2014

Cognitive Improvement After Microsurgical Revascularization for the Treatment of Moyamoya Disease

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Cognitive Improvement After Microsurgical Revascularization for the Treatment of Moyamoya Disease

By

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A thesis submitted to the Department of Psychology

in partial fulfillment of the requirements for the degree of

Master of Arts in General Psychology

UNIVERSITY OF NORTH FLORIDA

COLLEGE OF ARTS AND SCIENCE

July, 2013

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Dedications and Acknowledgements

I would like to acknowledge gratefully all of the following whose guidance, insight, and encouragement made this possible. Fist, the Mayo Clinic for their cooperation in letting me utilize the facility and data, especially Dr. Hanel for his endless support and assistance on this project, including giving me the opportunity to research such a fascinating disease. Dr. Hanel is an exceptional neurosurgeon and researcher who offered crucial contributions. I was extremely fortunate to have Dr. Guss and Dr. Lange as my professors, advisors, and mentors. I am thoroughly grateful for all of their support. They provided guidance, motivation, advice, constructive criticism, perpetual energy, and enthusiasm. Their rigor and passion for research inspires me, and I am honored to have learned from them.

A special thanks to my family for all of their love and encouragement. My parents, who have always provided encouragement and supported me in all of my pursuits. Finally, I would like profoundly to thank my husband Julius and daughters Isabella and Beatrice for all the love and emotional support during this entire endeavor, for which I will be eternally grateful.

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Abstract

Moyamoya disease is a rare entity characterized by progressive narrowing of intracranial blood vessels. In most cases, Moyamoya does not respond well to medical therapy and often leads to surgical revascularization. The physiological benefits of the revascularization surgery for Moyamoya patients have been well documented, yet the effects of surgery on cognitive skills and abilities are far less studied. Participants in the current study were 33 patients, 24 to 85 years of age, who underwent revascularization surgery at the Mayo Clinic in Jacksonville, Florida. All patients underwent a physical and cognitive preoperative evaluation, where speech, memory, and intellectual processes were measured. After surgery, patients returned for three follow-up assessments over a period of six months. All patients experienced stabilization or improvement of physiological symptoms. Regarding cognitive functions, speech, memory, and intellectual processes improved significantly after surgery. Results showed not only a reduction of physiological symptoms, but also a significant cognitive improvement postsurgery. This study adds to the research of this disease and to the benefits of treatment. More research can only strengthen these findings and educate healthcare professionals; helping them reaffirm Moyamoya patients have a better quality of life, by reinforcing the benefits of revascularization surgery.

Cognitive Improvement After Microsurgical Revascularization for the Treatment of Moyamoya Disease.

Japanese doctors first described Moyamoya as hypoplasia of the bilateral internal carotid arteries in 1957 (Scott & Smith, 2009). Moyamoya is a Japanese word that literally means "something hazy, like a puff of cigarette smoke" (Ikezaki & Loftus, 2001, p. 1). Moyamoya disease leads not only to a different degree of stenosis and occlusions of large arteries of the anterior part of the Willis circle, but also to the development of the collateral vasculature that produces a typical angiographic image, that resemble a 'puff of cigarette smoke' (Tarasow, Kulakowska, Lukasiewickz, Kapica-Topczewska, Korneluk-Sadzynska, Brzozowska, Drozdowski, 2011). Moyamoya disease has also been termed "bilateral hypoplasia of the internal carotid arteries," "cerebral juxta-basal telangiectasia," "cerebral arterial rete," "rete mirabile," "cerebral basal rete mirabile," and, more commonly, "spontaneous occlusion of the circle of Willis" (Burke, Burke, Sherma, Hurley, Batjer & Bendok, 2009). Patients with bilateral pathognomonic arteriographic findings are said to have Moyamoya disease and patients with unilateral findings have the Moyamoya syndrome (Scott & Smith, 2009). The term quasi-moyamoya disease is typically used to refer to patients who display steno-occlusive lesions and associated collaterals in other areas of the brain or who have systemic disorders that account for the observed vasculopathy (Zipfel, Fox & Rivet, 2005).

For a patient to be diagnosed with Moyamoya disease, four criteria need to be met; first, stenosis or occlusion of the terminal portion of the internal carotid artery; second, a coexisting abnormal vascular network in the base of the brain or basal ganglia; third, bilaterality; and fourth, no other identifiable cause (Fukui, 1997). These criteria indicate that both sides of the brain have to demonstrate a narrowing of the arteries, causing an obstruction that leads to a diminishing blood flow in the brain. The brain will look for new routes to compensate for the blockage by creating an abnormal vascular network, and if the blockage is not caused by any other source, such as a tumor, it is said that the patient has Moyamoya disease.

The minister of Health and Welfare of Japan has subdivided Moyamoya presentation into 4 categories: ischemic (63.4%), hemorrhagic (21.6%), epileptic (7.6%), and other (7.5%). In the United States the most common mode of presentation is ischemia in both children and adults, whereas the hemorrhagic presentation is comparatively rare (Weinberg, Rahme, Aoun, Batjer & Bendok, 2011).

Although the pathophysiology of Moyamoya disease is yet to be fully understood, several angiogenic and cellular proliferative proteins have been associated with Moyamoya disease, such as Vascular Endothelial Growth Factor (a 45-kD homodimeric), upregulated expression of Vascular Endothelial Growth Factor A (VEGF-A), abnormal elevation in the cerebrospinal fluid of Basic Fibroblast Growth Factor (18-kD protein), significant increase in both Hepatocyte Growth Factor and its receptor c-Met in the tunica media and intima, upregulation of Transforming Growth Factor–b1, and an elevation of Granulocyte Colony-Stimulating Factor were all found in patients with Moyamoya disease (Weinberg, Arnaout, Rahme, Aoun, Batjer & Bendok,2011).

Moyamoya has been observed throughout the world in people with various ethnic backgrounds (Scott & Smith, 2009). The incidence peaks in two ages: the early peak around five years old and a later peak around 36 years old. The incidence of the disease in Japan is 0.35 per 100,000 persons, in the United States (US) is significantly lower 0.086 cases per 100,000 persons indicating a genetic component (Weinberg, Rahme, Aoun, Batjer, & Bendok, 2011). For every

White Moyamoya patient in the United States, reported incidence-rate ratios are 4.6 for Asian Americans, 2.2 for Blacks, and 0.5 for Hispanics (Scott & Smith, 2009).

There is an ethnic predisposition to Moyamoya disease, the incidence of the disease being the highest in the Asian population worldwide, over 10% of Moyamoya patients have affected blood relatives; concordance in the affection status has been proven in 80% of identical twins (Hashikata, Mineharu, Takenaka, Houkin,Kuroda, Kikuchi,kimura,Taki, Sonobe, Ban, Nogaki, Handa, Kikuta, Takagi, Nozaki, Hashimoto, Koizumi, 2008). The inheritance pattern of Moyamoya is autosomal dominant with incomplete penetrance, there is a major gene locus for autosomal dominant Moyamoya disease on chromosome 17q25.3 (Mineharu, Liu, Inoue, Matsuura, Inoue, Takenaka, Ikeda, Houkin, Takagi, Kikuta, Nozaki, Hashimoto, Koizumi, 2008).

The narrowing of the arteries of the anterior part of the Circle of Willis are produced by the thickening and cellular proliferation in the vessel wall, causing a cerebralvascular hemodynamic impairment in Moyamoya patients, which means the stenosis are causing a irregular blood flow in the brain (Festa, Schwarz, Pliskin, Cullum, Lacritz, Charbel, & Lazar, 2010). In the case of Moyamoya patients the narrowing of the arteries cause hypoperfusion, reduced blood flow, in the major vessels of the anterior circulation of the brain and can lead to various symptoms (Golby, Marks, Thompson, & Steinberg, 1999). Moyamoya patients' common physiological complaints are stroke, seizures, hemorrhage, headache, and transient ischemic attacks (TIAs) also known as mini-strokes causing slurred speech, loss or diminished vision and mental confusion, but unlike stroke, TIA symptoms can resolve within few minutes (Guzman, Lee, Achrol, Bell-Stephens, Kelly, & Do, 2009). In addition, it has been observed that Moyamoya disease can impair cognition.

Cognitive impairment is a long-term complication for adult with Moyamoya Disease (Su, Hai, Zhang, Yu & Wu, 2013). Although some cognitive decline is expected with aging, cognitive impairment is an intermediate stage between the expected cognitive decline of normal aging and the more serious decline of dementia (Salthouse, Atkinson, & Berish, 2003). It can involve problems with memory, language, thinking and judgment that are greater than normal age-related changes. Cognitive impairment caused by vascular diseases such as Moyamoya is known as Vascular Cognitive Impairment (VCI), it is a syndrome that takes into account the spectrum of cognitive severity, which often includes executive dysfunction and the various types of brain vascular disease that could underlie cognitive symptoms, including subclinical vascular brain injury, common in Moyamoya patients (Gorelick, Scuteri, Black, DeCarli, Greenberg, Iadecola, Launer, Laurent, Lopez, Nyenhuis, Petersen, Schneider, Tzourio, Arnett, Bennett, Chui, Higashida, Lindquist, Nilsson, Roman, Sellke, & Seshadric, 2011). When vascular damage occurs in the brain, it compromise neural activity and hence causing cognitive impairment (Burke, Hickie, Breakspear, & Götz, 2007).

Cognitive executive functioning, which includes working memory, reasoning, task flexibility, and problem solving, is the most affected in Moyamoya patients, followed by memory (short and long term memory) and intellectual impairment to some extent (Karzmark, Zeifert, Tan, Dorfman, Bell-Stephens, & Steinberg, 2008). Cognitive executive functioning can be described as the control processes responsible for planning, assembling, coordinating, sequencing, and monitoring other cognitive operations (Salthouse, Atkinson, & Berish, 2003). Analysis of existing literature revealed executive function to be considerably impaired in adult Moyamoya patients, due to its in executive function, the frontal lobe, is thought to be directly affected in adult Moyamoya patients. The subcortical and frontal system was also found to be impaired in Moyamoya patients due to chronic hypoperfusion (Weinberg, Rahme, Aoun, Batjer & Bendok, 2011).

On the study “Moyamoya disease: functional and neurocognitive outcomes in the pediatric and adult populations”, by Dr. Weinberg et al., indicate the 2 most common tests to assess memory in Moyamoya adult patients are the California Verbal Learning Test II (CVRS-II) and the Wechsler Memory Test – Revised Visual Reproduction System (WMT-RVRS). 31% of their patients showed memory dysfunction. For speech they used the Delis-Kaplan Executive Function System (D-KEFS) and they found that 47% of their patients showed fluency impairment. Although they recommend revascularization for treating Moyamoya, and they reported that the surgery is beneficial to both physiological and cognitive outcome, their study did not focus on post-operative results. (Weinberg, Rahme, Aoun, Batjer & Bendok, 2011).

The Institute of Moyamoya Disease at Stanford University, conducted a study on the “Effect of Moyamoya disease on neuropsychological functioning in adult”, the neuropsychological tests chosen by Dr. Steinberg and colleagues, to assess memory impairment was CVRS-II and the WMT-RVRS as well, their study showed that 19% of their patients had memory impairment. To assess speech impairment they used the D-KEFS, and 47 % of their patients demonstrated fluency impairment, and for intellectual process the test used was the Trail Making Test Part A; and 39 % of their patients presented impairment in that area (Karzmark, Zeifert, , Tan, Dorfman, , Bell-Stephens, & Steinberg,2008).

Although Moyamoya symptoms and signs do not differ much from the manifestation of other cerebral vascular diseases, Moyamoya presents a faster clinical and angiographic progression, so it should be diagnosed and treated as early as possible to minimize permanent neurological deficits (Ikezaki & Loftus, 2001), within several years onset if left Moyamoya disease untreated, the Moyamoya patient can progress to a vegetative state (Burke, Burke, Sherma, Hurley, Batjer & Bendok, 2009). Because of the similarity of symptoms with many cerebral-vascular diseases, Moymoya can only be confirmed and diagnosed when the four criteria cited earlier are met and can be confirmed by Magnetic Resonance Imaging (MRI) and angiograms. MRI is the investigative tool of choice for neurological disease because it gives a better visualization of the brain and is more sensitive than computed tomography. Furthermore, angiograms also allow the doctor to visualize the arterial and venous supply to the brain, making it possible to diagnose Moyamoya with precision (Ikezaki & Loftus, 2001, p. 5).

Moyamoya is a progressive disease and in most cases “does not respond to medical therapy with vasodilator or antithrombotic agents” (Steinberg et al., 1999, p. 50). Various medical regimens have been investigated for the treatment of Moyamoya disease, including aspirin, steroids, vasodilators, mannitol, low-molecular-weight dextran, and antibiotics, all of which have thus far proven ineffective (Zipfel, Fox & Rivet, 2005). If left untreated, the morbidity is estimated to be greater than 70% (Guzman & Steinberg, 2011). Surgical intervention has become the standard of treatment of patients with Moyamoya.

There are three surgical treatments for revascularization surgery: direct, indirect, and a combination of direct/indirect revascularization. There is no optimal surgical treatment for Moyamoya, the indirect bypass is considered easier and safer, and leads to fewer periprocedure complications (Starke, Komotar, & Connolly, 2009). The indirect procedure is the recommended surgical procedure in the treatment of children with Moyamoya disease, because of the fragility of their arteries (Matsushima, Inoue, Ikezaki, Matsukado, Natori, Inamura & Fukui, 1998). However the direct bypass procedure was found to result in the best postoperative collateral vessel formation and clinical improvement (Matsushima, Inoue, Ikezaki, Matsukado, Natori, Inamura & Fukui, 1998).

The encephalo-duro-arterio-synangiosis is a common indirect surgical method used for providing more blood flow to the brains of Moyamoya patients. It uses a branch of the superficial temporal artery, which is laid straight on the surface of the brain without doing a direct anastomosis. It takes between six to eight weeks to grow new arteries into the brain and therefore provide more blood flow (Ikezaki & Loftus, 2001, p. 44). All patients in the present study underwent the direct revascularization, called extracranial to intracranial bypass or EC-IC bypass. The direct bypass is a straightforward technique of anastomosis (reconnection) of the superficial temporal artery and middle cerebral artery (Houkin, Ishikawa, & Yoshimoto, 1997). This intervention is often chosen because its effects are immediate after the procedure, it offers a good collateral circulation, and it is more reliable than the indirect procedure in reducing hemodynamic stress to the Moymoya vessels (Ikezaki & Loftus, 2001).

Previous research indicates that all three procedures; direct, indirect and the combination of indirect/direct revascularization surgery in patients with Moyamoya disease is effective at preventing future ischemic event. Of all patients that presented with TIA, prior to the revascularization, 91.8% were free of transient ischemic attacks one year or later (Gudzman et al., 2009). Revascularization surgery seems to be effective in preventing strokes in Moyamoya patients. The risk of strokes decreases significantly with the direct revascularization. The stroke rate in asymptomatic patients is 3.2% per year, once a patient has become symptomatic, the risk of recurrent stroke is much higher, with the reported range in the literature being 10.3% per year to 16% per year or 80.95% at 5 years (Mallory, Bower, Nwojo, Taussky, Wetjen, Varzoni,Hanel, & Meyer, 2013). Patients that were under medication treatment only have a risk of recurrent stroke of 65% in five years. After bypass surgery, the risk of recurrent stroke or hemorrhage within five years is 5.5% (Guzaman & Steinberg, 2010). Surgical intervention reduces the risk of infarction by 89% (Weinberg, Rahme, Aoun, Batjer, & Bendok, 2011). It is well documented that surgical revascularization procedures promote sufficient development of collateral vasculature, preventing future TIAs and infarction, for that reason the surgical revascularization is the recommended treatment for people with Moyamoya disease (Weinberg, Rahme, Aoun, Batjer, & Bendok, 2011).

There was been very little neuropsychological research on Moyamoya in adults, especially on the cognitive functioning of Moyamoya patients. Previous research indicates that impairments in intellectual functioning, information processing speed, executive functioning, and visual spatial ability can occur (Kuriyama et al., 2008). These impairments are associated with the cerebral blood flow (CBF), where Moyamoya patients with a higher baseline of CBF seem to have better cognitive functioning (Mogensen et al., 2012). Although the study of improvement in cognition after revascularization in Moyamoya patients is in its early stages, there are indications that cognitive dysfunction in adults with Moyamoya disease may be potentially reversible provided that revascularization surgery is performed before extensive brain infarction develops (Calviere et al., 2011). Thus, the goal of the current study is to investigate the improvement of cognition in Moyamoya patients after a revascularization surgical intervention, adding to the much-needed research on Moyamoya. The following outcomes were hypothesized:

1. Diagnostically confirmed Moyamoya patients will show cognitive dysfunction.
2. Direct Revascularization will improve physiological symptoms

3. Direct Revascularization (EC-IC bypass) will reestablish regular blood flow, improving perfusion post-operatively, thus increasing cognitive functioning.

Method

Participants

In this study, 33 patients were diagnosed with Moyamoya accordingly to the criteria established by the Research Community on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare of Japan and treated at the Mayo Clinic, in Jacksonville, Florida. No incentives were given to participants in this study. The exclusion criteria for the current study were patients younger than 18 years old, patients without Moyamoya disease or Moyamoya syndrome, and patients not treated at the Mayo Clinic, Jacksonville. Five males and twenty-eight females participated in the study and the majority (82%) was Caucasian. All participants were at least 18 years of age ($M = 51.63$ years; $SD= 15.19$).

Procedure

All participants were treated in accordance with the ethical principles and Code of Conduct of the American Psychological Association. Between January 2008 and December 2012, 33 adult patients with neurodiagnostically confirmed Moyamoya disease underwent presurgical neuropsychological assessment and physiological evaluation and three postsurgical assessments.

A pre and posttest design was implemented for this study. All participants underwent pre-surgery physiological and cognitive evaluation that served as the baseline to cognitive improvement after surgery. After the revascularization surgery, patients returned for three assessments to evaluate progress on cognitive and physiological abilities: the first assessment was between day 7 and 10 postsurgery; the second assessment between day 30 and 45; and the third assessment after 5 to 6 months.

Assessments

Physiological evaluation. Neurosurgeons at the Mayo Clinic examined the patients and their medical history was taken into consideration. All patients were symptomatic for their preoperative evaluation. Data on whether they currently have or have had a history of TIA, strokes, seizures, hemorrhage, and headaches were recorded. Patients' mobility was recorded; if they were walking by themselves without any assistance, if the patient was using a medical walker, or if the patient was in a wheelchair. Patient's reflexes were also recorded.

Every patient in this study underwent a battery of brain imaging tests, including MRI, Computed tomography angiography (CTA), angiography, and a Magnetic Resonance Angiogram (MRA). Every one of these brain imaging tests can be used to diagnose Moyamoya. Currently, there is no preferable test to diagnose Moyamoya. The contrast provided by the MRI, between grey and white matters make it a good choice when dealing with cerebral vascular diseases like Moyamoya. The CTA is a computed tomography technique used to visualize arterial and venous vessels throughout the body. This procedure is able to detect narrowing of blood vessels, which is essential when diagnosing Moyamoya. The angiography is a medical imaging technique used to visualize the inside of blood vessels. The MRA is used to generate images of in order to evaluate them for stenosis and occlusions. The exams were necessary to confirm the disease and to find the location of the blockage.

During the postsurgery assessment, doctors looked for new symptoms, stabilization or improvements of old ones, new strokes, and the number of seizures since surgery had occurred. It was crucial to report patients' improvements in every aspect. Although some patient did report headache after the surgery, there was not any new strokes, episodes of seizure, nor hemorrhage in the postsurgery assessments. After the last assessment, patients underwent further MRA testing to confirm that regular cerebral blood flow had been reestablished.

Cognitive evaluation. A pre- and postsurgery evaluation was given to every Moyamoya patient. Doctors at the Mayo Clinic were interested in patient progress in memory, speech, and intellectual processes. The test used in this study is not a standard test used in neuropsychology, nonetheless it is a standard test used in all three Mayo Clinic sites when assessing Moyamoya patients. The same tests were used in the study "surgical outcomes of stroke in a North American White and African American Moyamoya population" published in 2013 by the Journal of Neurosurgery (Mallory, Bower, Nwojo, Taussky, Wetjen, , Varzoni, , Hanel, & Meyer, 2013).

For speech, it was analyzed if the patients were able to communicate with the doctor. The content of the conversations, and the fluency were taken into consideration. For fluency the doctors analyzed if the patient's speech had normal rate and rhythm, if it was slow, rapid, slurred, unintelligible, or mute. The content was reported if the answers were circumstantial, coherent, or hard to follow. Patients were rated from 0 to 2, where 0 means no impairment, 1 impaired, and 2 highly impaired.

For memory, patients were asked to name three common objects present on the doctor's office table; such as coffee mug, notepad, pencil, or paper clips. They were also asked four to five questions. Some questions referred to autobiographic and episodic memory (e.g., What is your name? What is your date of birth? What is the name of your oldest child? In what city were you born?) Questions of declarative memory were also asked, for example, Who is the president of the United States? What day is today? It was recorded if the patient knew the answer, understood the question but did not know the answer, or did not understand the question. The same scale for speech was used, with 0 meaning no impairment, 1 impaired, and 2 highly impaired.

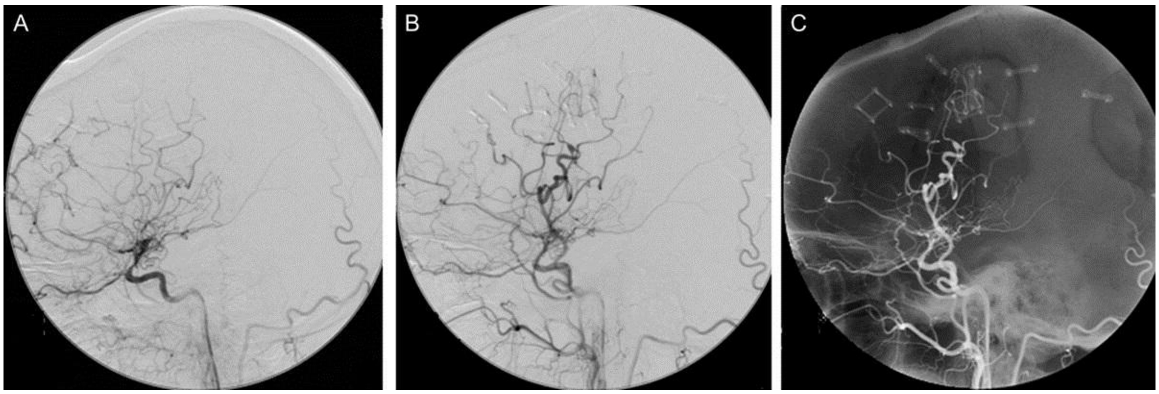
For intellectual processes, patients were asked to follow simple commands, such as “Please touch your nose with your index finger” or “Can you handle me the coffee mug next to the computer, please?” It was also recorded if the patients were aware of time, space, and person, which means if the patient knew who they were, where they were, and when the appointment was taking place. One patient, for example, knew she was at the hospital, but could not tell in what city the hospital was located, although she had been born and raised in Jacksonville, Florida. The same scale for speech was used, with 0 meaning no impairment, 1 impaired, and 2 highly impaired.

To be consistent, every patient saw the same doctor for the preoperative evaluation and the three follow-up assessments. These tests might seem simple, but many patients could not have undergone long standardized tests. Most patients presented with highly impaired speech, and it would have been very difficult to assess their cognitive functions using more complex methods.

Results

The direct revascularization, EC-IC Bypass, was successful for all 33 patients. The regular cerebral blood flow was reestablished improving perfusion post-operatively. Figure 1 shows preoperative and postoperative angiograms of a 48 years old female with Moyamoya disease who underwent the bypass. A, preoperative angiogram. B and C, postoperative angiogram after 5 to 6 months.

Figure 1. Pre-operative and post-operative angiograms



Physiological Symptoms

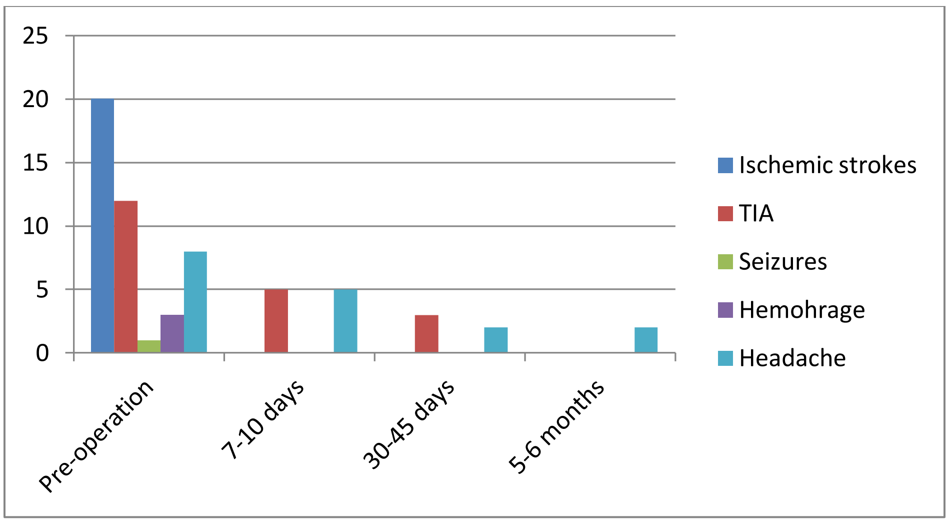
Table 1

Preoperative Symptoms in 33 patients undergoing revascularization for Moyamoya Disease

Symptoms	n(%) n=33
Hemorrhage	3(9)
TIA	12(36)
Ischemic Stroke	20(61)
Headaches	8(24)
Seizures	1(3)

Results showed a significant reduction of physiological symptoms. No patients reported new strokes, episodes of seizure, or hemorrhage in the postsurgery assessments. They reported less frequent episodes of transient ischemic attacks and headaches when compare their presurgical state. The MRIs, angiograms, CTAs, and MRAs showed that the regular blood flow had been reestablished, indicating that the direct revascularization, EC-IC bypass, had been successful. These results are consistent with results from previous research on Moyamoya, which indicates physiological improvement after revascularization (Guzman, 2008).

Figure 2. Decrease in physiological symptoms



Not only did physiological symptoms decrease, but also cognitive functioning improved postsurgery. Regarding the cognitive evaluation, there was a significant improvement in speech and memory. The next sections address the results for the memory, speech, and intellectual processes.

Memory

Figure 3. Memory improvement shown after surgery.

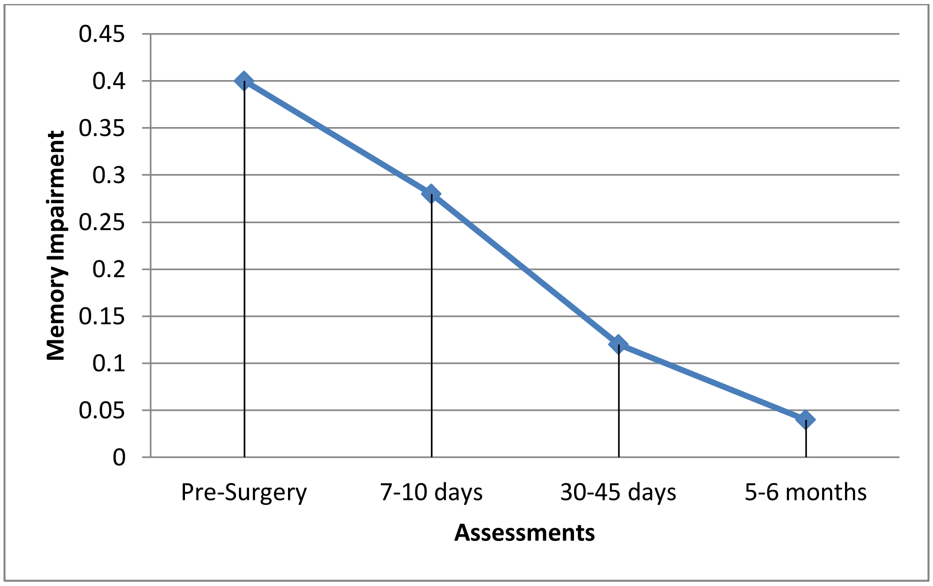


Figure 3 shows improvement in memory; it was calculated based on the decrease of memory impairment. The pre-surgical values demonstrate higher numbers, thus indicating greater impairment. The higher the number, the higher the impairment; the following assessments indicate lower scores for impairment, revealing improvement in memory. Table 2 shows the descriptive statistics for all participants from the memory test conducted postsurgery.

Table 2

Descriptive Statistics – Overall Memory Improvement

Assessments	Mean	SD	N
Pre-Surgery	.40	.76	25
7- 10 days	.28	.46	25
30-45days	.12	.33	25
5 – 6 months	.04	.20	25

Overall, there was a marginally significant improvement in memory from before surgery to after surgery (Wilks' Lambda = .79, $F(3, 22) = 2.00$, $p = .14$, partial eta squared = .21). Following Cohen (1988), effect sizes of .01 are small, .06 are moderate, and .14 are large. Thus, the effect size is very large.

Pairwise comparisons show significant difference (improvement) between condition pre-surgery and 30-45 days, pre-surgery and 5-6 months, and 7-10 days and 5-6 months, however there was no significant difference found between pre-surgery and 7-10 days and between 30-45 days and 5-6 months.

Speech

Figure 4. Speech improvement shown after surgery.

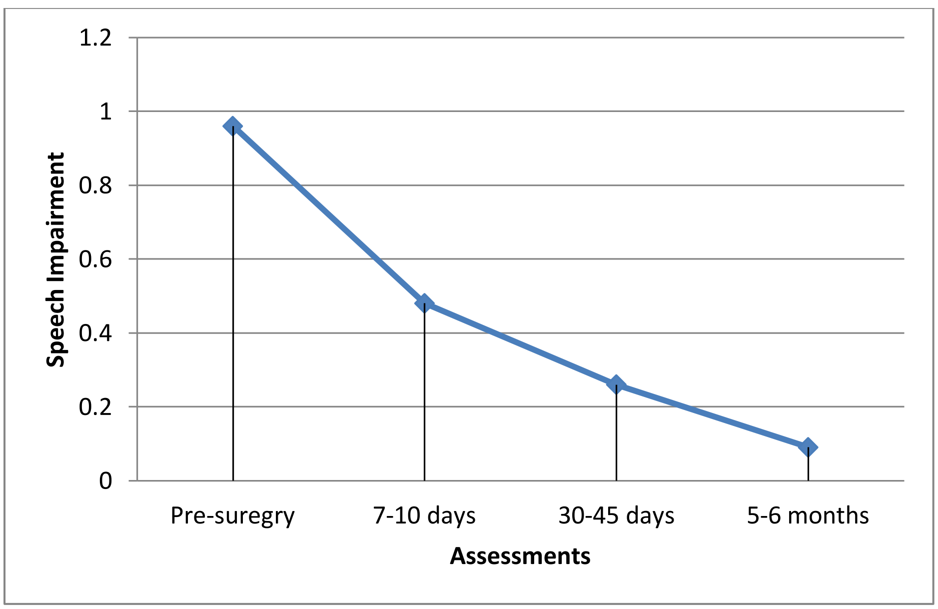


Figure 4 shows improvement in speech; it was calculated based on the decrease of speech impairment. The pre-surgical values demonstrate higher numbers, thus indicating greater impairment. The higher the number, the higher the impairment; the following assessments indicate lower scores for impairment, revealing improvement in speech.

Table 3 shows the descriptive statistics for all participants from the speech test conducted postsurgery.

Table 3
Descriptive Statistics – Overall Speech Improvement

Assessments	Mean	SD	N
Pre-Surgery	.96	.93	23
7- 10 days	.48	.59	23
30-45days	.26	.45	23
5 – 6 months	.09	.29	23

Overall, there was a significant improvement in speech pre and postsurgery (Wilks' Lambda = .51, F(3, 20) = 6.32, *p* = .003, partial eta squared = .49). Partial eta squared effect sizes of .01 are small, .06 are moderate, and .14 are large; thus, the effect size of our findings is very large.

Pairwise comparisons show significant differences between all four conditions, except between assessment 30-45 days and 5-6 months.

Intellectual Processes

Figure 5 shows improvement in intellectual process; it was calculated based on the decrease of intellectual process impairment. The pre-surgical values demonstrate higher numbers, thus indicating greater impairment. The higher the number, the higher the impairment; the following assessments indicate lower scores for impairment, revealing improvement in intellectual process.

Figure 5. Intellectual process improvement, pre and postsurgery.

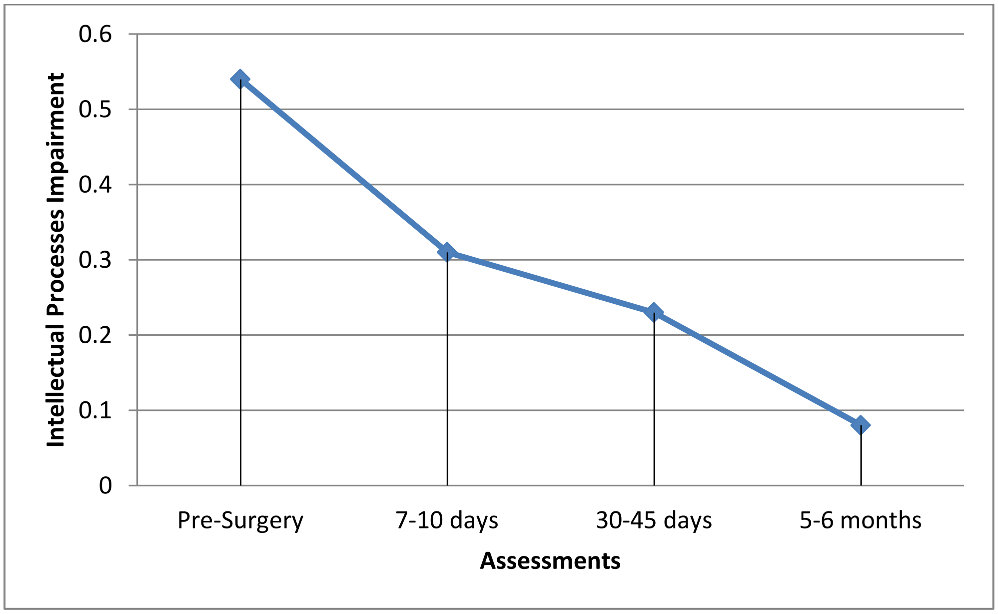


Table 4 shows the descriptive statistics for all participants from the intellectual processes test conducted postsurgery.

Table 4
Descriptive Statistics – Overall Intellectual Processes Improvement

Assessments	Mean	SD	N
Pre-Surgery	.54	.88	13
7 -10 days	.31	.63	13
30 - 45 days	.23	.44	13
5 - 6 months	.08	.28	13

Overall, there was no significant improvement in questions/general knowledge from before surgery to after surgery (Wilks' Lambda = .69, F(3, 10) = 1.48, p = .28, partial eta squared = .31). Since partial eta squared effect sizes of .01 are small, .06 are moderate, and .14 are large, the effect size of our findings is very large, showing the strength of the phenomenon. The non-significant result is probably due to the small sample size of 13. Pairwise comparisons show significant differences only between condition pre-surgery and 5-6 months.

Discussion

It was hypothesized that that hypoperfusion, decrease of blood flow, was the principal cause of cognitive decline in adults Moyamoya patients. In turn, improved perfusion post-operatively was hypothesized to correlate with improved cognitive functioning, and this study failed to reject this hypothesis. The findings are consistent with previous research on Moyamoya, physiological improvement was expected (Guzman, 2009), and in this study, we were able to confirm reduction of physiological symptoms postsurgery. This study is in agreement with researches that suggest that cognitive impairment can be expected in Moyamoya patients and that direct bypass is a reliable treatment for this condition. After the surgical procedure and direct bypass, and after regular blood flow had been reestablished, cognitive functions significantly improved in Moyamoya patients.

Patients presented a consistent significant improvement in speech during the first two assessments. Between 7 to 10 days and between 30 to 45 days after surgery, a significant improvement in speech was observed overall. Patients presented more fluency in their speech with more coherent conversation, and the doctors reported improvement in how and what was being said, not only the patients were pronouncing the words clearer, but the content of the conversation was more meaningful.

Memory showed improvement as well, but only one month after surgery. It appears to be a more progressive change, instead of a sudden improvement as was speech. Patients were able to recall not only names and birth dates of loved ones, but were also able to answer general knowledge questions, such as “Who is the president of the US?” They were also able to name common office objects like notepads, mugs, and paper clips.

Unfortunately, intellectual processes did not differ significantly between assessments; however, results showed a large effect size. A possible explanation could be the small sample size. Another possible explanation could be that for the first three assessments, over 80% of patients received a score of “0”. Thus, there was a floor effect. This means that when the patient received a “0”, not impaired, many times the doctor believed there was no need to keep asking the same question in subsequent assessments, causing the difference between number of participants and number of collected data. Example: there were 33 patients in this study, however only 13 patients complete the 3 postsurgical assessments for intellectual processes.

The results of this study support continuing clinical attention and intervention efforts directed at early identification and treatment, early surgical revascularization interventions to prevent further decline and improve cognitive outcome. Healthcare providers can utilize the findings of this research to prepare and help manage concerns of these patients pre- and postsurgery better.

Limitations to the Study

There were multiple limitations to this study. First and most saliently, our sample size, even though the number of participants (33) in the current study is considered an exceptional number for such a rare disease like Moyamoya, it is still a small sample, substantially limited analytical statistical power, as well as precluding use of multivariate techniques, because of our small sample size our finding should be considered preliminary and interpreted with caution. They need to be confirmed in a large number of patients. However, the findings were statistically significant and consistent with previous knowledge of Moyamoya disease. Second, one neurosurgeon rated all patients. It would be desirable to have multiple ratings to calculate interrater reliability. Third, the scale used in this study was from 0 to 2, if a more sensitive scaled were used, perhaps expanding the scale from 0 to 5, it could have shown more subtle improvements in cognition.

The sample demographics could arguably provide for biases. Study participants lacked diversity, as most patients were White women, over the age of 50 years, and of mid to high socioeconomic status, possibly contributing to limitations of the study's generalizability. Future studies could also include children with Moyamoya disease and more people from different ethnical groups.

Another limitation was that many patients were not from Florida where the surgery and assessment took place, and to complete all three postsurgery assessments was a logistical barrier. This was because when patients started to feel better, they wanted to go home and to their local neurologist for check up visits instead of coming to Florida, thus not all of the patients come to the third assessment.

Conclusions

Further research is warranted to bring awareness to this serious but treatable disease. Few studies both in the United States and around the world have been conducted using a large sample of Moyamoya patients and specifically assessing them on neuropsychological and psychological functioning. This study adds to the research as it has identified some unique issues of this disease and the benefits of the direct revascularization procedure to improve cognition. More research can only strengthen these findings and educate healthcare professionals, helping them assure the patients of a better quality of life and reinforcing the benefits of revascularization surgery for treatment of Moyamoya disease.

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