INVESTIGATING NEUROPSYCHOLOGICAL AND MENTAL HEALTH OUTCOMES AFTER SURGICAL INTERVENTION IN PEDIATRIC MOYAMOYA VASCULOPATHY

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Abstract

Moyamoya vasculopathy (MMV), a rare and progressive cerebrovascular disorder, is an important cause of pediatric stroke. This retrospective study explored post-revascularization neuropsychological and mental health outcomes. Eighteen patients from the Canadian Pediatric Stroke Registry at the Hospital for Sick Children (*MAge*=10, *SD*=4.073) who had revascularization surgery and completed neuropsychological assessments between 2012 and 2024 were selected. Outcome measures included academics, executive functioning, and mental health. Predictor variables were age at revascularization surgery, age at stroke/moyamoya diagnosis, and moyamoya diagnosis (confirmed or presumed). Two significant associations emerged: a strong positive relationship for children with a moyamoya diagnosis and caregiver-reported BASC-3 anxiety scores; and a strong positive correlation between moyamoya diagnosis and caregiver-reported BRIEF2 BRI total score. Age at revascularization and moyamoya diagnosis significantly predicted BRIEF2 caregiver-reported BRI total scores. These preliminary findings suggest our selected variables may predict caregiver and self-reported behavioural dysregulation and anxiety, requiring early intervention and ongoing support.

Keywords: pediatric stroke, moyamoya vasculopathy; moyamoya disease; moyamoya syndrome; clinical neuropsychology; mental health

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List of Acronyms

BASC-3= Behaviour Assessment System for Children, Third Edition

BRI= Behavioural Regulation Index

BRIEF2= Behaviour Rating Inventory of Executive Function, Second Edition

D-KEFS= Delis–Kaplan Executive Functioning System

FSIQ= Full Scale Intellectual Quotient

FRI= Fluid Reasoning Index

MMD= Moyamoya Disease

MMS= Moyamoya Syndrome

MMV= Moyamoya Vasculopathy

NF1= Neurofibromatosis type 1

PRI= Perceptual Reasoning Index

PSI= Processing Speed Index

SCD= Sickle-cell disease

TIA= Transient Ischemic Attack

VCI= Verbal Comprehension Index

WAIS-IV= Wechsler Adult Intelligence Scale, Fourth Edition

WIAT-III= Wechsler Individual Achievement Test, Third Edition

WISC-V= Wechsler Intelligence Scale for Children, Fifth Edition

WMI= Working Memory Index

WRAT-4= Wide Range Achievement Test, Fourth Edition

Introduction

Moyamoya vasculopathy (MMV) is an important cause of stroke and neuropsychological deficits in children and young adults. It is a rare and progressive cerebrovascular disorder characterized by the narrowing or blockage of the bilateral/distal internal carotid arteries (ICA), proximal middle cerebral arteries (MCA), and proximal anterior cerebral arteries (ACA), along with their respective branches within the circle of Willis (Hsu et al., 2014; Lehman et al., 2022; Liu et al., 2013). This narrowing often results in an increased risk of stroke or transient ischemic attacks (TIAs), especially in youth (Hsu et al., 2014; Lehman et al., 2022; Mitchell et al., 2023). Moyamoya disease (MMD) was first described in 1957 by Japanese surgeons who noted the appearance of the collateral blood vessels that form to bypass the blocked arteries (Takeuchi & Shimizu, 1957). The term 'moyamoya', meaning "puff of smoke" in Japanese, refers to the hazy network of small blood vessels seen on imaging scans, resembling the characteristic appearance (Mitchell et al., 2023; Suzuki & Takaku, 1969). In pediatric MMD, vessel stenosis occurs quite rapidly, often linking the level of vascular occlusion to the severity of cognitive impairment (Mitchell et al., 2023) and an increased risk for pediatric stroke (Kim, 2016; Lehman et al., 2022).

Furthermore, individuals with MMD often experience emotional and behavioural challenges, such as depression and anxiety (Oakley et al., 2024; Yeom & Oh, 2023). Managing a chronic illness may involve frequent medical appointments and potential learning difficulties, which can lead to emotional stress and behavioural issues that are seen in youth with MMD (Kim et al., 2018). Improvements in cognitive function were linked to the increased cerebral blood flow (CBF) to the MCA, specifically through surgical intervention after the age of 7 (Mitchell et al., 2023). Neurocognitive impairment in pediatric MMD is common and can have devastating

consequences if left untreated (Oakley et al., 2024). Therefore, formative research is important to understand the neuropsychological and mental health challenges faced by this population as it relates to their MMD diagnosis and pediatric stroke. It is crucial to note that existing developmental and neuropsychological theories, along with the current literature on pediatric moyamoya disease, offer critical insights into its developmental impact and the complex interactions and relationships that youth and their families will encounter over time.

Pediatric stroke

Pediatric stroke is a significant cause of acquired brain injury (Krishnamurthi et al., 2015; Sutherly & Malloy, 2020) and disability in children (Agrawal et al., 2009). Pediatric strokes are either perinatal (occurs between 28 weeks' gestation to 28 days after birth) or childhood (occurs at 29 days to 18 years of age) (Ferriero et al., 2019). Further, there are two primary classifications of stroke type: (1) ischemic stroke, the disruption of normal blood flow in the brain, and (2) hemorrhagic stroke, the occurrence of spontaneous bleeding in the brain due to the rupture or leakage of blood vessels (Festa et al., 2008). While the incidence rates for pediatric stroke vary in the literature (Hollist et al., 2021), it is estimated that ischemic stroke impacts an estimated 1.0 to 2.0 in 100,000 children per year in developing countries (Ferriero et al., 2019). Hemorrhagic stroke makes up about 50% of pediatric stroke cases, with an incidence of ~1 to 1.7 in 100,000 children per year in developing countries (Ferriero et al., 2019). Additionally, the Canadian Pediatric Ischemic Stroke Registry, a 16-year prospective national-based study, determined that the incidence of perinatal stroke was 10.2/100,000 and that the incidence of childhood stroke was 1.72/100,000 per year (deVeber et al., 2017). The mortality rate is higher for children who have suffered hemorrhagic stroke compared to ischemic stroke (Hollist et al., 2021). Research suggests that many pediatric stroke survivors experience significant and long-

term neuropsychological impairment, leading to cognitive deficits across many domains (Champigny et al., 2023; Greenham et al., 2017; Westmacott et al., 2010). These deficits often negatively impact other areas of a child's life, including social and cognitive functioning, academics (Champigny et al., 2020), and quality of life (Friefeld et al., 2004).

MMD prevalence rates and etiology

MMD is one of the diseases that is associated with stroke in childhood. The cause of MMD is not fully understood; however, research indicates that there are clear genetic underpinnings (Wang et al., 2018). Prevalence rates for MMD are much higher in East Asian countries such as Japan, Korea, and China, with 1 to 6 per 100,000 individuals (Kaseka et al., 2021), whereas in Europe and North America, the prevalence rates are as low as 0.1 per 100,000 individuals (Mitchell et al., 2023; Williams et al., 2012). The distribution of age of onset for MMD is bimodal and most commonly presents in children between the ages of 5 to 15 years old and in adults between the ages of 35 to 50 years old (Kim, 2016; Williams et al., 2012). MMD is more common in females, and there have been indications of RNF213 gene mutations linked to a family history of the disease (Liu et al., 2013; Kamada et al., 2011; Kuroda et al., 2022), increasing the risk by 30-40 times more than in the regular population (Kim, 2016). Children with MMD experience headaches, seizures, involuntary movements, cognitive impairment, hypertension, temporary or permanent blindness, hemiplegia, general paresis, loss of sensation, and aphasia (Kim, 2016; Mitchell et al., 2023; Lehman et al., 2022; Williams et al., 2012).

MMD diagnostic criteria

It is important to distinguish between Moyamoya disease (MMD) and Moyamoya syndrome (MMS) (Fukui et al., 2000; Kuroda et al., 2022). MMD is an illness of unknown etiology, whereas in MMS, there is an associated medical condition, such as neurofibromatosis

type I (NF1), autoimmune diseases (i.e., polyarteritis nodosa, Sjögren syndrome, etc.), meningitis, brain tumours, Down Syndrome, and Sickle Cell Disease (Fukui et al., 2000; Kuroda et al., 2022). Obtaining an accurate diagnosis of MMD is integral to ensuring that youth receive appropriate medical and neuropsychological interventions. The Research Committee on Moyamoya Disease created the diagnostic criteria for MMD in 1978, which have been revised several times to improve the accurate diagnosis of MMD (Kuroda et al., 2022). A definitive MMD diagnosis requires: (1) radiological imaging methods such as cerebral angiography, Magnetic resonance imaging (MRI), and Magnetic resonance angiography (MRA) are used to display bilateral occlusion of the terminal portion of the ICA and moyamoya vessels near the ICA lesions, and the proximal portion of the ACAs and MCAs; (2) Imaging that shows the characteristic "puff of smoke" (moyamoya vessels), specifically the abnormalities in the vascular networks that are in the areas of the occlusive or stenotic lesions in the arterial phase; (3) no other underlying conditions (Fukui et al., 1997; Fukui et al., 2000; Kuroda et al., 2022). The imaging typically corresponds with one of the six Suzuki stages (Kuroda & Houkin, 2008; Kuroda et al., 2022; Suzuki & Takaku, 1969; Takanashi et al., 1993). Similar criteria are used to diagnose moyamoya syndrome; however, the key difference is the presence of an underlying disease or comorbid condition (Fukui et al., 1997; Kuroda & Houkin, 2008; Kuroda et al., 2022; Takanashi et al., 1993). In cases of pediatric moyamoya disease, diagnostic imaging may locate lesions in the basal ganglia, thalamus, and white matter in the brain (Choi et al., 2022; Kuroda et al., 2022; Takanashi et al., 1993).

Suzuki and Takaku (1969) introduced moyamoya angiographic staging to evaluate the patterns of stenosis and collateralization of the disease in patients with MMD. The Suzuki angiographic stages are used to describe the specific stages of MMD; thus, stages 1 to 3 are

deemed early MMD, and stages 4 to 6 are deemed late (Choi et al., 2022; Suzuki & Takaku, 1969). The Suzuki stages provide an explanation of the start of stenosis in the terminal portion of the ICA and the appearance and eventual reduction of the collateral vessels that develop (Rupareliya & Lui, 2024; Suzuki & Takaku, 1969). It is suggested that the Suzuki stages correlate with vessel collateralization in children; however, this is not the case in adults with MMD (Baltsavias et al., 2015; Kim, 2016; Suzuki & Takaku, 1969).

Further, children with MMD will progress through some or all the Suzuki stages as quickly as adults (Suzuki & Takaku, 1969). In MMD, the brain responds to the steno-occlusive changes in the terminal ICA by developing collateral pathways and involves abnormal dilatation of the corresponding arteries (Takanashi, 2011). The "basal moyamoya" pathway includes the abnormal dilatation of the lenticulostriate and thalamoperforating arteries in the basal ganglia and thalamus (Takanashi, 2011). A subsequent pathway involves substantial dilatation of the anterior choroidal and posterior pericallosal arteries. The "ethmoidal moyamoya" pathway involves abnormal dilatation of the anterior and posterior ethmoidal arteries, largely from the ophthalmic arteries to the ACA branches. Finally, the "vault moyamoya" pathway comprises a vascular network in the cranial vault that is responsible for the collateral flow from the dural to the pial arteries. In pediatric MMD, the narrowing of the ICA, MCA, and ACA reduces blood flow to the brain, resulting in a cascade of neuroanatomical changes.

MMD and pediatric stroke

Various ethnic groups have higher incidence rates for pediatric stroke. For instance, Black and Asian children have a higher incidence rate than White children for pediatric stroke (deVeber et al., 2017; Ferriero et al., 2019; Fullerton et al., 2003; Hollist et al., 2021). Additionally, medical conditions such as MMD put some children at a greater risk than others for

pediatric stroke (deVeber et al., 2017; Hollist et al., 2021; Lehman et al., 2022; Mitchell et al., 2023; Williams et al., 2012). Youth with MMD are more likely to experience ischemic stroke compared to hemorrhagic stroke (Lehman et al., 2022). Cases of pediatric MMD present mainly with ischemic stroke (31.5%-67.8%) and TIAs (13%-40.3%) (Kim, 2016; Lehman et al., 2022). Occasionally, youth with MMD may present with hemorrhagic stroke (2.7%-2.8%) (Kim, 2016; Lehman et al., 2022).

Further, children with MMD can experience repeated TIAs or ischemic strokes due to hyperventilation, crying, stress, fatigue, infection, dehydration, eating hot foods, and playing the harmonica or flute (Kim, 2016). Research suggests revascularization surgery should be a clinical consideration for stroke prevention in pediatric MMD (deVeber & Kirkham, 2008).

Revascularization: Surgical treatment for pediatric MMD

It has been noted that the current standard of care for pediatric MMD is revascularization surgery, which is intended to improve cerebral blood flow in the brain and reduce the incidence of stroke (Lehman et al., 2022). Early studies examining surgical treatment options for MMD included direct, indirect, and combined bypass revascularization of the arteries impacted by MMD. A direct bypass of the superficial temporal artery (STA) to the middle cerebral artery (MCA) anastomosis was reported as the first successful surgical treatment for MMD (Funaki et al., 2018; Karasawa et al., 1978). Similar results were found in another study, where doctors used an indirect bypass, encephalo-duro-arterio-synangiosis (EDAS), and transplanted a scalp artery to treat MMD (Matsushima et al., 1981). EDAS is the most commonly used revascularization technique for MMD (Funaki et al., 2018) and keeps the distal and proximal arteries intact (Matsushima et al., 1981). Studies suggest that combined revascularization techniques are increasingly used in pediatric MMD, as they have been shown to have favourable outcomes

(Appireddy et al., 2019). A study examining revascularization outcomes in children with MMD found that neurocognitive functions are maintained pre- and post-surgery (Lee et al., 2011). The results suggest that early diagnosis and surgical intervention could assist in preserving neurocognitive functions that typically decline in children with MMD. In addition to pediatric stroke, risk factors, such as younger age, younger onset, and longer duration of symptoms, have been associated with decreased cognitive and intellectual function in pediatric MMD (Mitchell et al., 2023). There is a paucity of research on neurocognitive abilities and mental health functioning post-surgical intervention in pediatric MMD, thus leading to significant gaps in our understanding.

Post-revascularization cognitive and mental health outcomes in pediatric MMD

Research suggests that many pediatric stroke survivors experience significant and long-term neuropsychological impairment, leading to cognitive deficits across many domains (Westmacott et al., 2010), such as motor, cognitive, and language deficits (Greenham et al., 2017). For children with MMD, neurocognitive deficits related to executive functioning are seen in intelligence, processing speed, attention, and visuospatial functioning (Oakley et al., 2024). A recent systematic review examining post-surgery cognitive outcomes in pediatric MMD found that while revascularization maintained or improved full-scale intellectual quotient (FSIQ) and memory, approximately 70% of pediatric MMD patients experienced impaired cognitive function and poor academic performance (Mitchell et al., 2023). Any improvements in cognitive function were linked to the increased cerebral blood flow to the MCA (Mitchell et al., 2023). Other improvements in cognition were linked to surgery after age 7; however, if a child experienced an ischemic stroke pre-surgery, it was linked to poor cognitive function (Mitchell et al., 2023). These deficits often negatively impact other areas of a child's life, including social

and cognitive functioning, academics, and mental health (Friefeld et al., 2004). Children with MMD outside of East Asian countries are not studied as closely, thereby contributing to the lack of global knowledge and research in this area (Hogan et al., 2005; Mitchell et al., 2023). Researchers suggest that large studies with neuropsychological assessments that also examine academic performance are needed to understand the cognitive impairment experienced by children with MMD (Kronenburg et al., 2018).

Mental health outcomes in pediatric MMD

In addition to neuropsychological deficits, individuals with MMD often experience emotional and behavioural challenges, such as depression, anxiety, and behavioural issues (Oakley et al., 2024; Yeom & Oh, 2023). Additionally, symptoms such as irritability, emotional lability, hyperactivity, and inattention are observed in children with MMD (Oakley et al., 2024). MMD is associated with mood disorders such as depression and anxiety, with these comorbidities being difficult to treat (Oakley et al., 2024). Very few studies examining mental health outcomes in youth with MMD have been published (Mohapatra & Sahoo, 2016). It has been reported that individuals with MMD have increased psychological, physical, and mental burdens because of the fear of clinical complications of the disease, leading to a decline in their quality of life (Yeom & Oh, 2023). Living with a chronic medical condition such as MMD can have increasingly negative effects on children and can negatively impact their overall self-esteem and social relationships (Shim et al., 2015). Further, approximately 22-25% of children with MMD experience a significant increase in depression and anxiety and reported internalizing problems, as well as low scores on physical, emotional, and academic functioning (Shim et al., 2015).

Understanding the outcomes of daily functioning in children with MMD is important to providing clinical care. Theories of neurodevelopment provide a framework for understanding the variables that are important to explore in research. Key theories are presented below with a lens of how they may help us to understand outcomes in pediatric MMD.

Developmental Plasticity in Children Theory

The Developmental Plasticity in Children Theory, outlined by Dr. Maureen Dennis (2000), provides a theoretical framework for understanding the neuropsychological perspective on the central nervous system (CNS) sequelae experienced in childhood as well as the impact on developmental plasticity. This theory is useful in informing our neuropsychological understanding of pediatric MMD, particularly the complex interactions and relationships that youth and their families experience during their development (Dennis, 2000). Specifically, the theory examines the complex interaction between a youth's cognitive phenotype (areas of challenge as well as determinants of resilience) and the impact the sequelae have on the developing CNS. The theory posits that several factors moderate how a youth and their family navigate the challenges of a neuropsychological disorder, including: biological risk, the youth's age and developmental status, the time of onset of the disorder, and the reserve available for the youth, their family and their broader environment (e.g., community supports) (Figure 1). While the common belief is that a child's developing brain can recover after injury, research suggests that the early onset of neurovascular conditions, such as MMD, can result in long-term challenges related to brain function, learning, and overall behaviour (Ballantyne et al., 2008; Dennis et al., 2014). Existing research postulates that developmental plasticity in a youth's brain is either adaptive or maladaptive, depending on the type and timing of the brain injury, the youth's age, and resources available to them (Dennis et al., 2014; Westmacott & Baron, 2020).

Therefore, because MMD progresses through development, outcomes may be determined multi-factorially. For instance, youth with pediatric MMD are at an increased risk of stroke (biological risk), and the age of onset of the disease, as well as the timing at which they may be eligible for revascularization surgery, can influence developmental plasticity and recovery in the brain (Dennis et al., 2014; Westmacott & Baron, 2020). Dennis' model (2000) initially suggested that a youth with early-onset MMD, who receives early surgical intervention along with appropriate support (from family, healthcare providers, schools, etc.), may exhibit better neurocognitive outcomes than a youth with a later age of onset and lower reserve. The model emphasizes that age-related plasticity should not be inferred and that many factors, including reserve, family, and access to environmental resources, play a key role in the demands placed on a young brain (Dennis et al., 2014).

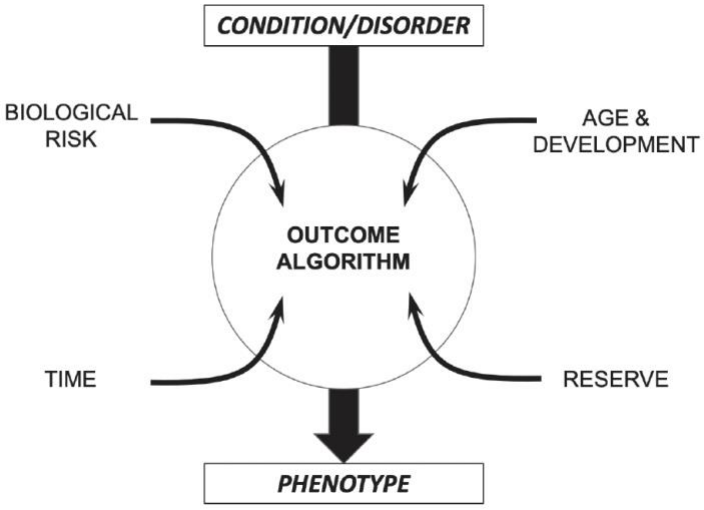

Figure 1. Image of the theory proposed by Dennis (2000), depicting the relationship between a youth's neuropsychological disorder and phenotype, as determined by biological risk and moderated by development, time, and reserve (Beauchamp et al., 2022).

The Bioecological Model of Human Development

The Bioecological Model of Human Development examines the complex interactions and relationships between an individual and their social and physical environments during

development (Bronfenbrenner, 1979; 1994; Bronfenbrenner & Morris, 2007). The model encompasses five subsystems: Microsystem, Mesosystem, Exosystem, Macrosystem, and Chronosystem, which help support human development and growth. The interactions that individuals have with others within their environment and the various subsystems are considered critical to human development (Bronfenbrenner, 1979; 1994). The microsystem (i.e., family and peers) refers to the immediate environment in which the child operates. This interaction forms a mesosystem, which is comprised of the relationships between two or more settings (i.e., the relationship between school and peers). The exosystem is an environment in which the child is not directly involved but still impacts them (i.e., the relationship between caregivers and their workplace). The macrosystem comprises larger societal structures and values (i.e., social, cultural, and religious) that do not directly impact the life of an individual child, but rather society as a whole. Finally, the chronosystem examines the influence of environmental changes on an individual's development over time. Specifically, the chronosystem focuses on "normative" (i.e., entering school) and "non-normative" (i.e., chronic illness) transitions that can occur across the lifespan and how they may indirectly impact development by affecting family processes. According to Bronfenbrenner (1979, 1994; Bronfenbrenner & Morris, 2007), when the interactions between different environments are compatible, they can have a positive influence on a child's developmental outcomes.

Researchers have applied Bronfenbrenner's model to youth with life-threatening conditions. Studies suggested that youth experience multiple stressors related to their diagnosis within many of Bronfenbrenner's subsystems related to their disease (Hosek et al., 2008; Kazak et al., 1995). The interplay between the stressors and subsystems places significant demands on the youth and their caregiver(s) and ultimately impacts relationships between families, health

care providers, and school administration (Hosek et al., 2008; Kazak et al., 1995). Within the context of pediatric MMD, for youth who experience TIAs, neurocognitive challenges, and unpredictable symptoms, the caregiver, school, and clinical supports are instrumental in helping the youth and their family navigate the complex interactions and relationships throughout their development (Cholley-Gomez et al., 2022).

Uncertainty in Illness Theory

Youth living with MMD and their families often experience uncertainty in daily living due to the unpredictability of unforeseen symptoms and complications related to the disease (Brown et al., 2020), including dehydration, physical exertion, hyperventilation, emotional stress, or the sudden onset of seizure or stroke symptoms. Mishel's Uncertainty in Illness theory (Mishel, 1988; 1990) provides a lens for understanding the cognitive, emotional, and behavioural impacts of pediatric MMD. Mishel conceptualizes uncertainty as an individual's inability to derive meaning from illness-related events and their incapacity to anticipate or predict health outcomes accurately. The theory posits that the complexity, ambiguity, and unpredictability related to the lack of resources or information associated with their disease create heightened psychological distress for youth and their families (Mishel, 1988; 1990). An individual's ability to accurately assess uncertainty allows them to determine if a stressor is a positive or negative and to effectively evaluate their ability to manage and respond to the stressor (Mishel, 1988, 1990; Zhang, 2017). According to Mishel, uncertainty can be mitigated with appropriate coping strategies to either reduce or maintain (i.e., positive or negative outcomes) (Mishel 1988, 1990). This theory was originally applied to adults with cancer and is now being applied in pediatric contexts, highlighting how uncertainty acts as a cognitive stressor impairing illness-related adjustment and quality of life for the youth and their caregiver(s) (Mishel, 1988; Stewart et al.,

2010; Zhang, 2017). The theory was reconceptualized to account for individuals who constantly live in a state of uncertainty related to their chronic illness (Mishel, 1990).

Youth with MMD and their families regularly navigate the difficulties of their disease, manage uncertainty, and tasks associated with their overall development (Baskin et al., 1998; Stewart et al., 2010; Zhang, 2017). Research suggests that in cases of adult MMD, uncertainty arises from the unpredictability of the disease with regard to the presentation of their symptoms, increased risk of stroke or TIAs, headaches, and seizures (Kaseka et al., 2021), thus contributing to psychological distress and poor quality of life (Zhang et al., 2024). Illness uncertainty, in the context of pediatric illnesses, relates to the experiences endured by the youth and their caregiver, their developmental stage, and the interactions they will encounter within their environment(s) (i.e., medical decisions, family coping, school, etc.) and the associated outcomes (Kerr et al., 2003; Szulczewski et al., 2017). The findings from a systematic review suggest that the notion of increased uncertainty for youth diagnosed with a chronic pediatric illness may be a fundamental element that negatively impacts overall psychological (e.g., anxiety, depression), social, and academic functioning, and coping strategies (Szulczewski et al., 2017).

Collectively, these theoretical frameworks can enhance our understanding of the challenges faced by youth MMD and their families from a clinical developmental and neuropsychological perspective. Additionally, they will assist clinicians in collaborating with youth and their families, as well as in policy development, advocacy, and creating supportive, informed interventions.

Summary

There is a lack of knowledge on the correlates of neuropsychological deficits and negative mental health outcomes seen in children with MMD with a history of stroke

(Berkelhammer et al., 2007). Including a variety of measures of outcome, including self-report, is important in precision health care, and leads to research that makes conclusions that can lead to important understanding of the abilities and needs of those with MMD. This proposed study aims to address a gap in the literature by studying the neuropsychological and mental health consequences of Moyamoya Disease (MMD) in a Canadian pediatric population.

Research Objectives and Hypotheses

The overarching objective of the proposed study is to examine neuropsychological and mental health outcomes in youth with pediatric MMD at the post-surgical intervention time point. This study aims to elucidate what impact surgical intervention has on outcomes that have not been researched in as much depth as cognitive functioning through performance measures; in particular, daily functioning through academic, mental health, and caregiver-reported executive functioning.

Research objectives:

1. To explore post-surgical intervention outcomes regarding neuropsychological and mental health profiles of youth with MMD through descriptive analyses.
2. To examine the association between MMD and stroke-related variables and their ability to predict post-surgical intervention academic achievement, everyday executive functioning, and mental health scores.

Based on extant literature, it is predicted that:

(1) Participants' MMD diagnosis (confirmed or presumed disease), presence of surgery, and age at stroke/moyamoya diagnosis will predict post-intervention academic achievement scores.

(2) Participants' MMD diagnosis (confirmed or presumed disease), presence of surgery, and age at stroke/moyamoya diagnosis will predict post-intervention scores on the BASC-3, in terms of mental health subscales.

(3) Participants' MMD diagnosis (confirmed or presumed disease), presence of surgery, and age at stroke/moyamoya diagnosis will predict post-intervention scores on the BRIEF2, measuring everyday executive function.

Method

This retrospective study examined individuals with Moyamoya disease enrolled in the Canadian Pediatric Stroke Registry at the Hospital for Sick Children in Toronto, Ontario (deVeber et al., 2017). The secondary data included in this study were obtained from the Children's Stroke Program at The Hospital for Sick Children, which is also part of the Canadian Pediatric Ischemic Stroke Registry (deVeber et al., 2017), as well as the Neuropsychology REDCap database within the hospital.

Participants

Participants were retrospectively identified for this study based on a neuropsychological assessment completed between 2012 and 2024, through their enrollment in the Canadian Pediatric Stroke Registry at the Hospital for Sick Children (deVeber et al., 2017). To be included in the study, participants needed to meet the following inclusion criteria: a moyamoya disease or moyamoya syndrome diagnosis, revascularization surgery, between 6 to 21 years of age, residing in Ontario, and proficient in English. Additionally, participants needed to have a complete neuropsychological assessment that also included mental health measures at post-surgical intervention. Youth were excluded from the study if they did not meet the age requirements or if they were diagnosed with concurrent neurological disorders (e.g., head injury, brain tumour).

Data included in this study was reviewed and cleaned from a larger dataset obtained from the Canadian Pediatric Stroke Registry (deVeber et al., 2017) of $N = 912$ participants. A review of clinical (medical) and demographic information from patient charts, as well as the exclusion criteria, led to some participants being eliminated because they did not have a confirmed MMD or MMS diagnosis, were deceased, or were missing patient information. Therefore, the dataset was reduced to $n = 66$ participants who were confirmed to have an MM diagnosis. After excluding participants without post-surgical intervention neuropsychological assessments, mental health measures, those who had no surgery, were outside the age range, or were diagnosed with neurological disorders, $n = 49$ participants remained. Next, I selected participants with the most complete assessments, including measures of intelligence, academics, executive functioning, and caregiver and, where applicable, self-report questionnaires. In some cases, this meant choosing a more recent and comprehensive assessment.

As part of patient care and assessment at the Hospital for Sick Children, youth diagnosed with MMD and MMS undergo clinical imaging for both diagnostic and prognostic purposes. Neuroimaging data and medical records were used to confirm MMD and MMS diagnoses and ensure that participants met study inclusion criteria. Therefore, a subset of the data ($n = 18$ participants) was included in the study. This information was used in the current study to examine the significance of various moyamoya disease and stroke variables (i.e., age at onset) as predictors of cognitive, academic, and mental health outcomes. The moyamoya diagnosis variable encompasses a confirmed or presumed disease diagnosis. Age at stroke/moyamoya diagnosis and age at revascularization were calculated based on the participants' year of birth and the date(s) of clinical presentation and revascularization surgery. The age at stroke/moyamoya diagnosis variable accounts for the age (in years) at which the child first

experienced an ischemic or hemorrhagic stroke or was formally diagnosed with moyamoya disease or syndrome, based on a review of medical records. If both a stroke event and moyamoya diagnosis are present, the earlier date (year) was used to calculate the participant's age.

Ethical considerations

Ethical approval was granted by the Hospital for Sick Children (REB number: 1000064788) and the York University Ethics Review Board (Certificate number: STU 2025-043) in Toronto, Canada. Since the data was sampled from the Canadian Pediatric Stroke Registry at the Hospital for Sick Children, informed consent and assent were provided to children and their caregivers at the time of assessment, for use of data for research purposes.

Measures

As part of the data collection process and hospital protocol, several questionnaires and measures, including demographic, neuropsychological, and mental health measures, were given to caregivers and youth (depending on age). All participants received neuropsychological assessments as part of their clinical workup for the Stroke Clinic. In addition to the assessment, caregivers completed questionnaires related to their mental health.

Demographic Questionnaire

Caregiver(s) completed demographic questionnaires to obtain information such as age, gender, ethnic background(s), age at stroke/moyamoya diagnosis, surgery status, other medical conditions, family characteristics, socioeconomic status, and caregiver(s) education.

Cognitive Descriptor Variables

The **Wechsler Intelligence Scale for Children, Fifth Edition: Canadian (WISC-V) (Wechsler, 2014).** The WISC-V is a standardized assessment that aims to measure intelligence and cognitive ability in children between the ages of 6 and 16, with Canadian standardized

norms. It provides five primary index scores: Verbal Comprehension Index (VCI), Visual Spatial Index (VSI), Fluid Reasoning Index (FRI), Working Memory Index (WMI), and Processing Speed Index (PSI). The WISC-V consists of 16 subtests, with 7 subtests generating a Full-Scale IQ (FSIQ) score. The index scores and the FSIQ have a mean of 100 and an SD of 15; scores ranging from 90 to 109 are considered to be average. The test-retest reliability ranges from 0.81 to 0.94.

The **Wechsler Adult Intelligence Scale, Fourth Edition: Canadian (WAIS-IV) (Wechsler, 2008).** The WAIS-IV is an assessment that aims to measure intelligence and cognitive ability in individuals between the ages of 16 to 90 years old, with Canadian standardized norms. It provides four primary index scores: Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI), and Processing Speed Index (PSI). The WAIS-IV is comprised of 10 core subtests and 5 supplemental subtests, with the 16 core subtests generating an FSIQ score. The index scores and the FSIQ have a mean of 100 and an SD of 15; scores ranging from 90 to 109 are considered to be average. The test-retest reliability ranges from 0.70 to 0.90.

Academic Outcomes

The **Wide Range Achievement Test, Fourth Edition (WRAT-4) (Wilkinson & Robertson, 2006)**. The WRAT-4 is an achievement test that aims to measure basic academic skills of reading, spelling, and arithmetic in individuals aged 5 to 94. The WRAT-4 includes four subtests: Math Computation, Spelling, Sentence Comprehension, and Word Reading. Split-half reliability scores range from 0.94 to 0.98.

The **Wechsler Individual Achievement Test, Third Edition (WIAT-III) (Wechsler, 2009).** The WIAT-III is an academic achievement that aims to identify strengths and

weaknesses, inform special education eligibility and/or placement decisions, inform the diagnosis of specific learning disabilities and aid in the design of instructional objectives and interventions. The WIAT-III includes 16 subtests. All subtest reliability coefficients fell between .83 and .97 (very good to excellent) except for Alphabet Writing Fluency (.69). All composite scores had excellent reliability, with scores ranging from .90 to .98.

Executive Functioning Outcomes

The ***Behavior Rating Inventory of Executive Function, Second Edition (BRIEF2) (Gioia et al., 2000).*** The BRIEF2 is a widely used, 63-item measure to assess the impairment of executive function in children and adolescents ages 5-18 years via caregiver(s) observations. The youth self-report form is for ages 11-18 years and contains 55 items. The BRIEF2 evaluates everyday behaviours associated with executive functioning at home and school and is comprised of three main indexes: behavioural regulation, emotional regulation, and cognitive regulation, and 9 subscales: inhibit, self-monitor, shift, emotional control, initiate, working memory, plan and organize, task-monitoring, organization of materials. Higher scores on this measure indicate low executive behaviour. The BRIEF2 is rated on a Likert scale with N = "*never,"* S = "*sometimes,"* or O = "*often"* to outline the frequency with which the child being evaluated performs an indicated behaviour. The reliability for the BRIEF2 caregiver proxy report is 0.90, and 0.80 for the youth self-report.

The ***Delis–Kaplan Executive Functioning System (D-KEFS) (Delis et al., 2001).*** The D-KEFS is a standardized neuropsychological assessment used to provide a profile of an individual's executive functioning capabilities and detect mild brain damage. Specifically, it is used to assess brain damage in the frontal lobes. The D-KEFS measures several verbal and non-verbal executive functions for individuals between the ages of 8 to 89 years old. It is comprised

of 9 subtests: Trail Making, Verbal Fluency, Design Fluency, Color-Word Interference, Sorting test, Twenty Questions, Word Context, Tower test, and the Proverb test. Secondary data results for this study include Standard Scores for the Trail Making, Colour-Word Inference, and Verbal Fluency subtests. Lower scores on this measure indicate challenges with executive functioning. This measure is used for descriptives.

Behavioural and Emotional Outcomes

The ***Behavior Assessment System for Children, Third Edition (BASC-3) (Kamphaus et al., 2015).*** The BASC-3 is a 28-item measure used to evaluate behavioural and emotional difficulties in youth and informs clinical diagnosis or needs for educational support. Items are rated on a 4-point Likert scale 1 = "*never*", 2 = "*sometimes*", 3 = "*often*", or 4 = "*almost always*". Higher scores on this measure are indicative of greater risk in behavioural and emotional difficulties. Caregiver and teacher proxy reports use the 4-point Likert scale ratings to provide their observations of the youth. The youth self-report asks respondents to answer questions about their personal thoughts and feelings, which are rated in one of two ways: T = "True" or F = "False" or N = "*never*", S = "*sometimes*", O = "*often*", or A = "*almost always*". The caregiver and teacher proxy-reports on executive functioning for school, social, behavioural, and emotional domains have been shown to be good predictors of any youth challenges (Hendrickson & McCrimmon, 2019).

Data Analysis Plan

Data exploration was conducted, involving the review of demographic information collected from the caregiver(s) and the youth with MMD. For the academic outcomes, given that only two participants who completed the WRAT-4, I created one overarching academic variable that used the scaled scores from the WIAT-III and WRAT-4 for Word Reading, Mathematics,

Spelling, and Reading Comprehension, which have been found to have significant and positive associations with each other (Smith & Smith, 1998; Vance & Fuller, 1995). For the initial data analysis, I conducted descriptive statistics and bivariate correlations to examine and understand the relationships between the study's dependent and independent variables.

Correlations

An exploratory analysis on relationships between predictors was conducted using Pearson's Correlation Coefficients and investigated using a correlation matrix. Variables which significantly predicted outcomes were determined. Next, significant correlations between variables were followed by linear regression procedures to determine relevant predictors of cognitive and mental health outcomes.

Simple Linear Regression

Preliminary tests related to the parametric assumptions about the data were met. A review of score distribution, descriptive statistics, graphs, and informed data normality was conducted. The assumptions for the linear regression model were tested, and no concerns were found for homoscedasticity, normality of errors and the independent errors all appear to be met. However, the small sample sizes across variables may have impacted the assumptions, and this should be considered when interpreting the results. Additionally, non-linearity was observed, thus indicating that the assumption of normality may not have been met. Regression diagnostics were conducted to assess multicollinearity, outliers and influential cases. Based on the overall details of the regression diagnostics, we can conclude that multicollinearity is not a concern. Similarly, the leverage, studentized residuals, and Cook's distance indicate no concern for outliers and influential cases. The final model of the simple linear regression includes the three predictor

variables and the academic, caregiver-reported mental health, and daily executive functioning outcome variables.

All data were analyzed using IBM SPSS Statistics Software Version 29. Two-tailed *p*-values were used for test results when hypotheses were non-directional, with $\alpha = .05$, and confidence intervals (CI) were set at 95%.

Results

Descriptive Statistics

Descriptive statistics were computed to assess the neuropsychological profiles and mental health scores at post-surgical intervention for participants. Descriptive statistics were computed for the cognitive (WISC-V; WAIS-IV), academic, mental health (BASC-3), and executive functioning (D-KEFS; BRIEF2) outcome measures, describing the centre, spread, and shape of the distribution of the variables. Of note is the variability within and the range of scores for the outcome measures.

Demographics and Clinical Presentation

Of the 18 participants, 10 (55.6%) identified as female and 8 (44.4%) identified as male. When caregivers were asked about moyamoya diagnosis, 15 (83.3%) selected 'confirmed', and 3 (16.7%) selected 'presumed'. Regarding clinical characteristics, the participants' age at revascularization surgery ranged from 4 to 17 years old (*MAge*=10, *SD*=4.073), and the participants' age at stroke/moyamoya diagnosis ranged from 1 to 17 years old (*MAge*=8.25, *SD*=4.282). The demographic and clinical characteristics for the youth and sociodemographic characteristics for the caregivers are presented in Tables 1, 2, and 3, respectively.

Table 1

Participant Demographic Characteristics

Gender, n (%)	
Female	10 (55.6%)
Male	8 (44.4%)
Child living arrangement, n (%)	
Biological caregiver (Mother)	2 (11.1%)
Both biological caregivers	11 (61.1%)
Missing	5 (27.8%)
Number of siblings, n (%)	
None	3 (16.7%)
1	5 (27.8%)
2	5 (27.8%)
3	1 (5.6%)
Missing	4 (22.2%)
Birth order, n (%)	
First	5 (27.8%)
Second	8 (44.4%)
Third	1 (5.6%)
Missing	4 (22.2%)
Handedness, n (%)	
Left	5 (27.8%)
Right	10 (55.6%)
Missing	3 (16.7%)
Handedness switch, n (%)	
Yes	1 (5.6%)
No	13 (72.2%)
Missing	4 (22.2%)

Note. There is incomplete data for some of the participants.

Table 2

Caregiver Sociodemographic Characteristics

Caregiver 1 – Highest education level, n (%)	
Elementary school	1 (5.6%)
Highschool	2 (11.1%)
Undergraduate degree or diploma	9 (50.0%)
Professional degree or graduate school	2 (11.1%)
Unchecked	4 (22.2%)
Caregiver 2 – Highest education level, n (%)	
Some Highschool	1 (5.6%)
Highschool	1 (5.6%)
Undergraduate degree or diploma	9 (50.0%)
Professional degree or graduate school	1 (5.6%)
Missing	6 (33.3%)

Caregiver Sociodemographic Characteristics

Estimated Household Annual Income, n (%)	
Under $20,000	1 (5.6%)
$50,001-$100,000	4 (22.2%)
$100,001-$150,000	6 (33.3%)
Over $150,000	4 (22.2%)
Marital Status, n (%)	
Never married	1 (5.6%)
Married	11 (61.1%)
Divorced	2 (11.1%)
Missing	4 (22.2%)

Note. There is incomplete data for some of the participants.

Table 3

Participant Clinical Characteristics

Moyamoya diagnosis, n (%)	
Confirmed	15 (83.3%)
Presumed	3 (16.7%)
Stroke/moyamoya diagnosis, n (%)	
Yes	16 (88.9%)
No	2 (11.1%)
Age at stroke/moyamoya diagnosis, n (%)	
1	1 (5.6%)
3	1 (5.6%)
4	2 (11.1%)
6	2 (11.1%)
7	1 (5.6%)
8	1 (5.6%)
9	2 (11.1%)
10	2 (11.1%)
11	1 (5.6%)
13	1 (5.6%)
14	1 (5.6%)
17	1 (5.6%)
Missing	2 (11.1%)
Stroke type, n (%)	
Childhood arterial ischemic stroke (AIS)	
Yes	12 (66.7%)
No	6 (33.3%)
Childhood cerebral sinovenous thrombosis (CSVT)	
Yes	0 (0%)
No	18 (100%)
Acute neonatal arterial ischemic stroke (NAIS)	

Yes	0 (0%)
No	18 (100%)
Acute neonatal cerebral sinovenous thrombosis (NCSVT)	
Yes	0 (0%)
No	18 (100%)
Presumed perinatal arterial ischemic stroke (PPAIS)	
Yes	0 (0%)
No	18 (100%)
Presumed perinatal cerebral sinovenous thrombosis (PPCSVT)	
Yes	0 (0%)
No	18 (100%)
Presumed periventricular venous infarction (PPVI)	
Yes	0 (0%)
No	18 (100%)
Arteriopathy without stroke	
Yes	11 (61.1%)
No	7 (38.9%)
Age at revascularization surgery, n (%)	
4	2 (11.1%)
6	1 (5.6%)
7	2 (11.1%)
8	3 (16.7%)
9	2 (11.1%)
10	1 (5.6%)
11	1 (5.6%)
12	1 (5.6%)
13	1 (5.6%)
15	2 (11.1%)
17	2 (11.1%)
Lesion laterality, n (%)	
Left hemisphere	5 (27.8%)
Right hemisphere	1 (5.6%)
Bilateral	2 (1.1%)
Missing data	10 (55.6%)
Lesion location, n (%)	
Cortical	
Yes	2 (11.1%)
No	16 (88.9%)
Subcortical	
Yes	3 (16.7%)
No	15 (38.9%)
Combined cortical-subcortical	
Yes	2 (11.1%)
No	16 (88.9%)
Cerebellum	

Yes	0 (0%)
No	18 (100%)
Brainstem	
Yes	0 (0%)
No	18 (100%)
White Matter	
Yes	4 (22.4%)
No	14 (77.8%)
Unknown/None of the above	
Yes	0 (0%)
No	18 (100%)
Cortical lesion type, n (%)	
Frontal	
Yes	3 (16.7%)
No	15 (83.5%)
Parietal	
Yes	1 (5.6%)
No	17 (94.4%)
Temporal	
Yes	0 (0%)
No	18 (100%)
Occipital	
Yes	0 (0%)
No	18 (100%)
Unknown/None of the above	
Yes	0 (0%)
No	18 (100%)
Subcortical lesion type, n (%)	
Basal Ganglia	
Yes	3 (16.7%)
No	15 (83.3%)
Thalamus	
Yes	0 (0%)
No	18 (100%)
Medial Temporal	
Yes	0 (0%)
No	18 (100%)
Unknown/None of the above	
Yes	0 (0%)
No	18 (100%)
Infarct size, n (%)	
Small	6 (33.3%)
Medium	3 (16.7%)
Missing	9 (50.0%)

Note. There is incomplete data for some of the participants.

Cognitive and Performance Executive Functioning Outcomes

The data for the IQ and performance EF are presented here for cognitive context but are not analyzed for the purposes of this study. The mean for the WISC-V FSIQ scores was *M*=92.80 (*SD*=23.31). The maximum and minimum scores were 46 and 131, respectively, with a range of 85. Overall, this suggests that the mean of the FSIQ scores fell generally within the clinically average range (Wechsler, 2014). The mean for the WAIS-IV FSIQ scores was *M*=84.29 (*SD*=20.94). The maximum and minimum scores were 61 and 107, respectively, with a range of 46. Overall, this suggests that the mean of the FSIQ scores fell generally within the average range (Wechsler, 2008). The maximum and minimum scores for the D-KEFS were 1 to 15, for most of the subtests, with ranges from 8 to 14. Overall, this may suggest that some of the participants experience significant post-surgical challenges with performance executive functioning, particularly for the Colour Naming, Word Reading, Number Sequencing, Number-Letter Switching subtests. The descriptive statistics computed for the academic, mental health, and daily executive functioning are presented in Table 5.

Table 4

Descriptives for Cognitive and Performance Executive Functioning Measures

	N	*M*	*Mdn*	*SD*	Range	Min	Max
WISC-V Cdn							
FSIQ	10	92.80	89.50	23.31	85	46	131
VCI	10	98.00	97.50	20.06	74	53	127
PSI	10	79.80	80.00	28.82	102	25	127
WMI	11	82.55	100.00	37.53	113	3	116
VSI	10	89.20	96.50	23.75	66	49	115
FRI	10	98.10	100.00	20.16	73	56	129
WAIS-IV Cdn							
FSIQ	7	84.29	82.00	20.94	46	61	107
VCI	7	89.71	90.00	12.51	35	70	105
PRI	7	87.00	87.00	27.68	62	54	116
WMI	7	84.00	82.00	15.03	38	67	105
PSI	7	85.14	85.00	15.42	43	63	106
D-KEFS[1]							
Trails MotorSpeedSS	14	9.79	10.00	2.81	8	6	14
Trails NumLettSwiSS	14	9.07	8.50	4.51	14	1	15
Trails LettSeqSS	14	9.57	9.0	3.34	11	4	15
Trails NumSeqSS	14	8.57	8.50	4.15	13	1	14
Trails VisScanSS	14	9.21	10.00	2.58	9	4	13
CatFluencySS	15	10.67	12.00	3.48	11	5	16
LetFluencySS	15	9.73	11.00	2.60	9	4	13
SwitchSS	14	9.50	9.50	2.62	8	5	13

Descriptives for Cognitive and Performance Executive Functioning Measures

	N	*M*	*Mdn*	*SD*	Range	Min	Max
InhibtimeSS	14	10.00	10.00	3.46	11	4	15
WordtimeSS	14	9.29	11.00	4.16	14	1	15
ColourtimeSS	14	8.93	9.50	3.97	14	1	15

Note. [1]Standard Scores used for the DKEFS. WISC-V = Wechsler Intelligence Scale for Children, Fifth Edition: Canadian; FSIQ = Full Scale IQ; VCI = Verbal Comprehension Index; , VSI = Visual Spatial Index; FRI = Fluid Reasoning Index; WMI = Working Memory Index; PSI = Processing Speed Index; WAIS-IV = Wechsler Adult Intelligence Scale, Fourth Edition: Canadian; VCI = Verbal Comprehension Index; PRI = Perceptual Reasoning Index; WMI = Working Memory Index; PSI = Processing Speed Index; Verbal Comprehension Index (VCI); Perceptual Reasoning Index (PRI). D-KEFS = Delis–Kaplan Executive Functioning System; Trail Making (Visual Scanning; Number Sequencing; Letter Sequencing; Number-Letter Switching; Motor Speed); Colour-Word Inference (Colour Naming; Word Reading; Inhibition; Inhibition/Switching); Verbal Fluency subtests (Letter Fluency; Category Fluency; Category Switching; Category Switching Accuracy).

Table 5

Descriptive Statistics for Academic, Mental Health, and Daily Executive Functioning Outcomes

	N	*M*	*Mdn*	*SD*	Range	Min	Max
Academic							
Basic Reading	6	105.3	100.5	22.74	65	80	145
Reading Comprehension	18	100.6	97.5	14.78	63	73	136
Spelling	14	100.1	98.0	21.27	73	72	145
Mathematics	15	89.0	86.0	22.13	84	45	129
BASC-3 Caregiver							
Anxiety	9	48.3	49.0	9.58	31	38	69
Depression	9	49.1	48.0	5.84	19	44	63
Ext. Prob	9	48.6	46.0	6.23	15	42	57
Int. Prob	9	48.6	47.0	4.36	12	43	55
BSI	9	50.4	48.0	7.47	19	42	61
BASC-3 Self-Report							
Anxiety	5	56.8	57.0	6.14	15	48	63
Depression	5	48.2	47.0	6.57	14	42	56
Int. Prob	5	52.0	47.0	9.67	23	43	66
ESI	5	53.2	53.0	8.87	22	44	66
BRIEF2 Caregiver							
BRI	11	52.8	52.0	8.65	29	42	71
ERI	11	56.8	59.0	8.45	25	45	70
CRI	11	56.6	51.0	10.69	31	43	74
BRIEF2 Self-report							
BRI	2	55.0	55.0	2.83	4	53	57
ERI	2	69.5	69.5	7.78	11	64	75
CRI	2	57.5	57.5	9.19	13	51	64

Note. [1]Standard Scores used for the Academic variables. BASC-3 = Behavior Assessment System for Children, Third Edition; Ext. Prob = Externalizing problems; Int. Prob = Internalizing problems; BSI = Behavioral Symptoms Index; ESI = Emotional Symptoms Index; BRIEF2 = Behavior Rating Inventory of Executive Function, Second Edition; BRI = Behavior Regulation Index; ERI = Emotion Regulation Index; CRI = Cognitive Regulation Index.

Correlations

Preliminary tests related to the parametric assumptions about the data were met. A review of score distribution, descriptive statistics, graphs, and informed data normality was completed. Bivariate correlations are presented in Table 6. A Pearson correlation was conducted to examine the relationship between the study's variables. The predictors for the regression were selected based on the correlation matrix. It was identified that age at revascularization surgery, moyamoya diagnosis (confirmed or presumed disease), and age at stroke/moyamoya diagnosis were highly correlated with key outcomes of interest.

The results of the correlation matrix show that age at revascularization surgery was negatively correlated with the BASC-3 caregiver-reported Behavioural Symptoms Index (BSI) total score, $r(7) = -0.75$, $p = .20$. While this relationship was not significant at the two-tailed $\alpha = .05$ level, it should be interpreted with caution, as it may suggest that younger age at surgical intervention may have increased levels of behavioural symptoms, as reported by their caregivers. It was also noted that age at revascularization surgery was significant and negatively correlated with the BRIEF2 caregiver-reported Behavioural Regulation Index (BRI) total score, $r(9) = -0.85$, $p = .001$. This suggests that those who had revascularization surgery at a young age may experience greater challenges with behavioural regulation, as reported by their caregivers. There were no other statistically significant relationships between the age at revascularization surgery and the remaining academic, daily executive functioning, and mental health outcome variables.

The results also found a strong and statistically significant positive correlation between a confirmed or presumed (confirmed or presumed disease) and BASC-3 caregiver-reported Anxiety score, $r(7) = 0.81$, $p = .008$, indicating that a moyamoya diagnosis (confirmed or presumed disease) is associated with increased levels of anxiety, as reported by their caregivers.

Further, it was also noted that a strong statistically significant positive correlation between moyamoya diagnosis (confirmed or presumed disease) and the BRIEF2 caregiver-reported BRI total score $r(9) = 0.70$, $p = .017$, indicating that children with a confirmed or presumed moyamoya diagnosis were reported by their caregivers to experience increased challenges with behavioural regulation. There were no other statistically significant relationships between the moyamoya diagnosis (confirmed or presumed disease) variable and the remaining academic, daily executive functioning, and mental health outcome variables.

For the age at stroke/moyamoya diagnosis variable, there was a strong and negative correlation with the self-reported BASC-3 Anxiety score, $r(2) = -0.93$, $p = .066$. Though this relationship was not statistically significant at the two-tailed level, the strength of the relationship may suggest that a younger age of stroke/diagnosis may be associated with increased challenges with anxiety. There were no other statistically significant relationships between the age at stroke/moyamoya diagnosis and the remaining academic, daily executive functioning, and mental health outcome variables.

Given the strength of the correlations, the following variables - age at revascularization surgery, age at stroke/moyamoya diagnosis, and moyamoya diagnosis (confirmed or presumed disease) - were used as predictors for the outcome variables in the linear regression model.

Simple Linear Regression

A simple linear regression was conducted to evaluate the extent to which age at revascularization surgery, age at stroke/moyamoya diagnosis, and moyamoya diagnosis (confirmed or presumed disease) variables could predict academic, caregiver-reported BASC-3, and caregiver-reported BRIEF2 outcomes.

Predictors of Academics

Academic basic reading standard scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and academic basic reading standard scores (Table 7). The regression equation revealed that none of the variables was a significant predictor of basic reading scores, $F(3, 2) = 1.80$, $p = .377$. The predictor variables accounted for approximately 73% of the variance in basic reading scores ($R^2 = .73$). Academic basic reading scores decreased for age at revascularization surgery, moyamoya diagnosis (confirmed or presumed disease) variables, and increased for age at stroke/moyamoya diagnosis variables for each standard score.

Table 7

Simple Linear Regression Analysis for Variable predicting Academic Basic Reading Standard Scores

				95% CI for *B*			
Variable	*B*	*SE. B*	*B*	LL	UL	*t*	*p*-value
Intercept	188.23	52.59		-37.99	414.54	3.58	.070
Age at revascularization Surgery	-22.66	13.90	-4.79	-82.48	37.16	-1.63	.245
Moyamoya diagnosis (C or P)	-52.44	28.00	-.94	-172.89	68.02	-1.87	.202
Age at stroke/moyamoya diagnosis	21.81	12.71	4.83	-32.86	76.47	1.72	.228

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Academic reading comprehension standard scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at

stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and academic reading comprehension standard scores (Table 8). None of the variables was found to be a significant predictor, $F(3, 12) = .71$, $p = .567$. The predictor variables accounted for a small portion of the variance in reading comprehension scores ($R^2 = .15$). Academic reading comprehension scores decreased for age at revascularization surgery, and moyamoya diagnosis (confirmed or presumed disease) variables, and increased for age at stroke/moyamoya diagnosis variable, for each standard score.

Table 8

Simple Linear Regression Analysis for Variable Predicting Academic Reading Comprehension Standard Scores

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	130.88	19.70		87.96	173.79	6.65	<.001**
Age at revascularization Surgery	-1.29	1.18	-.42	-3.85	1.28	-1.09	.296
Moyamoya diagnosis (C or P)	-15.01	11.67	-.39	-40.43	10.41	-1.29	.222
Age at stroke/moyamoya diagnosis	.286	1.08	.093	-2.06	2.63	.27	.795

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Academic spelling standard scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and academic spelling standard scores (Table 9). The regression equation revealed that none of the variables was a significant predictor, $F(3, 9) = 1.18$, $p = .369$. The predictor variables accounted for a small portion of the variance in spelling scores ($R^2 = .28$). Academic spelling scores decreased

for age at revascularization surgery and moyamoya diagnosis (confirmed or presumed disease) variables and increased for age at stroke/moyamoya diagnosis for each standard score.

Table 9

Simple Linear Regression Analysis for Variable predicting Academic Spelling Standard Scores

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*B*
Intercept	129.63	31.15		59.16	200.11	4.16	.002*
Age at Revascularization Surgery	-2.42	1.92	-.48	-6.77	1.93	-1.26	.240
Moyamoya Diagnosis (C or P)	-20.95	17.64	-.38	-60.86	18.95	-1.19	.265
Age at stroke/moyamoya diagnosis	2.70	1.71	.54	-1.17	6.57	1.58	.149

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Academic mathematics standard scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and academic mathematics standard scores (Table 10). None of the variables was found to be a significant predictor of mathematics outcomes, $F(3, 9) = .40$, $p = .758$. The predictor variables accounted for a small portion of the variance in mathematics scores ($R^2 = .12$). Academic mathematics scores increased for age at revascularization surgery, moyamoya diagnosis (confirmed or presumed disease) variables, and decreased for the age at stroke/moyamoya diagnosis variable, for each standard score.

Table 10

Simple Linear Regression Analysis for Variable predicting Academic Mathematics Standard Scores

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	65.18	38.79		-22.58	152.936	1.680	.127
Age at revascularization surgery	2.56	2.39	.452	-2.855	7.978	1.070	.313
Moyamoya diagnosis (C or P)	7.95	21.965	.130	-41.738	57.640	.362	.726
Age at stroke/moyamoya diagnosis	-.98	2.132	-.173	-5.802	3.844	-.459	.657

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Predictors of Mental Health (BASC-3)

Caregiver-reported BASC-3 Anxiety scores. A simple linear regression analysis was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables, and caregiver-reported BASC-3 Anxiety scores (Table 11). None of the variables was found to be a significant predictor of anxiety, $F(3, 4) = 3.12$, $p = .150$. The predictor variables accounted for approximately 70% of the variance in anxiety scores ($R^2 = .70$). The caregiver-reported Anxiety scores decreased for the age at revascularization surgery and age at stroke/moyamoya diagnosis variables and increased for the moyamoya diagnosis (confirmed or presumed disease) variable for each standard score.

Table 11

Simple Linear Regression Analysis for Variable predicting BASC-3 Anxiety Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value

Intercept	31.92	15.64		-11.51	75.35	2.04	.111
Age at revascularization surgery	-.31	.76	-.13	-2.42	1.79	-.42	.699
Moyamoya diagnosis (C or P)	19.79	8.81	.72	-4.66	44.24	2.25	.088
Age at stroke/moyamoya diagnosis	-.31	.79	-.11	-2.49	1.87	-.39	.714

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Caregiver-reported BASC-3 Depression scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and the caregiver-reported BASC-3 Depression scores (Table 12). None of the variables was found to be a significant predictor of depression, $F(3, 4) = .60$, $p = .650$. The predictor variables accounted for a small portion of the variance in depression scores ($R^2 = .31$). The caregiver-reported Depression scores decreased for the age at revascularization surgery variable and increased for the moyamoya diagnosis (confirmed or presumed disease) and age at stroke variables, for each standard score.

Table 12

Simple Linear Regression Analysis for Variable predicting BASC-3 Depression Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	48.39	14.78		7.35	89.43	3.27	.031*
Age at revascularization surgery	-.61	.72	-.42	-2.60	1.38	-.85	.444
Moyamoya diagnosis (C or P)	2.03	8.32	.12	-21.08	25.13	.24	.820

Age at stroke/moyamoya diagnosis	.75	.74	.44	-1.32	2.81	1.01	.371

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Caregiver-reported BASC-3 Externalizing problem scores. A simple linear regression was conducted to investigate the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and the caregiver-reported BASC-3 Externalizing Problem scores (Table 13). None of the variables was found to be a significant predictor of externalizing problems, $F(3, 4) = 1.13$, $p = .438$. The predictor variables accounted for a small portion of the variance in externalizing problem scores ($R^2 = .46$). The caregiver-reported Externalizing Problem scores decreased for the age at revascularization surgery variable and increased for the moyamoya diagnosis (confirmed or presumed disease) and age at stroke/moyamoya diagnosis variables, for each standard score.

Table 13

Simple Linear Regression Analysis for Variable predicting BASC-3 Externalizing Problem Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	54.53	14.30		14.82	94.24	3.81	.019*
Age at revascularization surgery	-.97	.69	-.61	-2.89	.96	-1.40	.236
Moyamoya diagnosis (C or P)	2.52	8.05	.14	-19.84	24.88	.31	.770
Age at stroke/moyamoya diagnosis	.07	.72	.04	-1.92	2.07	.10	.924

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Caregiver-reported BASC-3 Internalizing problem scores. A simple linear regression was conducted to explore the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis variables and the caregiver-reported BASC-3 Internalizing Problem scores (Table 14). None of the variables was found to be a significant predictor of internalizing problems, $F(3, 4) = 1.49$, $p = .345$. The predictor variables accounted for a small portion of the variance in internalizing problem scores ($R^2 = .53$). The caregiver-reported Internalizing Problem scores decreased for the age at revascularization surgery variable and increased for the moyamoya diagnosis (confirmed or presumed disease) and age at stroke/moyamoya diagnosis variables, for each standard score.

Table 14

Simple Linear Regression Analysis for Variable predicting BASC-3 Internalizing Problem Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	49.26	8.31		26.18	72.33	5.93	.004*
Age at Revascularization Surgery	-.53	.40	-.54	-1.65	.59	-1.32	.257
Moyamoya Diagnosis (C or P)	3.69	4.68	.32	-9.31	16.68	.79	.475
Age at stroke/moyamoya diagnosis	.12	.42	.11	-1.04	1.28	.30	.781

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Caregiver-reported BASC-3 BSI scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya

diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and the caregiver-reported BASC-3 BSI scores (Table 15). None of the variables was found to be a significant predictor of BSI, $F(3, 4) = 1.80$, $p = .287$. The predictor variables accounted for a small portion of the variance in BSI scores, $R^2 = .57$. The caregiver-reported BSI scores decreased for the age at revascularization surgery variable and increased for the moyamoya diagnosis (confirmed or presumed disease) and age at stroke/moyamoya diagnosis variables, for each standard score.

Table 15

Simple Linear Regression Analysis for Variable predicting BASC-3 BSI Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	62.13	14.78		21.11	103.16	4.21	.014*
Age at revascularization surgery	-1.43	.72	-.77	-3.42	.56	-2.00	.116
Moyamoya diagnosis (C or P)	.03	8.32	.001	-23.07	23.13	.003	.998
Age at stroke/moyamoya diagnosis	.13	.74	.06	-1.93	2.20	.18	.866

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Predictors of Daily Executive Functioning (BRIEF2)

Caregiver-reported BRIEF2 BRI scores. A simple linear regression was conducted to examine the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and the caregiver-reported BRIEF2 BRI scores (Table 16). The age at revascularization surgery and moyamoya diagnosis (confirmed or presumed disease) variables were found to be significant predictors of BRI, $F(3, 6) = 14.74$, $p = .004$. The predictor variables accounted for approximately 88% of the

variance in BRI scores (R^2 = .88). The caregiver-reported BRI scores decreased for the age at revascularization surgery variable and increased for the moyamoya diagnosis (confirmed or presumed disease) and age at stroke/moyamoya diagnosis variables, for each standard score.

Table 16

Simple Linear Regression Analysis for Variable predicting BRIEF2 BRI Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	50.11	7.57		31.58	68.64	6.62	<.001
Age at revascularization surgery	-1.46	.36	-.71	-2.34	-.57	-4.02	.007*
Moyamoya diagnosis (C or P)	12.51	4.58	.45	1.30	23.72	2.73	.034*
Age at stroke/moyamoya diagnosis	.43	.34	.20	-.41	1.26	1.25	.257

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Caregiver-reported BRIEF2 ERI scores. A simple linear regression was conducted to explore the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and the caregiver-reported BRIEF2 ERI scores (Table 17). None of the variables was found to be a significant predictor of ERI, $F(3, 6) = 3.41$, $p = .094$. The predictor variables accounted for approximately 63% of the variance in ERI scores (R^2 = .63). The caregiver-reported ERI scores decreased for the age at revascularization surgery variable and increased for the moyamoya diagnosis (confirmed or presumed disease), age at stroke/moyamoya diagnosis variables, for each standard score.

Table 17

Simple Linear Regression Analysis for Variable predicting BRIEF2 ERI Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	34.10	13.21		1.77	66.43	2.58	.042*
Age at revascularization surgery	-.60	.63	-.29	-2.14	.95	-.94	.383
Moyamoya diagnosis (C or P)	16.38	7.99	.59	-3.17	35.93	2.05	.086
Age at stroke/moyamoya diagnosis	1.38	.59	.66	-.07	2.83	2.33	.059

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Caregiver-reported BRIEF2 CRI scores. A simple linear regression was conducted to investigate the relationship between age at revascularization surgery, age at stroke/moyamoya diagnosis, moyamoya diagnosis (confirmed or presumed disease) variables and the caregiver-reported BRIEF2 CRI scores (Table 18). None of the variables was found to be a significant predictor of CRI, $F(3, 6) = .39$, $p = .766$. The predictor variables accounted for a small portion of the variance in CRI scores ($R^2 = .16$). The caregiver-reported CRI scores decreased for the age at revascularization surgery and age at stroke/moyamoya diagnosis variables and increased for the moyamoya diagnosis (confirmed or presumed disease) variable, for each standard score.

Table 18

Simple Linear Regression Analysis for Variable predicting BRIEF2 CRI Scores (Caregiver)

				95% CI for *B*			
Variable	*B*	*SE. B*	*β*	LL	UL	*t*	*p*-value
Intercept	59.06	22.84		3.18	114.95	2.59	.041*
Age at revascularization surgery	-.43	1.09	-.18	-3.10	2.25	-.39	.711
Moyamoya diagnosis (C or P)	3.81	13.81	.12	-29.99	37.61	.28	.792

Age at stroke/moyamoya diagnosis	-.50	1.02	-.21	-3.00	2.01	-.48	.646

Note. *p < 0.05, **p < 0.001. *B* = Unstandardized coefficient; *SE. B* = standard error; *β* = Beta (Standardized coefficient); CI = confidence interval; LL = lower limit; UL = upper limit; C = confirmed disease; P = presumed disease.

Discussion

The objectives of this study were twofold: first, to explore the post-surgical intervention neuropsychological and mental health profiles of Canadian youth with MMD through descriptive analyses; and second, to examine the association between MMD and stroke-related variables, and their ability to predict post-surgical intervention academic achievement, daily executive functioning, and mental health scores. To our knowledge, this is the first study to examine academic achievement, daily executive functioning, and mental health variables simultaneously in a cohort of Canadian youth with pediatric moyamoya vasculopathy. The study findings generated mixed results. Findings from the current study suggest that youth with pediatric moyamoya disease may present with academic, mental health and daily executive functioning challenges, which is consistent with the literature (Friefeld et al., 2004).

To examine the first research objective, I conducted descriptive analyses to generate neuropsychological and mental health profiles of youth with MMD. The study participants were generally equal in terms of gender. As seen in Table 2, participants were living with their biological caregivers, most of whom obtained a post-secondary education. Socioeconomic status for the participants was captured using estimated household annual income as reported by their caregivers, as follows: Under $20,000 (*n* = 1, 5.6%); $50,000 - $100,000 (*n* = 4, 22.2%); $100,001 - $150,000 (*n* = 6, 33.3%); Over $150,000 (*n* = 4, 22.2%). As for clinical characteristics, 88.9% (*n* =16) of the participants were diagnosed with childhood stroke (Ferriero

et al., 2019), which is a significant risk factor for those diagnosed with moyamoya disease or moyamoya syndrome (deVeber et al., 2017; Hollist et al., 2021; Lehman et al., 2022; Mitchell et al., 2023; Williams et al., 2012). The most prevalent stroke type for participants (n = 12, 66.7%) was childhood arterial ischemic stroke (AIS), which is also consistent with what has been described in the literature (Lehman et al., 2022).

In line with current literature, it was expected that the neuropsychological profiles for the participants in this study would show some variability. The FISQ means for the WISC-V (M = 92.80, SD = 23.31) and the WAIS-IV (M = 84.29, SD = 20.94) were within the average range; however, several participants had scores below this range. Similarly, there was variability in the scores for the D-KEFS, where several participants had low scores on the subtests. Lower scores on this measure of executive functioning may be associated with damage to the frontal lobes (Delis et al., 2001). Overall, the variability of the cognitive and executive functioning scores for participants in this study may highlight the challenges they experience associated with having moyamoya disease and emphasize the associated cognitive and executive functioning deficits that are present. This has also been noted in various studies examining the pediatric moyamoya population. Lesion laterality for the participants was in the left hemisphere (n = 5, 27.8%), right hemisphere (n = 1, 5.6%) or bilateral (n = 2, 11.1%). Further, 11.1% (n = 2) had cortical lesions, 16.7% (n = 3) had subcortical lesions, 11.1% (n = 2) had combined cortical-subcortical lesions, and 22.4% (n = 4) had white matter lesions. Regarding cortical lesion type, 16.7% (n = 3) of the participants had frontal lesions, and 5.6% (n = 1) had parietal lesions. Finally, 16.7% (n = 3) of the participants had subcortical lesions in the basal ganglia. Previous studies have found that a large portion of cognitive deficits experienced by individuals with MMD were attributed to

lesions in the frontal, parietal, and temporal lobes, which are regions important for intellectual and executive functioning (Kang et al., 2017; Kim et al., 2018).

For the second research objective, I examined the relationship between MMD and stroke-related variables and their ability to predict post-surgical intervention academic achievement, everyday executive functioning, and mental health scores. Pearson correlations were conducted to identify predictors. Interestingly, the findings showed that age at revascularization surgery was negatively correlated with the caregiver-reported BASC-3 Behavioural Symptoms Index (BSI) and the caregiver-reported BRIEF2 (Behavioural Regulation Index) BRI total scores. Although the relationship with BSI was not statistically significant, it suggests that earlier surgical intervention may be associated with higher levels of caregiver-reported behavioural symptoms. Conversely, the relationship with caregiver-reported BRI was negative and statistically significant, indicating that a younger age at surgery may be related to greater challenges with behavioural regulation, an aspect of executive functioning. Liang et al. (2025) found that in a cohort of Chinese children with moyamoya disease who exhibited challenges with behavioural regulation and executive functioning pre-revascularization surgery, they continued to experience persistent symptoms post-revascularization surgery. This aligns with the result of this study, suggesting that earlier surgical intervention may still place children at risk of increased caregiver-reported challenges with persistent behavioural regulation.

Furthermore, the results showed a strong and statistically significant positive relationship for children with a confirmed or presumed moyamoya diagnosis and caregiver-reported BASC-3 anxiety scores; this may indicate that a moyamoya diagnosis is associated with increased caregiver-reported levels of anxiety. Similarly, there was a strong statistically significant positive correlation between moyamoya diagnosis and the caregiver-reported BRIEF2 BRI total score,

suggesting that children with a moyamoya diagnosis were reported by their caregivers to experience greater challenges with behavioural regulation. These findings highlight the neuropsychological and emotional impact of moyamoya disease, as perceived by their caregivers. Neuropsychology theory posits that early onset of a neurological disorder, such as MMD, results in long-term challenges related to brain function, learning, and overall behaviour (Ballantyne et al., 2008; Dennis et al., 2014). Similarly, in line with the results of the study, researchers have found that regarding caregiver-reported emotional and behavioural problems, children with moyamoya showed significantly increased depression and anxiety, with internalizing problems (Shim et al., 2015).

The age at stroke/moyamoya diagnosis variable showed a strong, negative, and not statistically significant correlation with the self-reported BASC-3 anxiety scores. These results may suggest that a younger age of stroke onset may be associated with increased challenges with anxiety symptoms. In support of these results, studies have also found that patients with moyamoya disease experience challenges with quality of life, particularly in the areas of social, school, and work, as well as increased levels of anxiety (Ahmad et al., 2025; Ball et al., 2016; Nakamizo et al., 2018; Westmacott et al., 2025). Researchers suggest that youth with moyamoya disease could benefit from mental health support (Ball et al., 2016). Furthermore, in line with the uncertainty in illness theory and existing literature (Mishel, 1988; Stewart et al., 2010; Zhang, 2017), children with early onset of stroke and chronic illnesses often experience challenges with emotional regulation, such as anxiety due to the uncertainty related to their health (Zhang, 2017). Overall, the study results could suggest that earlier onset of stroke, earlier age at revascularization and a moyamoya diagnosis may increase caregiver and self-reported

behavioural regulation and mental health challenges, which will require early intervention and ongoing support.

In terms of predictors of academic, mental health, and daily executive functioning outcomes, statistical analyses did not demonstrate significant relationships for the regression models involving academic achievement scores and mental health subscales. It is possible that the linear regression analysis exploring these relationships was not significant due to the study's small sample size. Furthermore, there is also some natural variability within the sample size, which could explain why some of the regression models were not statistically significant. While the results were not statistically significant, studies have shown that in long-term follow-up post-surgical intervention, patients experienced significant difficulty in social and school settings due to intellectual impairment related to experiencing stroke onset at a young age (Nakashima et al., 1997; Liang et al., 2025).

When the predictor variables were regressed onto the BRIEF2 caregiver-reported BRI scores, age at revascularization and moyamoya diagnosis (confirmed or presumed disease), a statistically significant relationship was revealed. These results suggest that the deficits experienced by the participants seem to be related to their daily executive functioning rather than on tests of cognitive, academic, and executive functioning. Similar findings were observed in studies examining intellectual and executive functioning. Researchers found that children with moyamoya had impaired intellectual and executive function compared to normative and non-stroke groups (Gatti et al., 2024; William et al., 2012). A study investigating long-term neurocognitive outcomes in an adult population with moyamoya disease, with and without revascularization surgery, found that their neurocognitive functions (i.e., memory, attention, mental flexibility, and inhibitory control) declined over time for both groups (Nakamizo et al.,

2018). Moreover, studies have shown that post-revascularization cognitive dysfunction is often associated with lesions in the frontotemporal areas, as well as memory impairment and challenges with executive functioning (Hsu et al., 2014; Shim et al., 2015). Although our regression model indicates a statistically significant relationship, it is important to interpret the results cautiously due to the small sample size. This limitation is not unique to this population (Westmacott et al., 2025) or to studies using clinical, particularly medical data, which often have smaller sample sizes compared to other studies (Jenkins & Quintana-Ascencio, 2020). Although the findings may not be broadly generalizable, they are relevant to the pediatric moyamoya disease population and might also apply to others with chronic illnesses.

Limitations

Due to the rarity of MMD, the small sample size and retrospective nature of this study reflect some of the common limitations encountered when studying this population. The small number of participants also limits the ability to conduct parametric statistical analysis, which is a primary reason for including descriptive statistics for some of the variables. As a result, the sample size may have impacted the strength of the correlational relationships and the regression findings. Although strong correlations were noted, many were not significant. The findings should be interpreted with caution before establishing conclusions about this understudied population. Another limitation of the study is the lack of self-reported data, which is a common challenge in pediatric studies. In addition to having caregiver-reported data, having access to questionnaires completed by the youth and other informants (i.e., teachers) not only provides an accurate information about the youth, but will be integral for informing clinical practice; multi-informant perspectives are beneficial (De Los Reyes et al., 2015).

Clinical Implications

This study presents clinical findings that are important to consider when working with youth diagnosed with moyamoya disease. While it was important to gain an understanding of our sample, the findings from this thesis offer valuable information that may have broader implications for clinical practice. For instance, it could equip clinicians with data-driven knowledge to deliver precision healthcare, support, and interventions for these youth. Specifically, several of the mental health variables examined in this thesis were predicted by having a confirmed or presumed moyamoya diagnosis. It will be important to explore in more detail the anxiety and depression experiences of this population to ensure that youth with MMD are supported. Moreover, the findings from this study should inform questions about the youth's daily executive functioning and mental health so that caregivers and medical professionals can provide support in these areas where they may be experiencing difficulties. Specifically, these results should also inform interventions for executive functioning, such as cognitive rehabilitation, to assist in improving quality of life and overall well-being. These findings are also crucial for social and school functioning as youth with moyamoya disease often miss school and other social events due to attending frequent appointments or experiencing symptoms related to their disease (Kim et al., 2018; Oakley et al., 2024; Yeom & Oh, 2023). Furthermore, it will be important to include and examine the quality of life in youth with moyamoya disease, as most studies focus on cognitive functioning (Ball et al., 2016). This study provides an avenue to learn more about the pediatric moyamoya population, as most studies focus on the adult population.

Future Directions

The current study provided an opportunity to address a gap in the literature pertaining to the neuropsychological and mental health profiles of Canadian youth with moyamoya disease.

Future research should investigate similar profiles for youth at pre- and post-surgical intervention timepoints to provide a full picture of the potential challenges these youth may experience related to academics, mental health, and executive functioning. Growth curve modelling will provide researchers with an opportunity to explore differences in pre- and post-surgical interventions for these youth, thereby gaining a better understanding of their challenges in all aspects of their lives. Future research efforts should employ a multi-centre approach (e.g., Po et al., 2020) to fully understand this understudied population. The results from a multi-centre study could inform patient care and improve treatment and recovery, and neuropsychological rehabilitation strategies through the knowledge gained in studying a more robust, diverse and larger participant sample size. Further research is needed to gain knowledge in the neurocognitive impairments on mental health, academics, and overall quality of life related to moyamoya disease (Ball et al., 2016). Future studies should also consider the individual differences and the role that socioeconomic status plays (Bartha-Doering et al., 2021; Dennis et al., 2014) in the neuropsychological and mental health outcomes of youth with moyamoya disease. Finally, mixed-methods studies will help elucidate the self-reported experiences of youth with moyamoya disease, thereby understanding their needs and informing clinical practice.

Conclusion

Neuropsychological, academic, and mental health challenges in individuals with pediatric moyamoya disease are common despite having revascularisation surgery to prevent further decline. The goal of surgical intervention is to minimize the risks of adverse clinical outcomes associated with the disease; therefore, the hope is that it decreases symptoms, risk of stroke, and improves quality of life, thus enabling youth to focus more, perform well in school, socially, and in daily life. Exploratory research is important to understand the executive functioning,

academic, and mental health challenges faced by this population as they relate to their MMD diagnosis and pediatric stroke. This thesis not only addresses a gap in the literature as it relates to the pediatric population but also provides a valuable starting point for research into this understudied population and may be one of the first to examine all these outcomes together in a cohort of Canadian pediatric moyamoya patients.

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Tables

Table 6

Correlations Matrix

Variable		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1. Age at Surgery	*r*	--																		
	N	18																		
2. MM Dx. (confirmed or presumed)	*r*	-.41	--																	
	p	.087																		
	N	18	18																	
3. Age at Stroke/ moyamoya diagnosis	*r*	.65**	-.25	--																
	p	.007	.349																	
	N	16	16	16																
4. Basic Reading	*r*	.41	-.55	.45	--															
	p	.417	.263	.367																
	N	6	6	6	6															
5. Reading Comp	*r*	-.07	-.26	-.08	.69	--														
	p	.787	.305	.767	.128															
	N	18	18	16	6	18														
6. Spelling	*r*	.04	-.19	.35	.99**	.60*	--													
	p	.899	.511	.248	<.001	.024														
	N	14	14	13	6	14	14													
7. Math	*r*	.30	-.13	.05	.96**	.47	.36	--												
	p	.272	.638	.869	.002	.077	.204													
	N	15	15	13	6	15	14	15												
8. BASC-3 Anxiety (Caregiver)	*r*	-.47	.81**	-.32	-.95	-.18	-.29	-.59	--											
	p	.204	.008	.433	.200	.651	.449	.093												
	N	9	9	8	3	9	9	9	9											

9. BASC-3 Depression (Caregiver)	*r*	-.32	.25	.30	.87	.57	.63	.33	-.03	--							
	p	.401	.517	.472	.333	.106	.068	.380	.948								
	N	9	9	8	3	9	9	9	9	9							
10. BASC-3 Ext. Prob (Caregiver)	*r*	-.64	.45	-.15	.76	.47	.13	-.05	.13	.70*	--						
	p	.064	.226	.717	.454	.199	.732	.893	.637	.037							
	N	9	9	8	3	9	9	9	9	9	9						
11. BASC-3 Int Prob (Caregiver)	*r*	-.54	.55	-.11	.33	.60	.35	.06	.40	.81**	.84**	--					
	p	.138	.122	.793	.788	.085	.357	.881	.225	.009	.004						
	N	9	9	8	3	9	9	9	9	9	9	9					
12. BASC-3 BSI (Caregiver)	*r*	-.75*	.33	-.14	-.09	.26	-.06	-.31	.16	.53	.84**	.63	--				
	p	.020	.387	.738	.942	.493	.887	.412	.681	.143	.005	.068					
	N	9	9	8	3	9	9	9	9	9	9	9	9				
13. BASC-3 Anxiety (Self)	*r*	.20	.09	-.93	1.00**	.69	-.17	.38	.15	-.12	.40	.40	.22	--			
	p	.747	.977	.066	.	.201	.784	.529	.816	.855	.505	.503	.726				
	N	5	5	4	2	5	5	5	5	5	5	5	5	5			
14. BASC-3 Depression (Self)	*r*	.30	-.53	-.64	1.00**	.79	.003	.50	-.31	-.52	.09	.003	.12	.83	--		
	p	.629	.361	.359	.	.114	.996	.387	.609	.368	.887	.996	.851	.085			
	N	5	5	4	2	5	5	5	5	5	5	5	5	5	5		
15. BASC-3 Int Prob (Self)	*r*	.55	-.35	-.65	1.00**	.76	.24	.75	-.15	-.45	-.05	.06	-.20	.88*	.89*	--	
	p	.335	.567	.355	.	.140	.703	.146	.804	.446	.941	.925	.752	.046	.041		
	N	5	5	4	2	5	5	5	5	5	5	5	5	5	5	5	
16. BASC-3 ESI (Self)	*r*	.71	-.58	-.48	1.00**	.59	.24	.81	-.47	-.72	-.29	-.27	-.28	.74	.88*	.94*	--
	p	.182	.306	.520	.	.297	.699	.098	.419	.168	.642	.658	.652	.153	.048	.017	
	N	5	5	4	2	5	5	5	5	5	5	5	5	5	5	5	5
	r	-.85**	.70*	-.27	-.99	-.21	-.40	-.80*	.51	.67	.85**	.61	.83*	-.14	-.43	-.58	-.72	--
	p	.001	.017	.452	.084	.540	.290	.010	.199	.067	.008	.109	.011	.825	.467	.303	.170	

17. BRIEF2 BRI (Caregiver)	*N*	11	11	10	3	11	9	9	8	8	8	8	8	5	5	5	5	11	
18. BRIEF2 ERI (Caregiver)	*r*	-.30	.52	.35	-1.00*	-.10	-.42	-.87**	.50	.75*	.80*	.61	.85**	-.13	-.42	-.58	-.71	.63*	--
	p	.378	.103	.326	.010	.767	.262	.002	.211	.031	.017	.108	.008	.829	.479	.305	.183	.039	
	N	11	11	10	3	11	9	9	8	8	8	8	8	5	5	5	5	11	11
19. BRIEF2 CRI (Caregiver)	*r*	-.37	.20	-.33	-.58	-.05	-.81**	-.68*	.08	.25	.54	.29	.81*	.30	.27	-.06	-.07	.50	.33	--
	p	.260	.561	.355	.610	.876	.008	.045	.848	.557	.167	.495	.016	.622	.658	.926	.916	.116	.325	
	N	11	11	10	3	11	9	9	8	8	8	8	8	5	5	5	5	11	11	11

Note. MM Dx. = Moyamoya diagnosis. BASC-3 = Behavior Assessment System for Children, Third Edition; Ext. Prob = Externalizing problems; Int. Prob = Internalizing problems; BSI = Behavioral Symptoms Index; ESI = Emotional Symptoms Index; BRIEF2 = Behavior Rating Inventory of Executive Function, Second Edition; BRI = Behavior Regulation Index; ERI = Emotion Regulation Index; CRI = Cognitive Regulation Index. *$p < 0.05$. **$p < 0.01$.