Cerebral Circulation - Cognition and Behavior 2 (2021) 100003

Contents lists available at ScienceDirect

Cerebral Circulation - Cognition and Behavior

journal homepage: www.elsevier.com/locate/cccb

# Neurocognitive effects of Moyamoya disease and concomitant epilepsy

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ARTICLE INFO

*Keywords:*
Moyamoya
Vascular
Cognitive
Executive function
Epilepsy

ABSTRACT

*Objective:* Moyamoya disease (MMD) is a rare degenerative cerebrovascular disorder that leads to recurrent strokes and cerebral hypoperfusion. Seizures are not uncommon in MMD especially following surgical treatment for the disease. Cognitive changes that are largely executive in nature have been documented following MMD and surgical treatment, although research is limited in adults.

*Methods:* The present case report details the comprehensive neurocognitive evaluation of a patient with MMD and concomitant epilepsy.

*Results:* Neurocognitive findings revealed a prominent dysexecutive pattern and atypically poor performance in areas such as visual and verbal memory. The patient reported significant affective symptoms and functional decline.

*Conclusions:* This case offers insight into unique neurocognitive results that may present in adult MMD cases and underscores the importance of interpreting results in the context of neurological comorbidities in this rare disease.

## 1. Introduction

Moyamoya disease (MMD) is a degenerative cerebrovascular disorder characterized by blockage of the internal carotid artery at the Circle of Willis leading to fragile collateral vessels and subsequent cerebral hypoperfusion [10]. MMD is rare, with a prevalence of 0.086 per 100,000 in North American adults [9]. Patients with MMD present with recurrent infarcts, transient ischemic attacks (TIAs), and/or hemorrhagic bleeding due to fragile vessels [16]. Treatments for MMD include indirect bypass such as encephaloduroarteriosynangiosis (EDAS), a surgical intervention aimed at revascularization of the occluded vessels and reperfusion of affected cerebral areas [13]. The development of seizures has also been observed following MMD diagnosis and revascularization surgery [4,9].

While sequelae often include cognitive changes, few studies have examined neurocognitive functioning in adults with MMD. When reported, cognitive changes are typically characterized by executive dysfunction [2,7] beyond stroke alone [15]. Mood has been reported as generally stable across diagnosis and surgical intervention [7,17]. However, given the broad spectrum of cognitive and affective changes that can occur with severe hypoperfusion and chronic infarcts, further characterizations of adults with MMD are necessary to understand the scope of this disease. This case report reviews a patient with history of MMD post-EDAS with recurring seizures accompanied by cognitive decline, affective symptoms, and functional impairment in the context of psychosocial barriers to treatment.

## 2. Case presentation

The patient is a 53-year-old right-handed Caucasian male with 18 years of education. He is married and lives in rural southeastern United States. He discontinued his work in a professional position one year prior to the current evaluation secondary to MMD. Family history includes maternal and paternal myocardial infarction. The patient reported smoking approximately one pack of cigarettes per day for 35 years but denied alcohol use. He provided consent for this case report.

### 2.1. MMD history

The patient was diagnosed with MMD following a left M1 stroke in his early 50s and underwent left hemispheric EDAS surgery six months later. No further strokes were reported 14 months postoperatively. Angiogram revealed expected changes to the left internal carotid artery and formation of collateral vessels to distal middle cerebral artery branches. Post-surgical residual MMD symptoms included left-sided upper and lower extremity weakness, daily left-sided pain and pressure, blurred vision, diplopia, and bilateral hand tremor. He also described approximately six possible TIAs in the 15 months following the initial stroke

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https://doi.org/10.1016/j.cccb.2020.100003
Received 18 October 2020; Received in revised form 9 December 2020; Accepted 11 December 2020
Available online 16 December 2020

**Table 1**
Neurocognitive battery and standard scores.

| Cognitive Domain | Test | Standard Score |
|---|---|---|
| Mental Status | Montreal Cognitive Assessment (MoCA) | 22/30 (raw score) |
| Premorbid Functioning | Wechsler Abbreviated Scale of Intelligence-II (WASI-II) Vocabulary | 99 |
| Intellectual Functioning | WASI-II | VCI = 102<br>PRI = 86<br>FSIQ = 93 |
| Verbal Learning & Memory | California Verbal Learning Test-II (CVLT-II) | Trial 1–5 Total = 78<br>Long Delay Free Recall = 85<br>Recognition Discrimination = 40 |
| Visual Learning & Memory | Brief Visuospatial Memory Test-Revised (BVMT-R) | Total = 63<br>Long Delay = 63<br>Recognition = 81 |
| Executive Functioning & Attention | Wechsler Memory Scale-III (WMS-III) | WMI = 102<br>LNS = 105<br>Spatial Span = 100<br>Digit Span = 85 |
| | Trail Making Test Part B (TMT-B)* | 84 |
| | Stroop Color & Word Test | Color-Word = 78 |
| | WASI-II Similarities | 105 |
| | WASI-II Matrix Reasoning | 85 |
| Language | WASI-II Vocabulary | 99 |
| | Boston Naming Test – Second Edition (BNT-2)* | 87 |
| | FAS Test of Phonemic Fluency* | 69 |
| | Animal Naming* | 97 |
| Visuospatial | WASI-II Block Design | 90 |
| | Judgment of Line Orientation (JOLO) | 109 |
| | Taylor Complex Figure Copy | 84 |
| Processing Speed | Symbol Digit Modalities Test (SDMT) | Written = 73<br>Oral = 79 |
| | Trail Making Test Part A (TMT-A) | 82 |
| | Stroop Color & Word Test | Word Reading = 69<br>Color Naming = 73 |

*Note*: Standard score mean=100, standard deviation=15. Verbal Comprehension Index = VCI; Perceptual Reasoning Index = PRI; Full Scale Intelligence Quotient (FSIQ); Working Memory Index = WMI; Letter-Number Sequencing.
* Utilized demographically adjusted neuropsychological norms for Caucasian adults [6].

with symptoms including left-sided upper and lower extremity weakness and drooping mouth.

### 2.2. Additional medical history

Additional medical history includes recurrent complex partial seizures and staring spells with onset following a reported hypertensive emergency during hospitalization for cholecystectomy 2 years prior to his stroke. Notably, he reported cardiopulmonary arrest lasting approximately four minutes during that hospitalization. Seizure frequency was four to six seizures per week but increased to seven per week post-EDAS. At the time of evaluation, frequency had decreased to approximately two seizures per week with levetiracetam adherence. His aura was described as a feeling of intracranial pressure and pain, finger twitching, blurred vision, and facial numbness. Additional pertinent medical history included myocardial infarctions in 2010 and 2016; approximately five concussions during military service and secondary to falls during seizures with quick return to baseline; and insomnia (difficulty falling asleep, early morning waking).

### 2.3. Reported cognitive and functional changes

The patient reported onset of cognitive changes following the hypertensive emergency with exacerbation post-stroke two years later. Since that time, his cognitive difficutlies were reportedly stable. Cognitive changes included word-finding difficulties, worsened memory, and difficulty with executively-mediated skills such as multitasking and organizing information efficiently. He endorsed independence with all basic acts of daily living (ADLs) but required assistance for several instrumental ADLs. For instance, he reported incidents of a kitchen fire and flooding after failing to turn the stove and water off. He no longer managed the household finances due to cognitive difficulties and did not drive secondary to seizure precautions.

### 2.4. Neurocognitive evaluation

The patient participated in neurocognitive evaluation nine months post-EDAS surgery and approximately three and a half years following onset of perceived cognitive changes. Refer to Table 1 for the neurocognitive battery and standard scores. Performance was compared to normative data for each test, producing standard scores. Z scores were calculated based on deviation of standard scores from the patient's premorbid estimate. This premorbid estimate, per an expressive vocabulary task, was average range. Results revealed intact overall intellectual functioning, indicated by average range full scale IQ. However, he evidenced relative weaknesses in complex verbal learning along with impairment in visual learning and phonemic fluency. These performances likely represented executively mediated deficits characterized by restricted encoding affecting the learning process; memory retention and retrieval were fully intact (i.e., non-amnestic) and commensurate with best learning trials. His verbal processing speed and basic motoric speed were also slower than expected. Moderate anxiety and severe depressive symptoms were present (Beck Anxiety Inventory = 26; Geriatric Depression Scale = 22). See Fig. 1 for a graphical representation of Z scores for select neurocognitive results across cognitive domains assessed.

## 3. Discussion

The patient's results included executively-mediated learning difficulties and slowed processing speed. Such a pattern reflects bifrontal and

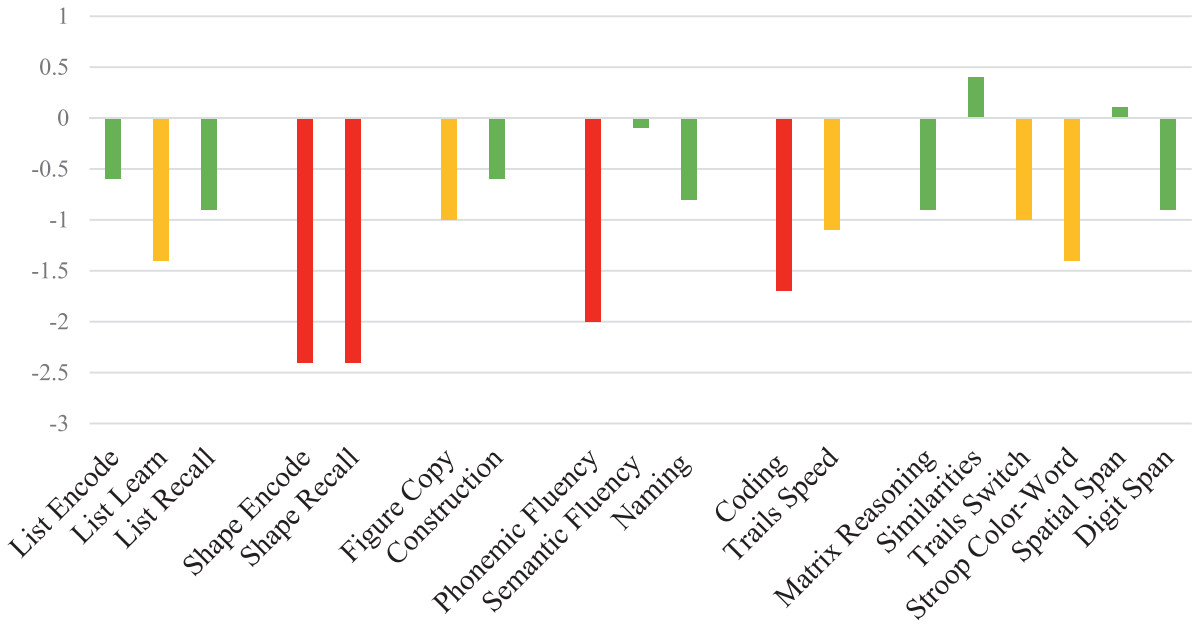


**Fig. 1.** Select standardized deviation scores of neurocognitive results.
Note: Scores are z-score deviations from estimated average premorbid functioning. Scores below −1.5 represent significant decrement (> 1.5 SD) from expected range (red bars). Yellow bars represent mild reductions (between 1 and 1.5 SD). Green bars represent scores within expected range. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

**Table 2**
Comparison of neurocognitive scores in the current case to existing literature.

| Cognitive Domain | Impairment in Current Case | Impairment in Existing Literature |
|---|---|---|
| Verbal Memory | List learning | – |
| Visual Memory | Learning and recall | – |
| Attention | – | Festa et al. [2]; Kazumata et al. [8] |
| Executive Functioning | Verbal inhibition | Festa et al. [2]; Karzmark et al. [7]; Kazumata et al. [8]; Lei et al. [11] |
| Language | Phonemic fluency | Karzmark et al. [7] |
| Processing Speed | Cognitive and motoric speed | Hara et al. [5] |

*Note*: Impairment in the current case indicated by scores one standard deviation or more below premorbid estimate.

subcortical involvement generally consistent with his significant vascular burden due to MMD and associated vascular event(s). However, this case reflects notable areas of additional impairment compared to the nascent MMD literature as summarized in Table 2. Most prominently, the patient's results were characterized by executive dysfunction. This dysexecutive pattern likely accounts for his difficulties with verbal memory through difficulties efficiently learning information. Verbal memory difficulties are inconsistent with existing literature [7,11]. Specifically, the patient exhibited severely restricted encoding of complex verbal information with intact recall commensurate with best learning; his impaired recognition is in keeping with newly documented differences between prospective and retrospective memory performance in MMD [14]. Similarly, his visual learning was notably restricted, again with intact visual recall relative to best learning trials; these deficits are inconsistent with existing literature [7,17]. Such a notable dysexecutive pattern may be attributable to the vulnerability of subcortical-frontal neural networks to ischemia regardless of their location in the brain [16]. Suppressed general cognitive processing speed was consistent with white matter compromise subsequent to chronic ischemia common in MMD. These white matter changes can be subtle and diffuse, spanning prefrontal, cingulate, and parietal cortices. It is disruption of these frontoparietal networks that is thought to affect executive function [8]. Specifically, white matter integrity in the left hemisphere has been associated with cognitive processing speed in MMD [5], again consistent with the unilaterality of the patient's MMD. Although Hara and colleagues [5] suggest that revascularization surgery may be neuroprotective due to reperfusion across frontoparietal white matter circuits, the patient demonstrated suppressed speed despite surgical intervention.

In addition to MMD, the patient's multiple concussions and reported insomnia may have impacted his cognitive performance, particularly in memory and executive functioning, although effects are generally small for concussion and may be moderate for insomnia [1,3]. More notably, his recurrent complex partial seizures likely affected his neurocognitive performance. Seizures are not uncommon in MMD: Twenty-four percent of adults with MMD have reported a history of one or more seizures, and epileptiform events have been estimated to occur in 18% of cerebral hemispheres following revascularization surgery [4]. Notably, the patient's seizures were largely unmanaged for a period due to difficulty maintaining prescriptions and medical appointments, a difficulty exacerbated by his location and inability to drive due to seizure precautions. This difficulty accessing healthcare services is especially salient given the association between regular follow-up care for MMD and lessened neurocognitive impairment [12].

Such a prolonged experience of seizure activity and difficulties with management may also manifest affectively. The patient endorsed a greater affective burden than is typical of most MMD presentations. Affective changes, such as depressive symptoms, irritability, and impulsivity, have been previously described in case studies (e.g., [16]), although larger scale investigations have indicated a general lack of affective involvement in MMD. Specifically, his severe range depressive

symptoms contrast with the only 5% of patients with MMD previously found to exhibit scores on self-report measures suggestive of clinically significant levels of depression [7]. Affective burden is a salient clinical issue in assessment of patients with MMD, however, as depression and anxiety in individuals who have experienced stroke are associated with poorer neurocognitive performance, functional outcome, and adherence to treatment, as well as higher mortality [12]. This patient's experience of recurring seizures may contribute to the discrepancy in affective burden between this case and extant findings. Seizures relative to MMD have been associated with higher rates of depressive symptoms due to their significant impact on functional activities. Difficulties in diagnosis of and medically managing seizures further contribute to mood disruption [7]. Accordingly, affective distress may have further contributed to cognitive performance in this case.

## 4. Conclusion

This case report details the comprehensive neurocognitive evaluation of a case of post-left hemispheric EDAS surgery MMD with preexisting epilepsy. Neurocognitive results indicate affective burden and a prominent dysexecutive pattern affecting verbal and visual learning and processing speed. In contrast to existing literature, suppressed verbal and visual memory was evident. To the authors' knowledge, this case is the first to underscore the impact of a vascular dysexecutive pattern on verbal and visual memory in this population. The experience of seizures in this case likely intensified affective burden and functional impairment. As seizures are common in this population [4], affective burden and its impact on cognitive performance is an important area of consideration when evaluating patients with MMD as is careful evaluation of psychosocial elements that may hinder regular medical follow-up.

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