mild residual impairments in executive and non-verbal recall memory. AW has made a good cognitive recovery from Encephalitis Lethargica, with return to work 8 months after her initial presentation.

It may be that a large part of AW's recovery occurred spontaneously, particularly as treatment and assessment were undertaken immediately following her acute presentation. However, as noted, little is known about the expected course of recovery from cognitive impairment secondary to Encephalitis Lethargica. Lishman [4] reported that adults tend to develop Parkinson's in the absence of 'dementia' and that adolescents have persistent cognitive and personality changes. Other authors have described the persistence of significant cognitive impairments [5] or a good cognitive recovery [6]. This latter report mirrors the recovery seen in AW. Whilst the contribution of spontaneous recovery must be considered, treatment was structured to target three cognitive areas—insight, memory and executive function.

Self-awareness or insight within the context of rehabilitation refers to the ability of a person to possess knowledge about their deficits and to understand the implications of these deficits [29]. AW did not appear to have intellectual awareness [30] of her deficits that could have limited the application of any compensatory techniques. Thus, an attempt was made to measure and develop her insight. A number of techniques have been described to measure a patient's level of awareness (e.g. Patient

Competency Rating Scale [31]; Awareness Questionnaire [32]) and denial of disability [33]. AW's level of awareness was assessed through unstructured interview, the EBIQ and daily completion of the memory diary. Insight was then targeted through education, including feedback of her test results and self-ratings of her everyday memory functioning. A comparison between AW's and her mother's report of everyday problems could have been made to increase insight. However, provision of information and completion of the diary did in itself allow self-awareness of deficits to develop and across sessions she was amenable to the application of compensatory strategies.

Memory problems are common after acquired brain injury and can have a significant impact upon an individual's everyday function [34]. As memory impairments were evident on neuropsychological assessment, compensatory strategies were discussed. Completion of a memory aids questionnaire indicated that AW already used external aids in her everyday life, including a diary, her mobile phone and Post It notes. She also used routine to remind her to complete activities, such as taking her medication after each meal. Her use of such strategies was reinforced and encouraged, particularly in the context of her return to work. It may be that her pre-morbid use of memory aids facilitated her use of aids post-injury [35]. AW was also provided with written information about memory strategies.

The degree of executive deficits on formal assessment suggested that it could be difficult for AW to return to her previous level of independence at work. Evans [24] advocates a problem-solving framework aimed at complete problems, with emphasis placed on different aspects of the framework and different strategies depending upon the patient's particular problems. von Cramon and Matthes-von Cramon [36] have also described the treatment of executive problems with a focus on problem identification and analysis. In a group study, training in structured problem-solving improved performance on neuropsychological tests. However, there was minimal generalization to everyday tasks. In another study [37] this analytical approach to problem-solving was adopted to assist a man who had sustained a traumatic brain injury to return to work. Under the premise of self-instructional training, the problem-solving rules were internalized over sessions until the subject could work independently.

AW was trained in the use of a structured approach to problem-solving [24]. Provided with a paper-based checklist and template, she was initially guided through the process and at later sessions was able to work through the outline independently. Particular attention was directed at her ability to

clarify and extract relevant information, definition of a problem and her reasoning abilities. Effort was made to give her examples that were relevant to her work duties. At the end of treatment, AW reported that she had been able to successfully return to work. Although not corroborated nor quantitatively measured, this suggests that she had been able to compensate for the executive difficulties evident on formal testing. Outcome of the problem-solving training could have been quantified with behavioural ratings from work colleagues or quantification of goal attainment. Assessment of internalization of the framework was not assessed at the end of therapy. However, her occupation as a teacher, with the need for pre-planned lessons, may have mirrored the problem-solving framework and so facilitated her application of this compensatory strategy.

Conclusions

Until now the cognitive sequelae and outcome following Encephalitis Lethargica has not been widely documented and the cognitive rehabilitation of such cases has not been addressed. The cognitive profile of a young lady following Encephalitis Lethargica has been described. Her outpatient programme focused upon increasing insight and on the management of memory and executive impairments. She has been able to return to work ~8 months after her initial presentation.

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