Cognitive Outcomes Following Arterial Ischemic Stroke in Children

DISSERTATION

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Abstract

Purpose: To determine whether children with arterial ischemic stroke (AIS) display deficits in cognitive functioning and explore factors that may account for individual variability in cognitive outcomes following AIS.

Participants and Methods: Participants included 36 children with AIS, which occurred from the perinatal period to childhood but at least 1 year prior to assessment. A comparison group of 15 children with asthma were included to control for acute medical illness requiring hospital admission. Participants ranged from 6 to 15 years of age at the time of the study. Children completed measures of general cognitive ability, attention and executive functions, and processing speed. Children also were assessed using the Pediatric Stroke Outcome Measure (PSOM), a standardized assessment of neurological function. Children in the AIS group also completed an MRI, which was used to determine stroke location and measure lesion volume.

Results: Mean cognitive scores fell within the average range for both groups. Compared to children with asthma, children with AIS performed significantly worse on a measure of inhibitory control. Group differences for the remaining cognitive measures were in the same direction but did not reach statistical significance. Children with AIS performed significantly lower than normative populations on several cognitive measures. The PSOM total severity score was significantly negatively correlated with general cognitive ability and processing speed. Stroke volume was significantly negatively

correlated with verbal skills and general cognitive ability. Results suggest that greater stroke severity was associated with lower cognitive functioning. Socioeconomic status (SES) was also related to verbal functioning, general cognitive ability, inhibitory control, and processing speed. Stroke location, lesion laterality, age at stroke, and sex were not significantly related to cognitive outcome. Regression analyses indicated that after controlling for SES, greater stroke severity accounted for significant variance in general cognitive ability, verbal skills, and processing speed.

Conclusions: Results suggest that following AIS, children performed in the low end of the average range on several cognitive measures. In the AIS group, overall neurological status, stroke severity, and SES were significantly related to general cognitive ability and verbal skills, as well as processing speed. After controlling for SES, stroke severity accounted for significant variance in cognitive functioning.

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Fields of Study

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Chapter 1: Introduction

Stroke in children results in high rates of mortality and morbidity and represents a significant public health concern (deVeber, 2002; Lynch, Hirtz, deVeber, & Nelson 2002). In recent decades, the awareness and detection of pediatric stroke has increased with technological advances in neuroimaging and medicine (deVeber, 2002). Pediatric stroke is 1 of the top 10 causes of death and occurs at a rate equal to or greater than that of pediatric brain tumors (Jordan & Hillis, 2007; Lopez-Vicente, Ortega-Gutierrez, Amlie-Lefond, & Torbey, 2010; Long et al., 2010; Mackay & Gordon, 2007; Mallick & Ganesan, 2008; Pappachan & Kirkham, 2008). Despite the belief that children recover better than adults, survivors of childhood stroke are vulnerable to neurological, cognitive, and behavioral sequelae (Gordon, Ganesan, Towell, & Kirkham, 2002; Jordan, 2006; Lo et al., 2008; Long et al., 2010; Mallick & Ganesan, 2008; Steinlin, Roellin, & Schroth, 2004). Available research suggests that children display mild deficits on cognitive measures and perform within the lower limits of the average range (Hogan, Kirkham, & Isaacs, 2000). However, existing studies have produced inconsistent results and many are limited by methodological flaws.

The following discussion will review pediatric stroke research to date, beginning with a brief description of the definition, epidemiology, and etiology of pediatric stroke. The remainder of the discussion will cover the state of the knowledge regarding pediatric

stroke outcomes, organized into three domains: sensorimotor, psychosocial, and cognitive functioning. The focus of this review is cognitive outcome following stroke, but a brief summary of sensorimotor and psychosocial outcomes is necessary to develop a more general understanding of the consequences of stroke in children. The review of cognitive outcome research will begin with a discussion of cognitive development and a brief comparison of adult and child outcomes following stroke. The cognitive outcome literature will be further divided into cross-sectional and longitudinal studies of general cognitive functioning (general cognitive ability, verbal, and nonverbal functioning), neuropsychological functioning (executive functions and memory), and studies examining lesion laterality. I will summarize and discuss predictors of outcome and methodological limitations of previous research. Finally, I will conclude with a meta-analysis of cognitive outcome studies.

Definition and Epidemiology

Stroke can occur as an ischemic (lack of blood flow) or hemorrhagic (accumulation of blood) event. The term ischemic stroke encompasses arterial ischemic stroke (AIS) and sinovenous thrombosis (Amlie-Lefond, Sebire, & Fullerton, 2008). AIS comprises the vast majority of ischemic stroke in children and is approximately four times more prevalent than sinovenous thrombosis (Hetherington, Tuff, Anderson, Miles, & deVeber, 2005; Kirton, Westmacott, & deVeber, 2007). The term AIS describes a brain infarction in an arterial distribution secondary to occlusion of cerebral arteries and sinovenous thrombosis is defined as venous blockage (e.g., thrombotic occlusion). Both AIS and sinovenous thrombosis can be caused by a blood clot obstructing arterial blood

flow. Sinovenous thrombosis occurs in the cerebral sinuses, which are part of the venous system responsible for draining blood from the brain (Pappachan & Kirkham, 2008). Hemorrhagic stroke includes intracerebral and subarachnoid hemorrhage and can arise spontaneously (i.e. ruptured aneurysm) or due to trauma (Jordan & Hillis, 2007). Research suggests AIS and hemorrhagic stroke are equally common in children, with an estimated incidence of approximately 1 to 3 out of 100,000 for each type (DeShryver et al., 2000; Jordan & Hillis, 2007; Mackay & Gordon, 2007; Roach et al., 2008).

Pediatric stroke is also differentiated based on age. The term 'perinatal stroke' refers to a cerebrovascular event occurring from early gestation through the first month of life (Mackay & Gordon, 2007; Roach et al., 2008; Stiles, Nass, Levine, Moses, & Reilly, 2010). The terms 'neonatal' and 'perinatal' are sometimes used interchangeably, although 'neonatal' technically refers only to events following birth and not to those occurring during gestation. The exact timing of stroke early in life is often hard to determine and thus, the term 'perinatal' is sometimes preferable (Amlie-Lefond et al., 2008; Golomb, Garg, Edwards-Brown, & Williams, 2008). Childhood stroke refers to cerebrovascular lesions occurring in children between 1 month and 18 years of age (Amlie-Lefond et al., 2008; Lynch et al., 2002; Mackay & Gordon, 2007).

Technological advances in neuroimaging techniques have increased the detection and diagnosis of childhood stroke (deVeber, Roach, Riela, & Wiznitzer, 2000). Advanced medical treatments have also increased the life expectancy of children with certain diseases associated with stroke, thus increasing the risk of vascular complications (deVeber, 2002; Pappachan & Kirkham, 2008). Estimates of the annual incidence of

childhood stroke have increased, although they vary based on the population studied. Research suggests that the incidence of childhood stroke ranges from 2 to 4 per 100,000 in the United States and may be as high as 13 per 100,000 children in France (Amlie-Lefond et al., 2008; Lo et al., 2008; Lynch et al., 2002; Jordan, 2006). Stroke is more common in neonates, with an estimated incidence of 1 per 5,000 live births (Amlie-Lefond et al., 2008). Perinatal stroke may be under-recognized and some researchers suggest the incidence may be as high as 1 per 4,000 live births (Lynch et al., 2002; Mackay & Gordon, 2007). Compared to girls, boys are at an increased risk for stroke (Golomb, Fullerton, Nowak-Gottl, & deVeber, 2009; Lopez-Vicente et al., 2010; Pappachan & Kirkham, 2008; Steinlin, Roellin, & Schroth, 2004). The sex disparity may be due to the higher prevalence of cardiovascular, mitotic, traumatic, and dysplasic etiologies in juvenile males compared to females (Braun et al., 2001). Although findings are inconclusive, hormonal differences may also account for sex differences. Specifically, researchers have hypothesized that estrogen may play a protective role in the onset and recovery from stroke in females (Golomb et al., 2009).

Etiology and Clinical Presentation

The etiology of pediatric stroke is broad and varies depending on the timing and type of cerebrovascular event. A complete discussion of the causes and clinical presentation of both ischemic and hemorrhagic stroke is beyond the scope of this study and therefore the current discussion will be limited to arterial ischemic stroke (AIS), not including sinovenous thrombosis. Likewise, studies that were restricted to children with unilateral lesions that did not have a specified origin, and studies that included comorbid

neurological disorders (i.e., cerebral palsy, sickle cell disease), will be excluded from the current review and subsequent meta-analysis.

Perinatal AIS

The vast majority of perinatal stroke is ischemic and typically involves the middle cerebral artery distribution, affecting large portions of one cerebral hemisphere (Kirton & deVeber, 2009; Stiles et al., 2010). Although the cause is often unknown, several maternal and fetal risk factors have been linked to perinatal AIS (Lynch et al., 2002; Mackay & Gordon, 2007). Maternal risk factors include history of infertility, chorioamnionitis (placental infection), premature or prolonged rupture of membranes, primiparity (first child), vacuum extraction, emergency cesarean section, preeclampsia (hypertension associated with kidney problems, and sometimes seizures), oligiohydramnious (decreased amniotic fluid), infection during pregnancy, coagulation disorders, autoimmune disorders, twin gestation, and advanced maternal age (Kirton & deVeber, 2009; Mackay & Gordon, 2007; Roach et al., 2008; Stiles et al., 2010). Fetal risk factors include birth trauma, heart rate abnormalities during birth, asphyxia, cardiac and other congenital abnormalities, low Agpar scores, resuscitation at birth, polycythemia (excess red cells), infection, coagulation disorders, and low birth weight (Mackay & Gordon, 2007; Roach et al., 2008; Stiles et al., 2010).

Approximately 70% of term infants with perinatal AIS present with seizures during the neonatal period. In approximately 75% of preterm infants with perinatal stroke, AIS is diagnosed following a routine ultrasound (Stiles et al., 2010). In a smaller group of children, perinatal AIS is not diagnosed until later, around 4 or 5 months of age,

when infants typically begin to exhibit early voluntary hand use (Lynch et al., 2002). Early hand preference can be indicative of hemiparesis. In these cases, children are diagnosed with presumed perinatal AIS after neuroimaging documents evidence of a previous stroke (Kirton & deVeber, 2009; Mackay & Gordon, 2007; Roach et al., 2008; Stiles et al., 2010).

Childhood AIS

A known predisposing cause can be identified in about 50% of the cases of childhood AIS at the time of infarction (Amlie-Lefond et al., 2008; Jordan, 2006; Pappachan & Kirkham, 2008; Roach et al., 2008). Traditional risk factors for stroke in adults include hypertension, hyperlipidemia, diabetes, smoking, and atherosclerosis (thickened artery walls resulting from high cholesterol), but these are rare in children (Bernard, Goldenberg, Armstrong-Wells, Amlie-Lefond, & Fullerton, 2008). The most common risk factors of childhood AIS include cardiac disorders, sickle cell disease, infection, coagulation disorders, vascular disorders, and other rare genetic disorders (Jordan, 2006; Lynch et al., 2002; Roach et al., 2008). Cardiac disorders, including both acquired and congenital heart disease, are the most common cause of childhood stroke, accounting for approximately 25% of cases of AIS (Jordan, 2006; Lynch et al., 2002). Sickle cell disease is the most common cause of stroke in African American children (Jordan, 2006; Lynch et al., 2002). AIS is more common in young children with sickle cell disease, whereas hemorrhagic events are more common in older children with this disease (Amlie-Lefond et al., 2008). Approximately one third of childhood AIS is caused by infections such as meningitis, encephalitis, systemic sepsis, human immunodeficiency

virus (HIV), and varicella zoster (Jordan, 2006; Lynch et al., 2002). Coagulation disorders may increase the risk for AIS because children with these disorders are more vulnerable to forming blood clots (Amlie-Lefond et al., 2008). Vascular disorders, including arterial dissection, moyamoya syndrome, and vasculitis, can also increase the risk of AIS. Arterial dissection most commonly occurs in the internal carotid and vertebral arteries and involves an abnormal tear in the arterial wall causing a small pocket to form and fill with blood (Pappachan & Kirkham, 2008). As this grows, the blood supply can be decreased or a clot can form and travel upstream to the brain. Moyamoya is Japanese for 'puff of smoke' and is associated with constricted vessels in the brain. This results in a tangled network of small blood vessels to compensate the blockage and resembles a puff of smoke on neuroimaging (Jordan, 2006; Lynch et al., 2002; Pappachan & Kirkham, 2008; Roach et al., 2008). In some cases, a thorough medical evaluation may identify multiple risk factors in a single patient (Roach et al., 2008).

Traditionally, recognition of pediatric stroke has been delayed because stroke is considered relatively rare in children and several disorders share similar symptoms (e.g. migraines, seizures, tumors, fever, demyelination disorders, and functional disorders) (Amlie-Lefond et al., 2008; deVeber et al., 2000b; Fox & Fullerton, 2010; Kirton et al., 2007). Furthermore, symptoms can be difficult for family members to identify and the presentation can vary depending on the location of infarct. AIS frequently involves the middle cerebral artery territory, and subcortical infarcts in the basal ganglia and thalamus are relatively common. Typical symptoms include hemiparesis, hemiplegia, seizures, and focal neurological signs, such as aphasia and visual disturbance (Amlie-Lefond et al.,

2008; McLinden, Baird, Westmacott, Anderson, & deVeber, 2007). AIS in the posterior circulation is less common and can present with ataxia, vertigo, or vomiting (Amlie-Lefond et al., 2008). Additional symptoms include altered mental state, acute neurologic deficits, and headache (Jordan 2006).

Given the array of physical symptoms and disorders that mimic stroke, a clinical diagnosis of AIS should have radiographic confirmation (Bernard et al., 2008; Kirtonet al., 2007). Several neuroimaging techniques can be used to aid in the diagnosis of stroke. Computed tomography (CT) is best used to identify large infarcts by imaging edema and blood (Kirton et al., 2007). Magnetic resonance imaging (MRI), specifically diffusion weighted imaging (DWI), is preferred over CT because it is more sensitive (Kirton et al., 2007). DWI uses gradient-echo imaging to image blood and can detect acute AIS within minutes of ischemia (Amlie-Lefond et al., 2008). Vascular imaging, such as a conventional angiogram, is often used in conjunction with neuroimaging to diagnose cerebral arteriopathy (Amlie-Lefond et al., 2008). Techniques such as transcranial carotid Doppler are used to monitor cerebral vasospasm and help prevent future stroke (Amlie-Lefond et al., 2008; Kirton et al., 2007).

Although the detection and treatment of stroke in adults have vastly improved in the past several decades, relatively little is known about AIS in children because of the purported rarity of this condition (Fox & Fullerton, 2010; Mallick & Ganesan, 2008). Treatment strategies for children with stroke have been extrapolated from the adult literature, but few studies have examined the safety and effectiveness of treatments in children (Amlie-Lefond et al., 2008; Fox & Fullerton, 2010; Jordan, 2006). Anticoagulant

therapy is a possible treatment, depending on the cause and type of stroke (Fox & Fullerton, 2010; Pappachan & Kirkham, 2008). Heparins are often used in the acute phase of AIS because they increase the activity of antithrombin, an intrinsic anticoagulant. Aspirin is typically used for the secondary prevention of recurrent AIS. However, consistent dosing guidelines for heparins and aspirin have not been established in pediatric populations (Bernard et al., 2008). Further research is needed to examine the effectiveness of available therapies in children and develop new treatment strategies.

Outcome of Pediatric Stroke

Recent estimates suggest the mortality rate of pediatric AIS ranges from 6 to 16% and may be higher in recurrent stroke (Bernard et al., 2008; Jordan, 2006; Pappachan & Kirkham, 2008). Perinatal AIS has a relatively low recurrence rate of approximately 3% to 5%; the recurrence rate of childhood AIS is higher and ranges from 20% to 40% (Mackay & Gordon, 2007). The risk for recurrence is related to the underlying pathology of stroke and may be higher in children with predisposing conditions such as sickle cell disease, complex congenital heart disease, or moyamoya (Roach et al., 2008). In survivors, the morbidity rate is high and at least 50% of children have neurological sequelae, learning difficulties, or seizures (Amlie-Lefond et al., 2008; Mackay & Gordon, 2007). Furthermore, in the US, the median cost for the first year of treatment of pediatric stroke is approximately $42,338 (Lo et al., 2008).

Sensorimotor Outcome

Sensorimotor functions are often affected following pediatric AIS, with paresis being a common outcome (Mallick & Ganesan, 2008). AIS involving subcortical regions

can cause a variety of motor impairments depending on the severity and site of the lesion. During typical development, corticospinal tracts originate in the motor cortex and the majority dessucate (cross to the contralateral side) in the medullary pyramids (Stiles, 2010). Thus, motor functions are contralaterally controlled in the cerebral cortex and unilateral lesions typically disturb motor functions on the opposite side of the body (Max, 2004). Whether upper or lower extremities are affected depends on the arterial distribution where the stroke occurs. As previously stated, AIS most commonly occurs in the territory of the middle cerebral artery (Gordon et al., 2002). The middle cerebral artery supplies blood to the brain regions responsible for controlling the upper extremities, head, and face. AIS is less common in the anterior cerebral artery distribution, which supplies brain regions responsible for controlling the lower extremities. AIS is also less common in the posterior cerebral artery territory, which distributes blood to the posterior fossa (cerebellum, brain stem). Following stroke, children may experience mild to severe hemiparesis, change in handedness, abnormal reflexes, motor asymmetries, and dystonia. Although the evidence is mixed, some research suggests motor impairment may diminish over time (Hogan, Kirkham, & Isaacs, 2000).

Psychosocial Outcome

Children may also experience psychosocial changes following AIS. Social impairment and personality changes have been well documented in adults following AIS, but have been less studied in children (Trauner, Nass, & Ballantyne, 2001). Early studies indicate infants with perinatal stroke may display more negative temperaments than

healthy infants. An increase in behavioral or psychiatric problems has also been noted in a sample of children with hemiplegia (Trauner, Nass, & Ballantyne, 2001). Children with early focal brain infarcts may display abnormal social behaviors. Researchers theorize the acquisition of complex social skills and moral rules may be impaired because of early, localized brain lesions. Trauner and colleagues (2001) compared children with perinatal stroke and a healthy control group. They did not find significant group differences in the level of social, emotional, or behavioral problems on the parent form of the Child Behavior Checklist. In another study, Max and colleagues (2002) used the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version to examine children with stroke and children with orthopedic injuries. They found that certain psychiatric disorders (i.e., attention deficit/hyperactivity disorder, anxiety disorders, mood disorders, personality disorders) were significantly more common among children with stroke than those with orthopedic injuries. Moreover, in the stroke group, they found that psychiatric disorders were independently and significantly correlated with factors such as low IQ, neurological abnormalities, and family psychopathology. They concluded that psychiatric disorders are more common following pediatric stroke, but that certain factors, such as average IQ and normal neurological examination, may be protective. In a long-term follow-up study examining 20 children with perinatal and childhood stroke, Steinlin, Roellin, and Schroth (2004) documented parent reported behavior problems in 44% of their sample. Based on parent report, they argued that behavior problems were related to brain dysfunction, rather than

parental and child frustration. Research in this area is still sparse, and future studies of psychosocial outcome after pediatric stroke are needed.

Cognitive Outcome Following Stroke

As stated previously, this review will begin with a discussion of cognitive development, followed by a comparison of cognitive outcomes that occur after stroke in adults and children. Theories that purport to account for the developmental differences observed in pediatric and adult populations will also be discussed. Cognitive outcome research will then be divided into cross-sectional and longitudinal studies examining general cognitive functions, specific neuropsychological functions, and laterality effects. The studies of general cognitive outcomes primarily used intelligence tests, such as the Wechsler Intelligence Scales. The studies examining specific neuropsychological outcomes typically included measures of verbal memory, nonverbal memory, attention, processing speed, and cognitive flexibility. The studies investigating the effect of lesion laterality included measures of functions typically mediated by left-hemisphere (i.e., language skills) and right-hemisphere (i.e., visuospatial processing) brain regions. The literature review will conclude with a summary of the results and limitations of previous studies and three separate meta-analyses examining general cognitive ability (Full Scale IQ), verbal skills (Verbal IQ), and nonverbal skills (Performance IQ).

Cognitive Development

Pediatric stroke research offers a unique opportunity to examine how the developing brain recovers following injury (Hogan, Kirkham, & Isaacs, 2000). The development of the human neocortex begins in utero, before gestational age 27 weeks,

and continues throughout childhood (Huttenlocher & Dabholkar, 1997). Synaptogenesis occurs in the third trimester of gestation and continues during the first 2 years of life. Following this period of rapid growth, the brain begins the process of pruning, or eliminating excess synapses. Research suggests the timing and duration of synaptogenesis and synaptic pruning differ based on brain region (Huttenlocher & Dabholkar, 1997). Neuroimaging studies have demonstrated linear increases in white matter and nonlinear changes in cortical gray matter (Giedd et al., 1999). Furthermore, volume changes are regionally specific. The primary cortical regions, involved in basic motor and sensory functions, develop first. Next, parietal regions, involved in space and language function, complete development during early adolescence. Finally, areas such as the prefrontal cortex begin to mature late in adolescence and continue to develop throughout early adulthood (Kolb & Fantie, 2009).

Neurodevelopment is a complex process and long-term outcomes of stroke may depend heavily on the site and size of the infarct and when the stroke occurs (Anderson et al., 2009; McLinden et al., 2007; Westmacott et al., 2010). Following stroke, children and adults may experience different patterns of cognitive recovery (Hurvitz, Warschausky, Berg, & Tsai, 2004). Adults struggle to regain lost skills, whereas children face a disruption in the normal trajectory of cognitive development (Dennis, 2000; Hurvitz et al., 2004). Furthermore, in early childhood, cognitive development typically increases at a much faster rate than later in life (Duval et al., 2008). Adults are also more likely to display lateralized deficits coinciding with lesion location, while this trend has not been

consistently documented in children. Finally, the outcomes of childhood AIS are less predictable compared to AIS during adulthood.

In healthy adolescents and adults, language functions are generally controlled by the dominant hemisphere, which is typically the left (Lidzba, 2005). Thus, in theory, damage to the left/dominant hemisphere leads to language impairment, while damage to the right/non-dominant hemisphere affects visuospatial skills (Montour-Proulx et al., 2004). However, this pattern has not been characteristic of children with unilateral brain damage. Current research suggests that both hemispheres are involved in early language development and acquisition. Neuroimaging studies suggest left hemispheric specialization for language may be age-dependent and the brain may become more lateralized over time (Lidzba, 2005). Hogan and colleagues (2000) suggest complete lateralization may not be evident until approximately 5 years of age. Following early injury to the left hemisphere, the brain can demonstrate reorganization, with language functions subsumed by the right hemisphere (Chilosi et al., 2005; Guzzetta et al., 2008; Lidzba, Staudt, Wilke, Kragelow-Mann, 2006). Indeed, in children with early stroke, language acquisition can be delayed, yet few verbal deficits are noted when they enter adulthood (Lidzba, 2005; Lidzba et al., 2006).

Cognitive Outcome Following Stroke in Adults versus Children

Few studies have directly compared adults and children following stroke. Available research is contradictory, but recent studies suggest outcomes in adults and children may be similar, with children demonstrating a lesser degree of recovery than adults in some cases. Mosch, Max, & Tranel (2005) matched 29 pairs of adults and

children based on lesion volume and location (right versus left hemisphere) to compare neuropsychological outcomes. Analyses indicate a similar pattern of deficits in pairs of adults and children with matched unilateral lesions. Learning and memory impairments were the most common weaknesses following stroke. In adults and children, results indicate lesion location and size may be more predictive of outcome than age. However, compared to matched adults, children with left hemisphere lesions were more likely to demonstrate visuospatial deficits and less likely to demonstrate speech and language deficits.

Montour-Proulx and colleagues (2004) examined intelligence test results from 417 children and 218 adults with a documented unilateral cortical lesion. Data were reportedly obtained from medical records (n = 340) and the scientific literature (n = 295). Cases were selected based on the availability of the following information: neuroradiological or surgical identification of a unilateral lesion, etiology, lesion location, age at lesion onset, age at testing, sex, and Wechsler Verbal IQ (VIQ) and Performance IQ (PIQ). Apart from listing the inclusion criteria, Montour-Proulx et al. (2004) did not describe how data were obtained from the scientific literature. Multivariate analyses revealed lesion volume accounted for the most variance in both VIQ and PIQ. Age at lesion was also significantly and positively correlated with VIQ scores, but not PIQ or overall IQ scores.

Duval and colleagues (2008) examined 725 medical records from adults and children (age range: 0 to 84 years) with documented unilateral focal lesions and IQ testing post-stroke. Age at lesion was positively correlated with mean full-scale IQ score

(FSIQ). Of the 725 charts reviewed, 240 individuals received more than one IQ test post-stroke. In this group, researchers found childhood lesions were associated with a greater decrease in FSIQ over time than adulthood lesions.

The difference in outcomes across ages is most likely associated with the neurological underpinnings of stroke. Schaller (2007) explains that although the biochemical cascade is the same across ages, the underlying pathophysiological mechanisms of ischemic brain damage affect age subgroups differently. It begins with the "rapid depletion of high-energy amino acids, high intracellular concentrations of calcium and the production of free radicals," (Schaller, 2007, p. 10). The degree of brain damage is largely dependent on age at stroke because of neurochemical and neurodevelopmental differences.

Although further research is needed, evidence suggests that the relationship between outcome and age may be nonlinear. Schaller (2007) suggests that the greatest impairment is frequently observed in extremely young or extremely old individuals. It is hypothesized that the intermediate age group may be more tolerant of hypoxic-ischemic brain damage because of unique neuroprotective factors (Schaller, 2007). Further complicating matters is the variable course of degeneration and subsequent plasticity following brain injury. Kolb, Teskey, and Gibb (2010) explain that the neurochemical cascade and associated cellular changes lead to a period of degeneration following brain injury. Eventually, the degeneration stabilizes and a process of regrowth and plasticity ensues. The exact timing and duration of the degeneration and plasticity is unknown and

most likely varies based on individual characteristics, such as age, environmental experience, and factors affecting gene expression.

Competing theories offer different explanations for the effects of injury in the developing versus adult brain. In the 1930s and 1940s, Kennard conducted some of the first studies of early brain injury in monkeys (Kennard, 1942; Kolb & Gibb, 2007). Her experiments involved ablating portions of the sensorimotor cortex in adult and infant monkeys. She noted that infants initially suffered less severe motor impairments compared to adult monkeys with similar ablations. Initial findings suggested earlier age at injury was associated with a greater potential for functional reorganization. However, she also observed that the infants exhibited delayed deficits that were not noted in the adult monkeys (Giza, Kolb, Harris, Asarnow, & Prins, 2009; Kennard, 1942; Levine, Kraus, Alexander, Suryakham, & Huttenlocher, 2005; Max, Bruce, Keatley, & Delis, 2010; Mosch, Max, & Tranel, 2005; Teuber & Rudel, 1962). Indeed, over time, the juveniles exhibited spasticity, uncoordinated fine motor movements, and difficulties with ambulation that persisted into adulthood (Giza et al., 2009). She concluded that the pattern of behavioral deficits differed between adults and infants (Dennis, Wilkinson, Koski, & Humphreys, 1995). She also observed that lesion size was predictive of outcome, with larger lesions predicting greater impairment (Kennard, 1942). Later research by Harlow and colleagues confirmed Kennard's initial findings supporting plasticity in infant monkeys. Their research suggested that infant monkeys with cortical damage recovered better than adolescent and adult monkeys with similar injuries (Akert, Orth, Harlow, & Schiltz, 1960; Kolb & Gibb, 2007). However, later studies conducted by

Goldman and Rosvold (1972) refuted the notion of early plasticity. Goldman and Rosvold's (1972) research suggested infant and juvenile monkeys with subcortical damage to the caudate nucleus displayed similar deficits on cognitive measures.

Neurodevelopmental research has continued to produce contradictory results, thus spurring the debate regarding plasticity versus vulnerability in the immature brain (Duval et al., 2008). In a review of neural plasticity research, Stiles (2000) explained that proponents of the 'plasticity' hypothesis suggest the young brain is less vulnerable to injury because healthy tissue is able to compensate for damaged tissue. According to this theory, functional and structural reorganization is possible because the immature brain is not yet specialized and can anatomically adapt to damage (Duval et al., 2008). Support for this theory comes from evidence of better recovery of critical motor and language functions after early brain injuries (Bates et al., 2001). However, opponents of the 'plasticity' theory have suggested that reorganization of brain functions is not always beneficial. Supporters of the 'early vulnerability' hypothesis suggest that the immature brain is more susceptible to damage. Researchers hypothesize that early injury disrupts the integrity of the developing brain and can cause problems later in development (Long et al., 2010). The 'early vulnerability' hypothesis postulates that the emergence of sophisticated cognitive functions relies upon the successful development of specific brain regions (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Long et al., 2010; Westmacott et al., 2010). Thus, children with early injuries may lack the foundation for later-maturing skills to develop, and deficits may not emerge until years after the stroke (Chapman, Max, Gamino, McGlothlin, & Cliff, 2003).

Research also suggests a 'crowding effect' may occur when healthy tissue subsumes the functions of damaged tissue and becomes functionally overloaded. The 'crowding effect' can lead to an overall decline in functions assumed by healthy tissue (Anderson et al., 2009). This may explain why certain functions, such as basic language skills, are preserved following left hemisphere damage, whereas complex visuospatial skills decline (Everts et al., 2008; Lidzba et al., 2006; Max, 2004). Lidzba and colleagues (2006) found evidence of the 'crowding effect' in a group of children with early left hemisphere lesions and language reorganization. Children with right hemisphere language lateralization demonstrated greater impairment on visuospatial tasks than non-head injured controls and children without right hemisphere language lateralization. The reason for the functional dominance of language as compared to visuospatial skills is still debated. Nevertheless, research consistently documents the reorganization of language skills following left hemisphere damage in children (Everts et al., 2008).

Cognitive Outcome Following Pediatric AIS

Initial cross-sectional studies examining the cognitive outcomes of pediatric AIS have yielded somewhat contradictory results (Stiles et al., 2010; Westmacott, MacGregor, Askalan, & deVeber, 2009). On one hand, some studies suggest children demonstrate little to no cognitive impairment following AIS. On the other, recent studies suggest only 12.5% to 14% of children fully recover without residual impairment following stroke (Christerson & Stromberg, 2010; Ganesan et al., 2000; Steinlin, Roellin, & Schroth, 2004). Furthermore, some research indicates that the average IQ of children following

AIS is at least one standard deviation below that of control children (Levine et al., 2005; Stiles et al., 2010).

In one of the first cross-sectional studies examining short-term outcome following AIS and sinovenous thrombosis, Hetherington and colleagues (2005) reported cognitive functioning was average following perinatal and childhood stroke. They compared 47 children with AIS and 25 children with sinovenous thrombosis to determine whether cognitive outcomes differ based on stroke type. Children in the AIS group were approximately 4.5 years of age at diagnosis and 4.9 years of age at assessment. Children in the sinovenous thrombosis group were approximately 3.7 years of age at diagnosis and 4.2 years of age at assessment. Children were administered age-appropriate cognitive instruments (i.e., Bayley Scales of Infant Development (BSID), Wechsler Preschool and Primary Scale of Intelligence-Revised Edition (WPPSI-R), Wechsler Intelligence Scale for Children-Third Edition (WISC-III), and Wechsler Adult Intelligence Scale-Revised (WAIS-R)) between 3 and 12 months post-stroke. The AIS and sinovenous thrombosis groups did not differ in terms of age at stroke, time since stroke, age at assessment, SES, or assessment instrument used. In addition to stroke type, researchers examined factors including etiology, seizures, neurologic disorders, lesion characteristics, developmental factors (age at onset, time since diagnosis, age at test), and SES. Children were divided into four groups based on lesion location: no parenchymal lesion (sinovenous thrombosis patients only), subcortical region (caudate, putamen, globus pallidus, substantia nigra, internal capsule, thalamus, brain stem, or cerebellum), cortical region, or combined subcortical and cortical region. Children were also divided into 3 groups based on age of

onset: infant onset (stroke in first 6 months of life), early onset (stroke between 6 months and 4 years of age), and late onset (stroke after 4 years of age).

Overall, children performed in the average range on cognitive measures (M = 98.5, SD = 12.1) and mean IQ scores did not significantly differ from the normative population mean (Hetherington et al., 2005). Mean IQ scores did not significantly differ between the AIS (M = 98.9, SD = 12.9) and sinovenous thrombosis (M = 97.8, SD = 10.4) groups. Children with combined cortical and subcortical lesions tended to perform the worst (M = 89.8, SD = 10.6), although this may have been confounded by lesion volume. Children with no apparent lesions (sinovenous thrombosis patients only) tended to perform the best (M = 101.2, SD = 11.9). The association between lesion location and cognitive outcome was not statistically significant. SES and IQ were associated, with lower SES predicting lower IQ score, but the relationship was not statistically significant. None of the other variables examined significantly predicted IQ scores. Although the sample was relatively large compared to other pediatric stroke studies, statistical power was still relatively low.

Unlike the results of the previous study, Pavlovic and colleagues (2006) documented cognitive deficits in the majority of their sample of children with AIS. Specifically, they examined children with AIS occurring in the neonatal period (n = 11) and during childhood, between 1 and 16 years of age (n = 33; M = 8.5 years). Participants in the neonatal group were assessed at a mean age of 1.8 years (range: 1.0 to 3.7 years); participants in the childhood AIS group were assessed at a mean age of 10.2 years (range: 2.1 to 18.2 years). Children in the neonatal stroke group were administered the BSID-II

(n = 10) (Motor M = 79.8; SD = 29.4; Mental M = 83.1; SD = 28.7) and the K-ABC (n = 1). Statistical analyses were not reported for the neonatal group. In the childhood AIS group, IQ was examined using the Kaufman Assessment Battery for Children (K-ABC) (n = 9), the German version of the WISC (Hamburg-Wechsler Intelligence Test for Children) (n = 8), the German version of the WAIS (Hamburg-Wechsler Intelligence Test for Children) (n = 3), and the BSID-Second Edition (BSID-II) (n = 2). Results are difficult to interpret because sample sizes are inconsistently reported throughout the study and the methods are poorly explained. FSIQ means were reported for 10 children who completed the WISC/WAIS (M = 99.2; SD = 12.9) and 9 children who completed the K-ABC (M = 93.9; SD = 17.0). FSIQ means did not significantly differ from normative population means. Significant differences between the childhood AIS group and normative population means were noted on the PIQ (M = 94.5; SD = 14.7), but not the VIQ (M = 103.3; SD = 13.9). Overall, the investigators concluded that following AIS, children perform in the low-average range with some isolated deficits. Notably, verbal skills appeared to be preserved whereas nonverbal skills were reduced, regardless of lesion laterality (Pavlovic et al., 2006). In addition, a quadratic regression analysis demonstrated that IQ and age at stroke were weakly related (R^2 = .23). Strokes occurring during middle childhood (5 to 10 years) were associated with favorable cognitive outcomes, whereas early (age < 5 years) and late (age > 10 years) strokes were associated with worse outcomes. Results are limited by the small sample, wide range of age distribution, and use of different cognitive measures (Pavlovic et al., 2006).

Conversely, Ricci and colleagues (2008) did not find evidence of significant impairment in their investigation of cognitive outcomes in children with perinatal AIS. Specifically, they examined 28 children with perinatal AIS between the ages of 5 years, 6 months and 10 years, 6 months (*Mdn* = 5 years, 8 months). They used MRI to document affected brain regions and to assess involvement of subcortical structures (i.e. basal ganglia, thalami, internal capsule). They measured cognitive outcomes using either the WPPSI-R or the WISC-III UK, depending on the child's age. The WPPSI-R was administered to 20 children and the WISC-III UK was administered to 8; 1 child was unable to complete testing. Twenty-one out of 27 children (78%) performed within the average range (*M* = 104; range: 82 to 144) on the FSIQ. The remainder of children performed below average (11%), with FSIQ scores from 71 to 79, or well below average (11%), with FSIQ scores below 70. Ricci et al. (2008) noted that children who performed below average also had abnormal imaging or clinical features. Approximately 80% of children performed within the average range on the PIQ and the VIQ. Almost half of the children (11 of 27, 41%) displayed a significant difference between VIQ and PIQ scores. Of these, nine scored significantly higher on the PIQ than the VIQ. The researchers did not perform statistical analyses to compare group IQ mean scores with normative data. They did not find significant correlations between cognitive impairment and size or location of infarct. Similarly, although children with seizures tended to display cognitive impairment, presence of seizures was not significantly related to cognitive outcome. Non-significant findings may be attributable to low power because of the small sample. In

addition, the sample was too small and heterogeneous to examine the effect of other variables such as socioeconomic status (SES) or cultural background.

To date, Westmacott and colleagues (2010) have conducted the largest cross-sectional study of cognitive outcomes following perinatal and childhood AIS. Their sample (N = 145) included children with perinatal AIS (n = 46), children with AIS occurring between 1 month and 5 years (n = 57), and children with AIS between 6 and 16 years of age (n = 42). Children were assessed at least 6 months post-stroke (M = 4.76 years post-stroke). The mean age at assessment was approximately 8 years in the perinatal and young child group, and 12 years in the older child group. Neurologists reviewed MRI/CT scans to determine lesion location and volume. Locations were classified as subcortical (basal ganglia and/or thalamus), cortical (cortical infarct without subcortical involvement), and combined (subcortical and cortical involvement). Lesion volume was classified as small (<10% of parenchymal volume), medium (10-25% of parenchymal volume), or large (>25% of parenchymal volume). Cognitive measures included the WPPSI-R (n = 12) or the WPPSI-III (n = 18) for preschool-aged children (n = 30) and the WISC-III (n = 51) or the WISC-IV (n = 64) for school-aged children (n = 115). Researchers noted that different editions were used in order to maximize sample size and include participants who were tested over a period of 13 years.

Although children performed within the lower end of the average range (FSIQ M = 94.47, SD = 14.70), all index measures for the participant group differed significantly from the WPPSI/WISC normative sample (Westmacott et al., 2010). Performance did not significantly differ between the subcortical and cortical lesion groups. Children with

combined subcortical and cortical lesions (FSIQ $M = 87.95$, $SD = 14.24$) performed significantly lower than children with restricted lesions (subcortical FSIQ $M = 98.23$, $SD = 14.68$; cortical FSIQ $M = 95.12$, $SD = 12.86$). The group difference remained significant after statistically controlling for the effect of lesion volume. Earlier age at stroke was also related to lower performance on cognitive measures. This association was modulated by lesion location, such that children with perinatal AIS and subcortical involvement demonstrated greater impairment than children with subcortical AIS later in childhood. Similarly, children with cortical AIS occurring between 1 month and 5 years of age performed significantly worse on cognitive measures than the other two groups. Consistent with previous research, Westmacott et al., (2010) did not find significant relationships between cognitive performance and sex or lesion laterality.

Westmacott et al.'s (2010) results support the 'early vulnerability' hypothesis, although lesion location modulates the relationship between age at stroke and cognitive outcome. The study has several shortcomings, including the absence of a healthy control group and the inconsistency of the interval between stroke and assessment, which was longer in the perinatal group than in the other two groups. Time since stroke was significantly negatively correlated with cognitive performance, possibly explaining the lower scores in the perinatal group. Future research is needed to further explore the relationship between time since stroke and cognitive performance.

The aforementioned cross-sectional studies present somewhat disparate results. Levine et al. (2005) attribute the discrepancy in findings to the age of children at the time of assessment. Their study indicates that following early unilateral brain injury, children

assessed before the age of 7 tend to display fewer deficits than those assessed later. They conclude that a decline in IQ may become more evident over time. Recent longitudinal studies have begun investigating long-term outcomes to examine the effect of age and determine whether cognitive functions are stable over time, or if deficits emerge later in development (Ballantyne, Spilkin, Hesselink, & Trauner, 2008; Levine et al., 2005).

In one of the first longitudinal studies of pediatric stroke, McLinden et al. (2007) administered the BSID to 27 children at 12 and 24 months post-stroke. A total of 18 children completed both assessments, 6 completed testing at 12 months only and 3 at 24 months only. The Bayley Mental Development Index was used to assess cognitive and language functioning. The Bayley Psychomotor Development Index was used to assess fine and gross motor development. Compared to the normative sample for the Bayley Scales, participants performed significantly lower on the Psychomotor Development Index at 12 months post-stroke ($M = 93.71$; $z = -2.05$) and 24 months post-stroke ($M = 93.48$; $z = -1.99$). Children performed significantly lower on the Mental Development Index ($M = 92.19$; $z = -2.39$) only at 24 months post-stroke. McLinden et al. (2007) suggest that following neonatal AIS, impairment may be evident as soon as 1 to 2 years post-stroke. Moreover, delays may become more pronounced over time as children with AIS begin to fall behind normally-developing peers. Notably, although children in this study performed significantly below normative expectations, their mean scores were within the average range. The study is limited in that it did not include a control group and neuroimaging data were not available. Additionally, to achieve the maximum sample size, researchers performed statistical analyses separately at the 12 and 24 month

assessments. It is unknown whether children who completed only one assessment differed from those who completed both.

Conversely, in a different longitudinal study, Ballantyne and colleagues (2008) found cognitive functions were stable and in the average range following perinatal AIS. As part of a 20-year longitudinal study examining language and learning, Ballantyne et al. (2008) examined a group of 29 pre-school to school-age children with perinatal unilateral AIS. Lesions were coded for laterality (right or left hemisphere) and severity. Severity was based on a 5-point scale ranging from '1' (focal ventricular dilation or atrophy seen on < 3 cuts on CT or MRI) to '5' (porencephaly or cortical atrophy involving multiple lobes). The researchers used a control group of 38 children with normal medical and developmental histories and with scores ranging from average to above average on cognitive measures. Although the use of a control group is a strength, it may not have been representative of the general population because controls had above-average cognitive performance.

The primary aim of this study was to examine cognitive outcomes longitudinally (Ballantyne et al., 2008). Children completed measures of IQ, academic achievement, and language functions using the same tests over a test-retest interval that averaged 3 years (interval range: 1 year, 5 months to 10 years, 1 month). The test battery included measures of general cognitive ability (WISC-R), achievement (Wide Range Achievement Test-Revised; WRAT-R), expressive and receptive language (Clinical Evaluation of Language Fundamentals-Revised; CELF-R), and/or receptive vocabulary (Peabody Picture Vocabulary Test-Revised; PPVT-R). Researchers attempted to assess 19 school-

age children with AIS and 24 control participants on two occasions, but some participants were unable to complete both testing sessions. It is unknown whether children who completed both sessions differed from those who did not. Children in the AIS group performed in the low-average to average range on measures of general intelligence and academic achievement at the first assessment (FSIQ $M = 94.7$, $SD = 20.4$; WRAT-R Reading $M = 85.0$, $SD = 16.1$; Spelling $M = 82.5$, $SD = 19.1$; Arithmetic $M = 91.5$, $SD = 10.2$) and second assessment (FSIQ $M = 96.1$, $SD = 20.4$; WRAT-R Reading $M = 89.4$, $SD = 13.3$; Spelling $M = 87.0$, $SD = 16.8$; Arithmetic $M = 94.2$, $SD = 18.7$). They performed below average on measures of expressive language ($M = 72.5$, $SD = 12.0$) and in the low-average range on measures of receptive language ($M = 84.2$, $SD = 10.9$). The AIS group performed significantly higher on measures of expressive language at the second assessment, although their scores were still below average ($M = 78.4$, $SD = 16.0$). Children in the control group performed in the average to high-average range on measures of intelligence and in the average range on measures of academic achievement and language skills at both assessments (FSIQ $M = 109.1$, $SD = 12.2$; WRAT-R Reading $M = 113.0$, $SD = 13.3$; Spelling $M = 106.2$, $SD = 15.9$; Arithmetic $M = 111.9$, $SD = 11.2$; Receptive $M = 109.1$, $SD = 12.2$, Expressive $M = 101.0$, $SD = 17.5$). Children in the control group performed significantly higher than children in the AIS group on all measures, at both assessments. Overall, results suggest that the majority of cognitive scores did not change significantly between assessments for either group. Based on their findings, Ballantyne et al. (2008) concluded that intellectual, academic, and language indices remain stable over time during the school-age years in the AIS group. They

suggest that functional plasticity is sufficient to maintain stable development and even improvement in some cases (Ballantyne et al., 2008). However, stable mean scores do not imply stable individual scores across time, and it is difficult to draw conclusions about individual change over time based on their data.

Ballantyne and colleagues (2008) also examined IQ change over a longer time interval using different age-appropriate test versions. Data collection was conducted over a longer test-retest interval, from pre-school (< 6.5 years of age) to school-age (> 6.5 years of age) (Ballantyne et al., 2008). Twenty-three children with perinatal AIS and 24 healthy control participants were administered the WPPSI or WPPSI-R when they were pre-schoolers and the WISC-R or WISC-III when they were school-aged. The investigators do not justify the use of test revisions. The test re-test interval was approximately 5 years (interval range: 1 year, 5 months to 11 years, 9 months). The length of test-retest interval was not correlated with performance. Children in both groups demonstrated a slight but significant improvement over time. Ballantyne et al. (2008) suggest that the increase could be a function of differences between test editions (WPPSI/WPPSI-R and WISC-R/WISC-III). The use of different test editions is a potential limitation because revised tests use updated norms, which may differ from previous editions. Furthermore, in a revised version, test developers may alter the content of items on the test, as well as the manner in which results are interpreted. These changes can make comparisons of data less reliable than is the case when using the same test edition. Indeed, Strauss, Spreen, and Hunter (2000) suggest that researchers should use the same test edition whenever possible in order to maintain continuity in research.

Further analyses indicated that presence of seizures was related to cognitive outcome (Ballantyne et al., 2008). In the longitudinal analysis of cognitive outcomes, children with a history of seizures performed significantly lower on measures of language and general cognitive ability compared to children without a history of seizures. In the analysis examining IQ change over time, the FSIQ of children with a history of seizures did not increase over time, whereas children without seizures improved significantly. Medication was not controlled in the study and it is unknown whether group differences are related to presence of seizures or anti-epileptic drugs. Additional factors, such as lesion laterality and severity, were unrelated to cognitive performance.

Most recently, in a longitudinal study of children with neonatal AIS, Westmacott and colleagues (2009) found evidence of cognitive impairment. Researchers examined 26 children with AIS diagnosed acutely in the neonatal period (between birth and 28 days of life). In all cases, children presented with seizures in the neonatal period and the diagnosis of stroke was confirmed with neuroimaging (MRI or CT). Children with presumed perinatal AIS were excluded. At the initial assessment, participant age ranged from 3 years, 6 months to 5 years, 11 months (M = 4.9 years, SD = 1.2 years). At the follow-up assessment, participant age ranged from 6 years, 1 month to 12 years, 5 months (M = 8.8 years, SD = 2.1 years). There was a minimum of 18 months between the initial assessment and follow-up (interval range: 1.53 to 6.92 years). Children first completed the WPPSI-Revised Edition (WPPSI-R) or the WPPSI-Third edition (WPPSI-III) in preschool. Children then completed the WISC-Third Edition (WISC-III) or the WISC-Fourth Edition (WISC-IV) in grade school. Again, the use of different editions of the

WPPSI and the WISC is not justified by the authors and is a potential limitation. Compared to the normative sample of the WPPSI, preschool-aged children did not significantly differ on FSIQ (M = 99.50, SD = 12.46), VIQ (M = 97.85, SD = 12.53), or PIQ (M = 99.81, SD = 13.24). When the same group of children was assessed with the WISC, significant differences were apparent. Compared to the normative sample of the WISC, school-aged children performed significantly lower on FSIQ (M = 92.81, SD = 12.81, z = -2.44), as well as Perceptual Reasoning (M = 95.15, SD = 13.90, z = -3.81), Working Memory (M = 88.77, SD = 14.21, z = -3.81), and Processing Speed Indices (M = 90.50, SD = 12.48, z = -3.23). Although school-aged children performed significantly lower compared to the normative sample, their scores were still within the average range. Children also tended to perform lower on the Verbal Comprehension Index (M = 95.35, SD = 12.34), but this difference did not reach statistical significance. Westmacott and colleagues (2009) suggest that results are indicative of emerging cognitive deficits. Analyses were limited by the lack of an appropriate control group and the use of different test editions.

Longitudinal analyses contrasting the first and second assessments revealed significant differences on indices of general cognitive ability and nonverbal ability, but not verbal ability (Westmacott et al., 2009). Approximately 70% of the sample showed a significant decline in at least one Index measure between assessments. Westmacott et al. (2009) posit that children with neonatal AIS may make slower gains compared to healthy peers. Furthermore, they explain that following AIS, children tend to display "subtle" weaknesses that may only affect complex cognitive skills (e.g., working memory,

processing speed, abstract reasoning). They did not find a significant relationship between lesion laterality and cognitive performance. Non-significant results may have been due to the small sample. They also analyzed the effect of sex and found males demonstrated a significantly greater decline in nonverbal ability compared to females. Additionally, males had a non-significant trend toward greater decline in FSIQ.

Neuropsychological Outcome Following Pediatric AIS

Initial studies investigating pediatric stroke outcomes primarily focused on gross neurologic and cognitive functioning. More recently, however, researchers have begun examining specific neuropsychological outcomes following pediatric AIS (Long et al., 2010). Studies suggest that although children with AIS may demonstrate average cognitive abilities, they may exhibit pronounced deficits on complex neuropsychological functions (Block et al., 1999; De Schryver et al., 2000; Everts et al., 2008; Westmacott et al., 2009).

In one of the first studies investigating neuropsychological functioning, Block, Nanson, and Lowry (1999) examined attention, memory, and language following unilateral pediatric AIS. Eleven children with AIS occurring between 6 months and 15 years of age were matched with healthy controls in terms of sex, age at testing, and SES. Children in the AIS group were assessed at least 2.5 years post-stroke (interval range: 8 to 23 years). The neuropsychological test battery included measures of divided attention (Symbol Digit Modalities Test; Trail Making Test, Parts A and B), and language and memory functioning (California Verbal Learning Test-Children's Version – CVLT-C; Rivermead Behavioural Memory Test; Revised Token Test; Reporter's Test). Compared

to controls, children with AIS performed significantly lower on the Symbol Digit Modalities Test. Groups did not differ in terms of accuracy but children in the AIS group took significantly longer to complete the measure. Similarly, children in the AIS group performed significantly slower on complex subtests of the Revised Token Test. Taken together, results suggest that following AIS in children, performance may be hindered by processing speed deficits rather than problems with accuracy. Analyses of verbal learning and memory tasks also revealed significant differences between groups. Investigators concluded that pediatric AIS is associated with mild, persistent deficits in verbal memory and processing speed. Notably, participants performed within normal limits, although children in the AIS group tended to perform within the lower bounds, whereas children in the control group tended to perform within the upper bounds of the average range. Block and colleagues (1999) also examined lesion location and compared seven children with right hemisphere lesions to four children with left hemisphere lesions. They did not find a significant effect of laterality on attention, memory, or language functioning. Comparisons were hampered by small sample sizes and heterogeneity of age at stroke and age at assessment.

In a larger study of long-term neuropsychological functioning following pediatric AIS, De Schryver and colleagues (2000) concluded that children recover fairly well. They examined a group of 27 children under 16 years of age. The interval between stroke and assessment was approximately 7 years (*Mdn:* 7 years, interval range: 3 months to 20 years). The wide range of follow-up time is a limitation. The neuropsychological test battery included measures of nonverbal problem solving (Raven Coloured and Standard

Progressive Matrices), verbal skills (Dutch version of the Vocabulary subtest of the WISC-R or the WAIS-R), and behavioral regulation and cognitive flexibility (Card Sorting Task for Children; CST-C). They also administered questionnaires examining quality of life, and a neurological examination. Eleven of the 27 children did not demonstrate functional impairment at follow-up. Participants performed significantly lower than the normative population on the Raven Matrices. On the Vocabulary subtest, approximately 80% of children with stroke performed in the average range and did not significantly differ from the normative population. On the CST-C, children with stroke were within normal limits. Children with seizures demonstrated significant deficits on cognitive measures compared to children without seizures. According to questionnaire data, 9 children required special education, 12 children repeated a grade level, and 17 children required remedial teaching. Although the degree of remediation is not mentioned, results suggest that children may be lagging behind their peers academically. Thus, although children with stroke may not demonstrate widespread cognitive deficits on formal measures, they may be struggling in the classroom setting. The findings are limited by the variable length of time between stroke and assessment.

Guimaraes, Ciasca, and Moura-Ribeiro (2007) examined intellectual and neuropsychological outcomes following childhood AIS (n = 14), occurring between 13 months and 10 years, 6 months. Children with AIS were compared to a randomly selected control group of healthy children (n = 14) matched for sex and age. Children were assessed at a mean age of 9 years, 10 months (age range: 7 years, 1 month to 14 years, 2 months). Age at stroke ranged from 13 months to 10 years and 6 months. Average time

between stroke and assessment was 4 years, 4 months (interval range: 8 months to 7 years, 9 months). The test battery included measures to assess general intelligence (WISC), perceptual motor development (Visual-Motor Gestalt Test), neuropsychological functioning (Luria-Nebraska Battery; LNB), and cognitive development (Test of Human Figure Drawing) (Guimaraes et al., 2007). Overall, 7 of 14 children in the stroke group performed in the average to above-average range on the WISC, whereas all 14 children in the control group performed average or above average. Apparently, researchers qualitatively judged group differences and concluded that the stroke group (FSIQ range: 60 to 123; VIQ range: 70 to 118; Execution/Performance IQ range: 48 to 125) performed lower than the control group (FSIQ range: 91 to 133; VIQ range: 90 to 124; Execution/Performance IQ range: 89 to 128). It is unknown whether group differences are significant because Guimaraes and colleagues (2007) only presented individual index scores and did not include means, standard deviations, or statistical analyses. Similarly, they stated that children with stroke performed lower than controls on LNB measures of motor skill, tactile skill, writing, reading, and memory (Guimaraes et al., 2007). Although the investigators improved on previous studies by including a control group, substantial methodological limitations are inherent in this study. The sample is heterogeneous in terms of age at stroke and time between stroke and assessment. It also included children with recurrent stroke, which may have confounded the findings. Furthermore, the report failed to include necessary statistics to support conclusions. Thus, the findings should be interpreted with caution.

Everts and colleagues (2008) examined neuropsychological functioning, behavior, and quality of life after pediatric AIS. Participants included 21 children with a mean age of 11.11 years (*SD* = 4.3, age range: 6 to 21 years). They compared sample means to the normative population and did not include a control group. Mean age at stroke was 7.3 years (*SD* = 4.6 years, age at stroke range: 1 month to 15 years) and time between stroke and assessment was approximately 4.9 years (*SD* = 3.10 years, interval range: 14 days to 14 years). Researchers administered the WISC-III or the WAIS, depending on participant age at assessment. Three children were examined with the Kaufman-Assessment Battery for Children. Additionally, researchers administered measures to assess visual short- and long-term memory (Rey-Osterrieth Figure), alertness and divided attention (Test of Attentional Performance), and verbal episodic memory (CVLT-C). Complete data were not available for the entire sample as some children were unable to complete the battery. Neuroimaging was available for 15 participants and coded for lesion location and size. It is unknown when imaging was performed post-stroke and whether MRI or CT scans were used in this study. Fourteen patients suffered from left hemisphere stroke and seven suffered from right hemisphere stroke. Three groups were formed based on lesion size: 1-2 cm (*n* = 4), 3-5 cm (*n* = 5), and 6-7 cm (*n* = 6). However, simply calculating lesion size in absolute units is inappropriate in studies of childhood stroke. Instead, researchers should calculate lesion size in relationship to total brain volume because brain volume significantly varies depending on a child's age (Jordan, Kleinman, & Hillis, 2009).

Everts and colleagues (2008) presented group means and individual data because of the relatively small sample. Similar to previous research, children with AIS performed

in the average range on the WISC-III and WAIS (FSIQ $M = 96.47$, $SD = 15$). Five of 17 patients performed below the average range on the FSIQ. Nine out of 18 patients performed below the average range on the PIQ. Notably, PIQ is dependent on intact motor functioning and several patients exhibited motor deficits. Thus, below-average PIQ scores may be explained, in part, by impaired motor skills. Thirteen out of 17 patients demonstrated a significant difference between VIQ and PIQ. Of these 13 children, nine performed significantly higher on VIQ. Laterality was not significantly related to the discrepancy between VIQ and PIQ. Cognitive functions including processing speed, auditory short-term memory, arithmetic skills, visuospatial skills, and attention were more often significantly reduced in this sample than expected in the normative population. Mean values for the CVLT-C and Rey-Figure were average and somewhat below average, respectively; however, sample sizes were too small ($n = 10$) to run statistical analyses. Researchers also found moderate impairment on measures of motor functions, behavior, and quality of life. A curve estimation analysis of age at stroke revealed a trend toward higher PIQ for children who sustained stroke between 5 and 9 years of age. Neither laterality nor presence of seizures was significantly related to cognitive performance. Shortcomings include lack of a control group, small sample size, and poorly defined inclusion/exclusion criteria. In addition, the sample was heterogeneous in terms of age at stroke, age at assessment, and stroke type. Analysis of the effects of age at stroke and laterality was hampered by the small sample size. Additionally, the study did not control for SES and other demographic factors. Despite

these limitations, the investigators concluded that, although group means were within normal limits, individual patients demonstrated isolated cognitive deficits.

Similarly, Long and colleagues (2010) examined the effect of lesion location on executive functions following ischemic (n = 21) or hemorrhagic (n = 7) stroke. Participants included 28 children with a mean age of 12.5 years (SD = 1.8, age range: 10 to 15 years) and diagnosed with stroke at least 18 months prior to the assessment. Specific functions of interest included attention control, goal setting, cognitive flexibility, information processing, and everyday executive functioning. Children completed several measures of executive functioning including Sky Search, Score!, Verbal Fluency Test, Color Word Interference Test, Trail Making Test, Tower Test, Creature Counting, Letter Number Sequencing, and Rapid Automated Naming. Additionally, parents and teachers rated children's daily functioning using the Behavioral Rating of Executive Function. Clinical MRI scans were available for 23 of the participants and CT scans were available for the remaining 5. A pediatric neurologist and neuropsychologist coded neuroimages for lesion characteristics including location, laterality, extent of lesion, and volume. Lesion volume was classified as small (<10% of parenchymal volume; n = 14), medium (10-25% of parenchymal volume; n = 8), and large (>25% of parenchymal volume n = 6), based on the entire brain including brainstem and cerebellum) (Long et al., 2010).

An examination of general cognitive ability was not a primary aim of this study, but Long and colleagues (2010) reported that children performed in the low-average range (M = 91.60, SD = 19.40) on the WASI. On measures of executive functioning, children with stroke tended to exhibit greater impairment compared to normative

populations. Children in their sample also had difficulty with daily executive functioning, as evidenced by significantly lower parent and teacher ratings compared to the normative population.

Long and colleagues (2010) also analyzed the effect of lesion location (frontal versus extra-frontal; cortical versus subcortical) and laterality. Children with frontal and extra-frontal lesions displayed significant impairment in executive functioning, most notably in cognitive flexibility. Compared to the extra-frontal group, children with frontal lesions tended to perform lower on measures of attentional control skills. Despite a large effect size, the group difference was not significant, likely because of small sample sizes and low power. Contrary to results found in the adult literature, children with extra-frontal lesions performed significantly lower on two measures of selective attention and working memory, compared to children with frontal lesions. These results suggest that extra-frontal lesions may lead to global impairment in children, although this trend is not typically observed in adults. Compared to children with subcortical lesions, children with cortical lesions performed significantly lower on a measure of processing speed (Long et al., 2010). However, in this sample, cortical lesions tended to be larger than subcortical lesions. Thus, greater impairment in the cortical group may have been related to lesion volume. Researchers did not find a significant effect of lesion laterality on executive functioning.

In preliminary analyses of age, the researchers found that children with earlier strokes (< 5 years) tended to perform lower on cognitive and behavioral measures than children with later strokes (> 5 years) (Long et al., 2010). In general, results support the

notion that early injury in the developing brain is detrimental to later developing skills, such as complex executive functions. Furthermore, the results suggest that, compared to adults, strokes in children may lead to global impairment that is less related to lesion location. This study is one of the first to examine long-term executive functioning in children following stroke. Results should be replicated with a larger, less heterogeneous sample of children with stroke and a control group.

Most recently, Kolk and colleagues (2011) examined long-term neuropsychological outcomes following neonatal (n = 21) and childhood (n = 10) stroke. They included children with either ischemic (n = 23) or hemorrhagic stroke (n = 8). Participants were between the ages of 4 and 12 years and included 31 children with stroke and 31 healthy children matched for age and sex. Children were assessed between 1 and 11 years following stroke. Although individual scores were not included, researchers reported that all participants obtained IQs over 80 on the Kaufman Assessment Battery. A pediatric neuroradiologist coded acute neuroimages for lesion characteristics. Researchers administered the Pediatric Stroke Outcome Measure (PSOM) and the Developmental Neuropsychological Assessment Battery (NEPSY) to measure neurological and neuropsychological functioning, respectively. Neurological status was moderately to severely impaired in approximately 65% of the children with neonatal stroke and 70% of the children with childhood stroke.

Kolk et al., (2011) converted subtest raw scores to z-scores to make scales comparable. They also compared effect sizes and tested group differences. Researchers compared the stroke and control groups using a covariance analysis to control for the

effect of age at testing, although some of the subtests of the NEPSY did not conform to the normality assumption. Overall, children in the stroke group performed significantly lower on measures of auditory and visual attention, language, sensorimotor functioning, and learning and memory (Kolk et al., 2011). Compared to children with childhood stroke, children with neonatal stroke performed significantly lower on measures of visuospatial skills. Analyses of lesion characteristics revealed a trend towards higher performance among children with right hemisphere lesions compared to children with left hemisphere lesions. Group differences were significant on Visuomotor Precision, Copying, Block Design, and Sentence Repetition subtests from the NEPSY. In addition, among children with neonatal stroke, epilepsy was associated with significantly lower performance on measures of visual attention, language, and verbal learning. This relationship was not observed in the childhood stroke group, but analyses may have been underpowered to detect a significant result. Unlike Long et al., (2010), Kolk and colleagues (2011) concluded that executive functions were relatively intact in their sample of children with stroke. However, null findings could be explained by the rarity of prefrontal lesions in this sample. This study is one of the first to use a prospective design, long-term follow-up, and a control group. Although the analyses were most likely underpowered, the size and composition of their sample is comparable to other studies. An inherent limitation in this study is the questionable validity of the statistical analyses. However, researchers explained that in order to control for the effect of age at stroke, analysis of covariance was the most appropriate procedure to use. Furthermore,

researchers describe this study as longitudinal, even though they appeared to follow a cross-sectional study design.

Laterality of Cognitive Function

Research has yielded consistent findings of hemispheric specialization for motor functions following stroke, but less is known about the laterality of cognitive functions following pediatric stroke (Hogan et al., 2000; Max, 2004). Traditionally, researchers believed language functions were entirely subsumed by the left hemisphere, whereas emotional and visuospatial functions were wholly subsumed by the right hemisphere (Ballantyne et al., 2008; Montour-Proulx et al., 2004). In adults, measures of verbal skills, such as VIQ on the WISC/WAIS, typically reflect left hemisphere function, and measures of nonverbal skills, such as PIQ, typically reflect right hemisphere function (Hogan et al., 2000). This notion has been supported by multiple studies examining cognitive outcomes following unilateral stroke in adults (Hogan et al., 2000).

Recent evidence, however, suggests the laterality of cognitive functions may be more complex than previously thought. Both hemispheres may be responsible for different aspects of language and visuospatial processing. The left hemisphere may control basic language functions such as speech production and comprehension, and the right hemisphere may be responsible for emotional aspects of language (understanding and expressing prosody, metaphor, and humor) (Max, 2004). Similarly, the right hemisphere may be responsible for global aspects of visuospatial processing and coordinate spatial judgments, whereas the left hemisphere may be more responsible for processing local aspects and categorical spatial judgments (Max, 2004; Schatz et al.,

2004). Both hemispheres are involved in spatial processing for the contralateral visual field (Schatz et al., 2004).

Furthermore, although neural development typically progresses along a well-organized path toward hemispheric specialization, the immature brain may possess a capacity for reorganization (Guzzetta et al., 2008; Lidzba & Staudt, 2008; Stiles, 2000). Although results are inconclusive, some research suggests that unlike the mature brain, the young brain may support the development of compensatory strategies following focal injury (Chilosi et al., 2005; Stiles, 2000). Thus, whereas adults with left hemisphere lesions typically exhibit a predictable pattern of language deficits, children's language functions tend to recover fairly well. Moreover, unlike the adult literature, few studies examining pediatric stroke have found a significant difference in verbal performance between left and right hemisphere lesions (Ballantyne, Spilkin, & Trauner, 2007; Bates et al., 2001; Hogan et al., 2000; Westmacott et al., 2010). Studies do suggest, however, that children with stroke typically display poorer visuospatial skills compared with language skills (Schatz, Craft, Koby, & DeBaun, 2004). Schatz and colleagues (2004) suggest this could be due to an inherent vulnerability in visuospatial skills or the "crowding effect". Indeed, an fMRI study of language function following left hemisphere perinatal AIS, confirmed right hemisphere language lateralization in 8 of 10 patients (Guzzetta et al., 2008). This topic remains controversial and reorganization of functions is most likely affected by a variety of factors including timing of stroke, underlying etiology, and presence of seizures (Guzzetta et al., 2008).

As part of a larger cross-sectional study of children with unilateral stroke (Max et al., 2002), Max (2004) sought to investigate laterality effects across a wide range of cognitive domains. Participants included 29 children with either AIS (n = 21) or hemorrhagic stroke (n = 8). Thirteen participants had left hemisphere lesions and 16 had right hemisphere lesions. Timing of stroke was classified as early (occurring from prenatal stage or up to 12 months of postnatal life; n = 17) or late (occurring at age 12 months or later; n = 12). Children ranged from approximately 5 to 19 years of age at the time of assessment. Max (2004) modified scoring rules for some measures. For children who fell outside of the age range of certain tasks, he used the normative data for the youngest or oldest age groups that were available. Max (2004) does not note which test scores were modified. This procedure increases the sample size at the expense of the validity of standard scores. Research MRI scans documented lesion location and volume for 26 participants. Review of clinical CT and MRI scans documented location and volume for the remaining three participants. Volume was calculated in absolute units, and before and after correcting for individual differences in brain volume.

The neuropsychological battery included measures of intelligence (WISC-IV), academic achievement (WRAT-R), language skills (Multilingual Aphasia Examination; Test of Written Language-Third Edition), visuospatial skills (Developmental Test of Visual-Motor Integration), memory (CVLT-C; Rey-Osterrieth Complex Figure Test), and executive functioning (Design Fluency; Wisconsin Card Sorting Test) (Max, 2004). Children performed in the low-average range on the majority of neuropsychological measures. Left and right hemisphere groups did not significantly differ on any measures

and most effect sizes were small, ranging from - 0.1 to - 0.65. In adults, lateralized findings would be expected; left hemisphere lesions would most likely result in language deficits, whereas right hemisphere lesions would result in visuospatial deficits. Findings suggest that the young brain may be capable of reorganization because significant lateralized deficits were not found. A control group of children with congenital clubfoot or scoliosis was recruited as part of the larger study (Max et al., 2002). Preliminary analyses indicated that compared to controls, children with stroke performed significantly lower on several measures. In contrast to the adult literature, these results suggest that children with stroke display milder but more diffuse impairment on neuropsychological measures compared to controls.

In later analyses examining the effect of age at lesion onset, Max and colleagues (2010) found a significant relationship between age and cognitive outcome. Specifically, compared to children with late-onset stroke, children with stroke occurring during the prenatal period through 1 year of age demonstrated lower scores on measures of intellectual function, language, visual and verbal memory, visuospatial function, and academic performance (Max et al., 2010). Conversely, children with late-onset stroke performed lower on measures of executive functions. Limitations of the study include small sample sizes, heterogeneity of stroke type (hemorrhagic vs. ischemic; early vs. late), and variable age at assessment.

In an offshoot of the same study (Max et al., 2002), Chapman and colleagues (2003) examined the recovery of higher-order, complex language skills. Unlike basic language skills, (i.e. vocabulary and grammar), complex functions such as discourse

processing continue to develop through adolescence. Therefore, impairments in higher-order language skills may not emerge for several years post-stroke. Chapman and colleagues (2003) examined discourse skills in a group of 17 children after AIS (n = 11) and hemorrhagic stroke (n = 6). To control for exposure to medical treatment and physical stigma, children with stroke were compared to children with congenital clubfoot (n = 9) or acquired scoliosis (n = 8), drawn from the larger study by Max et al. (2002). Children were individually matched for sex, ethnicity, SES, and age. Research MRIs were obtained for 14 of 17 children in the stroke group to analyze lesion size and location. Clinical CT or MRI scans were analyzed for the remaining three participants who did not undergo a research MRI. To assess discourse processing, children were asked to retell a detailed story consisting of 235 words and 2 episodes. The CVLT-C was used to measure verbal memory. The language structure (amount of words, length of retell) and information structure (content and organization) were analyzed for each child's story. Researchers were most interested in examining each participant's ability to use language to select, organize, and combine information in a meaningful way. Compared to orthopedic controls, children with stroke produced less accurate and more poorly organized stories. In addition, they included fewer details and had difficulty expressing the main ideas. Groups did not significantly differ on measures of verbal memory; thus, differences in discourse cannot be explained by memory deficits. Investigators concluded that the recovery of language functions depends largely on the complexity of tasks.

Chapman and colleagues (2003) also examined age at stroke effects, lesion volume, and laterality. Children with strokes before the age of 12 months produced significantly fewer words compared to children with strokes after the age of 12 months. Furthermore, children in the early stroke group included significantly fewer core propositions and important details compared to children in the late stroke group. Chapman et al. (2003) theorized that early stroke may disrupt neural networks responsible for supporting the development of complex language functions. Therefore, results support the 'early vulnerability' hypothesis. Children with left hemisphere lesions produced significantly longer utterances compared to children with right hemisphere lesions. Researchers did not find significant effects of lesion volume. Findings are limited by small sample sizes. Further research is needed to elucidate the effects of lesion size and location on discourse processing.

As part of the same cross-sectional study (Max et al., 2002; Max et al., 2010), Lansing and colleagues (2004) examined verbal learning and memory after childhood stroke. They compared 26 children with stroke to a control group of 26 children with either congenital clubfoot or scoliosis. Participants ranged from 5 to 17 years of age at the time of assessment. Children were matched on age, sex, ethnicity, and SES. Twenty-nine children were recruited in each group as part of the larger study. Three children with stroke and their controls were excluded because their ages exceeded the available normative data for the neuropsychological measures. Measures included subtests from the WISC-III to estimate PIQ (Picture Arrangement and Block Design), VIQ (Information and Similarities), and auditory attention and working memory (Digit Span).

The CVLT-C was used to measure verbal learning and memory. Compared to controls, children with stroke performed significantly lower on the estimated VIQ and PIQ, as well as the Digit Span subtest. Compared to controls, children in the stroke group demonstrated significant deficits in encoding on verbal learning and memory tasks. Children in the stroke group also recalled fewer total words immediately and after a delay. Furthermore, compared to the control group, children with stroke were less efficient in organizing words in semantic clusters to improve recall. Researchers did not find significant differences between children with right and left hemisphere lesions. Age at stroke was significantly related to verbal memory. Children with early strokes (before the age of 12 months) performed lower on the CVLT-C than those with late strokes (after the age of 12 months). Specifically, they had more difficulty with long delay free recall and were less accurate in their recognition memory. Similarly, a trend toward lower intellectual functioning was apparent in children with early stroke, although it did not reach significance. The sample was not large enough to examine effects of lesion location, lesion volume, or stroke type.

In one of the first fMRI studies investigating pediatric stroke, Guzzetta and colleagues (2008) examined lesion laterality in a group of 10 children following left perinatal stroke. Children were matched with a control group of 10 healthy children. Children in the stroke group ranged from 7 to 19 years of age (M = 11 years, 6 months) and children in the control group ranged from 11 to 19 years of age (M = 13 years, 8 months). Children in the stroke group performed within the average range on the Wechsler scales (M = 97; FSIQ range: 89 to 112). However, researchers did not state

which Wechsler scales were used, they did not include individual scores, and statistical analyses comparing mean scores with normative data were not performed. Both groups of children also completed a verbal rhyme generation task while undergoing an fMRI. Guzzetta et al. (2008) found that all control children demonstrated a clear left hemisphere lateralization for language on fMRI. Conversely, 8 out of 10 children with left hemisphere stroke demonstrated right hemisphere lateralization for language on fMRI. Researchers concluded that the immature brain is capable of re-organizing language networks and the right hemisphere is able to subsume left hemisphere functions.

Conversely, Beharelle and colleagues (2010) argue that the right hemisphere may not completely compensate for language functions following left hemisphere perinatal stroke. They conducted an fMRI study comparing 25 children with perinatal ischemic (n = 14) or hemorrhagic stroke (n = 11) to typically developing siblings (n = 27). Participants included children and adults with an average age of 14 years, 4 months at assessment (SD = 6 years, 9 months; age range: 7 years, 2 months to 29 years, 10 months). Participants completed tests of language outcome (WISC-III/WAIS-III VIQ), receptive vocabulary (PPVT-Third Edition), and expressive and receptive language (CELF). During the fMRI, participants also completed a category fluency task in which they were asked to verbally generate examples of categories.

Using MRI scans, researchers calculated lesion volume by tracing lesions on structural images and counting the voxels within the lesion (Beharelle et al., 2010). It is unclear whether researchers accounted for brain volume, which may be a limitation given the wide range of ages in their sample. MRI scans were also used to calculate a laterality

index to determine the laterality of language functions for anterior and posterior language regions. Anterior regions included the pars triangularis and pars opercularis of the inferior frontal gyrus and the ventral premotor region of the precentral gyrus and sulcus. Posterior regions included the posterior superior temporal gyrus and sulcus, supramarginal gyrus and angular gyrus (Beharelle et al., 2010). Analyses of fMRI data indicated a significant difference between the pattern of activation in children with early stroke compared to healthy siblings. As predicted, fMRI results of normally developing siblings demonstrated activation primarily in the left frontal and lateral temporal regions during a language activation task. Conversely, children with early left hemisphere stroke, demonstrated right hemispheric lateralization for anterior regions and bilateral activation for posterior regions.

The researchers also examined the relationship between laterality and language outcome (Beharelle et al., 2010). In children with early stroke, greater activity in the left frontal regions was associated with better verbal performance than right anterior lateralization. In posterior brain regions, bilateral activity in the temporal and parietal regions was associated with more favorable outcomes than unilateral activation (Beharelle et al., 2010). Results remained significant after controlling for lesion volume and extent of injury. Thus, even though several patterns of reorganization were noted following early brain injury, particular organizations were associated with advantageous outcomes. Moreover, results suggest that neural development may follow a normal progression, despite early injury. Results may be limited because of the small, heterogeneous sample, spanning a wide range of ages. Additionally, the categorical

fluency task may not have adequately assessed all areas of language processing. Future research should use different fMRI paradigms and to examine larger samples with less heterogeneity. Given the inherent limitations, results should be interpreted with caution until they can be replicated.

Predictors of Outcome

Lesion Characteristics

Efforts have been made to identify potential predictors of outcome following pediatric AIS. As previously stated, factors related to the lesion include severity, volume and location, laterality, and etiology (Bava, Archibald, & Trauner, 2007). Evidence suggests severity, as measured by lesion volume, may be predictive of cognitive and neurological outcome, as larger lesions are typically associated with worse outcomes (Ganesan, Ng, Chong, Kirkham, & Connelly, 1999; Everts et al., 2008; Hetherington et al., 2005; Hogan, Kirkham, & Isaacs, 2000; Westmacott et al., 2010). However, some studies have failed to find a significant relationship between lesion size and outcome (Chapman et al., 2003). The effect of lesion location has not been well documented in children. Research indicates combined subcortical and cortical lesions are more deleterious than lesions that are solely cortical or subcortical, but these results are often confounded by lesion volume (Hetherington et al., 2005; Hogan, Kirkham, & Isaacs, 2000; Montour-Proulx et al., 2004; Steinlin, Roellin, & Schroth, 2004; Westmacott et al., 2010). Likewise, research has failed to document a significant relationship between outcome and lesion laterality, but further examination is needed (Ballantyne et al., 2008; Hetherington et al., 2005; Hogan et al., 2000; Westmacott et al., 2010). Stroke etiology

has also been examined as a potential predictor of outcome, but research has failed to produce consistent results (Bava, Archibald, & Trauner, 2007). Moreover, this factor is difficult to examine because samples are typically heterogeneous in terms of stroke etiology.

Developmental Characteristics

Researchers have also focused on factors related to the child's development, such as age at stroke, age at assessment, and time between stroke and assessment. Examination of the link between age at stroke and outcome has produced mixed results. On the one hand, several studies suggest earlier strokes may be associated with worse outcomes, whereas others suggest later strokes lead to worse outcomes (Bava, Archibald, & Trauner, 2007; Chapman et al., 1998; Hogan, Kirkham, & Isaacs, 2000; Max et al., 2010; Montour-Proulx et al., 2004). Research also suggests the relationship between age and outcome may be U-shaped, with the least favorable outcomes occurring between 6 months and 4 to 5 years of age (Hetherington et al., 2005). Conversely, Max and colleagues (2010) found that children who sustained a stroke prenatally through 1 year of life suffered significantly worse outcomes than children with later strokes. However, the effect of age at lesion onset may vary depending on the neurocognitive function being measured (Max et al., 2010). Moreover, additional factors may modulate the relationship between age and outcome (Hetherington et al., 2005; Montour-Proulx et al., 2004; Westmacott et al., 2010).

Child Characteristics

A limited number of studies have begun to examine factors related to the child, such as presence of seizures, sex, and SES, as predictors of outcome following stroke. Presence of seizures has been loosely linked with reduced cognitive functioning, but this association is not consistent (Ballantyne et al., 2008; De Schryver et al., 2000; Everts et al., 2008; Fox & Fullerton, 2010; Ricci et al., 2008). Specifically, heterogeneous seizures with a high frequency and long duration may be associated with detrimental cognitive outcomes (Montour-Proulx et al., 2004). However, it is unknown whether the relationship between seizures and worse outcomes is related to the seizures themselves, the use of antiepileptic medication, or whether seizures are simply an indicator of a more severe brain injury (Fox & Fullerton, 2010). A small body of research has documented sex differences in cognitive outcomes following extreme prematurity, extremely low birth weight, and traumatic brain injury in adults and children (Braun et al., 2002). Likewise, studies examining unilateral lesions of mixed etiologies in children have suggested males may experience greater cognitive impairment than females. However, a sex disparity has not been consistently documented in children with AIS (Braun et al., 2002; Hetherington et al., 2005; Hogan et al., 2000). Available evidence suggests SES may be weakly associated with stroke outcome, but the effect of SES deserves further consideration (Hetherington et al., 2005).

Conclusions and Limitations in Existing Research

Overall, research examining cognitive and neuropsychological outcomes following pediatric stroke is mixed. Traditionally, the consensus was that following stroke, children perform within the lower limits of the average range on measures of IQ

(Ballantyne et al., 2008; Everts et al., 2008; Hetherington et al., 2005; Hogan, Kirkham, & Isaacs, 2000; Westmacott et al., 2010; Westmacott et al., 2009;). However, recent studies suggest children may exhibit pronounced deficits on more complex cognitive tasks (Block et al., 1999; De Schryver et al., 2000; Everts et al., 2008; Westmacott et al., 2009). Further research is needed because many of the existing studies are flawed in their methodology and research design.

A common limitation in the pediatric stroke literature is the failure to include an appropriate control group. Instead, children with stroke are typically compared to the normative population (De Schryver et al., 2000; Everts et al., 2008; Hetherington et al., 2005; McLinden et al., 2007; Ricci et al., 2008; Westmacott et al., 2010; Westmacott et al., 2009). A small number of studies have included a control group of healthy children, matched on factors such as age and SES (Ballantyne et al., 2008; Block et al., 1999; Trauner et al., 2001). Only one study has used an orthopedic control group consisting of children with congenital clubfoot or scoliosis (Max et al., 2002). The most appropriate control group for this population may be children with an illness not involving the central nervous system, to control for illness-related characteristics.

Due to the rarity of pediatric stroke, studies are also frequently hampered by small, heterogeneous samples. The largest study examining the outcomes of pediatric stroke was conducted by Westmacott and colleagues (2010), with a sample of 145 children. However, because of the low incidence rate of pediatric stroke, a sample this large is uncommon; typical sample sizes are smaller and range from approximately 10 to 50 participants. Furthermore, samples are often heterogeneous in terms of lesion

characteristics, including stroke type (AIS or hemorrhagic), lesion volume and location, and stroke etiology (Bates et al., 2001; Everts et al., 2008; Montour-Proulx et al., 2004; Westmacott et al., 2009). Stroke etiology may be associated with cognitive outcome, but this has not been examined in large-scale studies (Hogan et al., 2000). Westmacott et al., (2009) also caution against the inclusion of children with presumed perinatal stroke. Children with presumed perinatal stroke are typically not diagnosed until severe neurological problems emerge and it is difficult to pinpoint the stroke timing. Thus, future research should use stricter inclusion/exclusion criteria to control for the possible effects of etiology on cognitive outcome.

Additional limitations include heterogeneity of age at diagnosis and assessment and time since lesion onset (Ballantyne et al., 2008; Max et al., 2010). Levine et al. (2005) suggest that following early unilateral stroke, IQ may vary as a function of age at assessment. Their research indicates that IQ scores may decrease over time following early unilateral lesions. Results suggest that age at assessment should be controlled in cognitive outcome studies. Time since lesion onset should also be controlled because significant correlations between time since stroke and cognitive performance have been documented (Westmacott et al., 2010). Longitudinal designs provide an opportunity to examine the effects of time since lesion onset and change over time. However, longitudinal studies to date have been flawed because researchers have not controlled test-retest intervals (Ballantyne et al., 2008; DeShryver et al., 2000). Because single-site recruitment is difficult, Zahuranec and colleagues (2005) suggest that a collaborative,

multi-site, longitudinal study is necessary to obtain sufficient sample sizes of children with AIS.

Additional design flaws include poorly defined inclusion/exclusion criteria, use of different test versions, lack of standardized neuropsychological measures, inconsistencies in neuroimaging, and failure to control for extraneous factors, such as epilepsy medication (Ballantyne et al., 2008; DeShryver et al., 2000; Everts et al., 2008; McLinden et al., 2007; Westmacott et al., 2009). Relatively few studies to date have included standardized cognitive and neuropsychological measures. Instead, some rely upon parent ratings of school functioning as a proxy for neuropsychological functioning (Christerson & Stromberg, 2010; Steinlin, Roellin, & Schroth, 2004). However, parent ratings are an inadequate substitute for standardized measures of a child's cognitive functioning and make it difficult to compare results across studies. To increase sample sizes, some researchers have used different editions of the same test, despite the tests having different normative standards (Ballantyne et al., 2008; Westmacott et al., 2009). This makes a comparison of their results less reliable. The cognitive and neuropsychological side effects of antiepileptic drugs can also affect test results. Common side effects include reduced psychomotor speed, attention deficits, and memory impairment (Loring & Meador, 2004). Side effects such as these could significantly reduce cognitive test performance. Hence, the effect of antiepileptic medication should be examined or controlled for in future studies of pediatric AIS.

Preliminary Meta-Analysis

The magnitude of the effect of stroke on cognitive functioning is unknown. Results of previous studies vary in part because of the aforementioned methodological limitations. Therefore, we performed a preliminary meta-analysis to obtain an estimate of the effect of stroke on general cognitive outcome, as measured by FSIQ mean scores. We also performed two separate meta-analyses to obtain an estimate of the effect of stroke on verbal and nonverbal functioning, as measured by VIQ and PIQ mean scores, respectively. Studies of cognitive outcomes following childhood stroke were identified through computerized literature searches of ISI Web of Knowledge and PsychInfo using combinations of the following keywords: *stroke, arterial ischemic stroke, child, pediatric, perinatal, outcome, cognitive, neuropsychological, verbal, and nonverbal.* In addition, we examined the reference sections of previous stroke outcome studies and reviews. We included studies that were reported in English, were specific to pediatric stroke (AIS only, and combined AIS and hemorrhagic), and used standardized measures of general cognitive ability (FSIQ), as well as verbal (VIQ) and nonverbal functioning (PIQ). In addition, we included only studies which reported original quantitative data on the cognitive outcomes following perinatal or childhood stroke. Case studies and those that did not report adequate quantitative data were excluded. We also excluded studies that focused solely on children with sickle cell disease, cerebral palsy, 'hemiplegia', and lesions with unclear etiologies, as these factors may have confounded the results.

After completing a literature review, we selected 15 studies (see Table 1) for 3 separate meta-analyses examining general cognitive outcome (FSIQ), verbal outcome (VIQ), and nonverbal outcome (PIQ).

For the general cognitive outcome analysis, we chose 13 studies (Table 2). Measures of IQ included versions of the WPPSI, WISC, and WAIS, as well as the K-ABC and the BSID. The mean FSIQ derived from Wechsler Intelligence Scales was reported in nine studies. In one study, individual FSIQ scores for each participant were reported instead of a mean FSIQ for the stroke group (Guimaraes et al., 2007). Therefore, we used individual FSIQ scores to calculate a group mean and standard deviation. A modified mean FSIQ derived from a prorated VIQ and PIQ was reported in one study (Max et al., 2002). We calculated the mean FSIQ from the K-ABC, the WISC, and the WAIS FSIQ, as well as the BSID Mental Developmental Quotient data reported by Pavlovic et al., (2006). We chose to analyze the Mental Developmental Quotient because it more closely resembles the construct of FSIQ than the Motor Developmental Quotient. A mean FSIQ derived from the BSID, WPPSI-R, WISC-III, and WAIS-R was reported by Hetherington et al. (2005). Separate means were not reported for each individual test, but researchers did not find a significant effect of test type on IQ (Hetherington et al., 2005). Index scores from the BSID were reported in one study and we chose to analyze the Mental Development Index because it is more similar to FSIQ than the Psychomotor Development Index (McLinden et al., 2007). Three studies were longitudinal and included scores from an initial and a follow-up assessment. We chose to analyze the second assessment because the interval between stroke and assessment was large in other included studies.

We chose 10 studies for the verbal outcome meta-analysis (see Table 3) and 9 studies for the nonverbal outcome meta-analysis (see Table 4). Measures of VIQ and PIQ

included the WPPSI, WISC, and WAIS. The mean VIQ was reported in 7 of the 10 selected studies and a combination of the VIQ and Verbal Comprehension Index (VCI) was reported in one study (Westmacott et al., 2010). Two studies did not include mean VIQ scores and we used the reported individual VIQ scores to calculate a group mean and standard deviation (Guimaraes et al., 2007; Ricci et al., 2008). The mean PIQ was reported in seven of the nine selected studies and a combination of the PIQ and Perceptual Reasoning Index (PRI) was reported in one study (Westmacott et al., 2010). Two studies did not include mean PIQ scores and we used the reported individual PIQ scores to calculate the group mean and standard deviation (Guimaraes et al., 2007; Ricci et al., 2008).

Although three studies used control groups, we chose to use normative data in each meta-analysis to maintain consistency across studies. In addition, Ballantyne et al., (2008) used a healthy control group with above-average cognitive performance. As previous researchers have suggested, this group is not likely to be representative of the general population and may not serve as an appropriate comparison (Westmacott et al., 2009). For each of the 15 studies, we calculated the unstandardized difference between the mean cognitive test score (FSIQ, VIQ, and/or PIQ) and normative data ($M = 100$; $SD = 15$) (see Table 2). We also conducted one sample *t*-tests comparing sample means to normative data (see Table 2).

Fixed-effect or random-effects models can be used in a meta-analysis. The fixed-effect method relies upon the assumption that there is no heterogeneity and a single common effect underlies every study. On the other hand, the random-effects model

allows for heterogeneity and relies upon a more realistic assumption that studies are measuring different effects. Therefore, we chose the random-effects model for the three meta-analyses, which were computed using Review Manager 5 statistical software (The Cochrane Collaboration, 2008).

The analysis of FSIQ revealed a mean difference of 6.27 (95% CI, 4.70 – 7.83) between mean cognitive scores of children with stroke and the theoretical mean of the normative population, favoring the normative population. The difference was significant ($z = 7.86$; $p < .00001$; see Figure 1), and indicates that children with stroke scored significantly lower on measures of FSIQ compared to the normative population. The χ^2 test for heterogeneity of effect sizes was not significant ($\chi^2_{12} = 16.62$; $p = .16$). As a second test of heterogeneity, we examined the I-squared value, which is "the percentage of total variation across studies due to heterogeneity" (Higgins, Thompson, Deeks & Altma, 2003, p. 559). According to conventional guidelines, I-squared values less than 30% indicate moderate heterogeneity and values greater than 50% indicate significant heterogeneity. The I-squared value of the FSIQ meta-analysis ($I^2 = 28\%$) suggests moderate heterogeneity. We also conducted an additional analysis considering the nine studies that used the same FSIQ measurement. While the mean difference remained significant, the I-squared value slightly decreased ($I^2 = 16\%$).

The analysis of VIQ revealed a mean difference of 5.61 (95% CI, 3.32 – 7.89) between the mean VIQ scores of the children with stroke and the theoretical mean of the normative population, favoring the normative population. The difference was significant ($z = 4.81$; $p < .00001$; see Figure 2), indicating that children with stroke scored

significantly lower on measures of VIQ compared to the normative population. The χ^2 test for heterogeneity of effect sizes was not significant (χ^2_9= 5.29; p = .03). The I-squared value (51%) suggests moderate heterogeneity among effect sizes. We also conducted an additional analysis considering the seven studies that used the same VIQ measurement. The mean difference remained significant and the I-squared value did not change.

The analysis of PIQ revealed a mean difference of 6.62 (95% CI, 4.25 – 8.99) between the mean PIQ scores of the children with stroke and the theoretical mean of the normative population, favoring the normative population. The difference was significant (z = 5.48; p < .00001; see Figure 3), indicating that children with stroke scored significantly lower on measures of PIQ compared to the normative population. The χ^2 test for heterogeneity of effect sizes was not significant (χ^2_8= 14.53; p = .07). The I-squared value (45%) suggests moderate heterogeneity among effect sizes. We also conducted an additional analysis considering the six studies that used the same PIQ measurement. While the mean difference remained significant, the I-squared value decreased (I^2 = 9%).

The results of these meta-analyses indicate that children with stroke perform significantly lower than the normative population on measures of general cognitive ability, as well as verbal and nonverbal functioning. Furthermore, it appears that methodological differences among studies may partially account for heterogeneity in effect sizes, particularly variations in the tests used to assess cognitive functioning. Because of inconsistencies in study design and the small number of available studies, we

were unable to examine the effect of moderating factors on cognitive, verbal, and nonverbal outcome.

The Current Study

The primary aim of the current study is to determine whether children with AIS display deficits in cognitive functioning. The first two hypotheses were developed to address this aim. The first hypothesis is that children with AIS will perform lower on measures of cognitive functioning than children with asthma, a chronic illness not affecting the central nervous system. The second hypothesis is that children with AIS will perform significantly below the means of normative populations on standardized cognitive measures.

The secondary aim is to determine whether specific factors account for individual variability in cognitive outcome following pediatric AIS. In accord with this aim, the third hypothesis is that poorer neurological functioning (i.e., higher scores on the Pediatric Stroke Outcome Measure [PSOM]) will be associated with lower scores on standardized cognitive measures. The fourth hypothesis is that factors related to lesion severity, such as larger stroke volumes and combined subcortical-cortical infarcts, will be associated with greater deficits on standardized cognitive measures. Exploratory analyses also will examine lesion laterality, developmental factors (i.e., age at stroke, time between stroke and assessment), and child characteristics (i.e., presence of seizures, race, sex, SES) that may account for individual differences in outcomes. The final hypothesis is that greater stroke severity (higher PSOM scores, larger infarct volume, combined cortical and subcortical lesions, etc.) will account for significant variance in cognitive

outcome after taking significant developmental and child factors into account; the specific factors to include will be determined after performing exploratory analyses.

Chapter 2: Methods

Participants

The current study is part of a larger, multi-site study examining the social and cognitive outcomes of children following AIS as compared to children with asthma. Children were recruited from two different sites, Nationwide Children's Hospital (Columbus, Ohio) and Royal Children's Hospital (Melbourne, Australia). In total, 51 children were recruited: 36 with AIS and 15 with asthma. The retrospective recruitment process involved an initial screening of medical and radiology records to determine if children met criteria for participation. Children were eligible if they were from 6 to 15 years of age at the time of assessment, and if they met pre-specified inclusion/exclusion criteria.

In the AIS group, children had to meet both clinical and radiologic criteria for the presence of AIS during the perinatal period or childhood (i.e., documented non-progressive parenchymal lesion caused by a stroke). Exclusion criteria included certain stroke etiologies, other conditions affecting the central nervous system, and other conditions not affecting the central nervous system. Excluded stroke etiologies were hemoglobinopathies, including sickle cell disease; progressive neurometabolic disorders; malignancy; stroke during neurosurgery; moyamoya syndrome; brain trauma induced

hemorrhage; and autoimmune vasculitis. These conditions were excluded because they may have an impact on cognitive outcome independent of stroke (Hogan, Kirkham, & Isaacs, 2000). Other exclusionary conditions with central nervous system involvement were congenital hydrocephalus; intracerebral shunts; central nervous system infections; pre-existing mental retardation; prenatal exposure to alcohol/drugs; premorbid neurological disorder; genetic disorders with central nervous system involvement; and use of anti-psychotic medications. Other exclusionary conditions were pregnancy; previous organ or bone marrow transplant; any injury resulting from child abuse or assault; a history of severe psychiatric diagnosis requiring hospitalization; and any sensory or motor impairment that prevented valid administration of the measures (e.g., severe cerebral palsy).

Children with asthma were chosen for the control group because asthma is a chronic illness that does not involve the central nervous system. This group of children was also chosen because they had experienced an acute hospital admission, as had the children with AIS. Children in the control group were matched with children with AIS for age, sex, and time of hospital admission. Exclusion criteria for the control children were the same as the AIS group. In addition, children were excluded from the asthma group if they had a history of congenital or acquired neurological disorders; admission to the intensive care unit for acute asthma; organ failure; chronic outpatient use of oral steroids for asthma control; current use of psychotropic medication other than stimulants; or if they had experienced a significant hypoxic event.

Sample Size and Characteristics

The final group, consisting of 36 children with AIS and 15 children with asthma, did not significantly differ in demographic factors such as sex, racial distribution, age and maternal education. Children in both groups were also similar in age at presentation, age at assessment, and time between presentation and assessment (see Table 6).

Data from non-participants was available only from Nationwide Children's Hospital. Of children meeting the eligibility criteria, 23 children with AIS and 45 with asthma were able to be contacted. Participation rates (i.e., number of participants/number of eligible individuals who declined to participate) were 61% (14/23) in the AIS group and 18% (8/45) in the asthma group. These participation rates not atypical of clinical studies at Nationwide Children's Hospital, albeit somewhat lower than expected in the asthma group. Participants and non-participants did not differ significantly in age, sex, or race/ethnicity. However, according to census tract data, median income was significantly higher for participants compared to non-participants.

Classification of Stroke

All children in the AIS group completed an MRI at the time of assessment, at least 1 year following stroke. Previous research has documented that large lesions involving more than 10% of the intracranial volume are associated with less favorable outcomes. In the current study, lesion volume was estimated by tracing the outer margin of the lesion as displayed on MRI brain scan images, calculating a volume based on section thickness, and then summing up the volumes from all sections through the infarct. MRI images were also analyzed to characterize the location of the infarcts. Location was

qualitatively coded for hemisphere (right, left, bilateral, or brainstem/cerebellum) and cerebral location (cortical, subcortical, combined, or brainstem/cerebellum).

Measures

As part of a larger study examining social and cognitive outcomes following pediatric stroke, children and their parents completed standardized cognitive and neurological measures, as well as experimental measures of social information processing. Children in the stroke group also underwent an MRI. For the purposes of the present study, the cognitive and neurological measures will be described, as well as the MRI data obtained from children with AIS.

General Cognitive Ability

General cognitive ability was assessed using the two-subtest form of the Wechsler Abbreviated Scale of Intelligence (WASI IQ; $M = 100$, $SD = 15$) (Wechsler, 1999) consisting of the Vocabulary and Matrix Reasoning subtests ($M = 50$, $SD = 10$). The WASI was normed on a national stratified sample representative of the United States census. The two-subtest form serves as a valid estimate of overall cognitive ability (Wechsler, 1999). The two-subtest IQ has demonstrated satisfactory reliability in child samples ($r_{xx}^{a} = .93$) and adult samples ($r_{xx}^{a} = .96$). It yields a Full Scale IQ that is correlated with the IQ derived from the Wechsler Intelligence Scale for Children-Third Edition ($r_{12}^{c} = .81$) (Wechsler, 1999).

Executive Functions

Executive functions were assessed using subtests from the WISC-IV Processing Speed Index (PSI; $M = 100$, $SD = 15$) (Wechsler, 1991; Wechsler, 2003) and selected

subtests from the Test of Everyday Attention for Children (TEA-Ch) (Manly, Robertson, Anderson, & Nimmo-Smith, 1999). The PSI assesses focused attention and response speed and is comprised of two timed subtests: Coding and Cancellation (M = 10, SD = 3). The WISC-IV was normed on a large sample of children representative of the general population (Wechsler, 1991; Wechsler, 2003). The PSI has demonstrated satisfactory internal consistency (*alpha* = .88) and test-retest reliability (r = .79) in child samples (Wechsler et al., 2004).

The TEA-Ch Walk/Don't Walk subtest (M = 10, SD = 3) assesses inhibitory control. Children are asked to listen to a tape and mark one step on a paper path for every tone they hear. They must sustain their attention and listen carefully because the tones change unpredictably. When the tones change, children must stop making marks on the paper (Manly et al., 1999). The Code Transmission subtest (M = 10, SD = 3) lasts 12 minutes and assesses working memory. Children are required to sustain their attention while listening to a monotonous series of spoken numbers. They must listen for two 5s in a row and repeat the number that came immediately before the 5s (Manly et al., 1999). The Creature Counting subtest (M = 10, SD = 3) assesses mental flexibility. Children are required to repeatedly switch between counting aliens upwards (one, two, three) and downwards (three, two, one). The Creature Counting subtest produces two scores based on accuracy and time (Manly et al., 1999). The accuracy score is based on the number of trials children correctly complete. The timing score is based on the average time to complete each trial and is calculated for children who accurately complete at least three trials. The TEA-Ch is normed for children between the ages of 6 and 15. Test developers

have established satisfactory psychometric properties. Test-retest reliability is high for Creature Counting (r = .71), Walk/Don't Walk (71.0% test-retest agreement), and Code Transmission (r = .78). Satisfactory construct validity in measuring attention and executive functions has also been demonstrated (Manly et al., 1999).

Neurological Status

Stroke severity was assessed using the Pediatric Stroke Outcome Measure (PSOM; Appendix C; deVeber, MacGregor, Curtis, & Mayank, 2000). The PSOM is a structured neurological examination developed to measure the severity of neurological deficits following stroke in children. The PSOM is ordered along a developmental trajectory and can be used for children from birth through adolescence. The PSOM produces a composite severity score ranging from '0' (no deficits) to a maximum of '10'. The PSOM also yields 5 subscale scores (Right Sensorimotor Deficit, Left Sensorimotor Deficit, Language Production Deficit, Language Comprehension Deficit, and Cognitive or Behavioral Deficit). The subscales are rated on a scale ranging from '0' (no impairment) to a maximum of '2' (severe or profound impairment). The PSOM is completed by a neurologist based on direct examination of the patient's functioning. Areas of examination include "behavior, mental status, cranial nerves, motor functions (developmental, fine and gross motor, motor tone, power, reflexes, and involuntary movements), sensory function, cerebellar function, and gait function" (de Veber et al., 2008, p. 318). The examination is supplemented by parent report of cognitive and behavioral functioning. However, the neurological examination is more heavily weighted than the parental report in cognitive, emotional, and psychological domains. Preliminary

data indicates the PSOM has a concordance rate of 91% for summary scores assessed by two neurologists administering same-day assessments to 10 children ranging in age from young infants to older children, with a range of severity from normal to severe (deVeber et al., 2000a).

Procedures and Analyses

Of the 51 children in the study, 32 out of 36 children in the AIS group and 14 out of 15 children in the asthma group completed the entire cognitive battery. In the AIS group, one child was unable to complete the WASI Vocabulary, WISC-IV Coding and Cancellation subtests because of a medical emergency, unrelated to study procedures. Therefore, index scores for the WASI IQ and WISC-IV PSI were also missing. Several children between the ages of 6 and 7 were unable to complete the TEA-Ch subtests because they had difficulty understanding the task demands. One child in the AIS group was not able to complete any of the TEA-Ch subtests and one child was unable to complete Creature Counting and Code Transmission. One child in the AIS group and one child in the asthma group were unable to complete Creature Counting. Thirteen of the children in the AIS group and four of the children in the asthma group were missing Timing scores for the Creature Counting subtest. Four of these scores are missing because children could not complete the task. The remaining 13 children were able to complete Creature Counting but their accuracy scores were too low (< 3 correct) to calculate Timing scores. SES data was unavailable for two children because their data forms were not returned. Volumetric lesion data was available for 28 of the 36 children with AIS. One child was missing a measurement of total brain volume because the T1

weighted scan was not adequate to perform segmentation. Therefore, lesion volume was calculated as a percentage of total brain mass for 27 children. To address missing data in the following analyses, cases were excluded pairwise, instead of listwise, since the latter would have substantially decreased sample sizes.

Because of the small sample, data were examined graphically to determine whether outliers were present. To explore the relationship between cognitive performance and continuous variables (stroke volume, time between stroke and assessment), scatterplots for each cognitive measure in relation to each variable of interest were created. The scatterplots were visually inspected to determine whether outliers were present. To compare the distribution of cognitive scores across categorical variables, boxplots were created for each cognitive measure and each categorical predictor (AIS vs. asthma, stroke location, lesion laterality, sex, and SES). The pattern of cognitive scores for each group was examined and outliers were defined as data points that extended more than one and half the interquartile range from the median. All analyses were conducted twice: first including outliers and then with outliers removed, to examine their influence on results. Results of analyses that omitted outliers are only reported if the results differed from those that included the outliers.

The first aim of the current study was to determine whether children with AIS display cognitive deficits compared to children without AIS. To examine group differences between the AIS and asthma groups, they were compared using one-tailed independent samples *t*-tests, with significance of .05. The groups were compared on each of the seven cognitive subtests (WASI Vocabulary, Matrix Reasoning; TEA-Ch Creature

Counting, Walk/Don't Walk, Code Transmission; WISC-IV Coding, Cancellation) and the WASI IQ and WISC-IV Processing Speed composite scores. Cohen's *d* effect sizes were computed to determine the magnitude of group differences. According to Cohen (1988), an effect size of 0.2 is considered small, 0.5 is moderate, and 0.8 is large.

In line with previous research, the performance of the AIS group also was compared to normative populations using one-sample *t*-tests, with significance of .05. The AIS group's means on cognitive measures were compared to those of the normative populations. The same analyses were used to compare the asthma group's means to the normative populations. To provide the best evidence to date for cognitive outcomes following childhood AIS, we included the mean WASI IQ from the AIS sample in a final meta-analysis of FSIQ.

The second aim of the current study was to determine whether specific factors accounted for individual differences in cognitive outcome following pediatric AIS. Variables of interest included neurological status (PSOM scores), lesion characteristics (volume, location), developmental factors (age at stroke, time since diagnosis), and child characteristics (presence of seizures, race, sex, SES).

To examine the relationship between neurological status and cognitive outcome, Spearman's rank order correlations (ρ) were calculated between total PSOM scores and cognitive scores. Similarly, the relationship with lesion size was examined, calculated in absolute units (cubic mm) or in relationship to total brain volume because brain mass significantly varies depending on age (Jordan, Kleinman, & Hillis, 2009). Spearman

correlations were computed between lesion volume (absolute units and percentage of total brain volume) and cognitive scores.

To compare the effect of stroke location on cognitive outcome, a one-way between-groups analysis of variance (ANOVA) was conducted to compare mean cognitive test scores across four groups (cortical vs. subcortical vs. combined cortical and subcortical vs. asthma). Three children with brainstem/cerebellar lesions were excluded from analyses. Eta-squared effect sizes were calculated to examine the magnitude of group differences. According to Cohen (1988), an eta-squared of .01 is considered small, .06 is medium, and .14 is large. After examining the variability of scores for each group, it appeared that variances differed significantly on the TEA-Ch Code Transmission subtest. Therefore, the non-parametric Kruskal-Wallis test was used to confirm results for the TEA-Ch Code Transmission subtest. ANOVAs were also performed without the asthma group to confirm results.

Previous research has shown that combined infarcts are associated with lower cognitive scores than restricted lesions (Hetherington et al., 2005). Therefore, the location variable was collapsed into cortical/subcortical only versus combined cortical and subcortical lesions. ANOVAs compared mean cognitive test scores across three groups (cortical only or subcortical only vs. combined cortical-subcortical vs. asthma). Eta-squared effect sizes were calculated to examine the magnitude of group differences. Similar to previous analyses, group variances significantly differed on the TEA-Ch Code Transmission subtest, so results were confirmed using the Kruskal-Wallis Test. ANOVAs were also performed without the asthma group to confirm results.

Exploratory analyses examined the effect of lesion laterality on cognitive outcome. Specifically, ANOVAs compared mean cognitive test scores across four groups (left hemisphere vs. right hemisphere vs. bilateral vs. asthma). Three children with brainstem/cerebellar lesions were excluded from analyses. Eta-squared effect sizes were calculated to examine the magnitude of group differences. Group variances significantly differed on the TEA-Ch Code Transmission and WISC Cancellation subtests, so results were confirmed using the Kruskal-Wallis Test. ANOVAs were also performed without the asthma group to confirm results.

Additional exploratory analyses examined developmental factors, such as age at stroke and time between stroke and assessment. Age at stroke was dichotomized into prenatal/perinatal stroke and childhood stroke. ANOVAs compared mean cognitive test scores across three groups (pre/perinatal stroke vs. childhood stroke vs. asthma). Eta-squared effect sizes were calculated to examine the magnitude of group differences. Next, the asthma group was removed from the analyses, and two-tailed independent samples *t*-tests were conducted, with significance of .05, to compare the early and late stroke groups on cognitive measures. Cohen's *d* effect sizes were calculated to examine the magnitude of group differences. Spearman correlations also were computed to explore the relationship between performance on cognitive measures and time between stroke and assessment.

Analyses of child-related factors were somewhat limited due to the small sample. Statistical analyses of sex and SES were conducted, but sample sizes were too small to conduct statistical analyses examining the role of seizures or race. Two-way between-

groups analyses of variance (ANOVA) were conducted to determine whether sex differences were more pronounced in the AIS group compared to the asthma group. Partial eta-squared effect sizes were calculated to examine the magnitude of group differences. Next, the asthma group was excluded, and two-tailed independent samples *t*-tests, ($\alpha = .05$) compared males and females in the AIS group. Cohen's *d* effect sizes were calculated to examine the magnitude of group differences.

Maternal education was used as an estimate of SES. Participants were initially divided into six groups (9^{th} grade or less; $10^{th}/11^{th}$ grade; high school graduate; partial degree/professional qualifications; college/university graduate; graduate/post graduate degree). Because groups were somewhat small and unequal in size (see Table 6), the six categories were collapsed into three: (less than high school; high school graduate/partial college; college graduate). Two-way between-groups ANOVAs were conducted to determine whether SES differences were more pronounced in the AIS group compared to the asthma group. Partial eta-squared effect sizes were calculated to examine the magnitude of group differences. Next, the asthma group was excluded, and one-way between-groups ANOVAs were performed to examine the effect of SES in the AIS group. Eta-squared effect sizes were calculated to examine the magnitude of group differences.

The final hypothesis was that greater stroke severity would account for significant variance in cognitive outcome after taking other significant predictors into account. Initial analyses revealed that two indicators of stroke severity, total PSOM score and lesion volume, were significantly related to performance on cognitive outcome. SES was also

determined to be significantly associated with cognitive outcome. Therefore, hierarchical multiple regression analyses were conducted to determine how well the combination of these variables predict cognitive outcome, and whether stroke severity, as measured by total PSOM score and lesion volume, accounts for significantly greater variance in outcome than SES. Hierarchical multiple regression analyses were conducted for each cognitive measure with SES entered in the first step and total PSOM score and lesion volume entered in the second step. Total PSOM score and lesion volume were significantly correlated (.39), but neither variable was significantly correlated with SES.

Using GPOWER ($\alpha = .05$), we determined that the sample of 36 children with AIS and 15 children with asthma was sufficient to detect a small effect size of .20 with power of .16, a medium effect size of .50 with power of .48, and a large effect size of .80 with power of .82 (Erdfelder, Faul, & Bucher, 1996). Power analyses for comparisons within the AIS group, revealed that with alpha set to .05, the sample was sufficient to detect a small effect size with power of .09, a medium effect size with power of .30, and a large effect size with power of .64. In terms of the within-group correlational analyses, our sample of 36 children with AIS was sufficient to detect a small effect size of .10 with power of .15, a medium effect size of .30 with power of .58, and a large effect size of .50 with power of .96. Likewise, in regression analyses within the AIS group, with three predictors, a small effect size of .02 was detectable with power of .09, a medium effect size of .15 with power of .42, and a large effect size of .35 with power of .81. Thus, the study has sufficient power to detect large effect sizes, but limited power to detect medium or smaller effect sizes.

Chapter 3: Results

The first aim of the study was to determine whether children with AIS perform lower on cognitive measures than children with asthma. Table 6 shows the means, standard deviations, and effect sizes of the AIS and asthma group comparisons. Independent groups *t*-tests revealed a significant group difference on the TEA-Ch Walk/Don't Walk subtest scores [$t(48) = -2.29$, $p = .01$], with poorer performance in the AIS group. Analyses of the remaining six cognitive subtests and composite scores for the WASI IQ and the WISC-IV Processing Speed Index (PSI) revealed non-significant trends toward lower performance in the AIS group compared to the asthma group. Effect sizes ranged from small to medium (effect size range: .02 to .68). Outliers on cognitive tests were uncommon and results did not change after they were removed from analyses.

Analyses revealed significant differences between AIS group means and those of the normative populations on four of seven cognitive subtests (Vocabulary, Walk/Don't Walk, Code Transmission, Coding), as well as the TEA-Ch Creature Counting Timing score, the WASI IQ, and the WISC PSI (see Table 7). Similarly, analyses revealed significant differences between the asthma group and the normative population on three of seven cognitive subtests (see Table 7). Results did not change after removing outliers from the analyses.

Next, the mean WASI-IQ from the AIS sample was added to the meta-analysis of FSIQ following childhood stroke. We found a mean difference of 6.17 (95% CI, 4.75 – 7.60) between cognitive scores of children with stroke and the normative population, favoring the normative sample. The difference was significant ($z = 8.48$; $p < .00001$; see Figure 4), and indicates that children with stroke scored significantly lower on measures of FSIQ compared to the normative population. The χ^2 test for heterogeneity of effect sizes was not significant ($\chi^2_{13} = 16.74$; $p = .21$), and the I-squared value (22%) did not indicate significant heterogeneity.

Predictors of Outcome

The second aim of the study was to determine whether neurological severity (PSOM, lesion volume, lesion location), developmental factors (age at stroke, time between stroke and assessment), or child characteristics (presence of seizures, race, sex, SES) account for individual differences in cognitive outcome among children with AIS.

PSOM Total Score

Table 9 displays the distribution of severity ratings from the four PSOM subscales (0 = "no impairment," .5 = "mild impairment," 1 = "moderate impairment," 2 = "severe impairment"). The majority of children in the present study did not suffer from significant physical or functional limitations, as measured by the PSOM.

Table 9 contains the Spearman Rank Order Correlations (ρ) between total PSOM scores and cognitive test scores. In the current sample, relationships between PSOM scores and cognitive test performance were small to moderate (ρ range: -.01 to -.42), although all in the expected direction, with greater neurological severity related to poorer

cognitive test performance. Correlations between total PSOM scores and WASI IQ (ρ = -.35, p = .04), Vocabulary (ρ = -.34, p = .04), WISC PSI (ρ = -.30, p = .04), and WISC Coding (ρ = -.42, p = .01) scores were statistically significant.

Lesion Volume

Lesion volumes in absolute units were available for 28 of the 36 children with AIS and ranged from 213.80 to 160,988.68 cubic mm (M =24,580.35 cubic mm, SD = 42,430.97 cubic mm). Table 10 contains the Spearman correlations between absolute lesion volume and cognitive measures; correlations ranged from small to moderate in magnitude (range ρ: -.38 to .32), and were generally negative, so that larger lesion volumes were associated with poorer test performance. Correlations between volume and WASI IQ (ρ = -.38, p = .03) and Vocabulary (ρ = -.38, p = .03) scores were statistically significant. The remaining correlations did not reach statistical significance. After removing two outliers from analyses (see Table 10), correlations continued to range from small to moderate in magnitude (range ρ: -.50 to .39). The correlation between lesion volume and the TEA-Ch Creature Counting Total score (ρ = .39, p = .03) increased and reached statistical significance.

Lesion volume was calculated as a percentage of total brain mass for 27 children with available data. Lesions ranged from 0 to 14 percent of total brain volume (M = 2%, SD = 4%) (see Table 11). Correlations ranged from small to moderate in magnitude (ρ range = .02 to -.38), and again were generally negative. Correlations between volume percentage and the WASI IQ (ρ = -.38, p = .03), Vocabulary (ρ = -.36, p = .04), and Matrix Reasoning (ρ = -.34, p = .04) were statistically significant. The remaining

correlations did not reach statistical significance. After removing outliers from analyses (see Table 11), correlations continued to range from small to moderate (range ρ: -.47 to .29). The correlation between lesion volume and Matrix Reasoning decreased and was no longer statistically significant.

Lesion Location

Table 12 displays the means, standard deviations, and effect sizes from three stroke location groups (cortical; subcortical; combined cortical and subcortical); the asthma group is included as a reference. One-way ANOVAs revealed a significant effect of stroke location on TEA-Ch Walk/Don't Walk scores [$F(3, 43) = 3.41$, $p = .03$]. Post-hoc comparisons using the Tukey HSD test indicated that the mean score for the asthma group was significantly higher than that for the combined cortical and subcortical group. Eta-squared effect sizes ranged from very small to large (effect size range: .00–.24).

When cognitive test outliers were removed from the one-way ANOVAs, the groups significantly differed on WASI Matrix Reasoning [$F(3, 42) = 3.24$, $p = .03$] and WISC-IV PSI [$F(3, 39) = 3.05$, $p = .04$] scores. Differences were also significant on the Creature Counting Timing score [$F(3, 24) = 5.98$, $p = .00$]. However, after removing outliers, sample sizes were very small and unequally distributed. Post-hoc comparisons using the Tukey HSD test for the Matrix Reasoning subtest indicated that the mean score for the asthma group ($n = 15$, $M = 51.73$, $SD = 6.11$) was significantly higher than that for the combined cortical and subcortical lesion group ($n = 15$, $M = 43.93$, $SD = 7.47$). Post-hoc comparisons for the WISC-IV PSI indicated that the mean score for the subcortical group ($n = 11$, $M = 103.45$, $SD = 12.41$) was significantly higher than that for

the combined cortical and subcortical lesion group (n = 13, M = 88.54, SD = 13.57). Remaining group differences did not reach statistical significance and eta-squared effect sizes were modest in magnitude.

One-way ANOVAs examining the effect of lesion location in the AIS group alone (see Table 12) did not reveal significant group differences. Eta-squared effect sizes ranged from small to moderate in magnitude (effect size range: .00 to .08). After cognitive test outliers were removed, group differences on the WISC-IV PSI were significant [$F(2, 25) = 5.69$, $p = .01$]. Differences were also significant on the Creature Counting Timing score [$F(2, 15) = 7.39$, $p = .01$]. However, sample sizes were small and unequally distributed. Post-hoc comparisons for the WISC-IV PSI indicated that the mean score for the subcortical group (n = 11, M = 103.45, SD = 12.41) was significantly higher than that for the combined cortical and subcortical lesion group (n = 13, M = 88.54, SD = 13.57). Remaining group differences did not reach statistical significance and eta-squared effect sizes were modest in magnitude.

Next, we collapsed the lesion location variable into cortical/subcortical only and combined cortical and subcortical (see Table 13). ANOVAs comparing two lesion location groups and the asthma group revealed a significant effect of location on TEA-Ch Walk/Don't Walk [$F(2, 44) = 4.84$, $p = .01$]. Post-hoc comparisons using the Tukey HSD test revealed that the mean score for the asthma group was significantly higher than that for the combined cortical and subcortical group. Eta-squared effect sizes ranged from very small to large (effect size range: .003 to .18).

When cognitive test outliers were removed from one-way ANOVAs, differences on the WASI Matrix Reasoning subtest reached significance [$F(2, 43) = 4.38$, $p = .02$]. Post-hoc comparisons indicated that mean scores for the asthma group ($n = 15$, $M = 51.73$, $SD = 6.11$) and the cortical/subcortical only group ($n = 16$, $M = 50.69$, $SD = 9.49$) were significantly higher than that for the combined cortical and subcortical group ($n = 15$, $M = 43.93$, $SD = 7.47$).

Independent samples *t*-tests examining the effect of lesion location in the AIS group alone indicated that group differences were not significant (see Table 13). Cohen's *d* effect sizes were moderate (*d* range: .16 to .57). However, after removing cognitive test outliers, analyses revealed a significant difference on the Matrix Reasoning subtest [$t(29) = 2.19$, $p = .04$]. Specifically, the mean for the cortical/subcortical only group ($n = 16$, $M = 50.69$, $SD = 9.49$) was significantly higher than that for the combined group ($n = 15$, $M = 43.93$, $SD = 7.47$). Remaining group differences did not reach statistical significance and effect sizes continued to range from small to moderate in magnitude.

Lesion Laterality

Table 14 displays the means, standard deviations, and effect sizes for cognitive test scores based on lesion laterality (left hemisphere; right hemisphere; bilateral); the asthma group is included as a reference. ANOVAs did not reveal significant differences between groups and eta-squared effect sizes ranged from small to large (effect size range: .02 to .16). Group differences approached significance on the WASI Matrix Reasoning [$F(3, 43) = 2.35$, $p = .09$] and the TEA-Ch Walk/Don't Walk [$F(3, 43) = 2.72$, $p = .06$] subtests.

When cognitive test outliers were removed from analyses, groups differed significantly on the TEA-Ch Walk/Don't Walk subtest [$F(3, 23) = 3.60$, $p = .02$]. Post-hoc comparisons revealed that the mean for the asthma group ($n = 15$, $M = 6.73$, $SD = 2.87$) was significantly higher than that for the bilateral lesion group ($n = 6$, $M = 3.17$, $SD = 1.33$). Remaining group differences did not reach statistical significance and eta-squared effect sizes ranged from small to large in magnitude.

One-way ANOVAs examining the effect of lesion laterality in the AIS group did not reveal significant group differences. Effect sizes were modest in magnitude (effect size range: .00 to .14) and results did not change when we examined the effect of lesion laterality in the AIS group without outliers.

Age at Stroke

Table 15 displays the means, standard deviations, and effect sizes for cognitive test scores based on stroke timing (pre/perinatal, childhood stroke); the asthma group is included as a reference. ANOVAs did not reveal significant group differences and eta-squared effect sizes ranged from small to moderate (effect size range: .00 to .10). Results remained the same after we removed the asthma group from analyses and performed independent groups *t*-tests. Cohen's *d* effect sizes ranged from very small to moderate (effect size range: .02 to .45). Outliers on cognitive tests were rare and results did not change after they were removed from ANOVAs and independent groups *t*-tests.

Time between Stroke and Assessment

Table 16 contains Spearman correlations between cognitive test scores and time between stroke and assessment. Correlations between cognitive test scores and time

between stroke and assessment were modest (ρ range: .06 to .22) and did not reach statistical significance. Furthermore, correlations were inconsistent in direction. Although some correlations changed after removing cognitive test outliers from the analyses, none reached statistical significance (see Table 16).

Child Related Factors

Analyses of child-related factors were somewhat limited due to small, uneven sample sizes. Only three children presented with seizures at the time of assessment and only two children were members of a racial/ethnic minority. Therefore, we were unable to conduct quantitative analyses for those factors

Sex

Two-way ANOVAs exploring the influence of sex in the AIS and asthma groups did not reveal significant interactions or main effects (see Table 17). Partial eta-squared effect sizes for sex were small in magnitude (effect size range: .00 to .02). Therefore, sex differences were not more pronounced in the AIS group than in the asthma group. Results did not change after performing the ANOVAs without cognitive test outliers.

Similarly, we did not find a significant effect of sex on cognitive performance after removing the asthma group and performing independent groups *t*-tests in the AIS group (see Table 18). Cohen's *d* effect sizes ranged from very small to moderate (effect size range: .02 to .61). After removing cognitive test outliers from independent *t*-test analyses, groups differed significantly on the TEA-Ch Walk/Don't Walk subtest [$t(29.5) = -3.82$, $p = .00$]. Specifically, the mean score for females ($n = 20$, $M = 5.55$, $SD = 2.33$) was significantly higher than that for males ($n = 12$, $M = 3.17$, $SD = 1.19$). Remaining

group differences did not reach statistical significance and effect sizes continued to range from very small to moderate in magnitude.

Socioeconomic Status

Two-way ANOVAs exploring the influence of SES (coded as less than high school; high school graduate/partial college; and college graduate) in the AIS and asthma groups did not reveal significant interactions or main effects of SES. Partial eta-squared effect sizes for main effects of SES were small in magnitude (effect size range: .00 to .11). Therefore, SES differences are not more pronounced in the AIS group than in the asthma group.

When cognitive test outliers were removed from the two-way ANOVAs, the SES groups differed significantly on the WASI Vocabulary subtest [$F(2, 39) = 5.43$, $p = .01$], WASI IQ score [$F(2, 40) = 4.34$, $p = .02$], and the WISC-IV Cancellation subtest [$F(2, 41) = 3.99$, $p = .03$]. Post-hoc comparisons using the Tukey HSD test for the WASI Vocabulary subtest indicated that the mean score for college graduates ($n = 10$, $M = 53.5$, $SD = 8.90$) was significantly higher than that for those with less than high school ($n = 8$, $M = 39.63$, $SD = 4.14$) and high school graduates ($n = 27$, $M = 42.78$, $SD = 9.80$). Post-hoc comparisons for the WASI IQ score indicated that the mean score for the college graduates ($n = 10$, $M = 106.80$, $SD = 10.74$) was significantly higher than that for those with less than high school ($n = 10$, $M = 92.8$, $SD = 10.92$) and high school graduates ($n = 26$, $M = 91.92$, $SD = 11.76$). Post-hoc comparisons for the Cancellation subtest indicated that the mean scores for college graduates ($n = 10$, $M = 7.90$, $SD = 3.51$) and high school graduates ($n = 27$, $M = 8.85$, $SD = 3.35$) was significantly lower

than that for those with less than high school (n = 10, M = 12.0, SD = 2.21). Remaining group differences did not reach statistical significance and eta-squared effect sizes for SES continued to range from small to moderate in magnitude.

One-way ANOVAs examining the effect of SES in the AIS group (see Table 19), revealed a significant effect of SES on the WASI Vocabulary scores [F(2, 30) = 7.02, p = .00], WASI IQ scores [F(2, 30) = 6.42, p = .005], TEA-Ch Walk/Don't Walk scores [F(2, 30) = 3.98, p = .03], and WISC-IV Cancellation scores [F(2, 30) = 3.60, p = .04]. Post-hoc comparisons using the Tukey HSD test for the WASI Vocabulary subtest revealed that the mean score for college graduates was significantly higher than that for those with less than high school and high school graduates. Post-hoc comparisons for the TEA-Ch Walk/Don't Walk subtest and the WASI IQ indicated that the mean score for college graduates was significantly higher than that for high school graduates. Post-hoc comparisons for the WISC Cancellation subtest revealed that the mean score for the college graduates was significantly lower than that for those with less than high school. Eta-squared effect sizes were small to moderate in magnitude (effect size range: .01 to .30).

After removing cognitive test outliers from analyses examining SES in the AIS group, significant differences emerged on the WASI Matrix Reasoning subtest [F(2, 29) = 6.81, p = .00] and the WISC-IV PSI [F(2, 25) = 3.78, p = .04]. Post-hoc comparisons using the Tukey HSD test for the WASI Matrix Reasoning subtest indicated that the mean score for college graduates (n = 6, M = 56.0, SD = 7.04) was significantly higher than that for high school graduates (n = 20, M = 44.45, SD = 6.95). Post-hoc

comparisons for the WISC-IV PSI indicated that the mean score for college graduates (n = 6, M = 85.50, SD = 9.27) was significantly lower than that for those with less than high school (n = 6, M = 101.33, SD = 14.86). Remaining group differences did not reach statistical significance and eta-squared effect sizes ranged from small to moderate in magnitude.

Regression Analyses

The final hypothesis was that greater stroke severity would account for significant variance in cognitive outcome, after taking into account other significant factors. Initial analyses revealed that total PSOM score, lesion volume, and SES significantly influenced performance on several cognitive measures, whereas stroke location, age at stroke, time between stroke and assessment, and sex did not.

Hierarchical multiple regression analysis conducted for the WASI IQ score (see Table 20) revealed a significant overall regression model (F(3, 22) = 3.19, p =.04; R^2 = .30). When the effect of SES was controlled, total PSOM score and lesion volume did not collectively account for significant variance in WASI IQ scores (F(2, 22) = 2.68, p =.09; ΔR^2 = .17). SES accounted for unique variance in IQ scores (β = .43, p = .03), but total PSOM score and lesion volume did not. When cognitive test outliers were removed, the overall regression remained significant (F(3, 20) = 3.92, p =.02; R^2 = .37). When the effect of SES was controlled, total PSOM score and lesion volume collectively accounted for significant variance in general cognitive ability (F(2, 20) = 3.73, p =.04; ΔR^2 = .24). SES significantly accounted for unique variance in cognitive ability (β = .40, p = .04), but total PSOM score (β = -.25, p = .20) and lesion volume (β = -.36, p = .06) did not.

Hierarchical multiple regression analysis conducted for the WASI Vocabulary subtest (see Table 21) revealed a significant overall regression model ($F(3, 22) = 3.10$, $p = .05$; $R^2 = .30$). When the effect of SES was controlled, total PSOM score and lesion volume did not collectively account for significant variance in Vocabulary performance ($F(2, 22) = 2.01$, $p = .16$; $\Delta R^2 = .13$). SES accounted for unique variance in verbal skills ($\beta = .44$, $p = .03$), but total PSOM score and lesion volume did not. When cognitive test outliers were removed, the overall regression remained significant ($F(3, 20) = 4.34$, $p = .02$; $R^2 = .39$). When the effect of SES was controlled, total PSOM score and lesion volume collectively accounted for significant variance in verbal skills ($F(2, 20) = 4.01$, $p = .03$; $\Delta R^2 = .24$).

Hierarchical multiple regression analysis conducted for the WASI Matrix Reasoning subtest (see Table 22) did not reveal a significant overall regression model ($F(3, 22) = 1.59$, $p = .22$; $R^2 = .18$). When the effect of SES was controlled, total PSOM score and lesion volume did not account for significant variance in Matrix Reasoning ($F(2, 22) = 2.12$, $p = .14$; $\Delta R^2 = .16$). When a cognitive test outlier was removed, the overall regression did not reach significance ($F(3, 21) = 2.09$, $p = .13$; $R^2 = .23$).

Hierarchical multiple regression analysis conducted for the TEA-Ch Creature Counting Accuracy score (see Table 23) did not reveal a significant overall regression model ($F(3, 21) = .51$, $p = .68$; $R^2 = .07$). When the effect of SES was controlled, total PSOM score and lesion volume did not account for significant variance in mental flexibility ($F(2, 21) = .73$, $p = .49$; $\Delta R^2 = .07$).

Hierarchical multiple regression analysis conducted for the TEA-Ch Creature Counting Timing score (see Table 23) did not reveal a significant overall regression model ($F(3, 13) = 1.47$, $p = .27$; $R^2 = .25$). When the effect of SES was controlled, total PSOM score and lesion volume did not account for significant variance in performance ($F(2, 13) = 2.10$, $p = .16$; $\Delta R^2 = .24$). Outliers were not evident on the Creature Counting subtest.

Hierarchical multiple regression analysis conducted for the TEA-Ch Walk/Don't Walk subtest (see Table 24) did not reveal a significant overall regression model ($F(3, 22) = 1.14$, $p = .36$; $R^2 = .14$). When SES was controlled, total PSOM score and lesion volume did not account for significant variance in mental flexibility ($F(2, 22) = .39$, $p = .68$; $\Delta R^2 = .03$). Results did not change after cognitive test outliers were removed.

Hierarchical multiple regression analysis conducted for the TEA-Ch Code Transmission subtest (see Table 25) did not reveal a significant overall regression model ($F(3, 22) = 0.79$, $p = .5$; $R^2 = .10$). When SES was controlled, total PSOM score and lesion volume did not account for significant variance in processing speed ($F(2, 22) = 0.93$, $p = .41$; $\Delta R^2 = .08$). Results did not change after cognitive test outliers were removed.

Hierarchical multiple regression analysis conducted for the WISC-IV PSI (see Table 26) revealed a significant overall regression model ($F(3, 22) = 4.18$, $p = .02$; $R^2 = .36$). When SES was controlled, total PSOM score and lesion volume accounted for significant variance in processing speed ($F(2, 22) = 4.91$, $p = .02$; $\Delta R^2 = .28$). Total PSOM score significantly predicted processing speed performance ($\beta = -.52$, $p = .01$), but SES

and lesion volume did not. Results did not change after cognitive test outliers were removed.

Hierarchical multiple regression analysis conducted for the WISC-IV Coding subtest (see Table 27) revealed a significant overall regression model ($F(3, 22) = 3.18$, $p = .04$; $R^2 = .30$). When SES was controlled, total PSOM score and lesion volume accounted for significant variance in processing speed ($F(2, 22) = 4.75$, $p = .02$; $\Delta R^2 = .30$). Results did not change after cognitive test outliers were removed.

Hierarchical multiple regression analysis conducted for the WISC-IV Cancellation subtest (see Table 28) revealed a significant overall regression model ($F(3, 22) = 3.68$, $p = .03$; $R^2 = .33$). When SES was controlled, total PSOM score and lesion volume did not account for significant variance in processing speed ($F(2, 22) = 2.57$, $p = .10$ $\Delta R^2 = .16$). SES significantly predicted processing speed performance ($\beta = -.40$, $p = .04$), but total PSOM score and lesion volume did not. Results did not change after cognitive test outliers were removed.

Chapter 4: Discussion

Primary Aim

The first goal of the current study was to determine whether children display deficits in cognitive functioning following AIS. The hypothesis that children with AIS would perform significantly lower on cognitive measures than children with asthma could not be confirmed or rejected. The AIS group performed significantly lower than the asthma group on a measure of inhibitory control, but differences were not significant on measures of verbal and nonverbal functioning, processing speed, working memory, or cognitive flexibility. However, many group differences were in the expected direction and effect sizes ranged from small to moderate in magnitude. Although group differences did not reach conventional levels of statistical significance, we cannot be sure if that is due to an absence of significant differences or to the small sample size.

Convincing support was obtained for the second hypothesis that children with AIS would perform significantly lower on cognitive measures than normative populations. As predicted, mean scores of the AIS group were significantly lower than normative population means on measures of general cognitive ability, verbal functioning, inhibitory control, working memory, and one measure of processing speed. The AIS group exhibited a non-significant trend toward lower performance on measures of nonverbal functioning, cognitive flexibility, and processing speed, as compared to the

normative population. The asthma group performed significantly lower than normatively expected on measures of inhibitory control, sustained attention, and processing speed. Although children with asthma tended to perform slightly higher than children with AIS, results suggest children with asthma may also exhibit mild cognitive deficits.

Additionally, the inclusion of data from the current study did not alter the results of the meta-analysis of FSIQ following childhood stroke. That analysis revealed a small but significant mean difference across 14 studies demonstrating lower cognitive functioning in children with AIS compared to the normative population. Notably, only 5 of 13 published studies reported significant group differences between children with stroke and a control group or the normative population. The results of the meta-analysis highlight the importance of reviewing studies not only qualitatively but also quantitatively in order to fully summarize the findings.

Taken together, our findings provide support for the notion that children display mild cognitive deficits following AIS. The results are consistent with research documenting either non-significant trends toward lower cognitive functioning in children with stroke compared to normative population means (Everts et al., 2008; Heterington et al., 2005; Hogan et al., 2000; Long et al., 2010; Pavlovic et al., 2006) or significant differences between children with stroke and normative populations (McLinden et al., 2007; Westmacott et al., 2009; Westmacott et al., 2010). Moreover, the results of the final meta-analysis further strengthened the conclusion that children with stroke perform significantly below normative population means. Although most group differences between the AIS and asthma groups did not reach statistical significance, patterns of

performance were similar to previous findings. Specifically, Max and colleagues documented significant differences between children with stroke and a control group of children with orthopedic injuries (Max et al., 2002). However, further research is needed to determine whether children with AIS significantly differ from children with illnesses not involving the central nervous system.

Our results, along with findings from existing research, suggest that children with AIS perform at the low end of the average range on standardized cognitive measures administered in a controlled environment. Nevertheless, analyses of mean scores may mask individuals who exhibit more severe cognitive deficits. This study, along with others, indicates that some children with AIS perform significantly below average, as evidenced by group means in the low end of the average range (McLinden et al., 2007; Westmacott et al., 2009; Westmacott et al., 2010). Consequently, specific factors most likely distinguish this subgroup and account for decreased cognitive functioning among these children.

Secondary Aim

The second goal of the current study was to determine whether specific neurological, child-related, or developmental factors significantly predicted cognitive outcome following perinatal and childhood AIS. We found convincing evidence to support the hypothesis that greater stroke severity (i.e., higher PSOM scores and larger stroke volumes) would be associated with lower scores on standardized cognitive measures. Most correlations were in the expected direction, but they ranged from small to moderate in magnitude, and few reached statistical significance. Significant correlations

indicated that higher PSOM scores were related to lower performance on measures of general cognitive ability, verbal functioning, and processing speed. Similarly, significant correlations indicated that larger lesion volumes were related to reduced performance on measures of general cognitive ability and verbal functioning. Furthermore, total PSOM score and stroke volume were significantly correlated, suggesting that children with poorer neurological functioning were more likely to have larger lesions.

A relationship between stroke severity and cognitive performance was expected based on similar associations documented in research examining functional outcomes following stroke (Gordon et al., 2002; Kreiter et al., 2002). Although pediatric studies have not examined the PSOM as a measure of stroke severity, several studies have demonstrated a significant association between lesion volume and cognitive outcome (Beslow et al., 2010; de Veber et al., 2008; Duval et al., 2008; Everts et al., 2008; Ganesan et al., 1999; Hetherington et al., 2005; Hogan, Kirkham, & Isaacs, 2000; Jordan, Kleinman, & Hillis, 2009; Westmacott et al., 2010). Not all studies have found a significant relationship between lesion volume and outcome, but this is most likely due to small samples (Chapman et al., 2003).

Unlike previous findings, we did not find a significant effect of cortical lesion location on outcome. Lower cognitive performance was expected among children with combined cortical and subcortical lesions because some studies have demonstrated that trend (Hetherington et al., 2005; Hogan, Kirkham, & Isaacs, 2000; Montour-Proulx et al., 2004; Steinlin, Roellin, & Schroth, 2004; Westmacott et al., 2010). However, research is inconclusive and results are often confounded by lesion volume or limited by small

sample sizes. Similarly, we did not find a significant effect of lesion laterality on cognitive outcome. Contrary to adult studies, pediatric stroke research has failed to document a significant relationship between outcome and lesion laterality. More studies are needed to examine the effect of lesion location in terms of cortical region and laterality following childhood stroke (Ballantyne et al., 2008; Hetherington et al., 2005; Hogan et al., 2000; Kolk et al., 2011; Lefond et al., 2008; Ricci et al., 2008; Westmacott et al., 2010).

Likewise, no relationships were found between cognitive outcome and developmental factors, including age at stroke and time between stroke and assessment. Previous investigators have hypothesized that these variables may be related to cognitive outcome following stroke, but findings are inconclusive (Braun et al., 2002; Duval et al., 2008; Hogan et al., 2000; Max et al., 2010; Westmacott et al., 2009). Some recent studies suggest that earlier age at stroke may be associated with poorer outcomes compared to later stroke (Duval et al., 2008; Kolk et al., 2011; Lefond et al., 2008; Max et al., 2010; Montour-Proulx et al., 2004; Westmacott et al., 2010). On the other hand, other researchers suggest that the relationship may be curvilinear, with the greatest cognitive deficits documented in extremely young and extremely old individuals (Schaller, 2007). In the current study, null findings could have been due to the somewhat limited age range (6 to 15 years) of children. If a curvilinear relationship exists, the most vulnerable children in early childhood and late adolescence may have been omitted from our sample. Similarly, studies examining the interval between stroke and assessment have produced inconclusive results (Westmacott et al., 2010). Longitudinal studies of acquired brain

injuries suggest that the recovery trajectory is the fastest immediately following injury, then gradually tapers off over the next few years (Chapman et al., 2003; Yeates et al., 2007). More research is needed to examine the course of recovery following stroke during different developmental periods in childhood.

We also failed to find a significant relationship between cognitive outcome and sex, contrary to the adult literature. In adults with stroke, some evidence suggests that sex may influence outcome, with women outperforming men (Braun et al., 2002). On the other hand, recent findings indicate females may face more functional deficits than males (Duval et al., 2008; Roth et al., 2011). Although a small body of research suggests that girls may outperform boys following early brain insults, this trend has not been consistently observed in children following AIS (Braun et al., 2002; Hogan et al., 2000; Pavlovic et al., 2006; Westmacott et al., 2009; Westmacott et al., 2010).

SES, as measured by maternal education, had a moderate to significant effect on cognitive test performance in the AIS group. In general, higher levels of maternal education were associated with better performance on measures of general cognitive ability, verbal ability, and inhibitory control. Conversely, higher levels of education were associated with worse performance on a measure of processing speed. The reasons for the latter relationship, which was unexpected, are unclear. Perhaps children with higher SES were trying to compensate by being extra careful and taking their time. They may also have been taught to work slowly and check their answers to ensure their responses were correct. Other significant relationships were in the expected direction and consistent with previous research. Indeed, Hetherington et al. (2005) found a small, but non-significant,

trend toward an association between lower SES and lower cognitive functioning. However, studies examining this relationship in children with stroke are sparse. Often, groups are too small to run analyses or SES data is not routinely gathered at study sites (Westmacott et al., 2009). Researchers in the field of traumatic brain injury have more thoroughly examined the effect of SES and suggest that lower SES is associated with reduced cognitive functioning (Fay et al., 2010; Yeates, 2010).

Although the next goal was to examine the effect of presence of seizures and race on cognitive outcome, sample sizes were inadequate. The presence of seizures was considered potentially important because a small number of studies have documented a significant relationship between epilepsy and reduced cognitive functioning following stroke (Ballantyne et al., 2008; De Schryver et al., 2000; Duval et al., 2008; Everts et al., 2008; Fox & Fullerton, 2010; Kolk et al., 2011; Ricci et al., 2008). Less is known about the role of race in predicting outcome following pediatric stroke, but the adult stroke literature suggests African Americans may face a less complete recovery following stroke compared to white patients (Ottenbacher et al., 2008; Roth et al., 2011; Stansbury, Jia, Williams, Vogel, & Duncan, 2005).

Taken together, analyses revealed that total PSOM score, lesion volume, and SES significantly influenced performance on several cognitive measures, whereas stroke location, age at stroke, time between stroke and assessment, and sex did not. Analyses of predictors were hampered by small sample size, and power to detect significant results was low. Even though many correlations and effect sizes did not reach conventional levels of statistical significance, we cannot be sure whether this is due to an absence of

significance or because of the small sample. In addition to being small and underpowered, the current sample may have lacked sufficient variability to detect significant results. Compared to the current study, several of the studies that have reported significant results used larger samples of children with substantial variability in terms of stroke severity, age, and time between stroke and assessment. Replication of significant results will be needed to determine which neurological, developmental, and child related factors significantly predict cognitive outcome.

Regression Analyses

Overall, hierarchical regression results suggested that cognitive outcome following AIS depends on a combination of factors. Specifically, the combination of total PSOM score, lesion volume, and SES significantly predicted outcome on measures of general cognitive ability, verbal functioning, and processing speed in children with AIS. Collectively, poorer neurological functioning, larger lesion volume, and lower SES predicted lower scores on measures of general cognitive ability and verbal functioning. Similarly, together, lower neurological functioning, larger lesion volume, and higher SES predicted lower scores on a measure of processing speed.

The results also provided convincing support for the final hypothesis that greater stroke severity would account for significant variance in cognitive outcome, after taking other significant factors into account. Hierarchical regression analyses indicated that stroke severity accounted for significant variance in general cognitive ability, verbal performance, and processing speed, after controlling for SES. Furthermore, total PSOM score accounted for unique variance in processing speed performance. These results are

not surprising, given the previous findings that higher lesion volume was significantly related to lower general cognitive ability and verbal functioning, and higher PSOM scores were significantly related to lower processing speed. Montour-Proulx et al. (2004) reported similar regression results in a group of children and adults. Specifically, researchers found that lesion volume was a stronger predictor of cognitive outcome than age at stroke, interval between stroke and assessment, and recurrent etiology. Additional studies have also suggested stroke severity may be related to reduced cognitive functioning, but replication of these results is necessary (Ganesan et al., 1999; Duval et al., 2008; Everts et al., 2008; Hetherington et al., 2005; Hogan, Kirkham, & Isaacs, 2000; Westmacott et al., 2010).

Limitations

In designing an ideal study to examine cognitive outcomes in a population of children with AIS, one must consider the limitations apparent in the pediatric stroke literature and in the current study. The existing literature is relatively sparse and provides limited grounds for generalization because of methodological flaws. As previously stated, common limitations include small heterogeneous samples, inadequate control groups, poorly defined inclusion/exclusion criteria, and inconsistencies in neuroimaging and standardized test batteries (Bates et al., 2001; De Schryver et al., 2000; Everts et al., 2008; Hetherington et al., 2005; Hogan et al., 2000; McLinden et al., 2007; Montour-Proulx et al., 2004; Ricci et al., 2008; Westmacott et al., 2009; Westmacott et al., 2010). Limitations in the current study include a restricted neuropsychological test battery, cross-sectional study design, retrospective recruitment, and small sample size.

The primary aim of the larger study was to examine social outcomes following AIS in children, so cognitive testing was limited due to time constraints. As the meta-analyses indicate, several studies have examined general cognitive outcome, as well as verbal and nonverbal functioning, following childhood stroke. As a whole, findings indicate that children with stroke perform significantly lower than the normative population. Neuropsychological studies to date are limited, but suggest children may exhibit larger deficits on measures of complex neurocognitive skills (Block et al., 1999; Chapman et al., 2003; Max, 2004). Future research should expand upon these findings by using a more extensive neuropsychological battery. A comprehensive battery should include measures of verbal skills (receptive and expressive language skills, phonological processing, learning and memory), nonverbal skills (visual spatial skills, visual motor integration, learning and memory), executive functions (attention, working memory, cognitive flexibility), and motor functions. In addition, recent studies suggest children may exhibit deficits in the classroom that are not observed on standardized tests (De Schryver et al., 2000). Therefore, a brief assessment of academic achievement should also be administered following pediatric stroke. Furthermore, researchers have demonstrated that children may display deficits in daily executive functioning and adaptive behaviors (Hogan et al., 2000; Long et al., 2010). Therefore, parent and teacher reports of daily functioning and behavior should also be included.

In addition to limited neuropsychological testing, the current study is cross-sectional and retrospective, leaving unanswered questions about the long-term effects of pediatric AIS. Further prospective and longitudinal studies are needed to assess AIS at

multiple time points because studies to date have produced mixed results. Two studies indicate that children display decreased cognitive functioning over time, while one suggests that cognitive functions are stable (Ballantyne et al., 2008; McLinden et al., 2007; Westmacott et al., 2009). However, these studies are difficult to compare because researchers assessed functioning at different intervals following AIS. Longitudinal research with animal models has followed infant rats with strokes through childhood, adolescence, and adulthood (Kolk et al., 2010). Although less feasible with human participants, following children with AIS into adulthood would provide insight into the long-term prognosis of childhood stroke survivors. Retrospective recruitment may present an additional limitation. Participants recruited retrospectively may exhibit more deficits compared to those recruited through prospective, population-based studies (Roth et al., 2011).

Finally, the sample size was small, and statistical power was relatively low, although the sample size is comparable to or larger than those of previous studies. The limited sample size was anticipated, given the rarity of pediatric AIS, the difficulty in recruiting participants from this population, and the strict exclusion criteria. However, parents and children may not have received sufficient compensation for their time to participate. Given early challenges with recruiting children from this population, several modifications were made in eligibility criteria to increase sample sizes. The age range was expanded to include 6 to 7 year olds and 13 to 15 year olds, as well as children with perinatal stroke. The current sample also displayed limited variability in stroke severity, lesion volume, age, race, and presence of seizures. Overall, the sample included

predominantly young, white children, with relatively mild strokes (low PSOM scores; small AIS volumes) that occurred at very early ages (within the first year of life). Furthermore, few children presented with seizures at the time of stroke or assessment. Thus, in addition to being small and underpowered, the current sample may have lacked sufficient variability to detect significant results. Children with more severe impairments were most likely excluded because they would have been unable to complete the test battery due to sensory or motor impairments. Additionally, children with severe strokes typically have complicated medical histories and they may have been excluded based on the strict inclusion/exclusion criteria that were employed.

Strengths

Despite limitations, the current study successfully addressed many of the shortcomings inherent in previous research. A common limitation in pediatric stroke studies involves inconsistent inclusion and exclusion criteria, leading to heterogeneous samples. Selection criteria in the current study were strict and excluded a variety of conditions that could have confounded the findings. Furthermore, the criteria and selection process were characterized clearly and explicitly. Although the stringent criteria restricted the sample size, it was still comparable to previous studies.

Additionally, children with an illness not involving the central nervous system provided a control group that addressed the problem of the confounding effects of hospitalization and illness characteristics. Children with stroke do not represent a random sample that is representative of the general population, and children with an illness requiring acute hospitalization share unique characteristics.

Future Directions

The current study is one of the first to compare the cognitive outcomes of a group of children following AIS to a control group of children with asthma. Our results, along with findings from existing research, suggest that children with AIS perform at the low end of the average range on standardized cognitive measures administered in a controlled environment. In addition to cognitive impairment, children may also exhibit functional limitations that significantly impact their daily lives following stroke but are difficult to detect in standardized testing environments (Galvin, Randall, Hewish, Rice, & Mackay, 2010; Hogan et al., 2000). Although not examined in the present study, residual deficits in motor, language, academic, and behavioral domains are relatively common following pediatric stroke (Ganesan et al., 2000; Hogan et al., 2000; Yilmaz et al., 2011).

Despite the noted difficulties faced by children with stroke, few intervention programs have been developed for this population. Moreover, clinicians often focus on cognitive and physical recovery, while parents may be concerned with a broader range of functional domains (Galvin et al., 2010). Indeed, in a study of 26 children with pediatric stroke, approximately 90% of children and parents endorsed persistent functional disturbances in the domains of self-care, productivity, and leisure. Therefore, clinicians and therapists should routinely assess a child's degree of functional impairment following stroke. Given the cognitive, behavioral, and adaptive challenges children may face following AIS, development of effective rehabilitation programs is necessary. Interventions in this population are difficult to generalize, however, because the outcomes of AIS are variable and depend on a variety of factors, as described previously.

Although strongly needed, intervention and rehabilitation studies for children with stroke are lacking. However, some insight can be gained from the large body of translational animal research. Kolb and colleagues (2010) have used animal models of brain injury to study stroke and neural plasticity, and develop rehabilitation strategies that could potentially be used with humans. They explain that brain injury disrupts or severs connections in neural networks and specific rehabilitation strategies may help repair lost connections or create new ones.

Kolb and colleagues (2010) have found promising results when rats receive frequent physical activity, as well as enriched environmental, social, and tactile stimulation, following induced stroke. After a month of increased environmental and tactile stimulation, injured rats demonstrated improvements in cognitive, motor, and social functioning. Furthermore, they exhibited signs of neurological recovery including an increase in brain volume, synapses, and astrocytes. Kolb and colleagues (2010) hypothesize that the combination of behavioral and physical therapy facilitates cognitive and behavioral recovery in rats. Researchers note that a human translation of enriched environments and tactile stimulation may include intensive physical therapy and daily massage post-stroke (Kolb et al., 2010).

Similarly, clinical studies following traumatic brain injury in children has demonstrated a positive effect of enriched environments. Indeed, traumatic brain injury research suggests that children demonstrate greater adaptability and recovery in highly stimulating environments. For instance, family emotional and social support, broad social networks, and energizing physical activities appear to have a positive influence on the

course of functional recovery (Chapman & McKinnon, 2000). Moreover, intensive interventions with speech and language specialists, as well as physical and occupational therapists, can help improve children's functioning. Similarly, educational intervention and academic support from teachers and aides can facilitate recovery and help children adapt and cope with learning problems (Lansing et al., 2004). Finally, psychological counseling and behavioral therapy may foster recovery and alleviate stress for parents and children (Chapman & McKinnon, 2000).

Although research with human models is necessary, translational animal studies have demonstrated that increased physical, social, and environmental stimulation can facilitate recovery in brain injured rats. Likewise, studies of pediatric traumatic brain injury suggest that the combination of behavioral, physical, and psychological therapy is advantageous post-injury. However, it is unknown whether these findings can be generalized across the diverse population of children with stroke. Thus, future research is needed to develop and explore effective intervention strategies designed specifically for children with stroke.

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Appendix A: Tables

Study	Stroke type	Age at stroke (years)	Age at assessment (years) *M* (range)	N	Measures
Ballantyne et al., 2008	AIS	0	11.33 (7-12)	15	WISC-R
Beharelle, et al., 2010	AIS	0-18	14.33 (7.17-29.83)	25	WISC-III/WAIS-III (VIQ)
Duval et al., 2008	Unilateral lesion	0-18	NR	198	WISC/WAIS
Everts et al., 2008	Unilateral lesion	0.08-17.5	11.92 (6.75-21.17)	17	WISC-III
Guimaraes et al., 2007	AIS	1.25-10.5	9.83 (7.08-14.17)	14	WISC
Hetherington et al., 2005	AIS	0	4.9 (*SD*=5.4)	47	BSID/WPPSI-R/WISC-III/WAIS-R
Hogan et al., 2000	AIS	1.16-16.25	NR	38	WISC
Long et al., 2010	AIS/H	0-14.50	12.5 (10-15)	29	WASI
Max et al., 2002	AIS/H	0-18	5-19	29	WISC-III - Prorated
McLinden et al., 2007	AIS/SVT	0	1.67-12.33	21	BSID - Mental Development Index
Montour-Proulx et al., 2004	Unilateral lesion	0-17	NR	417	Weschsler VIQ and PIQ

Table 1. Characteristics of Studies Included in the Meta-analyses of Cognitive Outcome (FSIQ), Verbal (VIQ), and Nonverbal (PIQ) Functioning Following Pediatric Stroke

AIS = arterial ischemic stroke; H = hemorrhagic; SVT = sinovenous thrombosis; NR = not reported; N = number of children; WISC = Wechsler Intelligence Scale for Children; WAIS = Wechsler Adult Intelligence Scale; BSID = Bayley Scale of Infant Development; WPPSI = Wechsler Preschool and Primary Scale of Intelligence; K-ABC = Kaufman Assessment Battery for Children

Continued

Table 1 continued

Study	Stroke type	Age at stroke (years)	Age at assessment (years) *M* (range)	N	Measures
Pavlovic et al., 2006	AIS/SVT	0-16.3	1.8-18.2	30	K-ABC, WISC, WAIS
Ricci et al., 2008	MCA infarction	0	5.33-10.33	26	WPPSI/WISC
Westmacott et al., 2009	AIS	0	6.1-12.5	26	WISC-III/WISC-IV
Westmacott et al., 2010	AIS	0-16	9.08 (*SD*=3.83)	145	WPPSI/WPPSI-RWISC-II/WISC-III

AIS = arterial ischemic stroke; H = hemorrhagic; SVT = sinovenous thrombosis; NR = not reported; N = number of children; WISC = Wechsler Intelligence Scale for Children; WAIS = Wechsler Adult Intelligence Scale; BSID = Bayley Scale of Infant Development; WPPSI = Wechsler Preschool and Primary Scale of Intelligence; K-ABC = Kaufman Assessment Battery for Children

Study	N	FSIQ *M, SE*	Mean difference	Comparison	Significant difference	*t*	*p*
Ballantyne et al., 2008	15	94.7, 5.27	5.3	Controls	Yes	-1.01	.33
Duval et al., 2008	198	92.70, 1.20	7.3	None	NR	-6.09	< .01
Everts et al., 2008	17	96.47, 3.64	3.53	Norms	No	-0.97	.35
Guimaraes et al., 2007	14	90.5, 4.78	9.5	Controls	NR	-2.09	.06
Hetherington et al., 2005	47	98.9, 1.88	1.1	Norms	No	-0.58	.56
Hogan et al., 2000	38	93.84. 1.99	6.16	Norms	NR	-3.1	< .01
Long et al., 2010	28	91.60, 3.67	8.4	Norms	NR	-2.29	.03
Max et al., 2002	29	86.6, 3.34	13.4	Controls	Yes $t(56) = -4.08, p < .01$	-4.01	< .01
McLinden et al., 2007	21	92.19, 3.41	7.81	Norms	Yes $z(20) = -2.39, p = .01$	-2.29	.03
Pavlovic et al., 2006	30	91.71; 2.27	8.29	Norms	No	-3.64	< .01
Ricci et al., 2008	26	96.96; 4.19	3.04	None	NR	-0.72	.48
Westmacott et al., 2009	26	92.81; 2.60	7.19	Norms	Yes $z(25) = -2.44, p < .01$	-2.77	.01
Westmacott et al., 2010	145	94.74; 1.22	5.26	Norms	*Yes* $z(144) > 2.5, p < .01$	-4.31	< .01

Table 2. Means and Statistical Analyses of Studies Included in the Meta-analysis of FSIQ Following Pediatric Stroke

Note: Significant difference based on reported values; *t*-tests compared observed (*M, SD)* to normative population (*M* = 100; *SD = 15);* N = number; FSIQ = full scale intelligence quotient; M = mean; SE = standard error; NR = not reported.

Study	N	VIQ *M, SE*	Mean difference	Comparison	Significant difference	*t*	*p*
Ballantyne et al., 2008	15	98.7, 5.16	1.3	Controls	Yes $p < .01$	-.25	.81
Beharelle, et al., 2010	25	90.5, 4.16	9.5	Controls	NR	-2.28	.03
Everts et al., 2008	17	99.3, 3.47	3.53	Norms	NR	-0.20	0.84
Guimaraes et al., 2007	14	94.29, 3.81	5.71	Controls	NR	-1.50	0.16
Hogan et al., 2000	38	95.0, 2.77	5	Norms	No	-1.81	0.08
Max et al., 2002	29	90.9, 3.09	9.7	Controls	Yes $t(56) = -3.74, p < .01$	-2.97	< .01
Montour-Proulx et al., 2004	417	91.58, .82	8.42	None	NR	-10.25	< .01
Pavlovic et al., 2006	10	103.3, 4.40	-3.3	Norms	No	.75	.47
Ricci et al., 2008	26	94.88, 3.78	5.12	None	NR	-1.35	.19
Westmacott et al., 2010	145	95.99, 1.20	4.01	Norms	Yes $p < .01$	-3.35	< .01

Table 3. Means and Statistical Analyses of Studies Included in the Meta-analysis of Verbal Functioning (VIQ) Following Pediatric Stroke

Note: Significant difference is based on values reported in original articles; one sample *t*-tests were also performed independently to compare each study's observed (*M, SD)* to the normative population ($M = 100$; $SD = 15$); N = number of children; FSIQ = full scale intelligence quotient; M = mean; SE = standard error; NR = not reported.

Study	N	PIQ *M, SE*	Mean difference	Comparison	Significant difference	*t*	*p*
Ballantyne et al., 2008	15	93.5, 5.16	6.5	Controls	Yes $p < .01$	-1.26	.23
Everts et al., 2008	17	92.0, 5.02	8	Norms	NR	-1.59	0.13
Guimaraes et al., 2007	14	88.57, 5.34	11.43	Controls	NR	-2.14	0.05
Hogan et al., 2000	38	91.6, 2.64	8.4	Norms	Yes $p < .01$	-3.18	< .01
Max et al., 2002	29	84.5, 3.79	15.5	Controls	Yes $t(56) = -3.38, p < .01$	-4.09	< .01
Montour-Proulx et al., 2004	417	93.3, .91	6.7	None	NR	-7.39	< .01
Pavlovic et al., 2006	10	94.5, 4.65	5.5	Norms	No	-1.18	.27
Ricci et al., 2008	27	98.78, 4.01	1.22	None	NR	-.30	.77
Westmacott et al., 2010	145	96.48, 1.21	3.52	Norms	Yes $p < .01$	-2.92	< .01

Table 4. Means and Statistical Analyses of Studies Included in the Meta-analysis of Nonverbal Functioning (PIQ) Following Pediatric Stroke

Note: Significant difference is based on values reported in original articles; one sample *t*-tests were also performed independently to compare each study's observed (*M, SD)* to the normative population ($M = 100$; $SD = 15$); N = number of children; FSIQ = full scale intelligence quotient; M = mean; SE = standard error; NR = not reported.

Demographics	AIS	Asthma
N	36	15
Male (%)	16 (44%)	9 (60%)
White (%)	34 (94%)	14 (93%)
Age at presentation	4.17 ± 4.34	3.08 ± 3.97
Age at assessment	9.15 ± 3.02	9.84 ± 2.64
Time since presentation	4.97 ± 3.28	6.80 ± 3.23
Maternal education	34	15
9^{th} grade or less	0 (0%)	1 (7%)
$10^{th}/11^{th}$ grade	6 (18%)	4 (27%)
High school graduate	11 (32%)	2 (13%)
Partial degree/Professional qualifications	11 (32%)	4 (27%)
College/University graduate	4 (12%)	3 (20%)
Graduate/Post graduate degree	2 (6%)	1 (7%)

Table 5. Demographic Characteristics of AIS and Asthma Groups

Measure	AIS		Asthma		Cohen's *d*
	(n)	*M (SD)*	*(n)*	*M (SD)*	
WASI IQ	(35)	94.63 (13.92)	(15)	99.53 (11.78)	.38
Vocabulary	(35)	42.49 (12.30)	(15)	47.47 (9.94)	.44
Matrix Reasoning	(36)	48.97 (9.90)	(15)	51.73 (6.11)	.34
TEA-Ch					
Creature Counting Total	(33)	9.06 (3.20)	(14)	9.00 (3.66)	.02
Creature Counting Time	(23)	7.91 (3.10)	(11)	9.64 (2.94)	.57
Walk, Don't Walk*	(35)	4.94 (2.39)	(15)	6.73 (2.87)	.68
Code Transmission	(34)	8.32 (3.19)	(15)	7.27 (3.73)	.30
WISC PSI	(35)	93.69 (17.23)	(15)	95.20 (14.76)	.09
Coding	(35)	8.77 (3.38)	(15)	8.07 (3.47)	.20
Cancellation	(35)	8.94 (3.74)	(15)	10.20 (2.48)	.40

Table 6. Summary of Results for Cognitive Measures Based on AIS Group Compared to Asthma Group

*Groups significantly differed at $p < .05$

	AIS				Asthma			
Measure	*(n)*	Mean difference	*t*	*P*	*(n)*	Mean difference	*t*	*p*
WASI IQ	(35)	-5.37	-2.28	.03*	(15)	-.47	-.15	.88
Vocabulary	(35)	-7.51	-3.62	.00*	(15)	-2.53	-.987	.34
Matrix Reasoning	(36)	-1.03	-.62	.54	(15)	1.73	1.10	.29
TEA-Ch								
Creature Counting Total	(33)	-.94	-1.69	.10	(14)	-1.0	-1.02	.33
Creature Counting Time	(23)	-2.09	-3.23	.00*	(11)	-.36	-.41	.69
Walk, Don't Walk	(35)	-5.06	-12.53	.00*	(15)	-3.27	-4.42	.00*
Code Transmission	(34)	-1.68	-3.07	.00*	(15)	-2.73	-2.84	.01*
WISC PSI	(35)	-6.31	-2.17	.04*	(15)	-4.8	-1.26	.23
Coding	(35)	-1.23	-2.15	.04*	(15)	-1.93	-2.16	.05*
Cancellation	(35)	-1.06	1.67	.10	(15)	.20	.31	.76

Table 7. Summary of Results for AIS and Asthma Groups Compared to Normative Populations

*Significant difference at $p < .05$

Impairment	AIS Children				
	Right Sensorimotor Deficit *n* (%)	Left Sensorimotor Deficit *n* (%)	Language Production Deficit *n* (%)	Language Comprehension Deficit *n* (%)	Cognitive or Behavioral Deficit *n* (%)
None	20 (56%)	19 (53%)	31 (86%)	29 (81%)	18 (50%)
Mild (no functional impact)	7 (19%)	8 (22%)	1 (3%)	3 (8%)	4 11%)
Moderate (functional impact)	7 (19%)	5 (14%)	3 (8%)	3 (8%)	12 (33%)
Severe (missing function)	2 (6%)	4 (11%)	1 (3%)	1 (3%)	2 (6%)

Table 8. Frequencies of PSOM Severity Ratings on Subscales

	PSOM	
Measure	*(n)*	Correlation
WASI IQ	(35)	-.35*
Vocabulary	(35)	-.34*
Matrix Reasoning	(36)	-.27
TEA-Ch		
Creature Counting Total	(33)	-.27
Creature Counting Time	(23)	-.01
Walk, Don't Walk	(35)	-.06
Code Transmission	(34)	-.25
WISC PSI	(35)	-.30*
Coding	(35)	-.42*
Cancellation	(35)	-.20

Table 9. Spearman Rank Order Correlations (ρ) Between Total PSOM Score and Cognitive Measures

	Lesion Volume (cubic mm)			
	(n)	With Outliers	*(n)*	Without Outliers
WASI IQ	(27)	-.38*	(25)	-.44*
Vocabulary	(27)	-.38*	(25)	-.50*
Matrix Reasoning	(28)	-.29	(27)	-.25
TEA-Ch				
Creature Counting Total	(25)	.32	(23)	.39*
Creature Counting Time	(17)	.16	(17)	.16
Walk, Don't Walk	(27)	-.19	(25)	-.23
Code Transmission	(26)	-.13	(24)	-.07
WISC PSI	(27)	-.21	(25)	-.12
Coding	(27)	.02	(25)	.07
Cancellation	(27)	-.30	(25)	-.12

Table 10. Spearman Rank Order Correlations (ρ) Between Absolute Lesion Volume and Cognitive Measures

*Significant correlation $p < .05$

	Lesion Volume (percentage)			
	(n)	With Outliers	*(n)*	Without Outliers
WASI IQ	(26)	-.38*	(24)	-.44*
Vocabulary	(26)	-.36*	(24)	-.47*
Matrix Reasoning	(27)	-.34*	(26)	-.29
TEA-Ch				
Creature Counting Total	(24)	.24	(23)	.30
Creature Counting Time	(16)	.11	(16)	.11
Walk, Don't Walk	(26)	-.12	(24)	-.16
Code Transmission	(25)	-.06	(23)	-.02
WISC PSI	(26)	-.22	(24)	-.13
Coding	(26)	-.04	(24)	.02
Cancellation	(26)	-.25	(24)	-.19

Table 11. Spearman Rank Order Correlations (ρ) Between Percent Lesion Volume and Cognitive Measures

*Significant correlation $p < .05$

Measure	Cortical *(n) M (SD)*	Subcortical *(n) M (SD)*	Combined *(n) M (SD)*	Asthma *(n) M (SD)*	Eta-squared AIS	Eta-squared All
WASI IQ	(4) 99.25 (11.75)	(12) 95.58 (14.37)	(16) 92.5 (14.95)	(15) 99.53 (11.78)	.02	.05
Vocabulary	(4) 44.25 (9.64)	(12) 44.33 (11.46)	(16) 42.63 (10.65)	(15) 47.47 (9.94)	.01	.04
Matrix Reasoning	(4) 54.0 (11.75)	(12) 49.58 (8.93)	(17) 46.82 (10.74)	(15) 51.73 (6.11)	.04	.07
TEA-Ch						
Creature Counting Total	(3) 9.0 (3.61)	(12) 8.67 (2.93)	(16) 9.2 (3.55)	(14) 9.00 (3.66)	.01	.00
Creature Counting Time	(2) 3.0 (2.83)	(7) 8.29 (1.38)	(11) 8.64 (3.64)	(11) 9.64 (2.94)	.06	.24
Walk, Don't Walk*	(3) 6.33 (2.89)	(12) 5.08 (2.61)	(17) 4.06 (1.75)	(15) 6.73 (2.87)	.08	.19
Code Transmission	(3) 6.33 (2.08)	(12) 8.33 (1.72)	(16) 8.38 (4.21)	(15) 7.27 (3.73)	.00	.04
WISC PSI	(4) 89.0 (4.69)	(12) 100.25 (16.23)	(16) 91.06 (20.26)	(15) 95.20 (14.76)	.03	.06
Coding	(4) 8.50 (2.52)	(12) 9.50 (3.12)	(16) 8.56 (4.03)	(15) 8.07 (3.47)	.01	.03
Cancellation	(4) 7.75 (1.26)	(12) 10.42 (4.10)	(16) 8.25 (3.98)	(15) 10.20 (2.48)	.04	.10

Table 12. Summary of Results for Cognitive Measures Based on AIS Group (by lesion location) Compared to Asthma Group

*Significant difference $p < .05$

Measure	Cortical/Subcortical *(n) M (SD)*	Combined *(n) M (SD)*	Asthma *(n) M (SD)*	Cohen's *d*	Eta-squared
WASI IQ	(16) 96.5 (14.32)	(16) 92.5 (14.95)	(15) 99.53 (11.78)	.27	.04
Vocabulary	(16) 44.31 (10.72)	(16) 42.63 (10.65)	(15) 47.47 (9.94)	.16	.04
Matrix Reasoning	(16) 50.69 (9.49)	(17) 46.82 (10.74)	(15) 51.73 (6.11)	.38	.06
TEA-Ch subtests					
Creature Counting Total	(15) 8.73 (2.94)	(16) 9.2 (3.55)	(14) 9.00 (3.66)	-.14	.00
Creature Counting Time	(9) 7.11 (2.80)	(11) 8.64 (3.64)	(11) 9.64 (2.94)	-.47	.00
Walk, Don't Walk*	(15) 5.33 (2.61)	(17) 4.06 (1.75)	(15) 6.73 (2.87)	.57	.18
Code Transmission	(15) 7.93 (1.91)	(16) 8.38 (4.21)	(15) 7.27 (3.73)	-.14	.02
WISC PSI	(16) 97.44 (14.93)	(16) 91.06 (20.26)	(15) 95.20 (14.76)	.36	.03
Coding	(16) 9.25 (2.93)	(16) 8.56 (4.03)	(15) 8.07 (3.47)	.20	.02
Cancellation	(16) 9.75 (3.75)	(16) 8.25 (3.98)	(15) 10.20 (2.48)	.39	.03

Table 13. Summary of Results for Cognitive Measures Based on AIS Group (by collapsed lesion location) Compared to Asthma Group

*Significant difference $p < .05$

Cohen's *d* calculated between pre/perinatal AIS and childhood AIS groups; eta-squared calculated between pre/perinatal AIS, childhood AIS and asthma groups.

Measure	Left	Right	Bilateral	Asthma	Eta-squared	
	(n) M (SD)	*M (SD)*	*M (SD)*	*M (SD)*	AIS	All
WASI IQ	(16) 96.94 (15.08)	(9) 91.67 (14.02)	(7) 92.57 (15.16)	(15) 99.53 (11.78)	.03	.05
Vocabulary	(16) 43.06 (9.60)	(9) 43.45 (11.13)	(7) 44.29 (13.34)	(15) 47.47 (9.94)	.03	.06
Matrix Reasoning	(16) 52.50 (11.35)	(9) 45.11 (8.33)	(8) 45.13 (7.40)	(15) 51.73 (6.11)	.14	.14
TEA-Ch						
Creature Counting Total	(15) 9.33 (3.12)	(9) 9.11 (3.76)	(6) 7.83 (2.86)	(14) 9.00 (3.66)	.03	.02
Creature Counting Time	(11) 8.27 (3.90)	(4) 7.25 (1.71)	(5) 7.80 (3.27)	(11) 9.64 (2.94)	.02	.07
Walk, Don't Walk	(16) 5.0 (2.31)	(9) 4.67 (2.29)	(7) 3.86 (2.19)	(15) 6.73 (2.87)	.04	.16
Code Transmission	(16) 8.13 (2.47)	(9) 8.44 (3.01)	(6) 7.83 (5.53)	(15) 7.27 (3.73)	.00	.18
WISC PSI	(16) 99.63 (18.13)	(9) 88.67 (20.59)	(7) 89.14 (9.84)	(15) 95.20 (14.76)	.11	.07
Coding	(16) 9.88 (3.52)	(9) 7.22 (3.63)	(7) 8.86 (2.73)	(15) 8.07 (3.47)	.08	.09
Cancellation	(16) 9.94 (4.0)	(9) 8.67 (4.44)	(7) 7.29 (2.29)	(15) 10.20 (2.48)	.09	.09

Table 14. Summary of Results for Cognitive Measures Based on AIS Group (by lesion laterality) Compared to Asthma Group

Measure	Pre/perinatal AIS *(n) M (SD)*	Childhood AIS *(n) M (SD)*	Asthma *(n) M (SD)*	Cohen's *d*	Eta-squared
WASI IQ	(11) 97.64 (14.19)	(24) 93.25 (13.88)	(15) 99.53 (11.78)	.31	.05
Vocabulary	(11) 45.91 (10.40)	(24) 42.67 (10.17)	(15) 47.47 (9.94)	.32	.05
Matrix Reasoning	(11) 50.55 (10.29)	(25) 48.28 (9.85)	(15) 51.73 (6.11)	.23	.03
TEA-Ch					
Creature Counting Total	(11) 9.36 (3.59)	(22) 8.91 (3.07)	(14) 9.00 (3.66)	.14	.00
Creature Counting Time	(8) 7.0 (3.16)	(15) 8.40 (3.07)	(11) 9.64 (2.94)	-.45	.10
Walk, Don't Walk	(11) 4.91 (2.34)	(24) 4.96 (2.46)	(15) 6.73 (2.87)	-.02	.10
Code Transmission	(11) 8.73 (3.13)	(23) 8.13 (3.27)	(15) 7.27 (3.73)	.19	.03
WISC PSI	(11) 92.27 (20.46)	(24) 94.33 (15.98)	(15) 95.20 (14.76)	-.1	.00
Coding	(11) 9.09 (4.44)	(24) 8.63 (2.87)	(15) 8.07 (3.47)	.12	.01
Cancellation	(11) 8.18 (4.14)	(24) 9.29 (3.58)	(15) 10.20 (2.48)	-.29	.04

Table 15. Summary of Results for Cognitive Measures Based on AIS Group (by age at AIS) Compared to Asthma Group

Cohen's *d* calculated between pre/perinatal AIS and childhood AIS groups; eta-squared calculated between pre/perinatal AIS, childhood AIS and asthma groups.

	Time since AIS			
	(n)	With Outliers	*(n)*	Without Outliers
WASI IQ	(35)	-.07	(33)	-.24
Vocabulary	(35)	.05	(34)	-.15
Matrix Reasoning	(36)	-.17	(35)	-.21
TEA-Ch				
Creature Counting Total	(33)	-.13	(31)	-.30
Creature Counting Time	(23)	.20		
Walk, Don't Walk	(35)	-.18	(34)	-.25
Code Transmission	(34)	-.21	(33)	-.31
WISC PSI	(35)	.22		
Coding	(35)	.20		
Cancellation	(35)	.11		

Table 16. Spearman Rank Order Correlations (ρ) Between Time Since AIS and Cognitive Measures

*Significant correlation $p < .05$

	AIS		Asthma		
	Male	Female	Male	Female	Partial
Measure	*(n) M (SD)*	*(n)M (SD)*	*(n) M (SD)*	*(n) M (SD)*	Eta-squared
WASI IQ	(16) 95.50 (13.16)	(19) 93.89 (14.84)	(9) 101.22 (13.06)	(6) 97.0 (10.16)	.01
Vocabulary	(16) 43.88 (11.44)	(19) 43.53 (9.35)	(9) 48.0 (10.09)	(6) 46.67 (10.61)	.00
Matrix Reasoning	(16) 50.56 (7.59)	(20) 47.70 (11.45)	(9) 53.0 (6.56)	(6) 49.83 (5.35)	.02
TEA-Ch subtests					
Creature Counting Total	(14) 9.93 (3.91)	(19) 8.42 (2.48)	(9) 8.22 (3.11)	(5) 10.40 (4.51)	.00
Creature Counting Time	(11) 8.27 (1.35)	(12) 7.58 (4.17)	(7) 9.0 (2.0)	(4) 10.75 (4.27)	.01
Walk, Don't Walk	(15) 4.13 (2.30)	(20) 5.55 (2.33)	(9) 6.67 (3.43)	(6) 6.83 (2.04)	.02
Code Transmission	(14) 8.29 (2.05)	(20) 8.35 (3.84)	(9) 7.22 (3.60)	(6) 7.33 (4.27)	.00
WISC PSI	(16) 94.44 (14.16)	(19) 93.05 (19.81)	(9) 91.11 (14.35)	(6) 101.33 (14.32)	.02
Coding	(16) 8.44 (2.56)	(19) 9.05 (3.99)	(9) 7.11 (3.52)	(6) 9.50 (3.15)	.04
Cancellation	(16) 9.50 (3.98)	(19) 8.47 (3.57)	(9) 9.67 (2.69)	(6) 11.0 (2.10)	.00

Table 17. Summary of Results for Cognitive Measures Comparing Effect of Sex on AIS Group and Asthma Group

	AIS		
	Male	Female	
Measure	*(n) M (SD)*	*(n)M (SD)*	Cohen's *d*
WASI IQ	(16) 95.50 (13.16)	(19) 93.89 (14.84)	.21
Vocabulary	(16) 43.88 (11.44)	(19) 43.53 (9.35)	.05
Matrix Reasoning	(16) 50.56 (7.59)	(20) 47.70 (11.45)	.11
TEA-Ch			
Creature Counting Total	(14) 9.93 (3.91)	(19) 8.42 (2.48)	.46
Creature Counting Time	(11) 8.27 (1.35)	(12) 7.58 (4.17)	.22
Walk, Don't Walk	(15) 4.13 (2.30)	(20) 5.55 (2.33)	.61
Code Transmission	(14) 8.29 (2.05)	(20) 8.35 (3.84)	.02
WISC PSI	(16) 94.44 (14.16)	(19) 93.05 (19.81)	.18
Coding	(16) 8.44 (2.56)	(19) 9.05 (3.99)	.27
Cancellation	(16) 9.50 (3.98)	(19) 8.47 (3.57)	.08

Table 18. Summary of Results for Cognitive Measures Based on Males Compared to Females in AIS Group

Measure	Less than high school *(n) M (SD)*	High school graduate/partial college *(n) M (SD)*	College graduate *(n) M (SD)*	Eta-squared
WASI IQ*	(6) 93.83 (11.16)	(21) 90.57 (12.02)	(6) 110.0 (11.12)	.02
Vocabulary*	(6) 42.0 (8.44)	(21) 40.76 (8.65)	(6) 55.67 (9.03)	.01
Matrix Reasoning	(6) 51.50 (8.31)	(22) 46.64 (9.68)	(6) 56.0 (7.04)	.04
TEA-Ch				
Creature Counting Total	(6) 9.5 (3.62)	(19) 9.11 (3.33)	(6) 10.0 (1.67)	.01
Creature Counting Time	(5) 7.60 (1.52)	(13) 8.54 (3.36)	(5) 6.6 (3.64)	.06
Walk, Don't Walk*	(6) 4.67 (2.88)	(21) 4.33 (1.91)	(6) 7.17 (2.40)	.08
Code Transmission	(6) 7.67 (2.07)	(20) 8.35 (3.69)	(6) 9.17 (3.06)	.00
WISC PSI	(6) 101.33 (14.86)	(21) 93.33 (19.02)	(6) 85.5 (9.27)	.03
Coding	(6) 8.33 (2.07)	(21) 9.14 (4.02)	(6) 8.0 (2.19)	.01
Cancellation*	(6) 12.0 (3.41)	(21) 8.48 (3.71)	(6) 6.83 (2.4)	.04

Table 19. Summary of Results for Cognitive Measures Comparing SES Groups in AIS Group

*Significant difference $p < .05$

	WASI IQ					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*B*
Step 1						
Constant	11.80	9.15		77.67	9.65	
SES	8.42	4.39	.37	8.74	4.70	.37
Step 2						
Constant	80.06	8.94		83.19	8.96	
SES	10.01	4.24	.43*	9.42	4.22	.40*
PSOM Total Score	-2.10	1.58	-.24	-2.0	1.49	-.36
Lesion volume	-8.98E-5	1.58	-.26	-2.0	1.49	-.25
R^2	.30			.37		
F	3.20*			3.92*		
ΔR^2	.17			.24		
ΔF	2.68			3.73*		

Table 20. Hierarchical Multiple Regression Analyses Predicting WASI IQ Score from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	WASI Vocabulary					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
Step 1						
Constant	29.78	6.57		30.07	7.05	
SES	6.95	3.15	.41	6.82	3.44	.39
Step 2						
Constant	32.56	6.57		34.92	6.48	
SES	7.38	3.12	.44*	7.29	3.05	.42*
PSOM Total Score	-2.02	.00	-.34	-1.71	1.08	-.28
Lesion volume	-1.1E-5	1.16	-.05	.00	.00	-.34
R^2	.30			.39		
F	3.10*			4.34*		
ΔR^2	.13			.24		
ΔF	2.01			4.01*		

Table 21. Hierarchical Multiple Regression Analyses Predicting WASI Vocabulary Score from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	WASI Matrix Reasoning					
	With Outliers (n = 25)			Without Outliers (n = 24)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*B*
Step 1						
Constant	33.32	6.92		43.93	7.25	
SES	2.33	3.32	.14	2.56	3.53	.15
Step 2						
Constant	45.07	6.90		47.07	6.98	
SES	3.66	3.27	.22	2.86	3.29	.17
PSOM Total Score	0.99	1.22	-.17	-0.93	1.18	-.16
Lesion volume	-7.18E-5	.00	-.31	.00	.00	-.38
R^2	.18			.23		
F	1.59			2.09		
ΔR^2	.16			.21		
ΔF	2.12			2.83		

Table 22. Hierarchical Multiple Regression Analyses Predicting WASI Matrix Reasoning Score from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	TEA-Ch Creature Counting					
	Accuracy Score (n = 24)			Timing Score (n = 16)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*B*
Step 1						
Constant	8.51	2.31		9.03	2.75	
SES	0.27	1.12	.05	-.56	1.32	-.11
Step 2						
Constant	9.31	2.43		10.09	2.68	
SES	0.22	1.15	.04	-1.17	1.27	-.23
PSOM Total Score	-0.52	0.43	-.28	-0.49	0.47	-.27
Lesion volume	-7.05E-6	.00	.09	3.99E-5	.00	.55
R^2	.07			.25		
F	.51			1.47		
ΔR^2	.07			.24		
ΔF	.73			2.10		

Table 23. Hierarchical Multiple Regression Analyses Predicting TEA-Ch Creature Counting Score from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	TEA-Ch Walk/Don't Walk					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
Step 1						
Constant	2.39	1.60		2.39	1.71	
SES	1.28	0.77	.32	1.29	.83	.31
Step 2						
Constant	2.52	1.71		2.79	1.81	
SES	1.40	0.81	.35	1.35	.86	.33
PSOM Total Score	-0.13	.30	-.10	-.13	.30	-.09
Lesion volume	-6.66E-6	.00	-.12	-2.09E-5	.00	-.17
R^2	.14			.14		
F	1.14			1.11		
ΔR^2	.03			.04		
ΔF	0.39			0.52		

Table 24. Hierarchical Multiple Regression Analyses Predicting TEA-Ch Walk/Don't Walk from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	TEA-Ch Code Transmission					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
Step 1						
Constant	6.82	2.23		6.91	2.32	
SES	0.75	1.07	.14	0.78	1.13	.15
Step 2						
Constant	7.59	2.33		7.46	2.38	
SES	0.79	1.11	.15	0.69	1.12	.13
PSOM Total Score	-0.53	0.41	-.28	-0.57	0.40	-.31
Lesion volume	1.56E-6	.00	.02	3.69E-5	.00	.23
R^2	.10			.13		
F	0.79			1.03		
ΔR^2	.08			.11		
ΔF	0.93			1.31		

Table 25. Hierarchical Multiple Regression Analyses Predicting TEA-Ch Code Transmission subtest scores from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	WISC-IV PSI					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
Step 1						
Constant	109.75	11.67		109.48	12.51	
SES	-8.03	5.60	-.28	-7.77	6.09	-.26
Step 2						
Constant	117.00	10.57		118.88	11.02	
SES	-7.12	5.01	-.25	-7.29	5.19	-.25
PSOM Total Score	-5.20	1.86	-.52*	-4.96	1.83	-.49*
Lesion volume	-1.66E-5	0	-.04	0	0	-.20
R^2	.36			.39		
F	4.18*			4.26*		
ΔR^2	.28			.32		
ΔF	4.91*			5.25*		

Table 26. Hierarchical Multiple Regression Analyses Predicting WISC-IV PSI scores from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	WISC-IV Coding					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
Step 1						
Constant	9.11	2.38		9.03	2.56	
SES	-0.17	1.14	-.03	-0.11	1.25	-.02
Step 2						
Constant	10.72	2.17		10.84	2.31	
SES	-0.08	1.03	-.02	-0.06	1.09	-.01
PSOM Total Score	-1.11	0.38	-.56*	-1.06	0.39	-.53*
Lesion volume	-2.00E-6	0	.04	-1.57E-5	0	-.09
R^2	.30			.31		
F	3.18*			2.99		
ΔR^2	.30			.31		
ΔF	4.75*			4.48*		

Table 27. Hierarchical Multiple Regression Analyses Predicting WISC-IV Coding subtest scores from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

	WISC-IV Cancellation					
	With Outliers (n = 25)			Without Outliers (n = 23)		
Variable	*B*	*SE (B)*	*β*	*B*	*SE (B)*	*β*
Step 1						
Constant	14.18	2.39		14.16	2.57	
SES	-2.62	1.15	-.42	-2.59	1.25	-.40
Step 2						
Constant	15.31	2.35		15.72	2.45	
SES	-2.45	1.11	-.40*	-2.49	1.15	-.39*
PSOM Total Score	-0.82	0.41	-.38	-0.77	0.41	-.35
Lesion volume	-4.17E-6	0	-.05	-3.85E-5	0	-.20
R^2	.33			.36		
F	3.68*			3.71*		
ΔR^2	.16			.19		
ΔF	2.57			3.02		

Table 28. Hierarchical Multiple Regression Analyses Predicting WISC-IV Cancellation subtest scores from SES, Total PSOM Score, and Lesion Volume

*Significant at $p < .05$

Note. B = unstandardized beta; *SE (B)* = Standard error of unstandardized beta; *β* = standardized beta

Appendix B: Figures

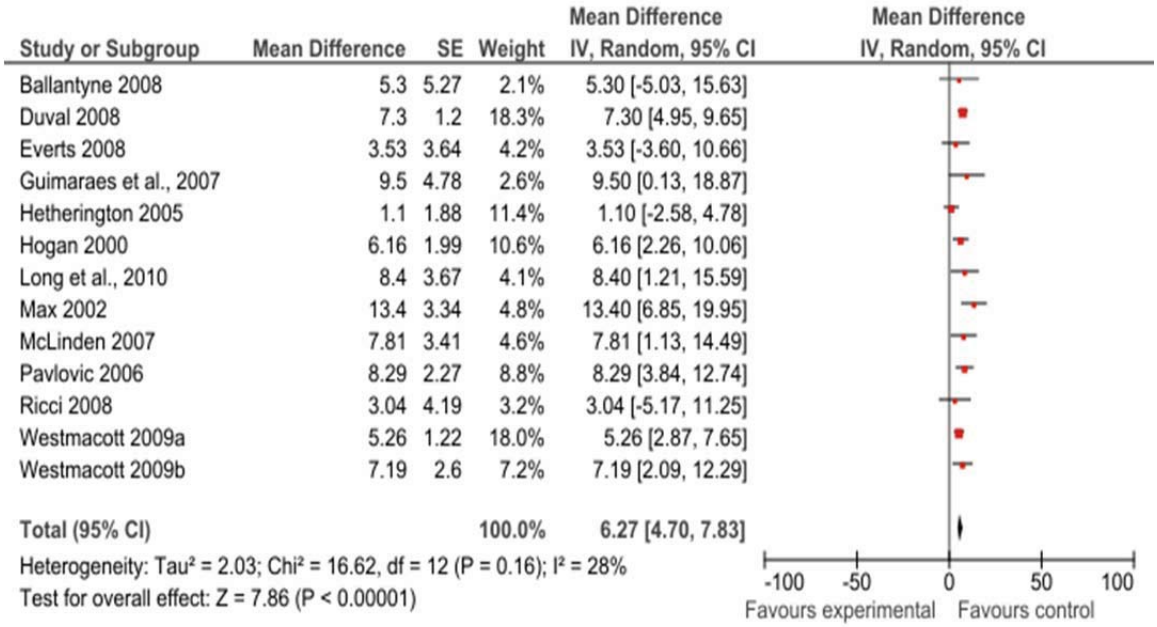


Figure 1. Random Effects Meta-analysis for Studies Examining Cognitive Outcome Following Pediatric Stroke

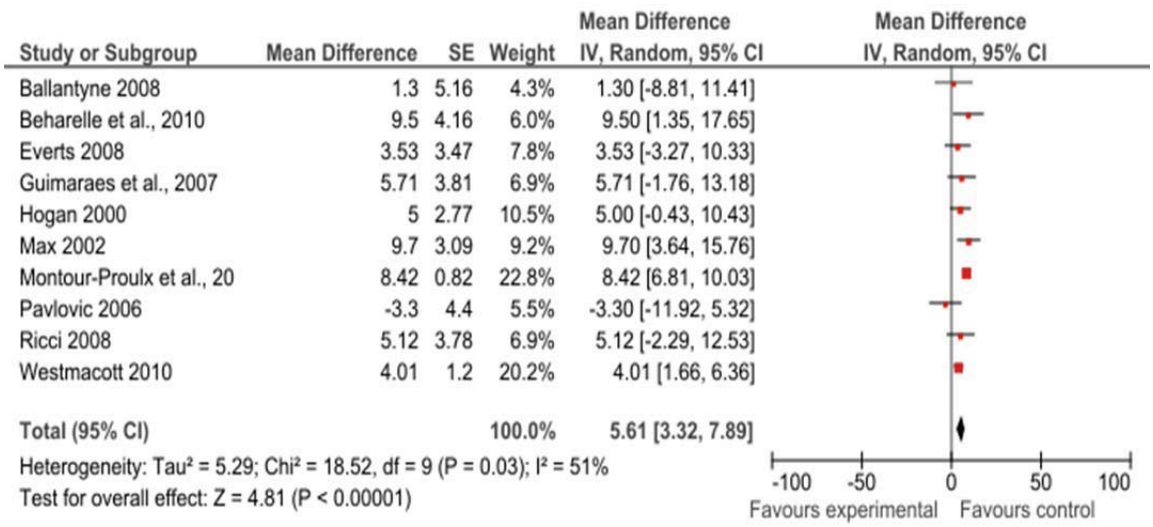


Figure 2. Random Effects Meta-analysis for Studies Examining Verbal IQ Following Pediatric Stroke

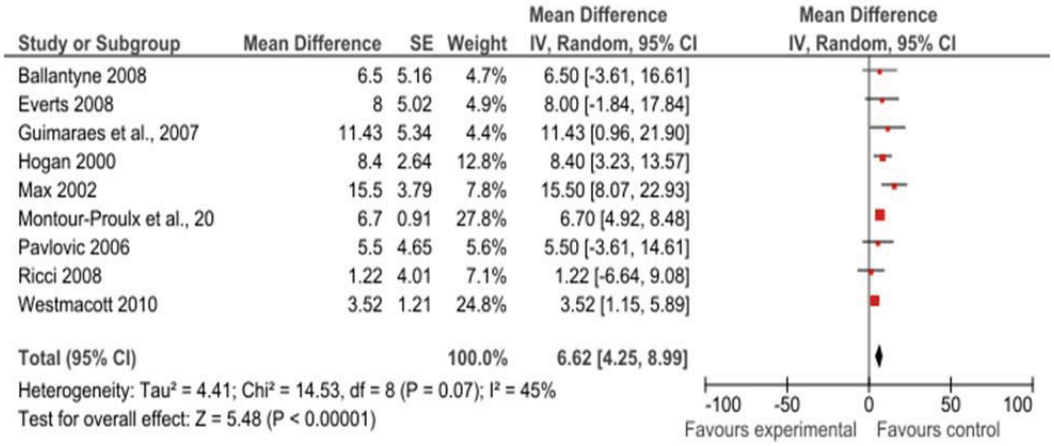


Figure 3. Random Effects Meta-analysis for Studies Examining Performance IQ Following Pediatric Stroke

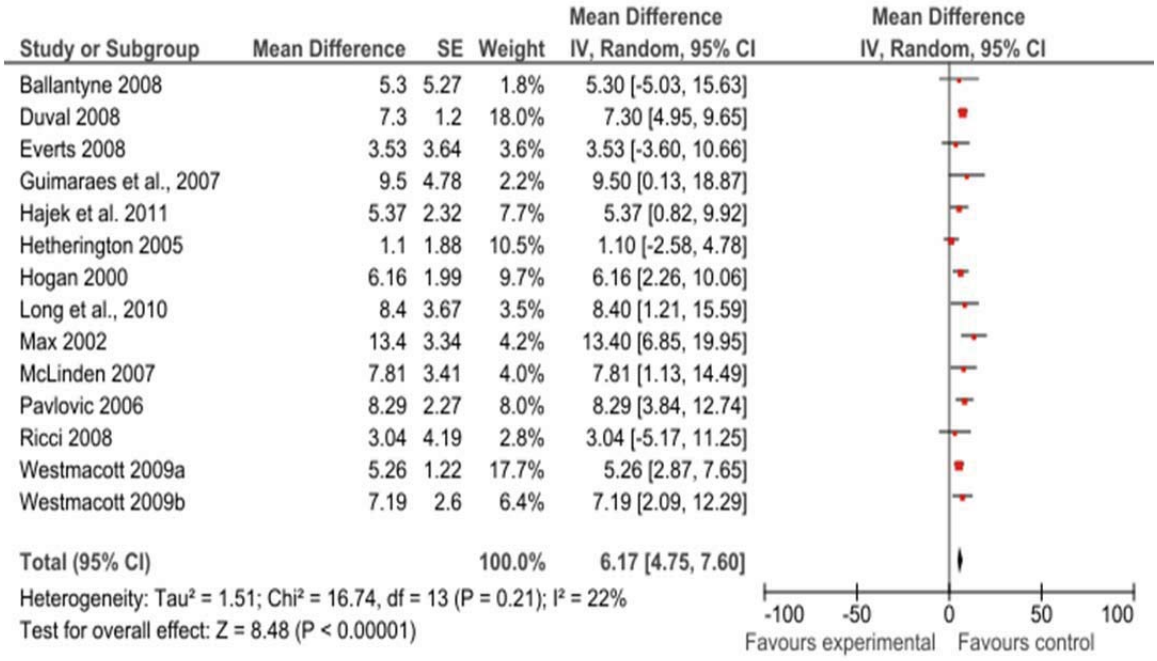


Figure 4. Random Effects Meta-analysis for Studies Examining IQ Following Pediatric Stroke with Current Study Data

Appendix C: Pediatric Stroke Outcome Measure (PSOM)

PAEDIATRIC STROKE OUTCOME MEASURE SHORT NEURO EXAM (PSOM-SNE) - CHILD VERSION (CHILDREN AGED 2 YEARS AND OLDER)

IDENTIFYING DATA

IPSS ID# _____ **Site:** _____ **Date of assessment** (yyyy-mm-dd): _____

Date of 1st Stroke (yyyy-mm-dd): _____ **Date of 2nd stroke** (yyyy-mm-dd): _____ **Date of 3rd stroke** (yyyy-mm-dd): _____

Type of Assessment: ☐ Initial visit ☐ Follow-up **Location of Assessment:** ☐ In-patient ☐ Clinic

INSTRUCTIONS: Check appropriate column for each item: Abnormal; Normal or Not Done (includes not age appropriate item)

LEVEL OF CONSCIOUSNESS

TEST ITEM	Normal	Abnormal	Notes
Level Of Consciousness			

BEHAVIOUR, MENTAL STATUS

TEST ITEMS	Normal	Abnormal	Not Done	Guidelines for Scoring
Activity Level				**Abnormal:** Excessively quiet, shy, removed, hyperactive, fidgety, gets up, uncontrollable, spills, into everything
Interpersonal Interaction				**Abnormal:** Clings to parent, aloof, withdrawn, gaze avoidance, punches
Cooperation				Age-dependent
Attention				**Abnormal:** Short, distractible, flits, ignores, preoccupied, disorganized, inattentive
Affect				**Abnormal:** Extremely shy, pouts or clings excessively or cries a lot for no reason, angry, totally flat, gaze avoidance, hyperactive, no sustained attention
Serial Numbers				Age **24** mos **-36** mos: **Ask:** *"Count as high as you can"* Age **4-8** years: **Ask:** *"Start at 20 count backwards"* Age **9-13** yrs: **Ask:** *"Start at 50 count backwards by 3's"* Age **13** yrs & up: **Ask:** *"Start at 100 count backwards by 7's"*
Drawing				**Ask** patient to draw circle, triangle, and cross, bisect vertical and horizontal lines, and draw clock on attached page
Right/Left Orientation				Test in patients older than 6 years age: "Show me your left hand" and "Show me your right hand"
Memory, Delayed Recall				**Instruct patient:** *"I need you to memorize 3 words and will ask you to repeat them in 5 minutes. The words are* ***"Chair", "Candle", "Dog"*** *"Repeat them now to see if you have them."*

LANGUAGE

TEST ITEMS	Normal	Abnormal	Not Done	Guidelines for Scoring
Speech Development				**Normal:** **0-4 mos**.- Coos **4-12 mos**. - babbles **by 12 mos**. - 1-2 words **12-18 mos**. - single words **2 years**. - 2 word phrase **3 years** - 3 word sentence, 200 words
Repetition				*"Stop"; "Stop and Go"; "If it rains we play inside"; "No ifs ands or buts"* *"The Prime Minister lives in Ottawa"* (or local version!)
Naming				Show patient attached sheet with pictures: skateboard, pencil, shirt, bicycle, and clock. Children ≥6 yrs. ask to identify: pencil, eraser, bicycle seat, buttons
Comprehension				**Simple Tasks**: *a. Close your eyes b. Touch your nose* *c. Point to the floor and then ceiling* **Complex 3 Step Command:** ask child to listen to the complete instruction, remember it, then do all 3 activities together when prompted: **"***Blink twice, stick out your tongue, then touch your finger to your nose*"
Letter Recognition / Reading				Test age 5 yrs. & up Ask patient to identify letters A, B, H
Writing				Ask patient to print first name (age 5-7) first and last name (age 8-9) or write first and last name in cursive

CRANIAL NERVES

TEST ITEMS		Normal	Abnorma	Not Done	Guidelines for Scoring and Notes (Describe Abnormalities)
Visual Fields	Right				Facing patient at 2 – 3 ft encourage to stare at your eyes and tell when they see object come into view from side (or note gaze shifting toward object)
	Left				
Pupillary Light Reflex	Right				Direct and Consensual
	Left				
Fundoscopy	Right				Note Abnormalities:
	Left				
Ocular Motility	Right				Move pen or red object or light smoothly from right to left and back testing full range. Watch for nystagmus or dysconjugate eye movements
	Left				
Optokinetic Nystagmus	Right				Test from 6 mos: move measuring tape slowly from right to left and back through full range encourage to 'watch the numbers as they go by'
	Left				
Facial Sensation	Right				Touch each side with light touch and cold object asking if child can feel or for older, 'is it the same on both sides' comparing forehead, cheek and chin R / L
	Left				
Facial Movements	Right				Ask patient to smile, count to 10 watching mouth symmetry Maximal eye closure strength *"Squeeze eyes shut as tightly as you can"*
	Left				
Hearing	Right				Finger rub for infants or whisper at 2-3 feet away. For older have child repeat letters/numbers
	Left				
Swallow					
Palate and gag	Right				Observe during open mouth crying or Demonstrate with tongue protruded *'Say 'ahhhhh."* Listen to voice quality
	Left				
Trapezius Strength	Right				Test Shoulder Shrug
	Left				
Tongue Movements Side-To-Side	Right				
	Left				

MOTOR EXAM

MOTOR TESTING

	POWER			TONE			INVOLUNTARY MOVEMENTS*		
	Normal	Abnormal	Not Tested	Normal	Abnormal	Not Tested	Normal (None)	Abnormal (Present)	Not Tested
Neck/Trunk Muscles									
Right Arm									
Proximal									
Distal									
Left Arm									
Proximal									
Distal									
Right Leg									
Proximal									
Distal									
Left Leg									
Proximal									
Distal									

***Type of Involuntary Movements Seen**
Check all that are present

TYPE	?Present
Limb Tremor	
Choreoathetosis	
Dystonic Posturing	
Tics	

FINE MOTOR COORDINATION

TEST ITEMS		Normal	Abnormal	Not Done	Guidelines for Scoring
Pincer Grasp	Right				Encourage to pick up small 2–3 mm. ball of rolled up paper
	Left				
Rapid Sequential Finger Movements	Right				**Demonstrate:** thumb touches tip of individual fingers back and forth 5 times *"As fast as you can"*
	Left				
Rapid Index Finger Tap	Right				**Demonstrate:** seated, finger taps table top or own thigh X 20 times, *"As fast as you can"*
	Left				
Finger To Nose Testing	Right				
	Left				
Heel To Shin Testing	Right				
	Left				
Rapid Foot Tap	Right				**Demonstrate:** feet flat on floor, foot taps floor X 20 *"As fast as you can"*
	Left				
Sitting/ Standing Balance					

SENSORY

TEST ITEMS		Normal	Abnormal	Not Done	Guidelines for Scoring
Light Touch	Right				Use cotton swab and **ask:** *" Is it the same on both sides?*
	Left				
Pin Prick Or Cold Sensation	Right				Use cool metal from tuning fork or reflex hammer
	Left				
Proprioception	Right				Great Toe up and down with eyes closed *(* **ask:** *"up or down?")*
	Left				
Graphesthesia/ Stereognosis	Right				Test >6 yrs: Eyes closed, draw number in palm & foot dorsum with closed pen tip
	Left				

TENDON REFLEXES

TEST ITEMS		Normal	Abnormal	Not Done	Guidelines for Scoring
Biceps	Right				
	Left				
Brachioradialis	Right				
	Left				
Triceps	Right				
	Left				
Knee Jerk	Right				
	Left				
Quadriceps	Right				
	Left				
	Left				
Ankle Jerk	Right				
	Left				
Babinski	Right				Upgoing toe is normal up to one year
	Left				
Elicited ankle clonus	Right				
	Left				

GAIT

TEST ITEMS		Normal	Abnormal	Not Done	Guidelines for Scoring
Gait Walking					By ≥ 16 mos.
Gait Running					By 2 yrs age
Gait on Heels					
Gait on Toes					10 steps
Tandem Gait					Heel to toe: test > age 6 yrs; walk on line forward (10 steps)
Jump on 2 Feet					By ≥ 36 mos.
Hop on Foot repetitively	Right				25 x *(age 7 yrs to 9 yrs.)*
	Left				*50 x (age 9 yrs or older)*
Station on one leg sustained	Right				Test age 7 and up. Count seconds out loud and compare stability.
	Left				
Romberg's Sign					*"Eyes closed, feet together, arms stretched forward".*

PARENTAL IMPRESSION QUESTIONS

Has your child recovered completely from the stroke? ☐ Yes ☐ No

Does your child need extra help with day-to-day activities compared with other children of the same age? ☐ Yes ☐ No

RECURRENCE

Date of Recurrence (yyyy-mm-dd): _____ ☐ Unknown ☐ No Recurrence

Recurrence Type: ☐ AIS ☐ CSVT-New ☐ CSVT-Extension ☐ TIA ☐ Silent Infarct

CT or MRI Date (yyyy-mm-dd): _____ ☐ Not Done

CT or MRI Findings (Describe New Abnormalities): _____

SCORING SHEET FOR PSOM-SNE

SUMARY OF IMPRESSIONS

After completing the PSOM-NE or equivalent detailed neurologic examination, summarize and grade your impressions in the following categories:

A. Sensorimotor Deficit (ANY motor or sensory abnormality including Cranial Nerve Deficits, Visual, and Hearing deficits)

	R side	L side
None	0	0
Mild but no impact on function	0.5	0.5
Moderate with some functional limitations	1	1
Severe or Profound with missing function	2	2

Select the Sensorimotor Deficits You Observed (select all that apply)

☐ Global developmental delay ☐ Global hypotonia or hypertonia

☐ Hemiparesis ☐ Hemifacial weakness ☐ Hemiataxia ☐ Dysarthria ☐ Other Motor deficit

☐ Hemisensory deficit ☐ Other Sensory deficit

☐ Difficulty with vision

☐ Difficulty with drinking, chewing or swallowing

☐ Other, describe: _____

B. Language Deficit – Production (exclude dysarthria)

None	0
Mild but no impact on function	0.5
Moderate with some functional limitations	1
Severe or Profound with missing function	2

Describe the Language Production Deficits You Observed Here: _____

_____

C. Language Deficit - Comprehension

None	0
Mild but no impact on function	0.5
Moderate with some functional limitations	1
Severe or Profound with missing function	2

Describe The Language Comprehension You Observed Here: _____

_____

D. Cognitive or Behavioural Deficit (specify which)

None	0
Mild but no impact on function	0.5
Moderate with some functional limitations	1
Severe or Profound with missing function	2

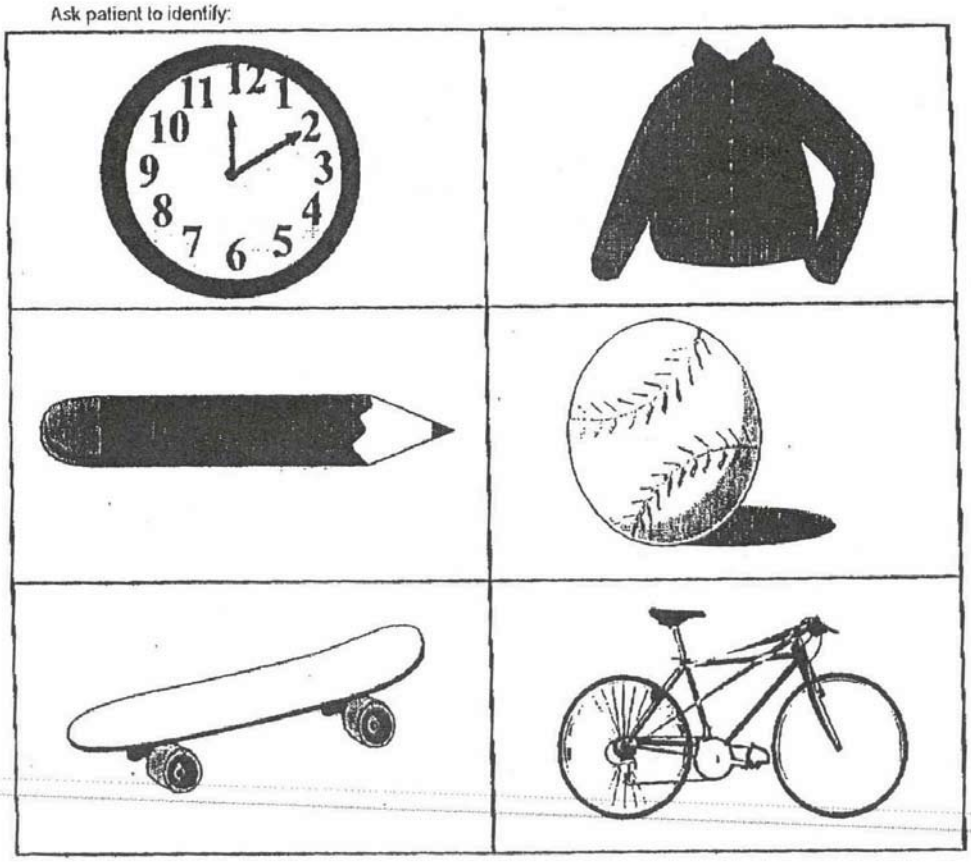
Describe the Cognitive or Behavioural Deficits You Observed Here: _____

_____

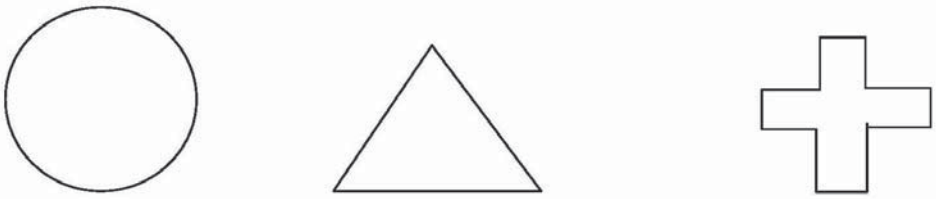
TOTAL SCORING: _____/10

PICTURES TO ASSESS 'NAMING' (see Language on Page 1) (adapted from STOP study: E. S. Roach)

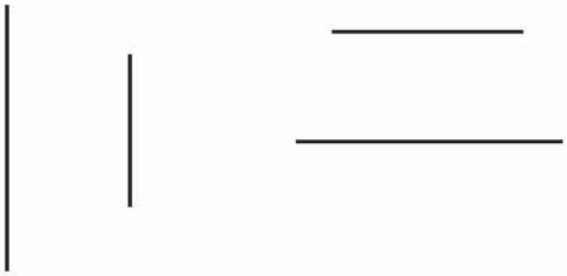
Ask patient to identify:



WORKSHEET FOR DRAWING: DRAWING Copy the Following Shapes



Place an 'X' at the middle of each of the 4 lines below



*Children **> 12 yrs**.: Draw a Clock and put the numbers on it (use back of this page if needed):