Effects of Perinatal Stroke on Executive Functioning in Children

by

Wan Qing Li

A thesis submitted in partial fulfillment of the requirements for the degree of

Master in Education

in

SCHOOL AND CLINICAL CHILD PSYCHOLOGY

Department of Educational Psychology

University of Alberta

© Wan Qing Li, 2018

Abstract

Background: Individuals with childhood stroke often experience neurological injury that manifests as lifelong cognitive and behavioural impairment; however, research is scarce regarding the neurobehavioural outcomes of children with perinatal stroke. One important aspect of neurobehavioural functioning and cognitive development is executive functioning (EF). EF is predictive of functional life outcomes across many domains, of which include social and cognitive development, and behavioural, emotional, and mental health. EF is poorly understood in the childhood stroke population, and particularly in those with perinatal stroke (which occurs during pregnancy or within the first month after birth).

Goals: The objectives of this research project were to: 1) elucidate the EF profiles of children with perinatal stroke from a cool and hot EF model, and 2) describe the association between demographic and clinical factors associated with EF outcomes following stroke.

Participants: Eighteen children aged 6-16 with a diagnosis of perinatal stroke were recruited through the Alberta Perinatal Stroke Project (APSP) in Edmonton, Alberta. Participants were identified through the IRB-approved APSP stroke registry or by patient care clinics of pediatric neurologists.

Method: Children underwent a neurobehavioural assessment, which was a measure of cool EF outcomes. Parents/guardians completed behavioural rating measures regarding their child's EF in real-life situations, which was a measure of hot EF outcomes. Additionally, parents/guardians also filled out questionnaires that captured the child's demographic background (age, sex, ethnicity, and family socioeconomic status) as well as medical characteristics (lesion size, lesion location, epilepsy presence).

Results: On measures of cool EF, children with perinatal stroke were more impaired than the normative sample on almost all measures, including Animal Sorting, Response Set, Design Fluency, and Inhibition-Naming, Inhibition-Inhibition, and Inhibition-Switching (all $p < 0.05$). Auditory Attention was not significantly impaired in the perinatal stroke group. With regards to measures of hot EF, children with perinatal stroke were rated as significantly more impaired than the normative sample on domains of Shift, Working Memory, Task-Monitoring, Organization/Planning, and the Cognitive Regulation Index (all $p < 0.05$). Male children and children with a history of epilepsy demonstrated worse performance on several cool EF measures; age did not have a significant impact. At the group level, children with perinatal stroke performed within the low-average range on measures of global intellectual functioning (IQ), which was significantly lower than the normative population. Additionally, children with perinatal stroke who had a global IQ score in the below-average range had significantly worse EF outcomes than those with global IQ scores in the average range.

Conclusions: Children with perinatal stroke demonstrated significantly more deficits than the normative population on measures of cool and hot EF. Additionally, children who were male and/or had comorbid epilepsy had more impairments in cool EF domains.

Preface

The research project, of which this thesis is of a part, received research ethics approval from the University of Alberta Health Research Ethics Board, Project Name: Neurobehavioral Outcomes of Children with Perinatal Stroke, HREB No. Pro00066087, DATE ETHICS APPROVAL WAS GRANTED.

This project is part is part of a larger research initiative called the Alberta Perinatal Stroke Project, led by Dr. Adam Kirton at the University of Calgary, with Dr. Carmen Rasmussen being the lead investigator at the University of Alberta. The data analysis and concluding analysis are my original work, as well as the literature review and introduction.

Acknowledgements

This thesis is an accumulation of the interactions I have had with study participants and their families; the edifying meetings with my supervisors; and the hours I have spent in front of my computer, pondering and writing. Over the past two years, I have been part of an amazing interdisciplinary team, a team that has passed on their research knowledge to a little fish (me!) who was starting out in a bigger pond. This thesis is not just a product, but rather a process; through this process, I was supported by incredible individuals who I wish to acknowledge.

I would first like to thank my supervisors, Dr. Carmen Rasmussen and Dr. Jacqueline Pei. Carmen—I am grateful for your continued guidance, encouragement, and careful scrutinization of my work (as my eye for detail can be improved). My growth as researcher is only possible because you provided me an opportunity to work on a project you had built through your previous hard work. Jacquie—you have always been a source of strength and support, both academically and emotionally. You have helped me develop as a student, a researcher, and a person, and I feel assured by your continual confidence in my abilities, even when others had their doubts. I'd also like to thank Dr. Lisa Smithson, who has been my unofficial third supervisor. Additionally, I want to thank Dr. Mandhane, Dr. Tamana, and Ms. Chikuma from CHILD lab for providing me with statistical and career advice. Finally, I would like to thank Dr. Christina Rinaldi for generously offering her time and support as a member of my thesis committee.

Outside of school, I have experienced the love and guidance from several sources. I thank God for everything I have in this life. My mother, who has been my rock and my inspiration through and through. Es, my comedian and icon. Ian, my Borat, financier, and #1 shoulder to cry on—thank you for pushing me towards being a better person, even though it is tough sometimes.

I also want to thank my pre-program friends (Cherry, Moses, and Margot), as well my sisters of the school and clinical child psychology program.

Finally, I am grateful for all the families that were involved in the research project; your contribution means the world to the lab, and also to the futures of children and families for generations to come. I am also indebted to Canadian Institutes Health Research, the University of Alberta, and Women and Children's Health Research Institute for their generous funding.

Table of Contents

List of Tables

List of Figures

Introduction

Stroke is one of the leading causes of mortality in children under the age of 18 years across North American and Europe (Benjamin et al., 2017; Lynch, Hirtz, deVeber, & Nelson, 2002; Murphy, Xu, Kochanek, Curtin, & Arias, 2017). Newborns less than one month of age are 17 times more likely to experience an episode of stroke in comparison to older infants and children (Wu, Lynch, & Nelson, 2005). One type of stroke that occurs in childhood is perinatal stroke, and it is defined as a localized, cerebrovascular event that takes place between 20 weeks gestation and 28 days of life (Raju, Nelson, Ferriero, & Lynch, 2007). Perinatal stroke is estimated to occur between 1 in 2,800 to 5,000 in live births, which makes it one of the leading causes of neurological injury in children (Chabrier, Husson, Dinomais, Landrieu, & Nguyen The Tich, 2011; Nelson, 2003; Novak, Hines, Goldsmith, & Barclay, 2012; Sigurdardottir et al., 2010).

Of the children who survive perinatal stroke, the majority experience pronounced life-long physical disability that is often comorbid with cognitive, linguistic, and/or sensorimotor impairments as a result of the neurological damage (Bosenbark, Krivitzky, Ichord, Jastrzab, & Billinghurst, 2018). Although perinatal stroke is a major contributor to chronic neurological disability, much is unknown about its presentation and severity of long-term cognitive outcomes which requires comprehensive assessments and long-term follow-up (Murias, Brooks, Kirton, & Iaria, 2014). Most researchers examining cognitive outcomes in patients with perinatal stroke focuses on intellectual functioning, with mixed conclusions: some researchers report little to no impairment whereas others report significant delays (Hajek et al., 2014; Murias et al., 2014). Few researchers studying perinatal stroke patients have investigated neuropsychological aspects of cognitive functioning, including executive functioning (EF), an important predictor of

functional life outcomes. EF is made up of cognitive skills that are necessary for the successful completion of goal-oriented and/or highly complex activities (Anderson, 1998). Outcomes that are often examined by researchers in EF literature include the ability to successfully carry out activities of daily living (Jefferson, Paul, Ozonoff, & Cohen, 2006), academic performance and classroom engagement (Brock, Rimm-Kaufman, Nathanson, & Grimm, 2009; van der Sluis, de Jong, & van der Leij, 2007), as well as engagement and maintenance of social relationships (Moriguchi, 2014). Unfortunately, research on cognitive outcomes of patients with perinatal stroke are based on small samples that use varied tests (with different normative samples), mixed populations that included other diffuse injuries, and inconsistent diagnostic protocols. Additionally, there are no evidence-based practices that address the sequelae of neuropsychological deficits. Thus, the primary aim of this present study is to investigate and describe EF outcomes in children following perinatal stroke.

Definition and Epidemiology

Stroke is defined as a cerebrovascular event that causes a disruption of blood supply to the brain, which results in an acute disturbance in central nervous functioning (Jacobson, Marcus, & Pugsley, 2018). Strokes can be broadly categorized as ischemic or hemorrhagic (Amlie-Lefond, Sébire, & Fullerton, 2008). An ischemic stroke is defined by infarction (i.e., death of a tissue; Jacobson et al., 2018), which is caused by lack of blood supply to a localized area of the brain for a certain period of time. A hemorrhagic stroke is defined as an infarction due to intracerebral or subarachnoid bleeding (Amlie-Lefond et al., 2008).

Perinatal stroke. Ischemic strokes can be further classified using three additional variables: timing, symptomaticity, and location/type of vessel affected (Kirton & deVeber, 2006). The first variable is timing, which refers to the developmental time frame at which the

stroke occurs. Perinatal stroke falls under the broader classification of pediatric stroke, which refers to strokes that occur from in utero to 18 years of age (Kirton & deVeber, 2009). Perinatal stroke applies to events that occur between 28 weeks gestation to the first month of life, and it overlaps with fetal strokes which occur between 8 weeks gestation to delivery (Lynch et al., 2002; Nelson & Lynch, 2004). Neonatal strokes apply to events that occur anytime from birth to 28 days gestation (Kirton & deVeber, 2009). Childhood stroke apply to events that occur between 1 month and 18 years of age (Amlie-Lefond et al., 2008; Gordon, 2007; Lynch et al., 2002), and the term has been further subdivided into early childhood stroke (29 days to 5 years) and late childhood stroke (5 to 18 years; Westmacott, Askalan, Macgregor, Anderson, & deVeber, 2010).

The second variable is symptomaticity, which refers to timing of when symptoms appear. Perinatal stroke presents with a wide range of possible symptoms (Lynch et al., 2002). In particular, symptoms related to perinatal strokes may not be readily brought to medical attention until preferential use of a limb is observed, developmental milestones are delayed, or when seizures occur (Hartel, Schilling, Sperner, & Thyen, 2004; Nelson, 2007). However, when motor functions are not impacted, diagnoses may be further delayed. Since symptoms often emerge when cognitive demands increase, deficits are more readily observed in school settings (Westmacott, MacGregor, Askalan, & deVeber, 2009). Thus, this group of stroke is always or often diagnosed retrospectively using neuroimaging, and they are classified as presumed perinatal stroke (Kirton & deVeber, 2013).

The third variable is location, which refers to the type of blood vessel affected: artery or vein. Arterial ischemic events refers to a blockage or closing of blood vessel (i.e., occlusion) which is presumably due to a blood clot (i.e., thrombosis), fat globule, or gas form (i.e.,

embolism) in the cerebral arteries (Amlie-Lefond et al., 2008; deVeber, MacGregor, Curtis, & Mayank, 2000; Kirton & deVeber, 2006, 2009). Venous infarctions following sinovenous thrombosis (usually hemorrhagic) refers to an occlusion of cortical or deep cerebral veins/venous sinuses, which is the venous system dedicated to draining blood from the brain (Amlie-Lefond et al., 2008; Kirton & deVeber, 2006; Pappachan & Kirkham, 2008).

With the progressive advances in neuroimaging technology, the detection and identification of pediatric stroke has improved drastically (deVeber, Roach, Riela, & Wiznitzer, 2000). Recent estimates suggests that a stroke episode occurs in 1 in 2,500 to 4,000 live births for neonates (Agrawal, Johnston, Wu, Sidney, & Fullerton, 2009), and perinatal stroke is estimated to occur in 1 per 4,000 live births (Lynch et al., 2002; Mackay & Gordon, 2007). As such, cerebrovascular disorders have become one of the top 10 causes of mortality and neurological disability in children, and especially in those younger than one year of age (Lynch et al., 2002).

Etiology and clinical presentation of perinatal stroke. The four clinical presentations of perinatal stroke are as follows: neonatal arterial ischemic stroke (NAIS), cerebral sinovenous thrombosis (CSVT), presumed perinatal ischemic stroke (PPIS) and periventricular venous infarction (PVI; Kirton & deVeber, 2013). For this study, the discussion will focus on perinatal ischemic stroke syndromes, which include NAIS, PPIS, and PVI.

NAIS. This subgroup of perinatal stroke patients are classified as having NAIS, which is the most commonly occurring form of perinatal stroke (Kirton & deVeber, 2009; Kirton & deVeber, 2013). Approximately 60% of children are symptomatic in the first 3 days of life (Raju et al., 2007). These symptoms usually appear as focal or generalized seizures, which may be accompanied by signs of neurological damage (Raju et al., 2007). The presence of an acute

arterial infarct is confirmed 7-10 days preceding the event using magnetic resonance imaging (MRI), a popular neuroimaging technique. NAIS are marked by the occlusion of a cerebral artery, caused most often by a blood clot in an intracranial or extracranial vessel, heart, or placenta which travels to the brain to disrupt blood flow (Lynch & Nelson, 2001). The disruption of blood flow leads to cell death, which can lead to primary and secondary cell death. Primary cell death occurs when cells do not receive the necessary oxygen and glucose (i.e., energy sources), which is normally transported through blood (Werner & Engelhard, 2007). Secondary cell death refers to the harmful biochemical reactions that are produced by as a result of disrupted blood flow that a product of the body switching to anaerobic metabolism due to the energy deficient state (e.g., cerebral edema, excitatory neurotoxicity, etc.) which may perpetuate further energy loss (Perlman, 2006). Depending on the severity of energy loss, these effects are associated with adverse neurodevelopmental outcomes at 1 and 4 years (Roth et al., 1997).

PPIS. Of the remaining 40% of children who are asymptomatic at birth, the emergence of symptoms may occur at four to eight months of age (Kirton, deVeber, Pontigon, Macgregor, & Schroff, 2008). These symptoms may present as motor impairments (e.g., preferential use of hands or legs), delay of developmental milestones, cognitive deficiencies, or seizures (Golomb, 2009). Thus, this subset of stroke presentations is labeled as PPIS, due to the uncertainty surrounding time of injury which can only be confirmed retrospectively through neuroimaging. PPIS include both arterial presumed perinatal ischemic stroke (APPIS) and PVI syndrome, which manifest through different clinical presentations (Kirton et al., 2008). APPIS is defined by a focal infarction in an artery and is likely to have occurred at term (Kirton, Shroff, Pontigon, & DeVeber, 2010). According to MRI scans, NAIS and APPIS are produced from the same process of disease progression, with only timing and symptomaticity (i.e., more seizures and non-motor

delays in APPIS cases) differentiating the diagnoses (Kirton et al., 2010). However, it should be noted that this difference may be due to selection bias: symptomatic children are the only ones undergoing neuroimaging for stroke detection (Kirton et al., 2010).

PVI. PVI is defined by a remote focal infarction in the subcortical white matter of the periventricular region, and is likely to have occurred prior to 34 weeks gestation (Kirton & deVeber, 2009). At 34 weeks gestation, the germinal matrix (i.e., highly vascular region of prenatal and premature brain located beneath the lateral ventricle) is prone to hemorrhaging (Mong & Pollock, 2011). The hemorrhage is a product of obstruction in the medullary veins that support the draining of blood from the periventricular region, which leads to an infarct (Kirton & deVeber, 2009). Second to APPIS, PVI is the most commonly occurring subtype of PPIS (Kirton et al., 2008).

Diagnosis of the PPIS subtype is usually confirmed through radiographic, neuroimaging techniques, such as MRI and computed tomography (CT) (Kirton & deVeber, 2009). The acuity with which diffused-weight MRI determines the location and timing of the stroke makes it currently the gold standard among imaging techniques (Nelson & Lynch, 2004).

Risk Factors. The causes of perinatal stroke are often unknown, although several risk factors have been identified in the literature (Ilves et al., 2016; Lynch et al., 2002; Nelson & Lynch, 2004). Maternal and fetal factors are among the most common risk factors, and they include disorders related to the placenta, cardiac system (particularly congenital heart disease), thrombotic abnormalities, infections, drugs, and complications during birth (Chalmers, 2005; Ilves et al., 2016; Lynch, 2009; Nelson & Lynch, 2004; Raju et al., 2007). Additionally, the risk factors may have differential impact on the types of perinatal stroke (Kirton et al., 2010). Compared to children with PVI, those born with arterial stroke are more likely to be delivered

through medically-assisted methods, require neonatal resuscitations, as well as experience greater complications during birth (Ilves et al., 2016).

Cognitive Outcomes in Perinatal Stroke

Perinatal stroke is a one of the leading causes of long-term neurological injury (Bemister, Brooks, Dyck, & Kirton, 2014). The injury can result in in cerebral palsy, sensory- and motor-impairments, epilepsy, developmental delay, and emotional and behavioural problems (Bosenbark et al., 2018; Golomb, 2009; Raju et al., 2007; Sreenan, Bhargrava, & Robertson, 2000). With regards to cognitive outcomes, children with perinatal stroke are at risk of developing cognitive deficits that are likely to be reflected in linguistic and spatial impairments (Kirton & deVeber, 2013; Murias et al., 2014; Nelson & Lynch, 2004). Some researchers have demonstrated that cognitive outcomes may be affected by lesion size and location (Kirton et al., 2008; Lee et al., 2005). However, predicting perinatal stroke outcomes at diagnosis is rather limited. In most cases, maternal health and pregnancy is normal. Over the long-term, children with perinatal stroke may experience anything from typical neurological functioning to severe quadriplegia (Lynch et al., 2002). Outcomes may also vary across perinatal stroke subtypes. For example, motor impairments are found in all stroke types, but non-motor outcomes such as cognitive impairments and behavioural problems are more commonly found in children with cortical arterial strokes (Kirton et al., 2008).

Researchers studying cognitive outcomes in children with perinatal stroke have generally focused on global intellectual functioning, as measured by standardized tests of intelligence (IQ). In some studies, children with perinatal stroke perform within the average range on measures of IQ (Hetherington, Tuff, Anderson, Miles, & deVeber, 2005; Ricci et al., 2008). Others have found that children with perinatal stroke have significantly lower (i.e., low average range) global

intellectual functioning than the normative sample (Hajek et al., 2014; Hartel et al., 2004; Westmacott et al., 2009, 2010). Within the different domains of global intellectual functioning, performance-based skills (i.e., hands-on and visual-spatial tasks) are often delayed in children with perinatal stroke compared to health controls, while verbal-based skills are not affected. This pattern of performance may be due to the time sensitivity of performance-based tasks, which poses as a challenge for those with motor deficits (Hartel et al., 2004; Muter, Taylor, & Vargh-Khadem 1997; Vargha-Khadem, Isaacs, van der Werf, Robb, & Wilson, 1992). This suggests that the use of global IQ scores as assessment measures in this population may not be sensitive enough to detect specific cognitive deficiencies and strengths (Chabrier et al., 2011).

It has been suggested that problems within intellectual domains become more apparent when children with perinatal stroke reach school-age (Chabrier et al., 2011), and with age their impairments become increasingly more pronounced compared to the normative population (van Buuren et al., 2013; Westmacott et al., 2010). Westmacott and colleagues found that IQ scores at preschool ages were at the Average range; however, as the children became school age, their IQ scores were lower than their school-aged peers (Low average range), which suggested that the children's abilities were failing to keep up with that of their peers (2009). In contrast, Ballantyne and colleagues found that children with perinatal stroke demonstrated stable performance on IQ measures even as they aged, which suggests that their ability remained constant across time (Ballantyne et al., 2008). Future researchers should focus on expanding the sample size and age groups, and use cognitive measures that allow for cross-study comparisons. The complex processes involved in neurodevelopment make long-term outcomes of children with perinatal stroke difficult to predict, although few studies have shown that the impact on cognitive functioning is modulated by the location, size, and timing of the stroke event (Gil, 2003;

McLinden, Baird, Westmacott, Anderson, & deVeber, 2007; Westmacott et al., 2010). Since the injury occurs at an early stage of brain development, there is debate as to whether this results in more favourable outcomes compared to individuals who experience stroke at a later age. Although some researchers report no evidence of increasing gaps in cognitive functioning over time (Ballantyne et al., 2008), others have found children with perinatal stroke have increasing difficulty with keeping with their same-aged peers (Westmacott et al., 2009). As such, researchers in pediatric neurology debate which model of cognitive development is the best fit for this area of study: *plasticity* or *early vulnerability*.

Plasticity model. Proponents of the plasticity model argue that young children are capable of functional reorganization in their brain. This comes from evidence that the physiology and anatomy of the brain have greater capacity for modification in early life, and the functions of the damaged tissues are shunted to that of healthy tissues (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005). This rests on the assumption that immature brain lacks specialization, and can therefore reorganize its anatomy and corresponding functions to adapt to insults (Anderson et al., 2009). This idea was born from Margaret Kennard's work on monkey models: infant monkeys had fewer motor impairment than adult monkeys when both parties received comparable lesions in the sensorimotor cortex (Kennard, 1938; 1942). This phenomenon became known as the "Kennard Principle", and it based on Kennard's observations in the monkey model: in comparison to mature brains, immature brains experience lesser degree of structural damage and fewer functional impairments due to its stronger recovery capabilities (Anderson et al., 2005). This pattern of findings has been reported in behavioural, cognitive, and language outcomes studies on children who have experienced early brain injury (as reviewed in Anderson,

Spencer-Smith, & Wood, 2011). Therefore, outcomes should reflect fewer impairments in those who have had early life injuries compared to older children and adults with comparable injuries.

Vulnerability model. In contrast to the plasticity model, supporters of the vulnerability model suggest that immature brains are susceptible to greater damage than more developed brains. The vulnerability model posits that functional reorganization may be more harmful than helpful for the individual, since the brain lacks the necessary cerebral structures devoted to performing functions that mature at a later date (Chapman, Max, Gamino, McGlothlin, & Cliff, 2003). Thus, cognitive functions that are contingent on the proper development of specific brain regions will be irreversibly impaired following the stroke (Anderson, et al., 2005; Long et al., 2010; Westmacott et al., 2010). The cumulative effects of early brain injury not only results in challenges acquiring skills at the time of injury, but it also interferes with the child's ability to build upon these skills in the future (Anderson et al., 2005). Although there is evidence that the immature brain is able to undergo neural restitution (i.e., neural regrowth and/or anatomical reorganization; Giza & Prins, 2006, Kolb, Teskey, & Gibb, 2010), full recovery from the injury is limited by improper formation of neural connections (Stein & Hoffman, 2003; Kolb et al., 2011) and/or the "crowding effect". The "crowding effect" refers to the phenomenon where following functional reorganization, healthy tissues that subsume the task of the damaged tissues becomes "functionally overloaded", resulting in the decline of abilities that are normally executed by the healthy tissue (Aram & Eisele, 1994; Vargha Khadem et al., 1992). For example, in the perinatal stroke population, certain skills such as language are relatively spared following injury to the left hemisphere, however, this is also associated with the decline of sophisticated visuospatial skills (Everts et al., 2008; Lidzba, Staudt, Wilke, & Krageloh-Mann, 2006).

Currently, researchers in the field of perinatal stroke tend to work from the vulnerability model. Children who have experienced a lesion in the first year of life have consistently demonstrated the poorest functional outcomes (Anderson et al., 2009). When comparing outcomes following stroke in pediatric and adult populations, adults tend to display more lateralized deficits depending on lesion location and they struggle to regain lost skills (Lidzba & Krageloh-Mann, 2005; Montour-Proulx et al., 2004). However, in children with unilateral brain damage, the effects of such insults are not found; instead functional reorganization occurs resulting in the "crowding effect" (Anderson et al., 2009). Researchers suggest that the greatest impairment is usually seen at the extreme ends of the age group (i.e., the young and the old), with those in the intermediate age group demonstrate the best tolerance for brain damage due to neuroprotective factors, such as ischemic tolerance (i.e., endogenous mechanism that protects neurons against ischemic damage; Schaller, 2007). Based on rat models, those who experienced stroke during their second year of life had the best outcomes, and those who experienced stroke in the perinatal period have the worst outcomes (Kolb & Gibb, 2000). In the pediatric stroke population, those who have had stroke in early childhood (age 1-6 years) had fewer performance delays than children with stroke onset in neonatal and early childhood (age <1 year), as well as those in later childhood (age >6 years) (Allman & Scott, 2013). In particular, children who experience injury in the neonatal stage have outcomes that may be further modulated by plasticity that follows.

Predictors of Cognitive Outcomes

There are several factors that have been associated with the cognitive deficits that observed in the perinatal stroke population. Outcomes in children tend to vary across studies due

to differences in stroke type, assessment measures, and demographics of the population. Thus, for some factors there remains uncertainty about the role it plays in impairment.

Sex. There have been no sex differences reported on measures of cognitive performance in children with perinatal stroke (McLinden et al., 2007; Muter et al., 1997). However, the impairments reported in these studies appear to be more prevalent in males than in females.

Lesion location (anatomy and lateralization) and lesion size. In the perinatal stroke population, lesions have been characterized by its 1) anatomic location (cortical vs. subcortical vs. combined) and 2) laterality (right hemisphere vs left hemisphere vs bilateral; Bosenbark et al., 2017). Findings are mixed regarding the impact of lesion location on cognitive outcomes in children with perinatal stroke. Kirton and colleagues found that cognitive and behavioural deficits were more likely to be found in children with middle cerebral arterial infarctions (cortical lesion) compared to those with subcortical lesion (2008). Westmacott and colleagues found that patients who had subcortical lesion during the perinatal period experienced particularly adverse cognitive outcomes (compared to those who experienced lesions in childhood). In typical brain development, subcortical structures tend to precede the development of cortical structures, making it more vulnerable to damage in the perinatal period (Pfefferbaum et al., 1994). Since the development of the cortical structures are contingent on that of subcortical structures, the functioning of cortical structures may be impaired resulting in deficits in the higher-order cognitive abilities (Chapman & McKinnon, 2000).

There has been no consistent relationship established between lesion laterality and cognitive performance (Ballantyne et al., 2008; Chapman et al., 2003; Everts et al., 2008; Goodman & Yude, 1996; Ricci et al., 2008; Vargha-Khadem et al., 1992; Westmacott et al., 2009; Westmacott et al., 2010). However, when multiple brain regions are involved in stroke, a

larger area is impacted, making it not uncommon to see relatively poorer outcomes in this group (Hetherington et al., 2005; Westmacott et al., 2010). Children with bilateral lesions involving both cortical and subcortical regions have demonstrated worse performance on measures of cognitive functioning compared to those with no lesion or restricted lesion (Hajeck et al., 2013; Hetherington et al., 2005; Westmacott et al., 2010). In contrast, other researchers have found no differences in cognitive functioning between children with differing lesion size (Ballantyne et al., 2008; Ricci et al., 2008).

Epilepsy and seizures. Epilepsy following stroke is more common in children than in adults (Ganesan et al., 2000). Seizures are reported to occur in approximately half of all children with neonatal stroke (Trauner, Chase, Walker, & Wulfeck 1993), and it is a common symptom of ischemic stroke subtypes (Chabrier et al. 2011). Approximately 60% of children with PAIS will experience recurrent focal seizures in the first 3 days of life (Bosenbark et al., 2017). Epilepsy and seizures negatively impact subsequent cognitive development since they limit the brain's plasticity and dampen recovery (Ballantyne et al., 2008; Golomb et al., 2006). Some researchers have found that children with perinatal stroke who have experienced seizures associated with early cerebral injury are more likely to have cognitive deficits (supported by lower performance on measures of general intellectual functioning) compared to those with pediatric stroke and those who do not experience recurring seizures (Ballantyne et al., 2008; Hartel et al., 2004, Murias et al., 2014; van Buuren et al., 2013). However, Fox and Fullerton have argued that it is unclear whether seizures result in worse cognitive outcomes, for it may be due the use of antiepileptic medication and/or seizures may be an indicator of more severe brain insult (2010).

Executive Function (EF)

Executive functions (EF) are a group of cognitive functions comprised of a heterogenous set of skills, including inhibitory control, cognitive flexibility, and working memory (Anderson, 2008; Gioia, Isquith, Kenworthy, & Barton, 2002; Novak, Hines, Goldsmith, & Barclay, 2012; Weierink, Vermeulen, & Boyd, 2013). These skills work together to support higher-order, metacognitive processes that are designed to help carry out problem-solving behaviours and the completion of future-oriented plans (Anderson, 1998). EF develops at a rate that appears to parallel that of the prefrontal cortex (PFC)—EF improves most quickly during preschool (Zelazo et al., 2017) and continues to develop into young adulthood (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001). EF is an important predictor of life outcomes including academic performance (Bull & Scerif, 2001; Knouse, Feldman, & Belvins, 2014), risk-taking and health (Albert & Steinberg, 2011; Cauffman et al. 2010; Seepage et al., 2009), and social relationships (Ellis, Weiss, & Lochman, 2009; Hay, Payne, & Chadwick, 2004; Zorza, Marino, & Mesas, 2016).

Traditionally, EF has been studied from a cognitive perspective: EF was defined by an individual's ability to engage in attentive control, working memory, and cognitive flexibility in affectively neutral situations (Zelazo & Muller, 2002). Cool EF conforms to the traditional cognitive definition of EF, whereas *hot EF* is a form of reward or emotion-mediated cognition in that it relies on inhibition and emotional control (Zelazo & Muller, 2002). The "cool" component of EF is considered as relatively more logic- and reason-based form of cognitive processing, and it is used in abstract, decontextualized settings (Chan, Shum, Toulopoulou, & Chen, 2008; Grafman & Litvan, 1999). Cool EF draws upon on skills such as attention, working memory, planning, inhibition, and shifting set (Miyrake et al., 2000). Cool EF has been loosely mapped onto the dorsolateral prefrontal cortex (DL-PFC) and dorsal regions of the caudate and putamen,

which are involved in decision-making, problem-solving, and reasoning (Chan et al., 2008). Neuropsychological assessments, including the Developmental Neuropsychological Assessment, Second Edition (NEPSY-II; Korkman, Kirk, & Kemp, 2007) include many of the classic cool EF measures, such as card sorting and self-ordered point tasks that are measures of attention, inhibitory control, working memory, task-monitoring, and flexible rule use (Hongwanishkul et al., 2005).

In contrast to cool EF, hot EF is an emotion- and motivation-based form of cognitive processing (Zelazo & Muller, 2002). Hot EF plays an important role in social and emotional-decision decision making and delay of gratification (Zelazo & Muller, 2002). Hot EF have some shared cognitive processes with cool EF, such as inhibitory control and self-regulation (Welsh & Peterson, 2014). Like cool EF, hot EF is also mapped onto a region of the PFC, which include the orbitofrontal cortex (OFC) and ventromedial prefrontal regions (VM-PFC), which is part of the fronto-striatal system with connections to the limbic system (Zelazo & Muller, 2002). The OFC is involved in the integration of affective information, as well as in the regulation of motivated behaviour (Zelazo & Muller, 2002). Hot EF has been widely assessed using behavioural tasks, including delay gratification (e.g., Mischel, Shoda, & Rodriguez, 1989), gambling and risk-reward decision making (e.g. Bechara et al., 1994), and delay discounting (e.g. Mitchell, 1999; Prencipe, Kesek, Cohen, Lamm, Lewis, & Zelazo, 2011). An alternative tool to behavioural tasks is behaviour rating scales, such as the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) that draw upon observations of the child's behaviours and reactions to emotionally charged circumstances (Skogli, Egeland, Andersen, Hovik, & Oie, 2014). Behavioural tasks are similar to rating scales

because they are both designed to measure adaptive decision-making skills and goal-orientated behaviours for reward(s) (Welsh & Peterson, 2014).

Although hot and cool EF interact in a functional system, and the same genetic and environmental factors may play a role in shaping PFC development, there are mixed findings on correlation patterns between the two constructs (Welsh & Peterson, 2014). In younger children (aged 3 to 6 years), cool and hot EF have similar rates of development (as reviewed in Welsh & Peterson, 2014), which researchers have postulated to reflect the lack of specialization of the early brain (Zelazo & Carlson, 2012). In school-aged children and adolescents, hot EF has been shown to have a prolonged development compared to cool EF (Prencipe et al., 2011), Additionally, cool and hot EF are differentially correlated with measures of general intellectual functioning and temperament (Hongwanishkul et al., 2005), as well as academic achievement outcomes and behavioural problems (Brock et al., 2009; Kim et al., 2013; Thorell, 2007; Willoughby, Wirth, & Blair, 2012). In clinical samples of children with ADHD, performance on hot and cool EF measure tended to predict different symptoms (Skogli et al., 2014; Thorell, 2007). Thus, it is possible that the two types of EF are differentially impacted in children with perinatal stroke, and a unique EF profile that will emerge.

Executive functioning following perinatal stroke. At the group level, it appears that children with perinatal stroke tend to perform within the low average to average range on assessments of intellectual ability. However, these findings may not be generalizable to their EF outcomes. Research on the pediatric stroke population has revealed that children may perform extremely poor on tasks that draw on complex neuropsychological functions (De Schryver et al., 2000; Everts et al., 2008; Westmacott et al., 2009).

There are few studies that focus on EF in the perinatal stroke population. Findings are inconsistent across studies due to the "mixed" sample which includes several stroke types (e.g., both perinatal/neonatal and childhood stroke), and/or use of different neuropsychological measures. In a mixed cohort study on EF outcomes in the neonatal and pediatric stroke population (age range = 4 to 10 years; $N = 30$), Kolk and colleagues found that EF functions that belong to the cool domain (i.e., attention, inhibition, cognitive flexibility, and planning) were relatively unaffected (2011). In contrast, Hajek and colleagues found that children with perinatal and pediatric AIS (age range = 6 to 15 years; $N = 36$) performed significantly worse on measures of attentive control, response speed (via processing speed test), and inhibitory control compared to controls (2014). Similar EF deficits were also reported by Bosenbark and colleagues in their study with children with PAIS (age range = 3 to 16 years; $N = 40$), which includes both NAIS and APPIS subtypes (2016). The children were assessed on cool and hot EF domains, including attention, inhibition, verbal (word) retrieval, flexibility/shift, planning and organization, processing speed, and working memory using the NEPSY-II (Korkman, et al., 2007) and a parent rating questionnaire (BRIEF; Gioia et al., 2000). At the group level, they found that children with PAIS performed significantly worse than the normative population on all domains except for working memory (Bosenbark et al., 2018). Despite the absence of working memory deficits at the group level, the researchers found a mediating effect of age: working memory performances worsened with increasing age. The greatest impairment was observed in inhibitory control. Older participants experienced additional difficulties in the areas of attention and planning and organization; these areas of functioning could not be assessed in younger children since the scales had a restricted age range (Bosenbark et al., 2018). Attention deficit/hyperactivity disorder (ADHD)-related symptoms was also reported in almost 60% of the

participants, which is far greater than the 5% prevalence within the general population (American Psychiatric Association, 2013). Consistent with these findings, ADHD is a comorbidity in approximately half of all pediatric stroke cases (Everts et al., 2008; Max et al., 2003).

Present Study

The purpose of this study was to elucidate the executive functioning (EF) outcomes of children with perinatal stroke. Although perinatal stroke has been shown to impair cognitive development in children, research on EF outcomes is scarce and no studies to date have examined EF outcomes in the perinatal stroke population from a hot/cool model

This is the first study to explore such outcomes through a hot/cool EF model. Since EF is a strong predictor of functional outcomes, an increased understanding of EF deficits has implications in constructing targeted and generalized interventions that may address underlying needs and thereby improve outcomes in the perinatal stroke population. The research hypotheses were developed based on existing literature:

Proposed aims and hypotheses. The aims of the study were to assess and describe the executive functioning profile (EF) in children with perinatal stroke compared to normative population data, as well as examine the relationship between EF and its clinical predictors. The goals of this study are as follows:

Aim 1. To determine the hot and cool EF profile of children with perinatal stroke.

Hypothesis 1.1: Children with perinatal stroke will demonstrate the most impaired performance on measures of attention (Auditory Attention, Response Set) and inhibition (Inhibition-Naming, Inhibition-Inhibition, Inhibition-Switching; cool EF) compared to the normative population. Children with perinatal stroke will demonstrate moderate

impairment on measures of cognitive flexibility/shift, self-monitoring and planning tasks (Animal Sort, Design Fluency; cool EF) compared to the normative population.

Hypothesis 1.2: Children with perinatal stroke will perform worse than the normative population on measures of emotional regulation, as measured by the Shift and Emotional Control subscales of the parent-rating measure (hot EF). Children with perinatal stroke will not perform significantly worse than the normative population on all other subtests of the parent-rating measure (hot EF).

Hypothesis 1.3: Performance on cool EF measures of inhibition (Inhibition-Naming, Inhibition-Inhibition, Inhibition-Switching) will be significantly related to Self-Regulation and Inhibitory Control subscales on parent-ratings of hot EF.

Aim 2. To determine the association between hot and cool EF with different clinical predictors, including sex, age, and epilepsy.

Hypothesis 2.1: Sex-related effects should be null or minimal (no difference between males and females on all measures of EF).

Hypothesis 2.2: When compared to the normative population, EF impairments will become more pronounced for the perinatal stroke group relative to the normative sample with increasing age.

Hypothesis 2.3: Children with a history of seizures will demonstrate worse EF outcomes on both cool and hot EF measures compared to those who have not had a seizure episode.

Aim 3. To determine the relationship between hot and cool EF performance and general intellectual functioning.

Hypothesis 3.1: Performance on all cool EF measures will increase as general intellectual scores increase.

Hypothesis 3.2: Performance on hot EF measures of Cognitive Regulation Index (comprised of Initiate, Working Memory, Plan/Organize, Task-Monitor, and Organization of Material) will increase as general intellectual scores increase.

Methods

Participants

Eighteen children with perinatal stroke between the ages of 6 to 16 with a documented medical history of perinatal stroke participated in the current study. This study uses a case-controlled research design. Participants with perinatal stroke were identified through the Alberta Perinatal Stroke Project (APSP) registry. APSP is a multi-site, population-based research cohort based in Calgary and Edmonton, AB. For this study, participants were identified either through retrospective ascertainment, perinatal stroke programs, and/or the Canadian Cerebral Palsy Registry—Alberta. Children were selected based on the following inclusion criteria: 1) 6 to 16 years of age at the time of assessment; 2) clinico-radiographic confirmation of perinatal stroke diagnosis by a pediatric neurologist; and 3) English as a first language. The diagnosis of perinatal stroke includes children with neonatal arterial ischemic stroke (NAIS), arterial presumed perinatal ischemic stroke (APPIS), and periventricular venous infarction (PVI), which follows the subtype definitions of stroke established by National Institutes of Health (NIH) Common Data Element (Grinnon et al., 2012). Children with the following diagnoses were excluded from the present study: 1) prematurity (<37 weeks gestation at birth); 2) age greater than 17 years; 3) lack of radiologic images available for review; and 4) significant medical comorbidity, other than seizures and epilepsy. Of the possible comorbidity, these include: cerebral hemorrhage not associated with ischemic infarction (i.e., germinal matrix hemorrhage <32 weeks gestation;

hypoxic ischemic event with diffuse or bilateral infarction alone; neurodevelopmental or psychiatric conditions not explained by stroke.

Data sources. For this study, data was collected through participant demographic forms, caregiver report, and assessments of general intellectual functioning and neuropsychological functioning. During the day of testing, caregivers were asked to report on their demographic information, as well as on the neuropsychological functioning of their child. The primary data collected from this project was part of a larger study, "Neurobehavioural Outcomes of Children with Perinatal Stroke", and the aims of the study are concurrent with those of the larger study.

Demographic and health information. The following variables were collected for each participant during the day of testing: age, sex, current living situation, family health history, caregiver factors (including marital status, highest level of education, household income bracket), as well as child's medical history (including epilepsy/seizures).

General intellectual functioning. Wide Range Intelligence Test (WRIT; Glutting, Adams & Sheslow, 1999) is a measure of general intellectual functioning (IQ) for individuals aged 4 to 85 years. The WRIT assesses both verbal (Verbal IQ) and nonverbal abilities (Visual IQ), and when combined forms the general intellectual functioning score (General IQ).

Cool EF. NEPSY–Second Edition (NEPSY-II; Korkman et al., 2007a) is a standardized, neuropsychological measure designed to evaluate a variety of cognitive abilities in children aged 6 to 16 years. Specifically, NEPSY-II is used as a measure of "cold" or reasoning-based component of executive functioning (EF). The Attention/Executive Functioning subtests assess a child's ability to formulate concepts, selectively attend to stimuli, flexibly engage in mental shifts, inhibit automatic responses, as well as initiate and monitor behavior (Korkman et al., 2007b). Children were administered Animal Sorting, Auditory Attention and Response Set,

Design Fluency, and Inhibition. Across all age groups, the inter-correlations between NEPSY-II subtests indicate that it has strong construct validity. The NEPSY-II also demonstrates adequate concurrent validity with measures of intellectual functioning, criterion validity with diagnostic data, as well as divergent validity across developmental disabilities. Finally, the NEPSY-II demonstrates high inter-rater reliability (.98 to .99, Davis & Matthews, 2014).

Animal Sorting. On the NEPSY-II animal sorting task, the child is presented with eight cards, and asked to sort the cards into two groups of four according to self-initiated rules. This subtest is designed to examine a child's ability to formulate basic concepts, sort cards based on those conceptual categories, and then to flexibly shift from one concept to another. In terms of reliability coefficients for NEPSY-II animal sorting, this subtest has excellent internal consistency (.95 to .96) and good test-retest reliability (.64-.75).

Auditory Attention and Response Set. The NESPY-II auditory attention and response set is a two-part test. On both subtests, the child is instructed to touch the appropriate coloured circle when he/she hears a target word being read aloud from a list. Auditory attention is designed to examine a child's ability to sustain auditory attention, and selectively attend to auditory stimuli. Response set places new cognitive demands on the child in addition to sustained and selective auditory attention. Response set tests a child's ability to shift, maintain, and follow a new and complex set of rules. The new rules require that the child inhibits of a previously learned response, and successfully act on matching or contrasting stimuli. In terms of reliability coefficients for NEPSY-II auditory attention, this subtest had good to excellent internal consistency (.71 to .91) and good test-retest reliability (.60-.74). Response set also demonstrated good internal consistency (.88) and adequate-to-good test-retest reliability (.55-.85).

Design Fluency. On the NEPSY-II design fluency subtest, the child is presented with two pages of five dots, one in random array and the other in structured array. This subtest is designed to examine the child's ability to draw as many unique designs by connecting two or more dots. In terms of reliability coefficients for NEPSY-II design fluency, this subtest has adequate internal consistency (.59) and adequate test-retest reliability (.44-.63).

Inhibition. In the NEPSY-II inhibition subtest, the child is presented with a series of black and white shapes or arrows, for which they name aloud its shape or direction, respectively. Depending on the rules of the task, the correct response to each shape or arrow will vary. This subtest is designed to measure a child's ability to inhibit automatic responses, act upon novel rules, and to switch between a repertoire of rule-based response under time constraints. In terms of reliability coefficients for NEPSY-II inhibition, this subtest has good to excellent internal consistency (.73 to .96) and adequate to excellent test-retest reliability (.64-.94).

Hot EF. Parents completed the Behavior Rating Inventory of Executive Function, Second Edition (BRIEF-2; Gioia et al., 2000), which is a measure of EF in children aged 5 to 18 years. The BRIEF-2 includes items that may capture some aspects of "hot" or emotionally-laden EF in children. It has been associated with the appraisal of environmental cues that are linked to reward and punishment, such as learning appropriate situations to express negative emotions (Seguin, Arseneault, & Tremblay, 2007). Specifically, the BRIEF-2 is designed to capture parent/guardian observations of their child's real-world behaviours and daily executive problem-solving skills through a behavioural ratings scale.

These types of EF are reflected in the caregiver's ratings of their child's strengths and weaknesses in the areas of behaviour and emotional regulation, reasoning, flexibility, organization, self-monitoring, and working memory. BRIEF-2 correlates with other well-

validated behavioural measures of inattention, impulsivity and learning skills (CBCL, BASC-2, Conners-3, ADHD-RS-IV); it also correlates with measures of intellectual ability (RIAS, WISC-IV, WAIS-IV; Gioia et al., 2000). Although several versions of the BRIEF-2 are available, the BRIEF-2-Parent Form was selected over the self-report version since it captures a wider age range (5 to 18 years vs. 13 to 18 years). With regards to inter-rater reliability, the parent report presents with fair to moderate inter-rater correlation with teacher (r = .28) and self-report (r = .50). The BRIEF-2 also demonstrates high internal consistency (α = .80-98) and test-retest reliability (r = .82). Finally, BRIEF-2 has been used in both normative and special populations, including those with developmental or acquired neurological disorders.

Behavioral Regulation Index (BRI): The Behavior Regulation Index (BRI) measures a child's ability to monitor and regulate their behavior in an effective manner. It is comprised of the Inhibit and Self-Monitor subscales. The Inhibit subscale assesses the child's ability to resist and employ self-control over impulsive behaviours. The Self-Monitor subscale assesses the child's awareness and ability to track one's behaviour on others.

Emotional Regulation Index (ERI): The Emotional Regulation Index (ERI) measures a child's ability to regulate emotional responses and to unconsciously shift attention and cognitive strategies to respond to the changing environment. It is comprised of the Shift and Emotional control subscales. The Shift subscale assesses the child's flexibility towards changing environments or situations, and their ability to adapt accordingly. The Emotional Control subscale assesses the child's ability to regulate their emotional response in an appropriate manner.

Cognitive Regulation Index (CRI): The Cognitive Regulation Index (CRI) measures a child's ability to control and manage cognitive processes and to problem solve effectively. It is

comprised of the Initiate, Working Memory, Plan/Organize, Task-Monitor, and Organization of Material subscales. The Initiate subscale assesses the child's ability to self-start on tasks/activities, as well as independently generate ideas. The Working Memory subscale assess the child's ability to maintain and manipulate information in their mind for the purpose of completing a task/activity. The Plan/Organize subscale assesses the child's ability to anticipate future events, develop plans ahead of time to complete tasks/activities, carry out tasks in a systematic manner, and clearly communicate their understanding of idea of concepts. The Task-Monitor subscale assesses the child's ability to engage in self-check and self-correction of work during or after finishing a task. The Organization of Materials subscale assesses the child's ability to keep areas of work and play organized and orderly.

Global Executive Composite (GEC): The Global Executive Composite is a summary score that is comprised of all BRIEF-2 subscales, which provides an overview of the child's executive functioning compared to same-aged peers.

Procedure

This study was approved by the Health Research Ethics Board-Health Panel through the University of Alberta. At the time of testing, consent was obtained from all participants and their caregivers for clinical data to be used in future research. Data was collected between May 2017 and May 2018. All participants underwent testing at the Glenrose Rehabilitation Hospital, Edmonton.

Initial screening. Participants were identified through APSP or upon referral to study investigators by APSP neurologists. Parents/guardians of children who were eligible for the study had consented to being contacted for research. Parents/guardians were notified through telephone and/or email to determine their interest in study participation. Contact information for

each participant was obtained through the institutional database. In the phone call and/or email, parents/guardians were provided information about the nature of the study, neuropsychological testing, as well as information regarding informed consent and voluntary participation which is in line with ethical policies set forth by the Health Research Ethics Board-Health Panel through the University of Alberta. A telephone and/or email script was used to standardize the process.

Testing session. For the families that consented, children were assessed at the Glenrose Rehabilitation Hospital in Edmonton, AB. Participants were evaluated in a single testing session, during which short breaks were provided as need. The neuropsychological testing lasted between 120 to 180 minutes (depending on age and ability), and it was completed in a quiet room with a single administrator. Neuropsychological assessments were administered by the study coordinator/co-investigator or the supervised graduate student, after they underwent training with a registered psychologist.

Parents/guardians provided demographic information and evaluations of their child's functioning in the domains of cognition, social/emotional, academic, and behavioural development through paper and pencil rating forms. These forms were completed while their child was being assessed. Undergraduate research assistants reviewed record forms and assisted with data entry, for which they were trained under a registered psychologist.

After the testing session, children received a $5 Indigo gift card for their participation. If needed, parking fees were covered for families during their study visit, and families that drove >50km to the study site were reimbursed for gas and maintenance fees ($0.50 per km driven). Several weeks/months after the testing session, parent/guardians were provided with a summary letter that briefly stated the assessment results via email. The letter could be used to inform school and medical services, if the parents so chose to.

Statistical Analysis

Scaled scores were used for all analyses. Relevant data were transferred into a Stata data file, including coded information from the demographic form. The initial phase of data analysis included analyzing the demographic features of our sample, such as participant age, sex, and SES. Analyses were performed using Stata/SE software for Windows, Version 14.2 (StataCorp LP, College Station, TX). Data was checked for normal distribution and homogeneity of variance. To address the first study aim, we conducted one-sample t-tests with corrections for the multiple comparison made between EF outcomes in the perinatal stroke population and the normative sample (found in published, normative results) using false discovery rates (i.e., Bonferroni correction). To address the second study aim, two-tailed independent sample t-tests (corrected for multiple comparisons) and Fisher's exact test were used to assess differences in EF outcomes due to sex (male vs. female) and occurrence of seizure (present vs not present). Pearson correlation was conducted between age and EF scores. To address the final study aim, Pearson correlation analysis (corrected for multiple comparisons) was used to examine the relationship between IQ scores and EF scores. A standard score of 90-109 on the intellectual ability measure is defined as falling within the Average range. The group was subsequently divided into two groups based on the descriptive categories: (low IQ ≤ 89; high IQ > 90), and a two-tailed independent sample t-test was used to assess differences in EF scales due to IQ (low vs. high). Significance was set a $p < 0.05$ for all analyses.

Results

Sample Characteristics

Demographic and clinical characteristics. At the time of examination, the mean age of the 18 participants (9 males) was 9.5 years (SD = 3.1; range 6-15). The study cohort consisted of

mainly participants of Caucasian race (83%), were from mid to high income families (61%) and had mothers who received university/college- equivalent education (50%). With regards to clinical characteristics, 10 children were diagnosed with APPIS, 6 were diagnosed with NAIS, 2 were diagnosed with PVI. 8 children had a reported history of seizure. Demographic and clinical characteristics of the study sample are summarized in Table 1.

Table 1. Participant Demographic and Clinical Characteristics

Demographic characteristics		
Sex, n, % male	9	50%
Age at testing in years, mean, mean (SD)	9.5 years	3.1 SD
Ethnicity (Caucasian), n, %	15	83%
Mother education (university/college equivalent), n, %	9	50%
Total household gross income (>$70,000), n, %	11	61%
Clinical characteristics		
Stroke presentation, n, %		
APPIS	10	56%
NAIS	6	33%
PVI	2	11%
Seizure present, n, %	8	44%

Sample cognitive outcome compared to the normative population. A summary of neuropsychological findings and parent-report on EF outcomes are presented in Table 2. Details regarding the global results are further described.

Table 2. Summary of Cool EF and Hot EF Outcomes

Measure	Variable	Test Mean	N	Range	Sample Mean (SD)	p	Cohen's d (Effect Size)	% Clinically Significant (1.5 SD deviation from the mean)
NEPSY-II	Animal Sorting	10	11	1-13	6.09 (3.14)	0.002*	1.25	55%
	Auditory Attention	10	15	2-13	8.40 (3.68)	0.114	0.42	36%
	Response Set	10	11	1-12	7.80 (2.93)	0.033*	0.75	9%
	Design Fluency	10	11	2-11	6.91 (2.77)	0.004**	1.12	27%
	Inhibition-Naming	10	14	1-9	5.21 (2.52)	0.000**	1.90	36%
	Inhibition-Inhibition	10	12	2-11	6.17 (3.07)	0.001**	1.24	33%
	Inhibition-Switching	10	9	3-11	6.67 (2.50)	0.004**	1.33	33%
BRIEF-2	Behavioural Regulation Index	50	17	37-85	53.24 (14.64)	0.376	-0.22	29%
	Emotional Regulation Index	50	17	39-89	56.12 (13.41)	0.078	0.46	24%

	Cognitive Regulation Index	50	17	40-77	56.30 (12.06)	0.047*	-0.52	24%
	Global Executive Composite	50	17	39-83	56.41 (13.12)	0.061	-0.49	24%
WRIT	Verbal IQ	100	16	70-107	87.25 (11.81)	0.001**	1.08	25%
	Visual IQ	100	15	68-119	89.67 (14.11)	0.013*	0.73	20%
	General IQ	100	15	44-115	86.07 (13.13)	0.001**	1.06	20%

*$p < .05$; ** $p < .01$

Global Intellectual Functioning

Fifteen of the eighteen children were assessed using WRIT subtests. One child did not complete the WRIT subtests due to their inability to communicate through verbal or written methods. Two other children asked to discontinue the testing session before completing all the subtests, resulting in missing values and inability to calculate their composite scores. General IQ estimates revealed that overall functioning fell in the Low Average range (M = 86.07; SD = 13.13; range 66-115), and scores of children with perinatal stroke were significantly lower than the normative sample [t(14) = -4.11, p = 0.001, d = 1.06] (Table 2).

Executive Functioning Outcomes

NEPSY-II. Figure 1 shows the group-level neuropsychological performance test data on the NEPSY-II 7 subtests. There were different sample sizes across the subtests due to the differing age restrictions of each test. Children with perinatal stroke performed significantly lower than the normative population on nearly all subtests: Animal Sorting, Response Set, Design Fluency, Inhibition-Naming, Inhibition-Inhibition, and Inhibition-Switching (summarized in Table 2). At the group level, children with perinatal stroke did not perform significantly worse than the normative sample on Auditory Attention.

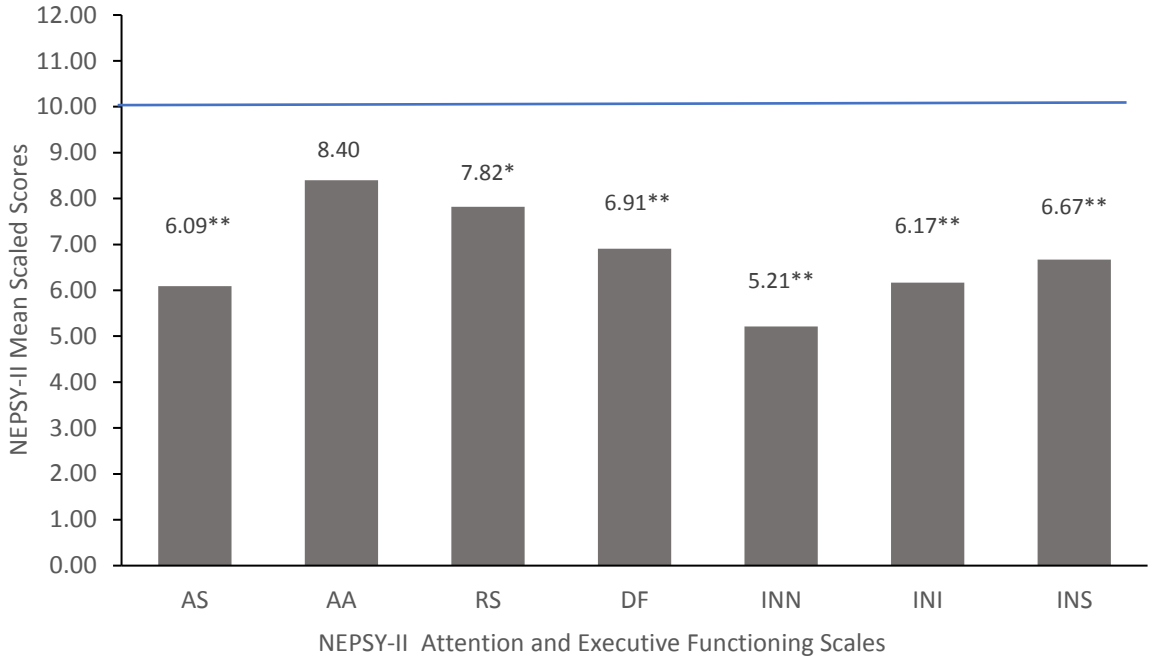

Figure 1. NEPSY-II Domain Results
AS = Animal Sorting (n=11); AA = Auditory Attention (n=14); RS = Response Set (n=11); DF = Design Fluency (n=11); INN = Inhibition-Naming (n=14); INI = Inhibition-Inhibition (n=12); INS = Inhibition-Switching (n=9). *Note*. *$p < .05$; ** $p < .01$.

BRIEF-2. Figure 2 presents the group mean T-scores for each scale, index, and composite of the BRIEF-2. In the perinatal stroke population, there were significant differences found for everyday EF domains compared to their same-aged peers, based on parent-rating: Shift, Working Memory, Task-Monitoring, Organization/Planning, and the Cognitive Regulation Index (summarized in Table 2).

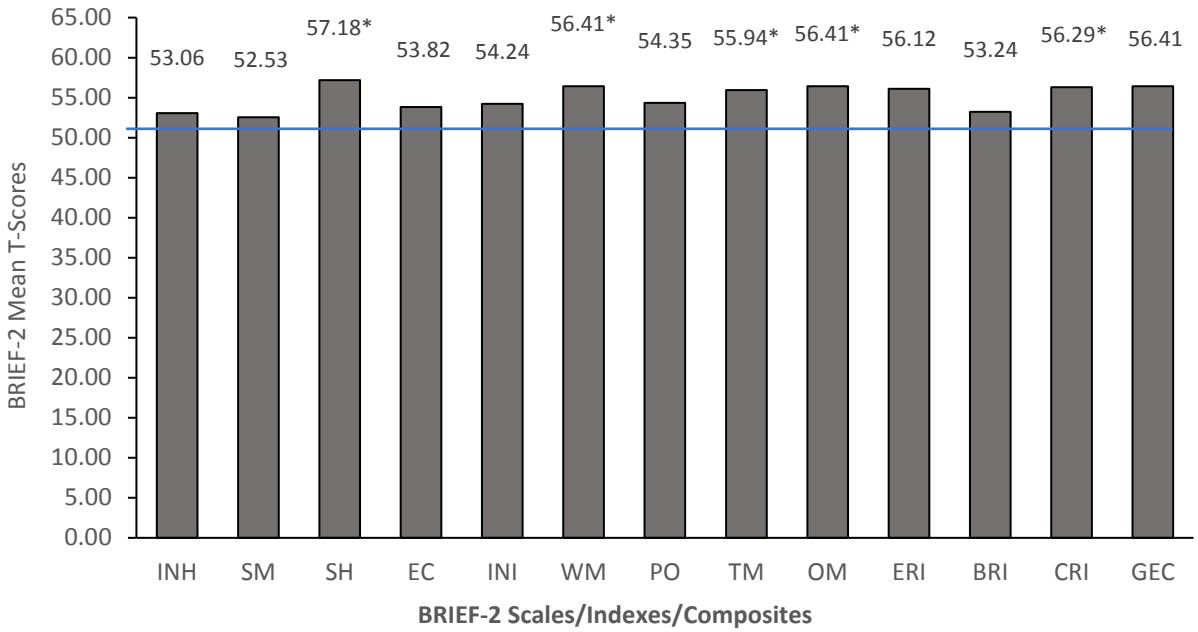

Figure 2. BRIEF-2 Domain Results
N = 17. INH = Inhibition; SM = Self-Monitor; SH = Shift; EC = Emotional Control; INI = Initiate; WM = Working Memory; PO = Plan/Organize; TM = Task-Monitor; OM = Organization of Materials; ERI = Emotion Regulation Index; BRI = Behavior Regulation Index; CRI = Cognitive Regulation Index; GEC = Global Executive Composite. *Note.* *$p < .05$; ** $p < .01$.

NEPSY-II as related to BRIEF-2. Figure 3 presents the Pearson correlation analysis between NEPSY-II and BRIEF-2 scores. Better performance on the Inhibition-Switching subtest of the NEPSY-II was associated with worse parent-ratings on four scales of the BRIEF-2: Inhibition ($r = 0.83$, $p = 0.006$); Shift ($r = 0.82$, $p = 0.007$), Behavioural Regulation Index ($r = 0.78$, $p = 0.012$), and Emotional Regulation Index ($r = 0.74$, $p = 0.022$).

Table 3. Relationship between NEPSY-II and BRIEF-2 Scores

	NEPSY-II						
BRIEF-2	Animal Sorting	Auditory Attention	Response Set	Design Fluency	Inhibition-Naming	Inhibition-Inhibition	Inhibition-Switching
Inhibit	-0.07	-0.06	-0.10	-0.25	0.26	-0.06	0.83**
Self-Monitor	-0.21	-0.16	-0.31	-0.14	0.12	-0.14	0.53
Behaviour Regulation Index	-0.10	-0.12	-0.21	-0.22	0.23	-0.09	0.78*
Shift	-0.14	-0.04	-0.16	-0.16	0.06	0.03	0.82**
Emotional Control	-0.22	-0.13	-0.09	-0.41	0.47	0.28	0.58
Emotion Regulation Index	-0.19	-0.10	-0.13	-0.32	0.31	0.20	0.74*
Initiate	-0.37	-0.36	-0.45	-0.46	-0.22	-0.24	0.45
Working Memory	-0.27	-0.32	-0.52	-0.34	-0.08	-0.32	0.17
Plan/Organize	-0.29	-0.06	-0.38	-0.21	-0.38	-0.24	0.30
Task-Monitor	-0.01	-0.14	-0.20	-0.20	-0.38	-0.02	0.50
Organization of Materials	-0.02	0.03	-0.15	0.18	-0.02	0.04	0.42
Cognitive Regulation Index	-0.24	-0.18	-0.40	-0.25	-0.20	-0.15	0.40
Global Executive Composite	-0.16	-0.20	-0.27	-0.30	-0.05	-0.10	0.59

*$p < .05$; ** $p < .01$.

Effect of Demographic and Clinical Factors on Executive Function Outcomes

Age. Pearson correlational analyses did not reveal a statistically significant relationship between age and NEPSY-II scores. No relationship was identified between age and BRIEF-2 scores. Findings are summarized on Table 4 and 5.

Table 4. Pearson Correlation Results for Age and NEPSY-II Subtests

	Age	
NEPSY-II	r	p
Animal Sort	-0.46	0.153
Auditory Attention	0.29	0.292
Response Set	-0.49	0.127
Design Fluency	0.13	0.705
Inhibition-Naming	0.01	0.970
Inhibition-Inhibition	-0.09	0.770
Inhibition-Switching	-0.34	0.368

Table 5. Pearson Correlation Results for Age and BRIEF-2 Composites

	Age	
BRIEF-2	r	p
Behavioural Regulation Index	-0.36	0.151
Emotional Regulation Index	-0.22	0.393
Cognitive Regulation Index	-0.03	0.900
Global Executive Composite	-0.21	0.418

Sex. With regards to sex differences on NEPSY-II performance, females performed significantly better than males on the Inhibition-Naming task [$t(12) = -2.68$, $p = 0.020$; $d = -1.448$). On other measures of performance-based EF, there were no significant differences observed between the two groups. No significant sex differences were found on BRIEF-2 parent-rating scales.

Seizures. Children with a history of seizures performed significantly worse than those without a history of seizures on the Inhibition-Switching task of the NEPSY-II [$t(6) = -2.85$, $p = 0.025$; $d = -1.88$). On other measures of performance-based EF, there were no significant

differences observed between the two groups (Table 6). No significant differences were found between the two groups on BRIEF-2 parent-rating scales (Table 7).

Table 6. NEPSY-II Subtest T-Test Results for Effect of Co-Morbid Seizures

NEPSY-II	Seizure							
	Present		Absent					
	M (SD)	N	M (SD)	N	t	df	p	d
Animal Sorting	7.00 (4.00)	3	5.57 (2.76)	8	0.63	4	0.556	0.44
Auditory Attention	7.80 (2.95)	6	8.70 (4.11)	9	-0.49	10	0.637	-0.24
Response Set	8.75 (2.50)	3	7.29 (3.20)	8	0.84	7	0.423	0.49
Design Fluency	6.67 (3.79)	3	7.00 (2.62)	8	-0.14	2	0.898	-0.11
Inhibition-Naming	4.80 (2.17)	6	5.44 (2.79)	9	-0.48	10	0.641	-0.25
Inhibition-Inhibition	5.75 (2.99)	5	6.36 (3.29)	7	-0.33	6	0.751	-0.20
Inhibition-Switching	4.75 (1.71)	4	8.20 (1.92)	5	-2.85	6	0.025*	-1.88

*$p < .05$; ** $p < .01$.

Table 7. BRIEF-2 Scales T-Test Results for Effects of Co-Morbid Seizures

BRIEF-2	Seizure					
	Present (n = 7)	Absent (n = 10)				
	M (SD)	M (SD)	t	df	p	d
Behavioural Regulation Index	49.71 (17.94)	55.70 (12.24)	-0.77	9	0.461	-0.41
Emotional Regulation Index	57.71 (18.09)	55.00 (9.90)	0.36	8	0.727	0.20
Cognitive Regulation Index	55.71 (14.30)	56.70 (11.03)	-0.15	10	0.881	-0.08
Global Executive Composite	55.71 (16.82)	56.90 (10.82)	-0.16	9	0.873	-0.09

*p < .05; ** p <.01.

General intellectual functioning. When comparing children with Global IQ scores (Low IQ group) below the Average range to those with Global IQ scores (High IQ group), those within the Low IQ group performed significantly worse on only two measures: Auditory Attention and Inhibition-Naming (Table 8). On other measures of performance-based EF, there were no significant differences observed between the two groups. No significant differences were found between the two groups on BRIEF-2 parent-rating scales (Table 9).

Table 8. NEPSY-II Subtest T-Test Results for Global Intellectual Functioning

NEPSY-II	Global IQ Score					
	Low (n = 9)	High (n = 6)				
	M (SD)	M (SD)	t	df	p	d
Animal Sorting	5.80 (4.44)	6.60 (2.07)	-0.37	5	0.728	-0.23
Auditory Attention	6.75 (3.92)	10.83 (2.14)	-2.49	11	0.030*	-1.24
Response Set	7.20 (3.49)	8.40 (2.88)	-0.59	7	0.570	-0.37
Design Fluency	6.67 (3.01)	7.20 (2.77)	-0.31	8	0.767	-0.18
Inhibition-Naming	3.71 (2.56)	7.00 (1.26)	-2.99	9	0.015*	-1.58

Inhibition-Inhibition	5.00 (3.32)	7.00 (3.10)	-1.03	8	0.334	-0.63
Inhibition-Switching	5.67 (1.53)	7.20 (3.19)	-0.91	5	0.397	-0.56

*$p < .05$; ** $p < .01$.

Table 9. BRIEF-2 Scales T-Test Results for Global Intellectual Functioning

BRIEF-2	Global IQ Score					
	Low (n = 9)	High (n = 6)				
	M (SD)	M (SD)	t	df	p	d
Behavioural Regulation Index	47.33 (11.78)	55.17 (13.24)	-1.17	9	0.268	-0.63
Emotional Regulation Index	50.22 (7.43)	56.33 (11.66)	-1.14	7	0.289	-0.66
Cognitive Regulation Index	52.67 (11.30)	55.33 (9.39)	-0.50	12	0.629	-0.25
Global Executive Composite	51.56 (11.04)	56.00 (9.78)	-0.82	11	0.429	-0.42

*$p < .05$; ** $p < .01$.

Discussion

Findings and Implications

Research aims. The goal of this study was to determine the profiles of executive functions (EF) of children with perinatal stroke, from the hot and cool EF model. Additionally, we sought to determine the impact of specific demographic factors, clinical variables, and general intellectual functioning on executive functions in this population.

Hypothesis 1.1. At the group level, as hypothesized, children with perinatal stroke performed significantly lower than the normative sample on almost all EF subtests administered. Specifically, children with perinatal stroke were more impaired than the normative sample on the following subtests: Animal Sorting, Response Set, Design Fluency, and all Inhibition subtests (i.e., Naming, Inhibition, and Switching). These subtests are designed to measure cool EF

constructs including attention, inhibitory control, flexibility/shifting, task monitoring, planning/organization, working memory, and processing speed. The greatest difference between the scores of children with perinatal stroke and the normative sample was on Inhibition-Naming, with the standard score falling more than 1.5 standard deviations below the normative mean. Weak performance in this area indicates that there are deficits in the areas of inhibitory control and processing speed, as this subtest requires switching between the correct naming of stimuli under time pressure. Moderate deficits (i.e., falling between 0.75 to 1.0 standard deviation below the normative mean) were observed in the areas of Animal Sorting, Response Set, Design Fluency, Inhibition-Inhibition, and Inhibition-Switching. Mild deficits (i.e., falling between 0.5 standard deviation below the normative mean) were observed on Auditory Attention, although this was not statistically significant from the normative mean. This indicates that children with perinatal stroke may not be significantly impaired on tasks that involve selective/sustained attention and/or tasks with low working memory demands that does not require the children to act according to multiple, complex rules.

Hypothesis 1.2. On parent-report measure of hot EF, children with perinatal stroke were rated as behaving significantly more impaired than the normative mean on only one composite scale, which was the Cognitive Regulation Index. Of the subtests that comprise the Cognitive Regulation Index, Working Memory, Task-Monitoring, and Organization/Planning was also rated as being significantly higher than that of the normative mean. This indicates that children with perinatal stroke are rated by their parents/guardians as having deficits with their ability to perform daily activities of functioning. Skills that support this area of functioning include the ability to remember and manipulate incoming information for a short period of time. Additionally, parents/guardians of children with perinatal stroke also perceive their child as

having greater difficulty with tasks that require foresight and thinking about the future. These skills draw up on more abstract, cognitive abilities; these abilities have relatively more overlap with cool EF constructs than Behavioural and Emotional Regulation Ind. It should also be noted that Shift was also significantly impacted. Shift is designed to measure the child's ability to flexibly adapt to challenges and changes in their environment, especially their emotional state. This may suggest that children with perinatal stroke may have greater difficulty than the normative population in recognizing, then changing their mood state to suit the atmosphere of their surroundings. Although children with perinatal stroke were rated as significantly more impaired than the norm on several subscales, their mean scaled scores (ranging from 55 to 57) still fell within the average range. From our sample, approximately 24% (4 of 17 participants) had scores that fell within the clinically impaired range.

Hypothesis 1.3. Significant correlations were observed between the children's performance on cool EF measures and the parent-ratings measures of hot EF. Better performance on the NEPSY-II task of Inhibition-Switching was associated with worse parental ratings on the BRIEF-2 in the areas of Inhibit, Shift, and Behavioral and Emotional Regulation Indices. Inhibition-Switching is designed to measure a child's ability to enact inhibitory control (maps onto Inhibit), be flexible and attentive to new rules, and to shift their responses based on the rules (maps onto Shift). This suggests that the association between performance measures and parent observations may not be measuring the same aspects of EF. Bodnar and colleagues (2007) found that well-validated, performance-based measures of EF (Conners' Continuous Performance Tests-II and Tests of Variables of Attention) are poorly correlated with parent-ratings (BRIEF-2). Their sample consisted of a mixed outpatient clinical group, and they hypothesized that the BRIEF-2 may be measuring different elements of EF compared to those assessed in

performance-based tasks (2007). work on construct validity Additionally, the lack of relationship between the other constructs of the performance-based tests and parent-rating measures suggests that there may be several other contributory factors. First, the formats of the measures should be considered when interpreting correlations. McAuley and colleagues noticed this pattern of weak correlation between different performance-based and parent-rating measures of EF (2010), which was also reported in Bosenbark and colleagues' study (2018). Second, the positive and/or weak correlations could be due to the divergence in constructs measured. However, this was deliberate, since cool EF and hot EF are employed differentially, depending on the task. Performance tasks assess abstract, de-contextualized cognitive component of EF, whereas parent report assess the application of EF-related skills in settings where the child may encounter emotionally-charged situations. The environment (i.e., school, home) plays an important role in differentiating the two measures, which is a hypothesis that was first proposed by Bosenbark and colleagues (2018). Third, researchers have been argued that performance-based measures of EF are administered in environments that may not be the most representative of the environment where children typically employ their EF skills. Compared to school and home environments, the measure was administered in rooms that had minimal distractions (i.e., stimuli including other children, toys, noises, etc.), and were administered by trained assessors who provided clear directions and goals as well as immediate reinforcement and feedback (Burgess, 1977). Overall, these findings suggest that the constructs being measured by parent-rating reports and performance-based measures are divergent.

Hypothesis 2.1, 2.2, and 2.3. With regards to predictors variables, sex and history of seizure was associated with poorer performance on all neurobehavioural measures. Based on the findings from this study, male children and children with a history of seizures tended to perform

worse than their counterparts on measures of inhibitory control. In general, there is evidence to suggest that ratings of impulsiveness are higher in males than in females, and that disorders of impulse control are more common among males (as reviewed in Rubia et al., 2013). Based on neuroimaging studies, females showed greater activation of frontal mechanisms (responsible for inhibitory control) compared to males, whereas males showed greater activation of parietal mechanisms (responsible for visual-spatial abilities; Rubia et al., 2013) when participants of both sex completed tasks of attention and inhibitory control. Thus, females and males tend to activate different areas of the brain during a test of attention and inhibitory control, which suggests that they may use different cognitive strategies, and possess relative strengths and weaknesses (Rubia et al., 2013). With regards to sex differences in stroke, Turtzo and McCullough determined that sex disparity exists between male and female patients with stroke, with males being at greater risk for perinatal stroke of both hemorrhagic and ischemic types, as well as cerebral palsy (2010). Additionally, Makrides and colleagues found that preterm males were less responsive to therapeutic interventions than preterm females, which the researcher concluded as evidence for intrinsic sex differences in the immature brain that can influence response to intervention (2009). Finally, in our study, males appear to have greater variability in their performance, and individual differences may provide an alternative explanation for this discrepancy.

The effect of seizure was only observed on one of the subtests from the performance-based measure of cool EF. This suggests that the presence of seizures may be detrimental to the development of inhibitory-control mechanisms, which builds upon the broader generalization that the presence of seizures may limit the brain's plasticity and change subsequent development of the brain, which is consistent with the findings of several studies (Ballantyne et al., 2008; Bosenbark et al., 2018; Chabrier et al., 2011; van Buuren et al., 2013; Westmacott et al., 2010).

However, it is inconclusive whether the differences between the seizure and non-seizure group are a result of the seizures, the ant-epileptic medicine administered, or a combination of both (Bosenbark et al., 2017). Additionally, our small sample size limited our ability to detect differences in other domains of functioning.

There were no significant predictors of hot EF as reported by parents. In comparison to the BRIEF-2 data, children demonstrated greater impairments on the NEPSY-II (performance-based measure). This suggests that parents may be underestimating and/or underreporting their child's deficits. Previously, researchers have found that parent ratings are often inconsistent with teacher ratings on measures of attention and behavioural regulation, a pattern that has emerged among other clinical pediatric populations (as reviewed in Bosenbark et al., 2018). This may be due to the differences in the degree of supports provided at home and school, the differing parental and teacher expectations, as well as the amount of time spent observing the children (Walsh et al., 2015; Wochos, Semerjian, & Walsh, 2014).

Hypothesis 3.1 and 3.2. In regard to the effects of global intellectual functioning, children with global IQ scores within or above the Average range performed better on Auditory Attention and Inhibition-Naming tasks than children with global IQ scores below the Average range. Auditory Attention and Inhibition-Naming are the only subtest that contain several test components, of which they have the least task demands and therefore, should be the easiest to complete with greater accuracy. Dennis and colleagues have argued that IQ and measures of such variable does not comprehensively encapsulate the domain of intelligence (2009). Instead, intelligence is a broad, cognitive construct that is comprised of several different cognitive abilities that may intersect with other domains of cognitive functioning, such as EF. As such, the effects of early brain insult due to perinatal stroke is typically accompanied by deficits in IQ, and

a slightly lower IQ is a result of the widespread impact of injury on the immature brain. This was consistent with our findings, as more than half of our participants with perinatal stroke Based on (9/15) performed below the Average range. However, since the two groups did not have significantly different performance on other measures, it is possible that IQ is not strong associated with EF outcomes as task complexity increases.

Limitations

This study the first to examine EF profiles of children with perinatal stroke through the cool and hot EF model. Additionally, it builds upon the existing literature regarding the impact of demographic, clinical, and cognitive factors that may affect EF outcomes. However, there are several limitations in the study. The first limitation was that there was an absence of a matched control group. Therefore, the neurobehavioural outcomes were compared to the age-standardized norms that were provided in test manuals that accompanied the child-specific measures.

Second, the sample size is smaller than those found in existing studies on the childhood stroke population. It was difficult to create proportionate groups based, such as one the one based on stroke subtypes (i.e., the PVI group was significantly smaller than the NAIS and APPIS) and seizure presence. However, clinical variables are difficult to control for when children are recruited, and consequently impacts the power of group comparisons. Although we found significant results (mostly at the group-level), effects that approached significance may reach significance with larger subgroups. However, previous studies that examined cognitive outcomes in childhood stroke conducted their assessments on mixed clinical population that included several different types of brain injury; in our study, we excluded those with hemorrhage strokes and sinovenous thrombosis which also limited our sample size. It should be noted that most children in our sample were from families of high SES backgrounds, with high maternal

education, and of Caucasian ethnicity; therefore, the findings may not be applicable to the general population of children with perinatal stroke.

Third, this study lacks a control group that is matched on sex and age. Typically, the purpose of a control group is to allow researchers to better discriminate patient characteristics and/or performance from an outcome that may be caused other factors, including history, observer, and/or patient expectation). It also protects the researcher from bias that may be found in an aspect of the research design, conduct, and analyses that would make the outcomes deviate from the true effect. Finally, for some children at the extreme ends of the age limits (i.e., age 6 and 16), they did not complete subtests on the performance-based measure because the test was exclusive to a restricted age range. This is likely due to the fact that skills in these areas are not fully developed at this time compared to older children, and are, therefore, more difficult to assess with the same tools.

Future Directions

The current study builds upon the existing research on EF outcomes in children with perinatal stroke, and additional research is needed to advance our understanding of cognitive outcomes in this population. In addition to the limitations that were presented in this study, it would be beneficial to have long-term follow-up with children from this population. The limits of a cross-sectional study only allow for generalization about how a certain age range may be impacted when compared to other age groups. By exploring the longitudinal effects in a cohort study, we could examine the trajectories of development, and how children's EF outcomes may be differentially affected by demographic and clinical variables.

Since this study only examined EF outcomes in children with perinatal stroke, future studies should also look at outcomes in other domains of neuropsychological functioning, which

include memory (working, short- and long-term memory; visual and verbal), visual-spatial skills, language, and learning. The measures of hot EF were only based on one parent report, which may not be a reliable or valid measure when used alone. Future studies may consider using an additional rating form (i.e., completed by teachers) and/or incorporating a performance-based or observation-based/role play task to identify hot EF deficits in children. Finally, it would be important to examine the association between cool EF and academic outcomes, as well as the that of hot EF and social/emotional functioning.

With regards to intervention, it is important to target the areas of deficit as evidenced in this study. It may be beneficial for parents and educational supports to become aware of the group-level impairments, so that a combination of adapted supports can be provided for the child. Children with traumatic brain injury and their families have been shown to benefit from family support (i.e., emotional and social), psychological services (i.e., behavioural therapy and counseling), as well as physical activities (Chapman & McKinnon, 2000). Additionally, children can benefit from specialized educational programming that provide accommodations to help them cope with cognitive deficits (Langsing et al., 2004). Although there is no standardized plan of intervention and/or rehabilitation with children with perinatal stroke, providing families and patients with an interdisciplinary team may be the first step to assessing and then addressing the complex needs of children from this clinical population.

References

Agrawal, N., Johnston, S. C., Wu, Y. W., Sidney, S., & Fullerton, H. J. (2009). Imaging data reveal a higher pediatric stroke incidence than prior US estimates. *Stroke; a journal of cerebral circulation*, *40*(11), 3415. doi: 10.1161/STROKEAHA.109.564633

Albert, D., & Steinberg, L. (2011). Judgment and decision making in adolescence. *Journal of Research on Adolescence*, *21*(1), 211-224. doi:10.1111/j.1532-7795.2010.00724.x

Allman, C., & Scott, R. B. (2013). Neuropsychological sequelae following pediatric stroke: A nonlinear model of age at lesion effects. *Child Neuropsychology*, *19*(1), 97-107. doi: 10.1080/09297049.2011.639756

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Amlie-Lefond, C., Sébire, G., & Fullerton, H. J. (2008). Recent developments in childhood arterial ischaemic stroke. *The Lancet Neurology*, *7*(5), 425–435. doi:10.1016/S1474-4422(08)70086-3

Anderson, V. A., Anderson, P., Northam, E., Jacobs, R., & Catroppa, C. (2001). Development of executive functions through late childhood and adolescence in an Australian sample. *Developmental neuropsychology*, *20*(1), 385-406. doi:10.1207/S15326942DN2001_5

Anderson, V. (1998). Assessing executive functions in children: Biological, psychological, and developmental considerations. *Neuropsychological rehabilitation*, *8*(3), 319-349. doi:10.1080/713755568

Anderson, V., Catroppa, C., Morse, S., Haritou, F., Rosenfeld, J. (2005). Functional Plasticity or Vulnerability After Early Brain Injury? *Pediatrics*, *116*(6), 1374–1382. doi:

10.1542/peds.2004-1728

Anderson, V., Spencer-Smith, M., Leventer, R., Coleman, L., Anderson, P., Williams, J., … Jacobs, R. (2009). Childhood brain insult: can age at insult help us predict outcome? *Brain*, *132*(1), 45–56. doi:10.1093/brain/awn293

Anderson, V., Spencer-Smith, M., & Wood, A. (2011). Do children really recover better? Neurobehavioural plasticity after early brain insult. *Brain*, *134*(8), 2197-2221. doi:10.1093/brain/awr103

Aram, D. M., & Eisele, J. A. (1994). Intellectual stability in children with unilateral brain lesions. *Neuropsychologia*, *32*(1), 85-95.

Ballantyne, A. O., Spilkin, A. M., Hesselink, J., & Trauner, D. A. (2008). Plasticity in the developing brain: Intellectual, language and academic functions in children with ischaemic perinatal stroke. *Brain*, *131*(11), 2975–2985. doi:10.1093/brain/awn176

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, *50*(1-3), 7-15. doi: 10.1016/0010-0277(94)90018-3

Bemister, T. B., Brooks, B. L., Dyck, R. H., & Kirton, A. (2014). Parent and family impact of raising a child with perinatal stroke. *BMC Pediatrics*, *14*(1), 182. doi:10.1186/1471-2431-14-182

Benjamin, E. J., Blaha, M. J., Chiuve, S. E., Cushman, M., Das, S. R., Deo, R., … American Heart Association Statistics Committee and Stroke Statistics Subcommittee, O. behalf of the A. H. A. S. C. and S. S. (2017). Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation*, *135*(10), e146–e603. doi:10.1161/CIR.0000000000000485

Bodnar, L. E., Prahme, M. C., Cutting, L. E., Denckla, M. B., & Mahone, E. M. (2007). Construct validity of parent ratings of inhibitory control. *Child Neuropsychology*, *13*(4), 345-362. doii 10.1080/09297040600899867

Bosenbark, D. D., Krivitzky, L., Ichord, R., Jastrzab, L., & Billinghurst, L. (2018). Attention and executive functioning profiles in children following perinatal arterial ischemic stroke. *Child Neuropsychology*, *24*(1), 106–123. doi:10.1080/09297049.2016.1225708

Bosenbark, D. D., Krivitzky, L., Ichord, R., Vossough, A., Bhatia, A., Jastrzab, L. E., & Billinghurst, L. (2017). Clinical predictors of attention and executive functioning outcomes in children after perinatal arterial ischemic stroke. *Pediatric neurology*, *69*, 79-86. doi: 10.1016/j.pediatrneurol.2017.01.014.

Brock, L. L., Rimm-Kaufman, S. E., Nathanson, L., & Grimm, K. J. (2009). The contributions of 'hot'and 'cool'executive function to children's academic achievement, learning-related behaviors, and engagement in kindergarten. *Early Childhood Research Quarterly*, *24*(3), 337-349. doi:10.1016/j.ecresq.2009.06.001

Bull, R., & Scerif, G. (2001). Executive functioning as a predictor of children's mathematics ability: Inhibition, switching, and working memory. *Developmental neuropsychology*, *19*(3), 273-293. doi:10.1207/S15326942DN1903_3

Burgess, P. W. (1997). Theory and methodology in executive function and research. In P. Rabbitt (Ed.), *Methodology of frontal and executive function* (pp. 81-116). Hove, England: Psychology Press.

Cauffman, E., Shulman, E. P., Steinberg, L., Claus, E., Banich, M. T., Graham, S., & Woolard, J. (2010). Age differences in affective decision making as indexed by performance on the Iowa Gambling Task. *Developmental psychology*, *46*(1), 193. doi:10.1037/a0016128.

Chabrier, S., Husson, B., Dinomais, M., Landrieu, P., & Nguyen The Tich, S. (2011). New insights (and new interrogations) in perinatal arterial ischemic stroke. *Thrombosis research*, *127*(1), 13-22. doi:10.1016/j.thromres.2010.10.003

Chalmers, E. A. (2005). Perinatal stroke - risk factors and management. *British Journal of Haematology*, *130*(3), 333–343. doi:10.1111/j.1365-2141.2005.05554.x

Chan, R. C., Shum, D., Toulopoulou, T., & Chen, E. Y. (2008). Assessment of executive functions: Review of instruments and identification of critical issues. Archives of clinical neuropsychology, 23(2), 201-216. doi: 10.1016/j.acn.2007.08.010

Chapman, S. B., Max, J. E., Gamino, J. F., McGlothlin, J. H., & Cliff, S. N. (2003). Discourse plasticity in children after stroke: age at injury and lesion effects. *Pediatric Neurology*, *29*(1), 34-41. doi:10.1016/S0887-8994(03)00012-2

Chapman, S. B., & Mckinnon, L. (2000). Discussion of developmental plasticity: Factors affecting cognitive outcome after pediatric traumatic brain injury. *Journal of Communication Disorders*, *33*(4), 333-344. doi:10.1016/S0021-9924(00)00029-0

Davis, J.L. & Matthews, R. (2010). NEPSY-II Review. *Journal of Psychoeducational Assessment, 28*(2), 175-182. doi: 10.117/0734282909346716

Dennis, M., Francis, D. J., Cirino, P. T., Schachar, R., Barnes, M. A., & Fletcher, J. M. (2009). Why IQ is not a covariate in cognitive studies of neurodevelopmental disorders. J Int Neuropsychol Soc, 15(3), 331-343.

deVeber, G. A., MacGregor, D., Curtis, R., & Mayank, S. (2000). Neurologic outcome in survivors of childhood arterial ischemic stroke and sinovenous thrombosis. *Journal of Child Neurology*, *15*(5), 316–324. https://doi.org/10.1177/088307380001500508

deVeber, G., Roach, E. S., Riela, A. R., & Wiznitzer, M. (2000). Stroke in children: recognition,

treatment, and future directions. In *Seminars in Pediatric Neurology*, *7*(4), 309-317. doi: 10.1053/spen.2000.20074

De Schryver, E. L., Kappelle, L. J., Jennekens-Schinkel, A., & Peters, A. B. (2000). Prognosis of ischemic stroke in childhood: a long-term follow-up study. *Developmental Medicine & Child Neurology*, *42*(5), 313-318. doi: 10.1111/j.1469-8749.2000.tb00096.x

Ellis, M. L., Weiss, B., & Lochman, J. E. (2009). Executive functions in children: Associations with aggressive behavior and appraisal processing. *Journal of Abnormal Child Psychology*, *37*(7), 945-956.doi: 10.1007/s10802-009-9321-5.

Everts, R., Pavlovic, J., Kaufmann, F., Uhlenberg, B., Seidel, U., Nedeltchev, K., ... & Steinlin, M. (2008). Cognitive functioning, behavior, and quality of life after stroke in childhood. *Child Neuropsychology*, *14*(4), 323-338. doi:10.1080/09297040701792383

Fox, C. K., & Fullerton, H. J. (2010). Recent advances in childhood arterial ischemic stroke. *Current atherosclerosis reports*, *12*(4), 217-224. doi:10.1007/s11883-010-0113-8

Ganesan, V., Hogan, A., Shack, N., Gordon, A., Isaacs, E., & Kirkham, F. J. (2000). Outcome after ischaemic stroke in childhood. *Developmental medicine and child neurology*, *42*(7), 455-461. doi:10.1111/j.1469-8749.2000.tb00348.x

Gil, A. M. (2003). Neurocognitive outcomes following pediatric brain injury: A developmental approach. *Journal of School Psychology*, *41*(5), 337–353. doi:10.1016/S0022-4405(03)00085-2

Gioia, G. A., Isquith, P. K., Guy, S. C., & Kenworthy, L. (2000). Test review behavior rating inventory of executive function. *Child Neuropsychology*, *6*(3), 235-238.

Gioia, G. A., Isquith, P. K., Kenworthy, L., & Barton, R. M. (2002). Profiles of everyday executive function in acquired and developmental disorders. *Child neuropsychology*, *8*(2), 121-137.

doi:10.1076/chin.8.2.121.8727

Giza, C. C., & Prins, M. L. (2006). Is being plastic fantastic? Mechanisms of altered plasticity after developmental traumatic brain injury. *Developmental neuroscience*, *28*(4-5), 364-379. doi:10.1159/000094163

Glutting, J., Glutting, J., Adams, W., & Sheslow, D. (1999). *WRIT: Wide Range Intelligence Test*. Wide Range Incorporated.

Golomb, M. R. (2009). Outcomes of perinatal arterial ischemic stroke and cerebral sinovenous thrombosis. Seminars in Fetal and Neonatal Medicine, 14(5), 318-322. doi:10.1016/j.siny.2009.07.003.

Goodman, R., & Yude, C. (1996). IQ and its predictors in childhood hemiplegia. *Developmental Medicine & Child Neurology*, *38*(10), 881-890. doi:10.1111/j.1469-8749.1996.tb15045.x

Gordon, A. (2007). Stroke in children. *Reprinted from Australian Family Physician*, *36*(11). Retrieved from https://www.racgp.org.au/afpbackissues/2007/200711/200711Mackay.pdf

Grafman, J., & Litvan, I. (1999). Importance of deficits in executive functions. *The Lancet, 354*(9194), 1921-1923. doi: 10.1016/S0140-6736(99)90438-5

Hajek, C. A., Yeates, K. O., Anderson, V., Mackay, M., Greenham, M., Gomes, A., & Lo, W. (2014). Cognitive outcomes following arterial ischemic stroke in infants and children. *Journal of Child Neurology*, *29*(7), 887-894. doi:10.1177/0883073813491828

Hartel, C., Schilling, S., Sperner, J., & Thyen, U. (2004). The clinical outcomes of neonatal and childhood stroke: review of the literature and implications for future research. *European Journal of Neurology*, *11*(7), 431–438. doi:10.1111/j.1468-1331.2004.00861.x

Hay, D. F., Payne, A., & Chadwick, A. (2004). Peer relations in childhood. *Journal of child psychology and psychiatry*, *45*(1), 84-108. doi: 10.1046/j.0021-9630.2003.00308.x

Hetherington, R., Tuff, L., Anderson, P., Miles, B., & deVeber, G. (2005). Short-term intellectual outcome after arterial ischemic stroke and sinovenous thrombosis in childhood and infancy. *Journal of child neurology*, *20*(7), 553-559. doi:10.1177/08830738050200070201

Hongwanishkul, D., Happaney, K. R., Lee, W. S. C., Zelazo, P. D., Wendy, S., Lee, C., & Lee, S. C. (2005). Developmental Neuropsychology Assessment of Hot and Cool Executive Function in Young Children : Age-Related Changes and Individual Differences. *Developmental Neuropsychology*, *28*(2), 617–644. doi: 10.1207/s15326942dn2802

Ilves, P., Laugesaar, R., Loorits, D., Kolk, A., Tomberg, T., Lõo, S., … Talvik, T. (2016). Presumed Perinatal Stroke: Risk Factors, Clinical and Radiological Findings. In *Journal of Child Neurology*, *31,* 621–628. doi:10.1177/0883073815609149

Jacobson, S., Marcus, E. M., & Pugsley, S. (2018). *Neuroanatomy for the Neuroscientist*. Springer International Publishing AG. doi:10.1007/978-3-319-60187-8

Jefferson, A. L., Paul, R. H., Ozonoff, A. L., & Cohen, R. A. (2006). Evaluating elements of executive functioning as predictors of instrumental activities of daily living (IADLs). *Archives of clinical Neuropsychology*, *21*(4), 311-320. doi:10.1016/j.acn.2006.03.007

Kennard, M. A. (1938). Reorganization of motor function in the cerebral cortex of monkeys deprived of motor and premotor areas in infancy. *Journal of Neurophysiology*, *1*(6), 477-496.

Kennard, M. A. (1942). Cortical reorganization of motor function: studies on series of monkeys of various ages from infancy to maturity. *Archives of Neurology & Psychiatry*, *48*(2), 227-240. doi:10.1001/archneurpsyc.1942.02290080073002

Kim, S., Nordling, J. K., Yoon, J. E., Boldt, L. J., & Kochanska, G. (2013). Effortful control in

"hot" and "cool" tasks differentially predicts children's behavior problems and academic performance. *Journal of abnormal child psychology*, *41*(1), 43-56. doi: 10.1007/s10802-012-9661-4

Kirton, A., & deVeber, G. (2006). Cerebral Palsy Secondary to Perinatal Ischemic Stroke. *Clinics in Perinatology*. doi:10.1016/j.clp.2006.03.008

Kirton, A., & deVeber, G. (2009). Advances in Perinatal Ischemic Stroke. *Pediatric Neurology*, *40*(3), 205–214. doi:10.1016/j.pediatrneurol.2008.09.018

Kirton, A., & deVeber, G. (2013). Life after perinatal stroke. *Stroke*, *44*(11), 3265–3271. doi:10.1161/STROKEAHA.113.000739

Kirton, A., deVeber, G., Pontigon, A.-M., Macgregor, D., & Shroff, M. (2008). Presumed perinatal ischemic stroke: Vascular classification predicts outcomes. *Annals of Neurology*, *63*(4), 436–443. doi:10.1002/ana.21334

Kirton, A., Shroff, M., Pontigon, A.-M., & DeVeber, G. (2010). Risk factors and presentations of periventricular venous infarction vs arterial presumed perinatal ischemic stroke. *Archives of Neurology*, *67*(7), 842–8. doi:10.1001/archneurol.2010.140

Knouse, L. E., Feldman, G., & Blevins, E. J. (2014). Executive functioning difficulties as predictors of academic performance: Examining the role of grade goals. *Learning and Individual Differences*, *36*, 19-26. doi:10.1016/j.lindif.2014.07.001

Kolb, B., & Gibb, R. (2011). Brain plasticity and behaviour in the developing brain. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, *20*(4), 265.

Kolb, B., Teskey, C., & Gibb, R. (2010). Factors influencing cerebral plasticity in the normal and injured brain. *Frontiers in human neuroscience*, *4*, 204. doi:10.3389/fnhum.2010.00204

Kolk, A., Ennok, M., Laugesaar, R., Kaldoja, M. L., & Talvik, T. (2011). Long-term cognitive

outcomes after pediatric stroke. *Pediatric neurology*, *44*(2), 101-109. doi: 10.1016/j.pediatrneurol.2010.08.012

Korkman, M., Kirk, U., & Kemp, S. (2007). NEPSY-II: Clinical and interpretive manual. *San Antonio, TX: The Psychological Corporation*.

Lee, J., Croen, L. a, Backstrand, K. H., Yoshida, C. K., Henning, L. H., Lindan, C., … Wu, Y. W. (2005). in the Infant, *293*(6), 723–729. doi:10.1016/j.siny.2009.07.009

Lidzba, K., & Krägeloh-Mann, I. (2005). Development and lateralization of language in the presence of early brain lesions. *Developmental medicine and child neurology*, *47*(11), 724-724. doi:10.1017/S0012162205001520

Lidzba, K., Staudt, M., Wilke, M., & Krägeloh-Mann, I. (2006). Visuospatial deficits in patients with early left-hemispheric lesions and functional reorganization of language: consequence of lesion or reorganization?. *Neuropsychologia*, *44*(7), 1088-1094.

Lynch, J. K. (2009). Epidemiology and classification of perinatal stroke. *Seminars in Fetal and Neonatal Medicine*, *14*(5), 245–249. doi: 10.1016/j.siny.2009.07.001

Lynch, J. K., Hirtz, D. G., deVeber, G., & Nelson, K. B. (2002). Report of the National Institute of Neurological Disorders and Stroke Workshop on Perinatal and Childhood Stroke. *Pediatrics*, *109*(1), 116–123. doi:10.1542/peds.109.1.116

Lynch, J. K., & Nelson, K. B. (2001). Epidemiology of perinatal stroke. *Current Opinion in Pediatrics*. doi: 10.1097/00008480-200112000-00002

Mackay, M. T., & Gordon, A. (2007). Stroke in children. *Australian Family Physician*, *36*(11), 896-902. Retrieved from https://www.racgp.org.au/afpbackissues/2007/200711/200711Mackay.pdf

Makrides, M., Gibson, R. A., McPhee, A. J., Collins, C. T., Davis, P. G., Doyle, L. W., ... &

Willson, K. (2009). Neurodevelopmental outcomes of preterm infants fed high-dose docosahexaenoic acid: a randomized controlled trial. *Jama*, *301*(2), 175-182. doi: 10.1001/jama.2008.945.

Max, J.E., Matthews, K., Manes, F.F., Robertson, B.A.M., Fox, P.T., Lancaster, J.L., Lansing, A.E., … Collings, N. (2003). Attention deficit hyperactivity disorder and neurocognive correlates after childhood stroke. *Journal of the International Neuropsychological Society, 9,* 815-829. doi: 10.10170S1355617703960012

McAuley, T., Chen, S., Goos, L., Schachar, R., & Crosbie, J. (2010). Is the behavior rating inventory of executive function more strongly associated with measures of impairment or executive function? *J Int Neuropsychol Soc, 16*(3), 495-505.

McLinden, A., Baird, A. D., Westmacott, R., Anderson, P. E., & deVeber, G. (2007). Early cognitive outcome after neonatal stroke. *Journal of Child Neurology*. doi:10.1177/0883073807305784

Mischel, W., Shoda, Y., & Rodriguez, M. I. (1989). Delay of gratification in children. *Science*, *244*(4907), 933-938. doi: 10.1126/science.2658056

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive psychology*, *41*(1), 49-100. doi: 10.1006/cogp.1999.0734

Mong, A., & Pollock, A.N. (2011). Chapter 62-Pediatric Neuroradiology. In Pretorius, E.S. & Solomon, J.A. (Eds.), *Radiology Secrets Plus-Third Edition* (434-438). doi:10.1016/C2009-0-55128-8

Montour-Proulx, I., Braun, C. M., Daigneault, S., Rouleau, I., Kuehn, S., & Bégin, J. (2004).

Predictors of intellectual function after a unilateral cortical lesion: Study of 635 patients from infancy to adulthood. *Journal of child neurology*, *19*(12), 935-943. doi: 10.1006/brcg.2001.1373

Moriguchi, Y. (2014). The early development of executive function and its relation to social interaction: a brief review. *Frontiers in psychology*, *5*, 388. doi:10.3389/fpsyg.2014.00388

Murias, K., Brooks, B., Kirton, A., & Iaria, G. (2014). A review of cognitive outcomes in children following perinatal stroke. *Developmental Neuropsychology*, *39*(2), 131–57. doi:10.1080/87565641.2013.870178

Murphy, S. L., Xu, J., Kochanek, K. D., Curtin, S. C., & Arias, E. (2017). Deaths: Final data for 2015. *National Vital Statistics Reports*, *66*(6). doi:10.1136/vr.h753

Muter, V., Taylor, S., & Vargha-Khadem, F. (1997). A longitudinal study of early intellectual development in hemiplegic children. *Neuropsychologia*, *35*(3), 289-298. doi: /10.1016/S0028-3932(96)00079-6

Nelson, K. B. (2003). Can We Prevent Cerebral Palsy? *The New Engl Journal of Medicine*, *349,* 1765-1769. doi:10.1056/NEJMsb035364

Nelson, K. B. (2007). Perinatal ischemic stroke. *Stroke*, *38*(2 PART 2), 742–745. doi: 10.1161/01.STR.0000247921.97794.5e

Nelson, K. B., & Lynch, J. K. (2004). Stroke in newborn infants. *The Lancet Neurology*, *3*(3), 150–158. https://doi.org/10.1016/S1474-4422(04)00679-9

Novak, I., Hines, M., Goldsmith, S., & Barclay, R. (2012). Clinical Prognostic Messages From a Systematic Review on Cerebral Palsy. *Pediatric*, *130*(5), e1285–e1312. https://doi.org/10.1542/peds.2012-0924

Pappachan, J., & Kirkham, F. (2008). Cerebrovascular disease and stroke. *Archives of disease in*

childhood, *93*(10), 890-898. doi:10.1136/adc.2008.142836

Perlman, J. M. (2006). Intervention strategies for neonatal hypoxic-ischemic cerebral injury. *Clinical therapeutics*, *28*(9), 1353-1365. doi:10.1016/j.clinthera.2006.09.005

Pfefferbaum, A., Mathalon, D. H., Sullivan, E. V., Rawles, J. M., Zipursky, R. B., & Lim, K. O. (1994). A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. *Archives of neurology*, *51*(9), 874-887. doi:10.1001/archneur.1994.00540210046012

Prencipe, A., Kesek, A., Cohen, J., Lamm, C., Lewis, M. D., & Zelazo, P. D. (2011). Development of hot and cool executive function during the transition to adolescence. *Journal of experimental child psychology*, *108*(3), 621-637. doi: 10.1016/j.jecp.2010.09.008.

Raju, T. N. K., Nelson, K. B., Ferriero, D., & Lynch, J. K. (2007). Ischemic perinatal stroke: summary of a workshop sponsored by the National Institute of Child Health and Human Development and the National Institute of Neurological Disorders and Stroke. *Pediatrics*, *120*(3), 609–616. https://doi.org/10.1542/peds.2007-0336

Ricci, D., Mercuri, E., Barnett, A., Rathbone, R., Cota, F., Haataja, L., ... & Cowan, F. (2008). Cognitive outcome at early school age in term-born children with perinatally acquired middle cerebral artery territory infarction. Stroke, 39(2), 403-410. doi:10.1177/08830738050200070201

Richards, J. B., Zhang, L., Mitchell, S. H., & De Wit, H. (1999). Delay or probability discounting in a model of impulsive behavior: effect of alcohol. *Journal of the experimental analysis of behavior*, *71*(2), 121-143. doi: 10.1901/jeab.1999.71-121

Roth, S. C., Baudin, J., Cady, E., Johal, K., Townsend, J. P., Wyatt, J. S., ... & Stewart, A. L. (1997). Relation of deranged neonatal cerebral oxidative metabolism with

neurodevelopmental outcome and head circumference at 4 years. Developmental Medicine & Child Neurology, 39(11), 718-725. doi:10.1111/j.1469-8749.1997.tb07372.x

Rubia, K., Lim, L., Ecker, C., Halari, R., Giampietro, V., Simmons, A., ... & Smith, A. (2013). Effects of age and gender on neural networks of motor response inhibition: from adolescence to mid-adulthood. *Neuroimage*, *83*, 690-703. doi: /10.1016/j.neuroimage.2013.06.078

Schaller, B. J. (2007). Influence of age on stroke and preconditioning-induced ischemic tolerance in the brain. *Experimental neurology*, *205*(1), 9-19. doi:10.1016/j.expneurol.2006.01.017

Seeyave, D. M., Coleman, S., Appugliese, D., Corwyn, R. F., Bradley, R. H., Davidson, N. S., ... & Lumeng, J. C. (2009). Ability to delay gratification at age 4 years and risk of overweight at age 11 years. *Archives of pediatrics & adolescent medicine*, *163*(4), 303-308. doi:10.1001/archpediatrics.2009.12

Séguin, J. R., Arseneault, L., & Tremblay, R. E. (2007). The contribution of "cool" and "hot" components of decision-making in adolescence: implications for developmental psychopathology. *Cognitive Development*, *22*(4), 530-543. doi: 10.1016/j.cogdev.2007.08.006

Sigurdardottir, S., Indredavik, M. S., Eiriksdottir, A., Einarsdottir, K., Gudmundsson, H. S., & Vik, T. (2010). Behavioural and emotional symptoms of preschool children with cerebral palsy: A population-based study. *Developmental Medicine and Child Neurology*, *52*(11), 1056–1061. https://doi.org/10.1111/j.1469-8749.2010.03698.x

Skogli, E. W., Egeland, J., Andersen, P. N., Hovik, K. T., & Øie, M. (2014). Few differences in hot and cold executive functions in children and adolescents with combined and inattentive subtypes of ADHD. *Child Neuropsychology*, *20*(2), 162-181. doi:

10.1080/09297049.2012.753998

Sreenan, C., Bhargava, R., & Robertson, C. M. (2000). Cerebral infarction in the term newborn: clinical presentation and long-term outcome. *The Journal of pediatrics*, *137*(3), 351-355. doi:10.1067/mpd.2000.107845

StataCorp LP. Released 2016. Stata/SE for Windows, Version 14.2. College Station, TX: StataCorp.

Stein, D. G., & Hoffman, S. W. (2003). Estrogen and progesterone as neuroprotective agents in the treatment of acute brain injuries. *Pediatric rehabilitation*, *6*(1), 13-22.

Trauner, D.A., Chase, C., Walker, P., & Wulfeck, B. (1993). Neurologic profiles of infants and children after perinatal stroke. P*ediatric Neurology, 9*, 383-386.

Thorell, L. B. (2007). Do delay aversion and executive function deficits make distinct contributions to the functional impact of ADHD symptoms? A study of early academic skill deficits. *Journal of Child Psychology and Psychiatry*, *48*(11), 1061-1070. doi: 10.1111/j.1469-7610.2007.01777.x

Turtzo, L. C., & McCullough, L. D. (2010). Sex-specific responses to stroke. *Future neurology*, *5*(1), 47-59. doi: 10.2217/fnl.09.66

Vargha-Khadem, F., Isaacs, E., van der Werf, S., Robb, S., & Wilson, J. (1992). Development of intelligence and memory in children with hemiplegic cerebral palsy. The deleterious consequences of early seizure. *Brain, 115*(Part 1), 315-329.

van Buuren, L. M., van der Aa, N. E., Dekker, H. C., Vermeulen, R. J., van Nieuwenhuizen, O., van Schooneveld, M. M., & de Vries, L. S. (2013). Cognitive outcome in childhood after unilateral perinatal brain injury. *Developmental Medicine & Child Neurology*, *55*(10), 934-940. doi:10.1111/dmcn.1218

van der Sluis, S., de Jong, P. F., & van der Leij, A. (2007). Executive functioning in children, and its relations with reasoning, reading, and arithmetic. *Intelligence*, *35*(5), 427-449. doi:10.1016/j.intell.2006.09.001

Walsh, K. S., Paltin, I., Gioia, G. A., Isquith, P., Kadan-Lottick, N. S., Neglia, J. P., & Brouwers, P. (2015). Everyday executive function in standard-risk acute lymphoblastic leukemia survivors. *Child Neuropsychology, 21*(1), 78-89.

Weierink, L., Vermeulen, R. J., & Boyd, R. N. (2013). Brain structure and executive functions in children with cerebral palsy: a systematic review. *Research in developmental disabilities*, *34*(5), 1678-1688. doi:10.1016/j.ridd.2013.01.035

Welsh, M., & Peterson, E. (2014). Issues in the conceptualization and assessment of hot executive functions in childhood. *Journal of the International Neuropsychological Society*, *20*(2), 152-156. doi: 10.1017/S1355617713001379.

Werner, C., & Engelhard, K. (2007). Pathophysiology of traumatic brain injury. *BJA: British Journal of Anaesthesia*, *99*(1), 4-9. doi:10.1093/bja/aem131

Westmacott, R., Askalan, R., Macgregor, D., Anderson, P., & deVeber, G. (2010). Cognitive outcome following unilateral arterial ischaemic stroke in childhood: Effects of age at stroke and lesion location. *Developmental Medicine and Child Neurology*, *52*(4), 386–393. doi:10.1111/j.1469-8749.2009.03403.x

Westmacott, R., MacGregor, D., Askalan, R., & deVeber, G. (2009). Late emergence of cognitive deficits after unilateral neonatal stroke. *Stroke*, *40*(6), 2012–9. doi:10.1161/STROKEAHA.108.533976

Willoughby, M. T., Wirth, R. J., & Blair, C. B. (2012). Executive function in early childhood: Longitudinal measurement invariance and developmental change. *Psychological*

assessment, *24*(2), 418. doi: 10.1037/a0025779

Wochos, G. C., Semerjian, C. H., & Walsh, K. S. (2014). Differences in Parent and Teacher Rating of Everyday Executive Function in Pediatric Brain Tumor Survivors. *The Clinical Neuropsychologist, 28*(8), 1243-1257

Wu, Y. W., Lynch, J. K., & Nelson, K. B. (2005). Perinatal arterial stroke: Understanding mechanisms and outcomes. *Seminars in Neurology*. https://doi.org/10.1055/s-2005-923536

Zelazo, P. D., Blair, C. B., & Willoughby, M. T. (2016). Executive Function: Implications for Education. NCER 2017-2000. *National Center for Education Research*.

Zelazo, P. D., & Müller, U. (2002). Executive function in typical and atypical development. *Blackwell handbook of childhood cognitive development*, 445-469. doi: 10.1002/9780470996652.ch20

Zorza, J. P., Marino, J., & Mesas, A. A. (2016). Executive functions as predictors of school performance and social relationships: Primary and secondary school students. *The Spanish Journal of Psychology*, *19*. doi: 10.1017/sjp.2016.23.