Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke

A Dissertation

Submitted to the Faculty

Of

Drexel University

By

Danielle D. Bosenbark

in partial fulfillment of the

requirements for the degree

Of

Doctor of Philosophy

June 2015

Acknowledgments

I am grateful for the support of my dissertation committee: Drs. Maria Schultheis, Jennifer Gallo, Lauren Krivitzky, Lori Billinghurst, and Brian Daly. I especially want to thank Dr. Krivitzky for spending numerous hours mentoring me on this project. I also appreciate all the enthusiastic involvement, collaboration, and support from the team of CHOP researchers and clinicians including Drs. Lori Billinghurst, Rebecca Ichord, Arastoo Vossough, Aashim Bhatia, and Ms. Laura Jastrzab. Thank you also to my lab members for providing helpful constructive criticism and guidance on this project.

Finally, I am grateful for the unwavering love and support of my husband and family. It is because of their encouragement that I have accomplished my personal and academic goals and will continue to do so.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

AED	Anti-Epileptic Drugs
ADHD	Attention Deficit Hyperactivity Disorder
ANOVA	Analysis of Variance
BRIEF	Behavior Rating Inventory of Executive Functioning
CHOP	Children's Hospital of Philadelphia
CT	Computed Tomography
DWI	Diffusion-Weighted Imaging
MRI	Magnetic Resonance Imaging
MR	Magnetic Resonance
NAIS	Neonatal Arterial Ischemic Stroke
PAIS	Perinatal Arterial Ischemic Stroke
PPAIS	Presumed Perinatal Arterial Ischemic Stroke
PSOM	Pediatric Stroke Outcome Measure
SES	Socioeconomic status
TBI	Traumatic Brain Injury
TEA-Ch	The Test of Everyday Attention for Children
TMT-A&B	Trail Making Test A & B
TOL-DX:2	Tower of London-DX: Second Edition
WASI-II	Wechsler Abbreviated Scale Of Intelligence, 2nd Edition
WMTB-C	Working Memory Test Battery for Children
WPPSI-IV	Wechsler Preschool and Primary Scales of Intelligence, 4th Edition

Abstract

Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke

Danielle D. Bosenbark, M.S.

Maria T. Schultheis, Ph.D.

Background: Despite its recognition as the most frequent form of stroke in children and being a major source of long-standing neurological sequelae, there is a dearth of research concerning the psychosocial and neuropsychological profile of perinatal arterial ischemic stroke (PAIS). Prior research has documented a high incidence of Attention Deficit Hyperactivity Disorder (ADHD)—a disorder characterized by prominent impairments in attention and executive functioning skills—among children with a history of PAIS, yet there are no prior studies comprehensively investigating this profile in these children. Moreover, medical and neurophysiological factors may contribute to outcomes in these domains are largely understudied in this population. A elevated understanding of the attention and executive functioning profile in PAIS will not only better inform clinicians of the cognitive outcomes, but may also lead to better interventions to address—or strategies for management of—the subsequent sequelae of PAIS.

Objectives: The present study sought to: 1) investigate and describe the profile of attention and executive functioning in children following perinatal stroke; and 2) examine the influence of clinical and demographic factors on attention and executive functioning outcomes in children following perinatal stroke.

Participants: Forty-one children aged 3-15 diagnosed with perinatal arterial ischemic stroke, recruited from the Children's Hospital of Philadelphia (CHOP) in Philadelphia, Pennsylvania. Patients were identified through the CHOP Pediatric Stroke Program's

ambulatory patient care clinic and IRB-approved Stroke Registry.

Method: Children underwent a single-session neuropsychological assessment focusing on attention and executive functioning domains at CHOP. Additionally, parents/legal guardians completed questionnaires regarding real-world functioning of attention and executive functioning during the visit as well, providing a functional measure of these domains. Demographic (age, sex, race, and family socioeconomic) and medical variables (lesion size, lesion location, presence of epilepsy) were collected for each participant.

Results: Although intellectual performance was in the lower normative range (mean = 94.38; *SD* = 15.90), it was significantly lower than FSIQ in the normative sample. Additionally, measures of attention, verbal fluency, inhibitory control, flexibility/shifting, planning/organizing, and processing speed were significantly lower in children with PAIS than in the normative sample (all $p<0.001$); working memory was not significantly different. The presence of comorbid epilepsy, larger stroke volume, and older age at time of testing significantly influenced performance on several attention and executive functioning measures, whereas sex, stroke location (anatomical), and stroke laterality did not.

Conclusions: Overall, children with PAIS evidenced significant attention and executive functioning impairment in comparison to typically developing peers in the normative population. Children with comorbid epilepsy, larger stroke volume, and/or older age were at increased risk for deficits in these cognitive domains.

1. INTRODUCTION

Stroke affects approximately 2-13 per 100,000 children under age 18 every year in Europe and North America, and ranks among the top 10 causes of death in this age group (Earley et al., 1998; Giroud et al., 1995; Lynch, Kirtz, deVeber, & Nelson, 2002). Moreover, ranking only second to adult age groups in the incidence of stroke, perinatal arterial ischemic stroke (PAIS) is estimated to occur in between 1 in 2800 to 1 in 5000 births (Chabrier, Husson, Dinomais, Landrieu, & Nguyen The Tich, 2011). PAIS is currently the most frequent form of cerebral infarction in children and is a major source of long-standing neurological sequelae. Long-term motor and cognitive deficits which interfere with activities of daily life and academic attainment affect 40-60% of childhood stroke survivors (De Schryver, Kappelle, Jennekens-Schinkel, & Boudewyn Peters, 2000; deVeber, MacGregor, Curtis, & Mayank, 2000; Ganesan et al., 2000; Ganesan, Prengler, McShane, Wade, & Kirkham, 2003). The public health significance of these problems is magnified when considering that children live with the sequelae of stroke for the duration of their childhood and throughout their adult lives.

Despite the magnitude of the public health impact of PAIS, there is a paucity of research concerning clinical outcomes in this population. Very few studies have comprehensively examined and described the psychosocial and neuropsychological profile of the disorder and what factors may contribute to these outcomes. To this point, many studies have included a variety of stroke types or only focused on intellectual functioning as an outcome, and none have incorporated preschool-aged children. Additionally, prior studies investigating prognostic factors for outcomes in PAIS have been few in number and varied in results due to small sample size, varied diagnostic

protocols, and limited follow-up duration. Moreover, there are no proven or widely accepted interventions to address—or strategies for management of—the neuropsychological sequelae of PAIS. Current practices are based on clinician experience and preference and extrapolation from adult clinical trials in stroke. Thus, there are two aims to the present study: Aim 1 seeks to investigate and describe the attention and executive functioning profile in children following perinatal stroke. Aim 2 seeks to examine the influence of clinical and demographic factors on these cognitive domains.

1.1 Perinatal Arterial Ischemic Stroke (PAIS)

Cerebrovascular disorders are among the top 10 causes of mortality in children with the rates highest in first year of life (Lynch et al., 2002). Stroke is estimated to affect 1 in 4000 neonates based on CT scan findings (Estan & Hope, 1997) and is 17 times more common in term newborns less than one month of age than in older infants and children (Wu, Lynch, & Nelson, 2005).

PAIS represents a specific entity in the spectrum of cerebrovascular events. It is defined as a cerebrovascular event that occurs between 28 weeks of gestation and 28 days of postnatal age in term or near-term infants, with pathological or radiological evidence of focal arterial infarction of the brain (Kirton & deVeber, 2006; Lynch et al., 2002). PAIS may be further subdivided according to clinical presentation. Approximately 60% of children who suffer from the disorder present with early symptoms—mostly recurrent focal seizures—in the first 3 days of life. MRI typically reveals an area of acute infarction that can be dated to the 7-10 days preceding the study when diffusion-weighted sequences are obtained. This subgroup is identified as neonatal arterial ischemic stroke (NAIS; Kirton & deVeber, 2013). In the remaining 40%, children do not have specific

symptoms in the neonatal period and are only recognized later with the emergence of motor impairment (e.g., early handedness, decreased hand use, rigidity of the upper limb or fisting), developmental delay, specific cognitive deficiency, or seizures. Neuroimaging of these cases reveals evidence of chronic infarction, which is presumed to have occurred in the perinatal period. Thus, this subgroup is identified as presumed perinatal arterial ischemic stroke (PPAIS; Kirton & deVeber, 2013).

Diagnosis of the disorder is readily confirmed by brain magnetic resonance imaging (MRI) and computed tomography (CT), though MRI is the preferred study for accurate delineation of stroke location, volume and age. Perinatal AIS does not recur when no prothrombotic or cardiac risk factors have been identified. PAIS is a significant antecedent of long-term neurological disability, including cerebral palsy, developmental delay, epilepsy, and cognitive and behavioral problems. Given the functional impact of these deficits, identification of outcome predictors regarding these sequelae (and the way to prevent or alleviate them) is of major interest.

1.2 Cognitive Functioning in PAIS

Children with perinatal arterial stroke are at risk of developing cognitive disturbances (Nelson & Lynch, 2004). Various levels of global cognitive function have been demonstrated in several studies, yet few reports have described the details of affected neuropsychological processes.

1.2.1 General Intellectual Functioning

Cognitive outcome research has yielded contradictory results (Westmacott, MacGregor, Askalan, & deVeber, 2009) with most studies reporting little impairment, but others suggesting that cognitive deficits are common. According to some previous

studies on global outcome measures after perinatal stroke, general intellectual functions are within the average range poststroke despite the significant evidence of motor deficits, seizure disorders, and cortical sensory deficits (Cappa et al., 1990; deVeber et al., 2000; Wulfeck et al., 1991). Specifically, performance on measures of intelligence (IQ) has fallen in the average range (Hetherington, Tuff, Anderson, Miles, & deVeber, 2005; Ricci et al., 2008) and Ballantyne et al. (2008) reported no evidence of decline in cognitive function over time in children with perinatal unilateral brain damage.

In contrast, other studies of global cognitive outcomes after PAIS have found measures of overall intelligence to be statistically lower (i.e., in the low end of the average range) in children who had had a stroke than in the normative sample (Hajek et al., 2013; as reviewed in Hartel et al., 2004; Westmacott et al., 2009). When examining the different domains of intellectual skills, performance-based skills (PIQ/PRI) but not verbal-based skills (VIQ/VCI) tend to be reduced in children with PAIS compared to controls. It has been suggested that this is a result of the injured brain preferentially sparing language functioning, as well as the methods employed to measure verbal-versus performance-based skills. For example, performance-based tasks often have a timed component which can present a challenge for these children, especially for those with poorer motor skills (as reviewed in Hartel et al., 2004; Muter, Taylor, & Vargha-Khadem, 1997; Vargha-Khadem, Isaacs, van der Werf, Robb, & Wilson, 1992). Thus, looking at full scale IQ differences may not be as meaningful in this population.

These controversial findings may be, in part, due to small sample sizes and the age ranges of the cohorts being studied, as it has been suggested that deficits in nonverbal

reasoning, working memory, and processing speed may not emerge until school-age (Chabrier, et al., 2011), and thus may be less detectable for some cohorts.

1.2.2 Attention and Executive Functioning

Studies including detailed neuropsychological evaluations of the perinatal stroke population are few in number. Even fewer in number are studies investigating the attention and executive functioning profile of this population, which is surprising given the fact that Attention Deficit Hyperactivity Disorder (ADHD; a disorder marked by attention and executive functioning deficits) is so prevalent in these children, as discussed in more detail below.

Executive functions (EF) have been defined as distinct, higher-order cognitive functions that work together to enable a person to engage successfully in independent, purposive, self-serving behavior (Anderson, 2008; Gioia, Isquith, Kenworthy, & Barton, 2002; Lezak, 1995). This domain includes supervisory or self-regulatory functions that organize and direct cognitive activity, emotional response, and behavior (Gioia, et al., 2002; Hughes & Graham, 2002). Development of EF skills coincide with the development of frontal brain systems/circuits, which typically become more salient in mid-late childhood and continue to develop into young adulthood (Anderson V., Anderson P., Northam, Jacobs, & Catroppa, 2001). Studies examining deficits in executive function among childhood stroke survivors are few and far between; those that exist often include a mixture of stroke types in the study cohort (e.g., perinatal/neonatal and childhood arterial ischemic stroke) and have used different neuropsychological measures, resulting in inconsistent findings. While one “mixed cohort” study reported a relative sparing of executive function (Kolk, Ennok, Laugesaar, Kaldoja, & Talvik, 2011)

others have reported deficits in this domain, including problems with inhibitory control, working memory, verbal fluency, processing speed, concept learning and mental flexibility (Everts, et al., 2008; Hajek et al., 2013; Lansing et al., 2004; Max et al., 2003; Pavlovic et al., 2006). Similarly, Long and colleagues (2011) specifically assessed executive functioning skills in childhood stroke and detected deficits in both cognitive (attentional control, cognitive flexibility, and information processing) and behavioral/everyday aspects of this domain, providing additional support for the necessity of evaluating this area of neuropsychological functioning in the stroke population.

Additionally, there is evidence to suggest that the prevalence of attention problems is increased after childhood stroke. Among poststroke behavioral disorders, ADHD is the most common in the pediatric population (Max et al., 2002; Max et al., 2003). ADHD is a disorder characterized by age-inappropriate symptoms of inattention, hyperactivity, and impulsivity (American Psychiatric Association [APA], 2013). Research has shown that those diagnosed with the disorder experience deficits in multiple domains of function, the most prominent impairments consistently occurring in speed of complex information processing, attention/executive functions (e.g., tasks of verbal fluency, inhibition, and set shifting), and working memory (Muir-Broaddus, Rosenstein, Medina, & Soderberg, 2002). Of the few PAIS studies currently in the literature, many of them have reported this finding. For example, outcomes of patients in Everts et al.'s (2008) work revealed that symptoms of ADHD occurred more often in children after stroke than in the normal population (50% vs. 3-17%). Max et al. (2002, 2003) also reported that ADHD was the most common disorder in this population (46% of

poststroke participants without prestroke ADHD as compared to 17% of postorthopedic controls). The concept of increased prevalence of ADHD after a pediatric neurological event or injury (e.g., traumatic brain injury, pediatric brain tumor treatments) is not uncommon and is often referred to as secondary ADHD (SADHD; Gerring, Brady & Chen, 1998, 2000; Herskovits, Megalooikonomou, & Davatzikos, 1999; Max et al., 1998a, 2004). Though the presentation of the disorder is acquired from a non-developmental etiology, the symptomology and neuropsychological difficulties experienced are similar in nature. What remains uncertain is whether the changes in phenotype and symptoms (e.g., fewer problems related to hyperactivity) that can occur throughout development in the traditional developmental view of ADHD—occurring as a result of delayed maturation of cortical areas involved in attention and executive functioning—also occur in clinical populations with SADHD, particularly since the etiology is a traumatic insult to their brain rather than a complex interaction of genetics and environmental influences (Alderson & Mullins, 2011). Thus, examining the profile of attention and executive functioning in children throughout development, ranging from preschool through late childhood, is further warranted.

In sum, the attention and executive functioning profile after perinatal stroke is not well known and although prior research has documented a high incidence of ADHD (suggesting that deficits in these cognitive skills are particularly germane to this population), there are no prior studies investigating these neuropsychological domains in PAIS alone. Others have suggested the importance of doing so (Kirton & deVeber, 2013; Westmacott, Askalan, MacGregor, Anderson, & deVeber, 2009), but it has yet to be done. Given the risk of developing problems in these domains, as well as the impact of

these skills on the child's home and school functioning, having a better understanding of what issues children with PAIS are most at risk for will hopefully lead to better management and/or treatment of these problems. Thus, an investigation into these skills is warranted in the PAIS population and will provide a better understanding of the neurocognitive profile and deficits that need to be addressed in treating children with this disorder as well as making recommendations for home and school interventions throughout development.

1.3 Predictors of Cognitive Outcome in PAIS

Multiple studies have attempted to identify specific factors that account for cognitive impairment following perinatal stroke. However, such factors remain poorly understood, as outcomes of children with PAIS vary among studies due to differences in stroke type, duration of follow-up, specific assessments, and population studied. The following variables have been studied to some degree and conflicting findings have been reported.

- Age (Time Since Stroke): In the PAIS population, all children are presumed to have experienced a stroke within the same age range. Therefore, age (at testing) represents the amount of time since the cerebrovascular event, which has been assessed in previous studies but has had mixed results. Ballantyne et al. (2008) reported stable IQ in a group of children with perinatal stroke as they aged. In contrast, Westmacott et al. (2009) found average IQ at preschool ages significantly declined to the low average range in the same children at school age, indicating a slowed rate of cognitive development. Moreover, children made

slower gains over time, gradually diverging from the norm as they aged (school age performance was significantly lower than the normative population).

- Sex: Few studies have investigated the impact of sex in PAIS but those that have reported no effects of sex on general cognitive performance (i.e., intellectual skills measured with either Wechsler or Bayley scales; (McLinden et al., 2007; Muter et al., 1997). No studies currently exist in terms of reporting sex differences in the PAIS population within the domains of attention and executive functioning. That said, impairments in these domains have been shown to be more prominent in males compared to females, with an ADHD male-to-female ratio of 3:1 in population based studies (Barkley, 2006; Gaub & Carlson, 1997) and between 5:1 to 9:1 in clinical samples (APA, 2013; Gaub & Carlson, 1997; Sandberg, 2002).
- Lesion Location (Laterality and Anatomic Location): Lesion location in perinatal stroke has largely been identified in two ways in the literature: (1) laterality (i.e., right hemisphere vs. left hemisphere vs. bilateral); and (2) anatomic location (i.e., cortical vs. subcortical vs. combined). Cortical-only strokes often refer to those that involve cortex and subjacent white matter; subcortical-only strokes are those that involve only the thalamus and/or basal ganglia (caudate, putamen or globus pallidus); combined strokes are those involving cortex, subjacent white matter, along with thalamus, and/or basal ganglia. Somewhat mixed results have been reported regarding these characteristics. With regard to lesion location, adverse cognitive and behavioral outcomes have been found to be associated with MCA infarctions with cortical-only involvement, as compared to subcortical-only involvement (Kirton, Deveber, Pontigon, Macgregor, & Shroff, 2008)—however,

a clear description of specific types of cognitive problems was lacking in this study, as only Pediatric Stroke Outcome Measure (PSOM) scores were reported. In contrast, Westmacott et al. (2010) reported subcortical-only lesions in the perinatal period to be particularly detrimental to future cognitive outcome (as compared to lesions occurring later in childhood). Because brain development typically proceeds with subcortical structures developing earlier than cortical structures (Pfefferbaum et al., 1994), the former is likely to be more vulnerable to damage during the perinatal period. Subsequently, because the development of later-maturing areas (i.e., cortical regions) is dependent upon proper development of early-maturing areas (i.e., subcortical regions; Gogtay et al., 2004; Kolb & Gibb, 2007), damage to subcortical regions may disrupt the development of cortical regions and, consequently, the higher order cognitive skills these brain regions are responsible for. Thus, it is plausible that very early subcortical damage is particularly detrimental to cognitive development because it disrupts later cortical and white matter maturation (Chapman & McKinnon, 2000).

With regard to laterality, there is some evidence that right hemisphere lesions result in poorer outcomes in childhood stroke (Cnossen et al., 2010). In contrast, the majority of the literature to date has concluded that there is no consistent association between cognitive performance and hemisphere of the infarct, particularly in perinatal stroke (Ballantyne et al., 2008; Chapman, Max, Gamino, McGlothlin, & Cliff, 2003; Everts et al., 2008; Goodman & Yude, 1996; Ricci et al., 2008; Studer et al., 2014; Vargha-Khadem et al., 1992; Westmacott et al., 2009; Westmacott et al., 2010). However, the interpretation of these null

laterality findings is complicated not only by the incorporation of heterogeneous populations, but the use of different measurements of cognitive outcome (general IQ versus specific cognitive domains), and cohorts that tend to consist of predominantly left-sided strokes.

Further, when multiple brain areas/structures are involved in the same contiguous stroke, worse outcomes tend to occur. Specifically, bilateral infarctions (Golomb et al., 2009) and lesions involving both cortical and subcortical regions (Hetherington et al., 2005; Westmacott et al., 2010) result in poorer intellectual and cognitive outcomes. However, this is likely to be related to the size of the lesion, as lesions involving multiple regions (e.g., both hemispheres, cortical and subcortical layers) are often larger than other lesion types.

- Lesion Size/Volume: Lesion size/volume has also been examined as a potential predictor in PAIS because larger lesions are typically associated with worse overall outcomes in childhood stroke (Everts et al., 2008; Hetherington, et al., 2005; Long et al., 2011; Westmacott et al., 2010). Studies with children post-PAIS have revealed controversial findings. While some have found no differences in general cognitive performance based on lesion size (Ballantyne et al., 2008; Ricci et al., 2008), others have demonstrated associations between the size of the lesion and cognitive outcome. More specifically, in these studies, larger infarctions (defined by some as “an infarct involving more than two thirds of a major cerebral artery distribution”) tended to be associated with poorer outcomes (Golomb et al., 2009; Hajek et al., 2013; Lee et al., 2005). PAIS is largely

understudied with regard to the impact of lesion size specifically on attention and executive functioning domains, but there is evidence to suggest that these skills are more negatively impacted by larger infarctions in childhood stroke (Long et al., 2001).

- Epilepsy: Unlike adults, children are particularly vulnerable to epilepsy after stroke (Chadehumbe et al., 2008; Fox, Glass, Sidney, Lowenstein, & Fullerton, 2013; Lee et al., 2009; Singh et al. 2012). Various studies have reported prevalence rates of the disorder ranging from 15% to 54% following stroke in the PAIS population (Kirton et al., 2008; Ricci et al., 2008; Wanigasinghe et al., 2010). A growing body of literature supports a relationship between the development of epilepsy and adverse neuropsychological outcomes (Ballantyne et al., 2008; Chabrier et al. 2011; Golomb et al., 2009; Ricci et al., 2008; Wanigasinghe et al., 2010). Early cerebrovascular lesions accompanied by comorbid epilepsy increased not only the incidence but also the degree of deficits in both verbal and non-verbal cognitive functions in neonatal stroke patients, irrespective of the lesion hemisphere (Muter et al., 1997). Although longitudinal studies of children with stroke have shown that FSIQs are near-normal and remain steady with time, subgroup analyses comparing children with and without comorbid epilepsy reveal substantial associations with deficits in intellectual, executive functioning, and behavioral outcomes (Ballantyne et al., 2008; Brinckman & Krivitzky, 2014). Beyond this, detailed epilepsy outcomes—specifically related to neuropsychological outcomes in PAIS—are not comprehensively described (Golomb et al., 2001; Lee et al., 2005).

Because there exists somewhat of an inconsistency in the variables above, it is evident that more research should be dedicated to delineating their role in stroke. Exploring the variables above and the impact they may have on outcomes in PAIS will allow clinicians to better predict how children who have suffered from the disorder will develop skills and function across various domains in comparison to their peers throughout development. This, in turn, will also help to inform future families whom have a child with PAIS, as concerned parents can be better informed about what to expect from their children in terms of cognitive capacities moving forward.

1.4 Present Study

In summary, perinatal stroke has been shown to affect cognitive development, particularly in the domains of attention and executive functioning, as evidenced by the high rates of poststroke ADHD diagnoses. However, few studies have specifically addressed these functional domains, nor have they detailed the profile of attention and executive functioning skills in children with PAIS. Moreover, as discussed above, specific factors which predict perinatal stroke outcome remain poorly understood in this population. Data on clinical outcomes of children with ischemic stroke acquired early in life is of great importance for the clinical management including intervention options, counseling parents, understanding of children's health related needs, and planning home and school services. In order to achieve this goal, the prognostic value of a variety of factors with an assumed impact such as sex, age, extent and location of lesion, and the presence of epilepsy on clinical outcome needs to be investigated. Also lacking in the current literature is studies that include children in the preschool age range who are

developing the above skills, and the impact a perinatal stroke has on cognitive development.

Thus, the present study was designed to fill the above void in knowledge in the literature and sought to investigate attention and executive functioning after perinatal stroke and to determine clinical factors expected to influence outcome. This study was not only the first to thoroughly examine the impact of perinatal stroke on attention and executive functioning in children, but also the impact of various medical and neurophysiological factors on these outcomes. Further, this study incorporated children in the preschool age range (3-5 years old) in order to examine the emergence of these skills at younger ages and how they differ from older children. The proposed study was the first to address this and offers particular utility, as this information may help to identify children at risk for academic difficulties (among others) when they enter school. The following hypotheses were developed based on the knowledge that is currently available in the literature, as reviewed above.

Formal Statement of Proposed Study Aims and Hypotheses

Aim 1: To investigate and describe the attention and executive functioning profile in children following perinatal stroke.

Hypothesis 1: Children with perinatal stroke will demonstrate poorer cognitive functioning in the domains of attention and executive functioning (as indicated by performance and parent-based measures), compared to the normative population.

Aim 2: To examine the influence of clinical and demographic factors on attention and executive functioning skills in children following perinatal stroke.

- **Hypothesis 2a**: Older children will demonstrate greater deficits in attention and metacognitive aspects (i.e., higher order thinking skills which involve active control over the cognitive processes engaged in learning and monitoring of performance) of executive functioning than younger children.
- **Hypothesis 2b:** Males will demonstrate higher overall rates of ADHD symptoms on parent report in terms of raw symptom counts. Prior research has revealed a greater prevalence of ADHD in males compared to females in other clinical pediatric populations (APA, 2013; Gaub & Carlson, 1997; Sandberg, 2002) and as such, it is expected that PAIS will show similar sex differences.

  Hypothesis 2c: Select medical variables (lesion characteristics, presence of epilepsy) will be differentially related to attention and executive functioning skills in children following perinatal stroke.
    - Children who have had a bilateral stroke are expected to demonstrate poorer performance in the domains of attention and executive functioning compared to those with only unilateral lesions. Additionally, we hypothesize no differences in attention and executive functioning skills when comparing left and right hemisphere lesions.
    - Children with larger lesions will demonstrate poorer performance in the domains of attention and executive functioning than children with smaller lesions.
    - Children with subcortical-only lesions (i.e., those involving only the thalamus and/or basal ganglia) will demonstrate poorer performance in the domains of attention and executive functioning than children with cortical-

only lesions (i.e., those involving only cortical and subjacent white matter). Additionally, children who have had a combined stroke (i.e., those involving a combination of cortex, subjacent white matter, thalamus, and/or basal ganglia) are expected to demonstrate poorer outcomes than both cortical-only and subcortical-only lesions.

- Children who have developed epilepsy after perinatal stroke will demonstrate poorer attention and executive functioning performance than those who have not developed epilepsy.

2. METHOD

2.1 Study Overview

A summary of the study design and flow can be seen below.

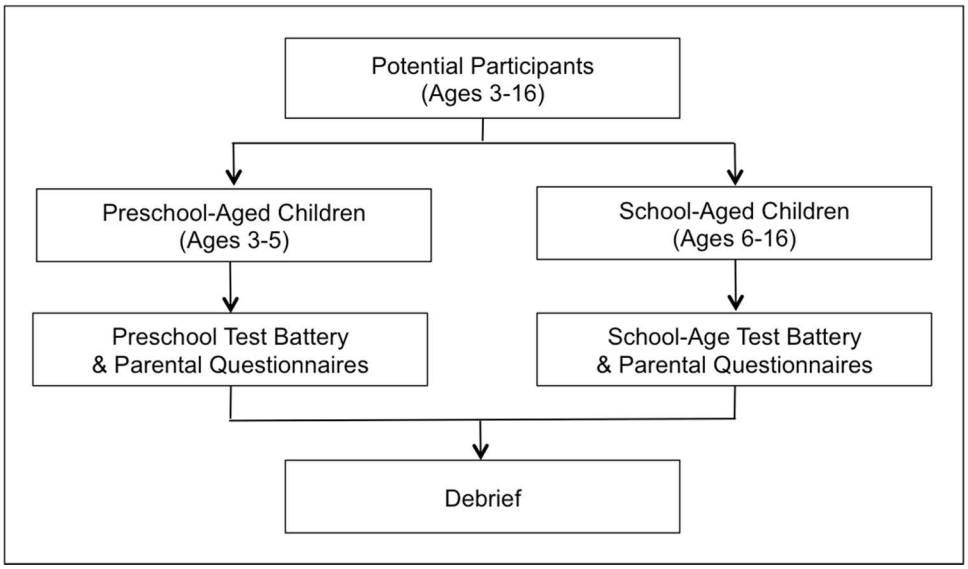

Figure 1. Study Design

2.2 Participants

Forty-one participants aged 3-15 who suffered a perinatal stroke were recruited from the Children's Hospital of Philadelphia (CHOP) in Philadelphia, Pennsylvania. One participant (from the preschool group) had to be excluded due to subsequent identification of an exclusionary medical comorbidity. Patients were identified through the CHOP Pediatric Stroke Program's Stroke Registry. A comprehensive and systematic medical chart review was conducted to identify eligible participants. Data from individuals meeting the following criteria were included in the present study. Specific inclusion criteria include: 1) Documentation by a physician of perinatal arterial ischemic stroke (i.e., a stroke occurring after 28 weeks of pregnancy through birth and the 1st

month of life); 2) Aged 3-16 years; and 3) English as first language. Participants meeting the following criteria were excluded from the present study: 1) Premature birth prior to 37 weeks; and 2) Significant medical comorbidity, other than epilepsy. Examples of comorbidities include: neonatal bleeds (e.g., intraventricular hemorrhages, germinal matrix hemorrhages); neonatal watershed infarcts associated with hypoxia; watershed strokes; hemoglobinopathies; progressive neurometabolic disorders; Down syndrome and other chromosomal abnormalities; malignancy; congenital and acquired CNS infections; significant head trauma; severe and profound mental retardation; syndromic vascular malformations; any severe sensory or motor impairment that prevents valid administration of the measures (e.g., severe cerebral palsy).

2.3 Recruitment Overview

A summary of the recruitment flow can be seen below.

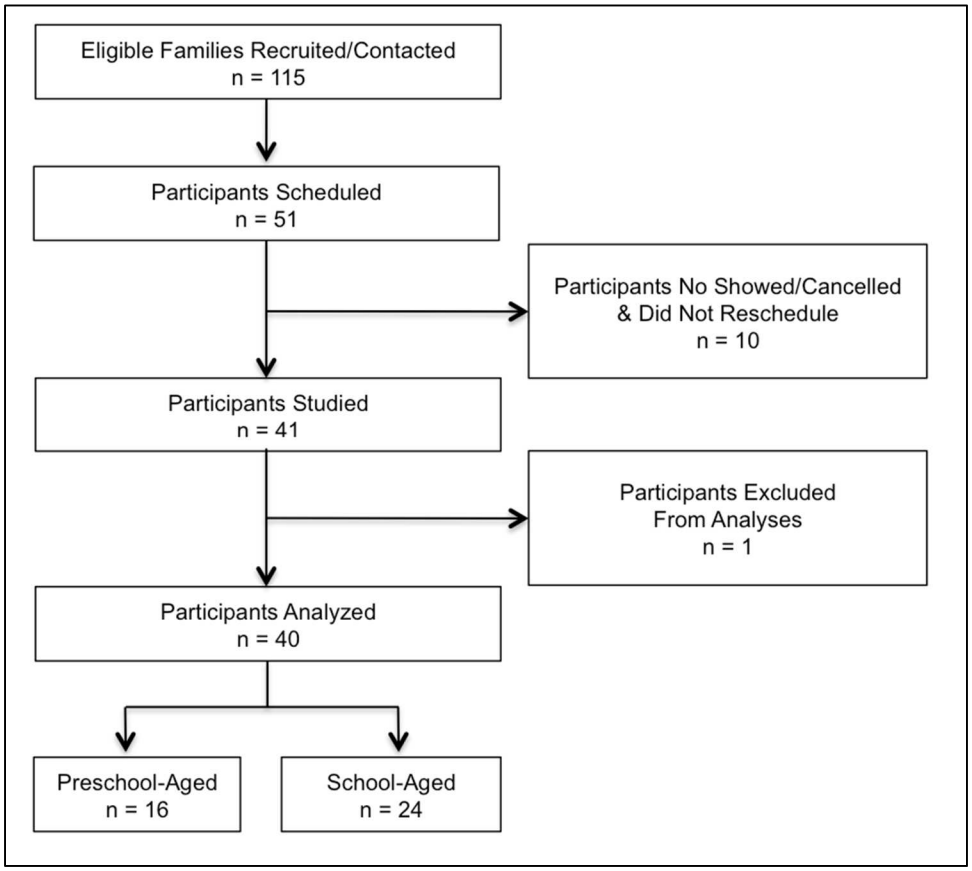

Figure 2. Study Recruitment

2.3.1 Recruitment

Primary recruitment occurred through the CHOP Pediatric Stroke Program's Stroke Registry. This registry includes a cohort of pediatric patients with stroke syndromes, 115 of whom were eligible children diagnosed with PAIS. Participants were also identified through the Pediatric Stroke Clinic. All eligible participants were contacted for recruitment.

2.4 Data Sources and Test Measures

Data for this study was collected from three sources: 1) medical records; 2) parental report; and 3) neuropsychological testing.

2.4.1 Medical Records

Multiple medical variables were collected from participants' medical records in this study. Information regarding the location and volume/size of patients' lesions was obtained and this neuroimaging data was analyzed by a CHOP neuroradiologist and a CHOP neurologist. With respect to lesion location, location was classified by laterality (left hemisphere, right hemisphere, bilateral hemispheres), and structures involved (cortical-only, subcortical-only, combined; definitions provided above). With respect to lesion volume/size, this was estimated using the Modified Pediatric Alberta Stroke Program Early Computed Tomography Score (ModASPECTS), which has been shown to be well-correlated with infarct volume (Beslow et al., 2012). This scoring system utilizes acute MR diffusion-weighted imaging. Designed to provide a quick and reliable semi-quantitative estimation of assessing infarct volume in children (Wusthoff et al., 2011), this method takes approximately 10 minutes per participant and can be completed without image reformatting, as is required in other techniques. Scoring is based on a 30-point scale; each hemisphere is subdivided into 15 regions, yielding a maximum of 15 points per hemisphere. Regions include: seven cortical middle cerebral artery regions, two cortical anterior cerebral artery regions, two cortical posterior cerebral artery regions, and four subcortical regions (caudate, lentiform nuclei, internal capsule, and thalamus). One point is assigned for each region involved in the infarct, even if it is only a small portion, including watershed areas or punctate foci. Of note, this procedure could only be applied

to participants whom presented with PAIS acutely in the neonatal period (i.e., NAIS) *and* had available acute MR imaging that had been obtained during that period. Thus, none of the PPAIS participants had modASPECTS data available for analysis of stroke volume.

Additionally, clinical data concerning the presence or absence of chronic epilepsy as well as antiepileptic medication (i.e., medication type and dosage) was retrieved and recorded from the child's CHOP medical records by a CHOP neurologist and Stroke program research coordinator. Study data were collected and managed using a secure, web-based electronic data capture tool, REDCap (Research Electronic Data Capture) hosted at CHOP (Harris et al., 2009). Epilepsy was defined as (1) one unprovoked seizure at > 30 days of age and one of the following (a) a routine EEG which showed epileptiform abnormalities (b) treatment with anticonvulsant; or (2) ≥ 2 unprovoked seizures occurring ≥ 24 hours apart at > 30 days of age. As previously discussed, these variables may be able to predict attention and executive functioning in children with PAIS. As such, we explored the relationships among these variables as a secondary goal of the current study. Imaging data was viewed on the institutional PACS system, but not obtained for storage once data was recorded.

2.4.2 Parental Report

Demographic information as well as information on parental (or guardian) perception of neuropsychological functioning was collected on the day of testing (while the child was completing the study tasks).

2.4.2.1 Demographic Information

Age, sex, race, family socioeconomic status (SES), and family mental health history was collected for each participant at the time of the study.

2.4.2.2 Questionnaires

Parents/primary caretakers completed the following parental questionnaires.

ADHD Rating Scale-IV

The ADHD Rating Scale-IV (DuPaul, Power, Anastopoulos, & Reid, R., 1998; McGoey, DuPaul, Haley, & Shelton, 2007) is an 18-item parent report questionnaire designed to assess for symptoms of both inattentive and hyperactive-impulsive subtype ADHD. Each item/statement is rated on a 4-point Likert scale using "Never or rarely," "Sometimes," "Often," or "Very often" as responses. Scores are totaled for both subtypes as well as a total score. Total significant symptom count (classified as responses of "often" or "very often") for Inattention (9 possible symptoms) and Hyperactive/Impulsive (9 possible symptoms) behaviors were calculated. Participants are then classified as having no overall significant elevation in symptom report based on age/sex norms (i.e., a score falling in the $<80^{th}$ percentile category based on normed data), subthreshold elevation (i.e., a score falling in the 80^{th} and 90^{th} percentile categories), or a clinical elevation (i.e., a score falling in the 93^{rd} and 98^{th} percentile categories).

Behavior Rating Inventory of Executive Function (BRIEF)

The BRIEF (Gioia, Isquith, Guy, & Kenworthy, 2000a) is a behavior rating scale that measures an individual's executive functioning skills in the context of real world functioning. Many performance measures fail to adequately observe diminished executive function capacity because they do not assess or sufficiently capture real-world behaviors and complex day-to-day executive problem-solving. In contrast, the BRIEF specifically targets those real-world behaviors. The BRIEF has also been shown to have convergent and discriminant validity with other measures of inattention, hyperactivity-

impulsivity, depression, atypicality, anxiety, and somatic complaints (Gioia et al., 2000a). Moreover, the BRIEF measures a child's executive function capacity by considering problems that have existed in specific behaviors within the past 6 months. Parents complete a series of questions by responding "Never," "Sometimes," or "Always" in regards to specific behaviors.

Several versions of the BRIEF are available, including a parent report for school age (for ages 5-18; Gioia, et al., 2000a) and a parent report for preschool age children (for ages 2-5 years; Gioia, Espy, & Isquith, 2003), both of which were used in the current study. The Parent Version assesses eight subdomains of executive function by asking about the prevalence of certain behaviors which are relevant across the age range. The first 3 subdomains make up the Behavioral Regulation Index (BRI) and include Inhibit, Shift, and Emotional Control. The other 5 subdomains compose the Metacognition Index (MCI) and include Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor. Scores from the BRI and MCI indices can also be combined to calculate the Global Executive Composite (GEC).

Similarly, the Preschool Version (also completed by parents) assesses five subdomains of emerging executive functioning: Inhibit, Shift, Emotional Control, Working Memory, and Plan/Organize. Indices derived from this version include the Inhibitory Self-Control Index (ISCI; Inhibit + Emotional Control), the Flexibility Index (FI; Shift + Emotional Control), and the Emergent Metacognition Index (EMI; Working Memory + Plan/Organize). Combined, these indices produce the Global Executive Composite (GEC).

2.4.3 Neuropsychological Test Battery

The neuropsychological measures included are well validated and commonly used in both clinical and neuropsychological assessment settings. Measures appropriate for age were used to assess intellectual ability and the primary study domains of attention and executive functioning. A preschool test battery was used to assess children aged 3-5 years and a school-aged battery was used to assess children aged 6-16 years.

2.4.3.1 Preschool Test Battery

Children aged 3-5 were assessed with the following set of measures.

Intelligence

- *Wechsler Preschool & Primary Scale of Intelligence—Fourth Edition (WPPSI-IV; 20-45 minutes):* The WPPSI-IV (Wechsler, 2012) is a measure of cognitive development for preschoolers and young children. Because there is no abbreviated measure of intelligence (e.g., WASI-II) available for the preschool age range, the full assessment was used.

Attention

- *WPPSI-IV Cancellation Subtest (5 minutes):* The Cancellation subtest of the WPPSI-IV (Wechsler, 2012) is a task in which children must work within a specified time limit to scan two arrangements of objects (one random, one structured) and mark target objects. This was originally proposed to be used to assess attention in the preschool group of children (those aged 4-5); however, see page 33 for further explanation why the test was not used as part of this domain.

Executive Functioning

- *WPPSI-IV Working Memory Subtests:* The Picture Memory and Zoo Locations subtests of the WPPSI-IV (Wechsler, 2012) were used to assess working memory.
    - *Picture Memory (5 minutes)*: This is a visual recognition task involving a child viewing stimulus pictures for 3-5 seconds and then the child selects the stimulus pictures from a larger selection of images.
    - *Zoo Location (5 minutes)*: This is a visual-spatial recall test in which child views locations of animals on cards for 3-5 seconds and then the child must place the proper animal with the correct location.
- *NEPSY-II:* The following NEPSY-II (Korkman, Kirk, & Kemp, 2007) subtests were used to assess various aspects of executive functioning.
    - *Word Generation (5 minutes)*: This subtest is designed to assess verbal productivity through the ability to generate words within specific semantic and initial letter categories. The child is given a semantic or initial letter category and asked to produce as many words as possible in 60 seconds.
    - *Speeded Naming (5-10 minutes):* This timed subtest is designed to assess rapid semantic access to and production of names of colors, shapes, sizes, letters, or numbers. The child is shown an array of colors and shapes; colors, shapes, and sizes; or letters and numbers. He or she names them in order as quickly as possible.
    - *Statue (5 minutes):* This subtest is designed to assess motor persistence and inhibition. The child is asked to stand and maintain a body position

with eyes closed during a 75-second period and to inhibit the impulse to respond to sound distracters.

2.4.3.2 School-Age Test Battery

Children aged 6-16 were assessed with the following set of measures.

Intelligence

- *Wechsler Abbreviated Scale of Intelligence (WASI-II; 15-30 minutes)*: The WASI-II (Wechsler, 2011) is an abbreviated, performance measure of general intellectual functioning to estimate a Full Scale IQ in individuals aged 6-90 years. The two-subtest version consists of Vocabulary and Matrix Reasoning subtests.

Attention

- *Test of Everyday Attention for Children (TEA-Ch):* The TEA-Ch (Manly, Robertson, Anderson, & Nimmo-Smith, 1999) is a normed and standardized battery of "game-like" tests that are designed to assess different types of attention in children aged 6-16. The following subtests were used to measure selective attention, sustained attention, and dual task performance in the school-aged group of children.
    - *Sky Search (SS; 5 minutes):* Participants are given a large printed sheet that is filled with pairs of spaceships, and asked to circle those pairs in which both spaceships are identical. Performance is calculated relative to a control task in which there are no distractors, resulting in a Focused Attention score.
    - *Score! (5 minutes)*: This subtest requires children to count the number of scoring sounds (i.e., beeps) they hear being played on a recording.

- *Sky Search: Dual Task (SSDT; 5 minutes):* This subtest requires participants to identify pairs of "target" spaceships (as in Sky Search, but using a new configuration), while still keeping count of the scoring sounds (as in the Score! subtest).

Executive Functioning

- *Working Memory Test Battery for Children (WMTB-C):* The WMTB-C (Pickering & Gathercole, 2001) is an assessment of working memory in children. The test is designed to reflect the three component structure of the Working Memory Model proposed by Baddeley and Hitch (1974): the Central Executive (CE), which is involved in the control and regulation of the Working Memory System; the Phonological Loop (PL), which is responsible for holding verbal information for short periods; and the Visuo-Spatial Sketchpad (VSSP), which holds information in visual and spatial form. In the current study, three subtests from the battery were used:
  - *Listening Recall (5 minutes)*: A measure of the CE. Children are presented with a series of sentences and for each sentence, they must first provide true/false judgments on the sentence's semantics, and then recall the sentence-final word.
  - *Word List Recall (5 minutes)*: A measure of the PL. Children are asked to temporarily store and then recall words.
  - *Block Recall (5 minutes)*: A measure of the VSSP. Children are seated in front of an array of randomly placed blocks. The examiner taps on the

blocks in a predetermined order and children are asked to then tap the blocks in the same order.

- *NEPSY-II:* Similar to the preschool group, the following NEPSY-II (Korkman, Kirk, & Kemp, 2007) subtests were used to assess various aspects of executive functioning.
    - *Word Generation (5 minutes)*: (See description in preschool section above.)
    - *Speeded Naming (5-10 minutes):* (See description in preschool section above.)
    - *Statue (5 minutes):* (See description in preschool section above.) Only 6 year-olds will complete this subtest, as it is not normed for older children.
    - *Inhibition (5-10 minutes)*: This timed subtest is designed to assess the ability to inhibit automatic responses in favor of novel responses and the ability to switch between response types. The child looks at a series of black and white shapes or arrows pointing up or down, and names either the shape, direction, or an alternate response, depending on the color of the shape or arrow.
- *Tower of London-DX: Second Edition (TOL-DX; 15-20 minutes):* The TOL-DX (Culbertson & Zillmer, 2005) is a measure of executive functioning, particularly planning and problem solving. The TOL-DX utilizes a tower structure with three pegs and three colored beads (red, blue, green), and requires the child to move the beads on his or her tower structure to match bead configurations presented by the

examiner (on the examiner's board) in as few moves as possible. This test was completed by children ages 7-16, as norms do not begin until age 7.

- *Trail Making Test A & B (TMT; 5-10 minutes):* The TMT (Reitan, 1958) measures attention, visual searching, mental processing speed, and the ability to mentally control simultaneous numerical and alphabetical patterns. In Part A, participants are asked to connect a series of circled numbers in numerical order on a worksheet. In Part B, participants are asked to connect an alternating series of numbers and letters to one another (i.e. 1 to A to 2 to B to 3 to C and so on) on a worksheet as quickly as possible. This test was completed by children aged 7-16, as norms do not begin until age 7.

2.4.4 Summary of Study Measures

Table 1 summarizes the intelligence and neuropsychological measures, as well as parental questionnaires administered in this study, categorized by age range.

Table 1. Summary of Proposed Assessment Battery By Age

Domain	Preschool (3-5 Years)	School-Age (6-16 Years)
Intelligence		
	WPPSI-IV	2-Subtest WASI-II
Attention		
		TEA-Ch Subtests
Visual Attention	WPPSI-IV Cancellation (ages 4-5)	• Sky Search (SS)
Auditory Attention	N/A	• Score!
Dual Attention	N/A	• Sky Search DT (SSDT)
Executive Functioning		
Working Memory	WPPSI-IV WMI Subtests	WMTB-C Subtests
	• Picture Memory	• Listening Recall
	• Zoo Locations	• Word List Recall
		• Block Recall
	NEPSY-II Subtests	NEPSY-II Subtests
Verbal Fluency	• Word Generation	• Word Generation
Rapid Naming	• Speeded Naming	• Speeded Naming
Inhibitory Control/Persistence	• Statue	• Inhibition
		• Statue (age 6)
Planning	N/A	Tower of London-DX (age 7+)
Shift/Sustain	N/A	Trail Making Test A & B (age 7+)

2.5 Procedure

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia reviewed and approved this study. Secondary approval was provided by the IRB at Drexel University.

2.5.1 Initial Screening

Participants were identified through the Pediatric Stroke Clinic or upon referral to study investigators by a CHOP neurologist. Eligible patients were then approached by one of the investigators in person or by telephone to inquire if they would be interested in participating in the study; if contacted via phone, contact information for each participant was obtained via the institutional database. Parents/guardians were provided with information about the nature of the study, neuropsychological testing, and Institutional

Review Board–related information regarding informed consent and voluntary participation. In addition to the principal investigators, a Stroke Program research coordinator was trained to obtain verbal consent from parents or guardians. A telephone script was utilized to facilitate this process.

2.5.2 Testing Session

For consenting families, children were assessed at CHOP in a single testing session; short breaks were provided if needed. Neuropsychological testing lasted 40-115 minutes (depending on age) and was completed in a quiet consultation room with an examiner trained to give the measures. The examiner was a trained research assistant and the testing was not billed to the family or insurance company.

Information on the child's real world emotional, behavioral, and cognitive functioning was also collected via parent questionnaire. Parents/guardians completed the questionnaires while their child was testing.

A few weeks after the testing session, the families were provided with a summary letter that briefly reviewed the results of the testing session and could be used to inform school services, if desired; this was mailed to them at a later time, after scoring of the tests has been completed. Children participants were given a $5 Target gift card and a small toy after participation. If needed, parking fees were covered for families during their study visit at CHOP.

2.6 Composite Scores

Composite scores were created for different attention and executive functioning domains. Based on a priori test design and confirmatory expert survey (i.e., agreement of multiple experienced neuropsychologists on which subtests belonged in which functional

domains), subtests and/or test subscores were categorized into seven domains of functioning: Attention, Working Memory, Verbal Retrieval, Inhibitory Control, Flexibility/Shifting, Planning/Organization, and Processing Speed (see Table 2).

Table 2. Subtests Included in Composite Scores

Domain	Preschool (3-5 Years)	School-Age (6-16 Years)
Attention	• -	• TEA-Ch SS (Attention) • TEA-Ch Score! • TEA-Ch SSDT
Working Memory	• WPPSI-IV WMI Index	• WMTB-C subtests
Verbal Retrieval	• NEPSY WG (Semantic) • NEPSY SN (Combined)	• NEPSY WG (Semantic & Letter) • NEPSY SN (Combined) • NEPSY Inhibition - Naming (Combined)
Inhibitory Control	• NEPSY Statue	• NEPSY Inhibition - Inhibition (Combined) • TOL-Dx - Rule Violations • NEPSY Statue (6 year-olds)
Flexibility/Shifting	• -	• NEPSY Inhibition - Switching (Combined) • Trails B-A
Plan/Organize	• -	• TOL-Dx Total Moves
Processing Speed	• NEPSY SN (Completion Time) • WPPSI-IV Cancellation • WPPSI-IV Bug Search	• NEPSY Inhibition - Naming (Completion Time) • NEPSY SN (Completion Time) • TEA-Ch SS (Target Time) • Trails A • TOL-Dx Problem Solving Time

Subsequently, *z* scores for each subtest (of the given domain) for each participant were calculated with reference to the means and standard deviations of the normative population. For tests with multiple process scores (e.g., Tower of London, NEPSY-II subtests), the summary score or the score that was felt to be most representative of the domain being assessed was included. Composite scores were then calculated by averaging the *z* scores of all subtests within that domain. These scores were then used in statistical comparisons.

Composite scores for Flexibility/Shifting and Planning/Organization could not be calculated for children whom were given the preschool battery, as these areas could not be assessed in these children, due to the lack of age appropriate measures. A composite score for Attention was also not calculated for the preschool participants, as expert survey clearly indicated that the subtest initially chosen as an attention subtest (WPPSI-IV Cancellation) better fit in in the processing speed domain.

2.7 Statistical Analyses

Analyses were performed using the Statistical Package for Social Sciences software for Mac, version 22 (SPSS, Chicago, IL). Subsequent to checking data for normal distribution and homogeneity of variance, we conducted 1-sample t-tests with corrections made for multiple comparison based on false discovery rates to compare cognitive outcome with that of the normative sample (i.e., based on published normative results). Additional, unplanned exploratory analyses were conducted to further examine executive functioning deficits in children with different levels of parent-reported attention symptoms using univariate ANOVAs with least significant difference (LSD) post-hoc corrections and independent samples t-tests (corrected for multiple comparisons). Further, the relationship between performance and parent-based measures of attention and executive functioning skills were explored via univariate ANOVAs with least significant difference (LSD) post-hoc corrections, independent samples t-tests (corrected for multiple comparisons), and Pearson correlational analyses (corrected for multiple comparisons).

Lastly, two-tailed independent sample t-tests (corrected for multiple comparisons) and Fisher's exact test were used to assess differences in attention and executive

functioning outcomes due to sex (male vs. female), lesion laterality (left vs. right), lesion cortical layer (cortical vs. cortical plus subcortical), and epilepsy (present vs. not present). For the sex analysis to test our hypothesis, we chose to look at raw symptom count on the ADHD-IV Rating Scale and not standardized parent report scores, as the standardized scores use sex specific norms to account for sex differences. Because we did not have a specific hypothesis about performance on the BRIEF or behavioral tasks, we performed an exploratory analysis to look at the role of sex on these measures. Pearson correlation analyses (corrected for multiple comparisons) and univariate analyses of variance (ANOVA) with least significant difference (LSD) post-hoc corrections were used to examine effects of age and lesion size (total modASPECTS score) on attention and executive functioning outcomes. Significance was set at $p<0.05$ for all analyses.

3. RESULTS

3.1 Sample Characteristics

3.1.1 Demographic Characteristics

At time of examination mean age of the 40 participants (23 males) was 85.7 months (*SD* 37.2 months, range 36-188 months). Compared to the U.S. Population (U.S. Census Bureau, 2012), the makeup of the study cohort was skewed slightly toward the Caucasian race and higher education levels. However, in terms of race, this is largely representative of the broader CHOP PAIS registry that the cohort was derived from, which is comprised of a total of 121 children with perinatal stroke: 82 Caucasian (67.8%); 18 African American (14.9%); 5 Latino (4.1%); 2 Other (1.7%); and 9 Unknown (7.4%). Education/SES specific to the PAIS population was not collected for the CHOP registry, nor for other large, population-based studies (e.g., Armstrong-Wells, Johnston, Wu, Sidney, & Fullerton, 2009; deVeber et al., 2000; Lee et al., 2005; Kirton & deVeber, 2013). Our sex distribution also was representative of the CHOP population, which is comprised of 66 males (54.5%). Additional demographic characteristics of the study sample are summarized in Table 3.

Table 3. Participant Characteristics

Sex, n (%) male	23	(57.5)
Age at Testing in months, m, mean (SD)	85.7	(37.2)
Race, n (%)		
American Indian or Alaska Native	0	(0.0)
Asian	1	(2.5)
Black or African American	3	(7.5)
Hispanic or Latino	2	(5.0)
Native Hawaiian or Other Pacific Islander	0	(0.0)
White	30	(75.0)
Multiracial	4	(10.0)
Mother Education, n (%)		
High School	13	(32.5)
College/Job Training	19	(47.5)
Graduate School	8	(20.0)
Family History, n (%)		
ADHD	3	(7.5)
Mood and/or Anxiety Disorders	21	(52.5)
Learning Disorders	4	(10.0)

3.1.2 Lesion and Clinical Characteristics

Medical characteristics of the study sample are summarized in Table 4.

Table 4. Lesion and Clinical Characteristics

LESION CHARACTERISTICS		
Laterality, n (%)		
Left	32	(80.0)
Right	7	(17.5)
Bilateral	1	(2.5)
ModASPECTS Score, mean (SD)*		
Total	6.0	(3.0)
Cortical	3.8	(2.2)
Cortical Involvement, n (%)		
Cortical Only	11	(27.5)
Subcortical Only	3	(7.5)
Cortical & Subcortical	26	(65)
CLINICAL CHARACTERISTICS		
Stroke Presentation, n (%)		
NAIS	28	(70)
PPAIS	12	(30)
Epilepsy Diagnosis, n (%)	10	(25.0)

*Only calculated for acute NAIS participants.

3.2 Sample Cognitive Outcome Compared to the Normative Population

A summary of all neuropsychological findings is presented in Table 5. Details regarding global results are further described below.

Table 5. Neuropsychological Assessment Subtest Results

Measure	Variable	Test Mean	N	Min	Max	Sample Mean	Sample SD	t	df	p	Mean Diff	d
Wechsler Scales	FSIQ	100	40	40	125	94.38	15.90	-2.24	39	0.031*	-5.63	0.35
	WPPSI-IV Receptive Vocab	10	6	9	16	12.00	2.97	1.65	5	0.160	2.00	0.67
	WPPSI-IV Object Assembly	10	6	6	13	8.83	2.48	-1.15	5	0.302	-1.17	0.47
	WPPSI-IV Information	10	16	1	15	9.81	3.37	-0.22	15	0.827	-0.19	0.06
	WPPSI-IV Block Design	10	16	1	14	7.63	3.20	-2.97	15	0.010*	-2.38	0.74
	WPPSI-IV Picture Memory	10	16	1	16	9.56	3.88	-0.45	15	0.659	-0.44	0.11
	WPPSI-IV Similarities	10	10	1	19	10.60	4.90	0.39	9	0.708	0.60	0.12
	WPPSI-IV Matrix Reasoning	10	10	1	16	8.10	4.56	-1.32	9	0.220	-1.90	0.42
	WPPSI-IV Bug Search	10	10	1	15	10.10	4.48	0.07	9	0.945	0.10	0.02
	WPPSI-IV Cancellation	10	9	3	15	10.22	3.70	0.18	8	0.862	0.22	0.06
	WPPSI-IV Zoo Locations	10	15	8	17	11.73	2.71	2.48	14	0.027*	1.73	0.64
	WPPSI-IV WMI Composite	100	15	84	137	105.80	13.26	1.69	14	0.112	5.80	0.44
	WASI-II Matrix Reasoning	50	24	30	65	43.17	8.88	-3.77	23	0.001**	-6.83	0.77
	WASI-II Vocabulary	50	24	38	64	49.38	7.67	-0.40	23	0.693	-0.63	0.08
TEA-Ch	SS Correct Targets	10	24	3	14	9.13	3.64	-1.18	23	0.251	-0.88	0.24
	SS Target Time	10	24	1	11	5.17	3.14	-7.53	23	0.000**	-4.83	1.54
	SS Attention Score	10	24	1	10	4.96	2.96	-8.36	23	0.000**	-5.04	1.71
	Score!	10	24	1	15	7.25	3.95	-3.41	23	0.002**	-2.75	0.70
	SSDT	10	24	1	18	5.29	5.15	-4.48	23	0.000**	-4.71	0.92
WMTB-C	Word List Recall	100	24	65	135	97.17	16.91	-0.82	23	0.420	-2.83	0.17
	Block Recall	100	24	55	113	82.42	16.85	-5.11	23	0.000**	-17.58	1.04
	Listening Recall	100	24	60	118	88.42	17.13	-3.31	23	0.003**	-11.58	0.68
NEPSY-II	Speeded Naming Completion Time	10	39	1	14	8.59	3.08	-2.86	38	0.006**	-1.41	0.46
	Speeded Naming Combined Score	10	39	4	16	9.31	2.76	-1.56	38	0.126	-0.69	0.25
	Word Generation Semantic Fluency	10	38	1	18	9.63	3.44	-0.66	37	0.513	-0.37	0.11
	Word Generation Initial Letter Fluency	10	20	4	12	7.40	2.21	-5.26	19	0.000**	-2.60	1.18
	Inhibition Naming Completion Time	10	24	1	14	7.08	3.19	-4.48	23	0.000**	-2.92	0.91
	Inhibition Naming Combined Score	10	24	1	15	7.54	3.82	-3.15	23	0.004**	-2.46	0.64

	Inhibition Inhibition Completion Time	10	24	1	13	6.75	3.14	-5.07	23	0.000**	-3.25	1.04
	Inhibition Inhibition Combined Score	10	24	1	12	6.50	3.72	-4.61	23	0.000**	-3.50	0.94
	Inhibition Switching Completion Time	10	20	1	13	6.50	3.12	-5.02	19	0.000**	-3.50	1.12
	Inhibition Switching Combined Score	10	20	2	12	6.70	2.68	-5.51	19	0.000**	-3.30	1.23
	Inhibition Total Errors	10	24	1	14	6.67	3.76	-4.34	23	0.000**	-3.33	0.89
	Statue	10	19	1	14	6.32	3.68	-4.36	18	0.000**	-3.68	1.00
TOL-Dx	Move Score	100	20	60	114	75.50	16.98	-6.45	19	0.000**	-24.50	1.44
	Total Correct	100	20	60	108	87.00	13.26	-4.38	19	0.000**	-13.00	0.98
	Rule Violations	100	20	60	108	71.60	20.17	-6.30	19	0.000**	-28.40	1.41
	Time Violations	100	20	60	108	78.20	18.57	-5.25	19	0.000**	-21.80	1.17
	Initiation Time	100	20	60	199	95.45	26.11	-0.78	19	0.445	-4.55	0.17
	Execution Time	100	20	60	114	80.80	19.22	-4.47	19	0.000**	-19.20	1.00
	Problem Solving Time	100	20	60	116	81.15	18.37	-4.59	19	0.000**	-18.85	1.03
TMT	TMT-A	50	20	10	46	20.85	13.16	-9.91	19	0.000**	-29.15	2.22
	TMT-B	50	20	10	49	19.15	14.97	-9.21	19	0.000**	-30.85	2.06
	TMT B-A	0	20	-3.1	2.7	-0.17	1.46	-0.52	19	0.609	-0.17	0.12
BRIEF	Inhibit	50	40	34	80	51.35	11.27	0.76	39	0.453	1.35	0.12
	Shift	50	40	37	84	52.55	11.11	1.45	39	0.155	2.55	0.23
	Emotional Control	50	40	35	83	51.48	11.54	0.81	39	0.424	1.48	0.13
	Initiation	50	24	39	86	54.46	12.62	1.73	23	0.097	4.46	0.35
	Working Memory	50	40	38	77	56.50	12.68	3.24	39	0.002**	6.50	0.51
	Plan/Organize	50	40	32	83	53.37	12.70	1.68	39	0.101	3.38	0.27
	Organization of Materials	50	24	35	72	49.79	12.30	-0.08	23	0.935	-0.21	0.02
	Monitor	50	24	32	76	55.33	9.59	2.72	23	0.012*	5.33	0.56
	Self-Control	50	16	33	82	51.19	12.50	0.38	15	0.709	1.19	0.10
	Flexibility	50	16	36	75	51.56	11.15	0.56	15	0.583	1.56	0.14
	Behavioral Regulation	50	24	33	85	52.33	11.56	0.99	23	0.333	2.33	0.20
	Metacognition	50	40	36	78	54.08	12.26	2.10	39	0.042*	4.08	0.33
	Global Executive Composite	50	40	30	81	53.33	12.79	1.65	39	0.108	3.33	0.26

* = $p<0.05$; ** = $p<0.01$; Red = statistically significant result; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

3.2.1Intellectual Outcome

Twenty-four of the 40 children were assessed using the WASI-II 2-subtest and 16 using the WPPSI-IV; one child completed the Wechsler measures but did not complete the remaining attention and executive functioning measures (below) due to extreme difficulty with and resistance to testing. Full-scale IQ estimates were derived from both measures and revealed overall functioning in the average range (mean = 94.38; *SD* = 15.90); range 40-125). Although scores were in the low end of the average range, results of independent t-tests found that this was significantly lower than FSIQ in normative sample [$t(39) = -2.24$, $p = 0.031$, $d = 0.35$] (Table 5).

3.2.2 Attention and Executive Functioning Outcomes

3.2.2.1 Performance-Based Outcomes

Figure 3 presents the group neuropsychological performance (i.e., paper/pencil) test data on the IQ measures and 7 attention/executive functioning composite domains.

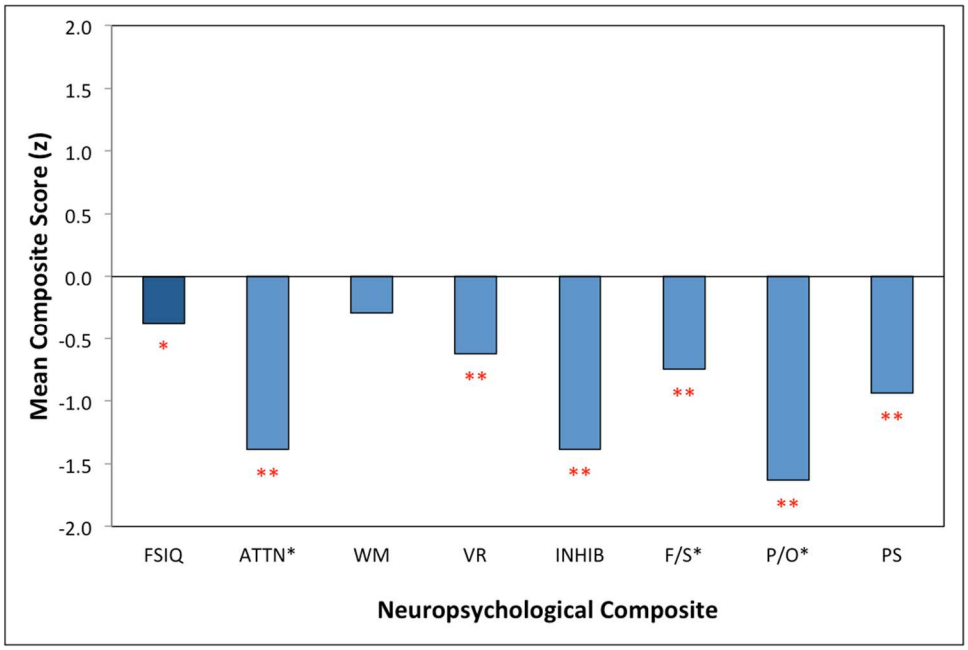

Figure 3. Attention and Executive Functioning Composite Results

Bar graphs showing the mean composite score for each neuropsychological domain tested. FSIQ = Full-Scale IQ (*n*=40); ATTN = Attention (*n*=24); WM = Working Memory (*n*=39); VR = Verbal Retrieval (*n*=40); INHIB = Inhibitory Control (*n*=39); F/S = Flexibility/Shifting (*n*=21); P/O = Plan/Organize (*n*=20); PS = Processing Speed (*n*=20). Attention, Flexibility/Shifting, and Plan/Organize domains are comprised of only the school-aged participants, as these domains were not calculable for preschool participants. Note: ** = $p<0.01$; Red = statistically significant result.

Children with PAIS performed significantly worse than the normal population in nearly all of the domain areas including the following composites: Attention, Verbal Retrieval, Inhibitory Control, Flexibility/Shifting, Plan/Organize, and Processing Speed (summarized in Table 6). Cohen's d values revealed large effect sizes for the Attention, Inhibitory Control, Flexibility/Shifting, Plan/Organize, and Processing Speed Composites, and medium effect size for the Verbal Retrieval Composite. In the group as a whole, Working Memory was the only domain not negatively impacted by PAIS. Six of the seven composite scores were correlated with FSIQ scores (Attention: $r = 0.50$, $p = 0.014$; Working Memory: $r = 0.71$, $p = 0.000$; Verbal Retrieval: $r = 0.70$, $p = 0.000$; Inhibitory Control: $r = 0.61$, $p = 0.000$; Flexibility/Shifting: $r = 0.30$, $p = 0.181$; Plan/Organize: $r = 0.71$, $p = 0.000$; Processing Speed: $r = 0.75$, $p = 0.000$).

Table 6. Neuropsychological Composite Results

Domain/Composite	Composite Mean	N	Min	Max	Mean	SD	t	df	p	Mean Diff	d
IQ	0	40	-4.00	1.67	-0.38	1.06	-2.24	39	0.031*	-0.38	-0.35
Attention+	0	24	-3.00	0.22	-1.39	0.97	-7.02	23	0.000**	-1.39	-1.43
Working Memory	0	39	-2.02	2.47	-0.29	1.02	-1.77	38	0.084	-0.29	-0.28
Verbal Retrieval	0	40	-3.33	1.44	-0.62	0.91	-4.34	39	0.000**	-0.62	-0.69
Inhibitory Control	0	39	-3.00	1.00	-1.38	1.12	-7.70	38	0.000**	-1.38	-1.23
Flexibility/Shifting+	0	21	-3.00	1.02	-0.75	0.95	-3.61	20	0.002**	-0.75	-0.79
Plan/Organize+	0	20	-2.67	0.93	-1.63	1.13	-6.45	19	0.000**	-1.63	-1.44
Processing Speed	0	40	-3.00	1.44	-0.94	1.16	-5.10	39	0.000**	-0.94	-0.81

+Comprised of only the school-aged participants; not calculable for preschool participants.
* = p<0.05; ** = p<0.01; Red = statistically significant result.

3.2.2.2 Parent Report-Based Outcomes

ADHD-IV Home

Although the ADHD-IV allows for a normative comparison to classify participants into severity percentiles, there are no quantitative normative scores that allow for a statistical comparison between clinical samples to a normative population. However, this measure provided important information regarding the distribution of both the inattention and hyperactive/impulsive symptoms within the study sample. On the Attention Scale, 42.5% of the study sample was identified as having no elevation; 30% with a subclinical elevation; and 27.5% with a clinical elevation. On the Hyperactivity Scale, 70% of the study sample was identified as having no elevation; 27.5% with a subclinical elevation; and 2.5% with a clinical elevation. Figure 4 summarizes the distribution of these 3 classifications for the symptoms on both scales.

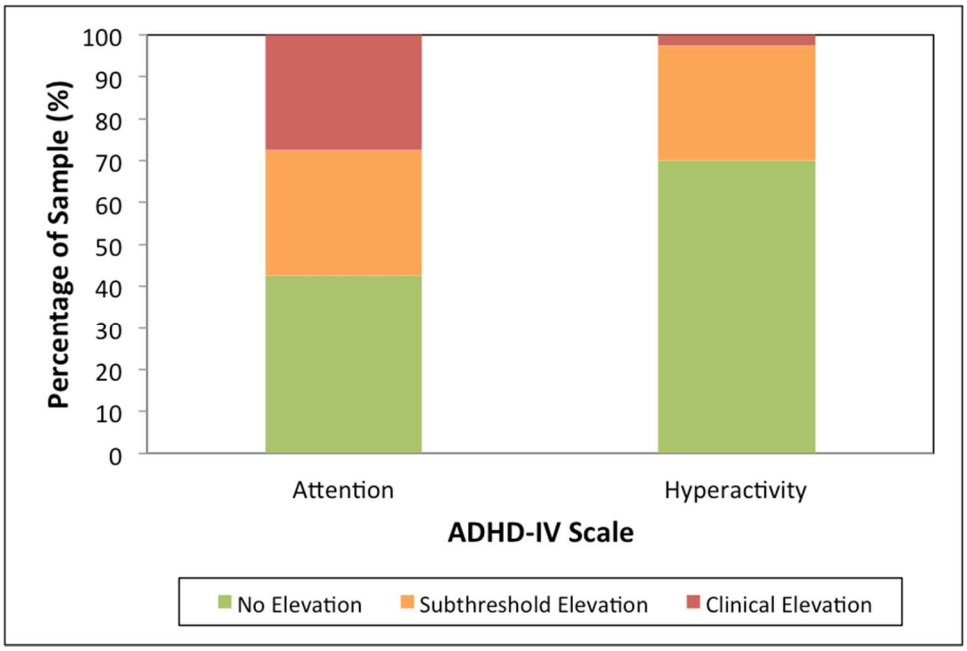

Figure 4. PAIS ADHD-IV Home Profile

Percentage of children with no elevation, subthreshold elevation, and clinical elevation in each scale of the ADHD-IV Scales (Attention *n*=40, Hyperactivity *n*=40).

BRIEF

In our PAIS sample, no significant differences were found for everyday executive function compared with same-aged peers, as rated by parents: Self-Control: t(15) = 0.38, $p = 0.709$, $d = 0.10$; Flexibility: t(15) = 0.56, $p = 0.583$, $d = 0.14$; Behavioral Regulation: t(23) = 0.99, $p = 0.333$, $d = 0.20$; Global Executive Composite: t(39) = 1.65, $p = 0.108$, $d = 0.26$. However, there was a trend toward higher T-scores (more impaired functioning) in the area of Metacognition: t(39) = 2.10, $p = 0.042$, $d = 0.33$; statistical significance was lost when correcting for multiple comparisons. Figure 5 presents group mean T-scores for each index.

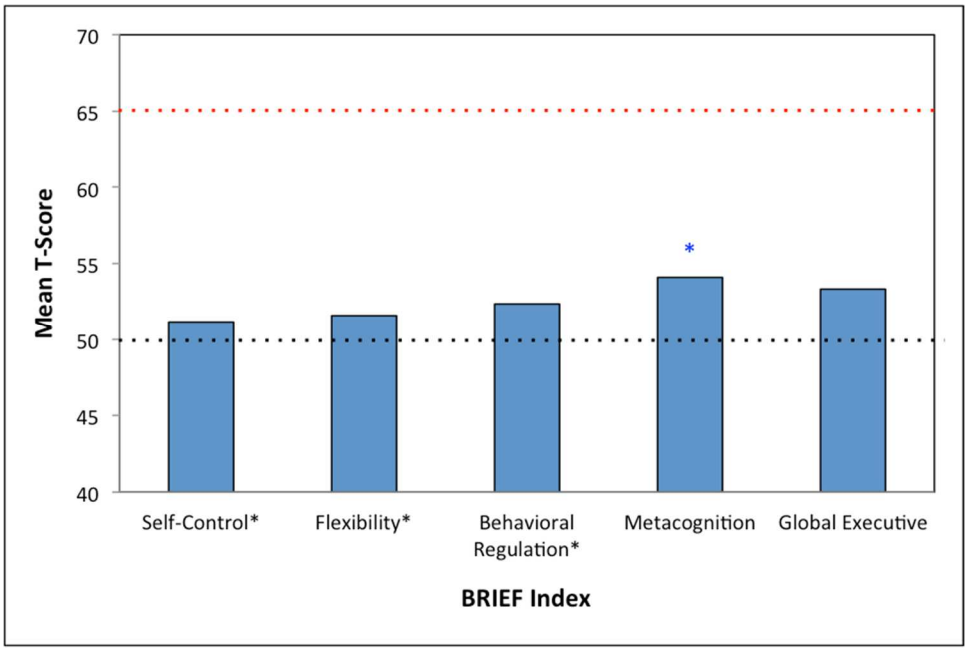

Figure 5. PAIS BRIEF Profile

Mean T-scores for BRIEF indices. Self-Control (*n*=16) and Flexibility (*n*=16) indices are only averaged for preschool-aged children (from BRIEF-Preschool measure only) and the Behavioral Regulation Index (*n*=24) is only averaged for school-aged children (from BRIEF-Parent measure only). Both the Metacognition and Global Executive Indices *n*=40. The black dotted line indicates the mean score of the BRIEF (T=50). The red dotted line indicates the threshold for classifying clinical elevations; higher scores indicate more severe deficits.

Combined ADHD-IV and BRIEF Results

A one-way ANOVA comparing scores on both parent report measures indicated statistically significant differences between ADHD-IV Attention severity groups (i.e., no-, subthreshold-, and clinical elevation) on all BRIEF Index T-scores (Figure 6, Table 7). Post-hoc results largely showed that children in the no elevation group on the Attention scale were significantly less impaired than both the subthreshold elevation and clinical elevation groups. Additionally, with the exception of the Metacognition index, there were no significant post-hoc differences found between the subthreshold elevation and clinical elevation groups (summarized in Table 8).

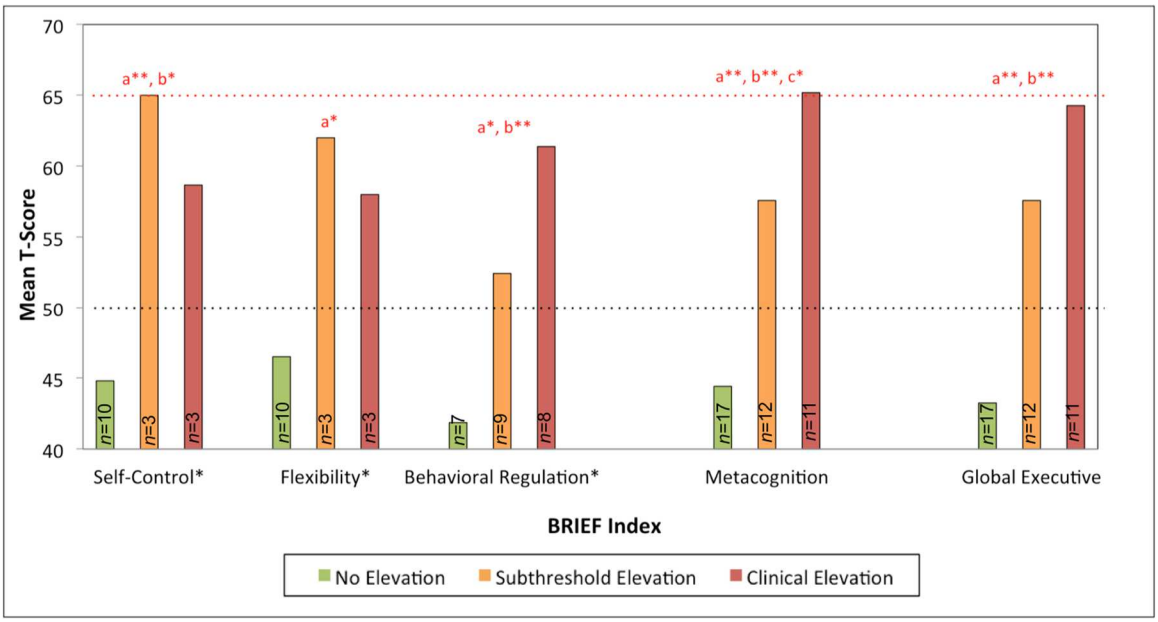

Figure 6. Comparison of BRIEF Indices Between ADHD-IV Attention Severity Groups
Mean T-scores for BRIEF indices between the No Elevation, Subthreshold, and Clinical Elevation groups on the ADHD-IV Attention Domain. Self-Control and Flexibility indices are only averaged for preschool-aged children (from BRIEF-Preschool measure only) and the Behavioral Regulation index is only averaged for school-aged children (from BRIEF-Parent measure only). The black dotted line indicates the mean score of the BRIEF (T=50). The red dotted line indicates the threshold for classifying clinical elevations; higher scores indicate more severe deficits. Note: a = post-hoc contrast between No Elevation and Subthreshold Elevation; b = post-hoc contrast between No Elevation and Clinical Elevation; c = post-hoc contrast between Subthreshold Elevation and Clinical Elevation. * = $p<0.05$; ** = $p<0.01$. Red = statistically significant result.

Table 7. BRIEF Index T-Score Differences Between ADHD-IV Attention Groups: One-Way ANOVA Results

BRIEF Index	ADHD-IV Attention Severity						df (Between, Within)	F	p	η^2
	No Elevation		Subthreshold		Clinical					
	Mean	(SD)	Mean	(SD)	Mean	(SD)				
Self-Control	44.80	(8.31)	65.00	(15.13)	58.67	(7.64)	2, 13	6.239	0.013*	0.490
Flexibility	46.50	(7.58)	62.00	(16.09)	58.00	(7.81)	2, 13	3.976	0.045*	0.380
Behavioral Regulation	41.86	(5.55)	52.44	(8.66)	61.38	(11.12)	2, 21	9.046	0.001**	0.463
Metacognition	44.41	(7.27)	57.58	(10.01)	65.18	(9.08)	2, 37	20.631	0.000**	0.527
Global Executive	43.24	(7.74)	57.58	(10.83)	64.27	(9.29)	2, 37	19.431	0.000**	0.512

* = $p<0.05$; ** = $p<0.01$; Red = statistically significant result.

Table 8. BRIEF Index T-Score Differences Between ADHD-IV Attention Groups: One-Way ANOVA Post-Hoc Results

Index	Post-Hoc Comparison			Mean Diff	Std. Error	p
Self-Control	No Elevation	vs.	Subthreshold Elevation	-20.20	6.32	0.007**
	No Elevation	vs.	Clinical Elevation	-13.87	6.32	0.047*
	Subthreshold Elevation	vs.	Clinical Elevation	6.33	7.83	0.433
Flexibility	No Elevation	vs.	Subthreshold Elevation	-15.50	6.21	0.027*
	No Elevation	vs.	Clinical Elevation	-11.50	6.21	0.087
	Subthreshold Elevation	vs.	Clinical Elevation	4.00	7.70	0.612
Behavioral Regulation Index	No Elevation	vs.	Subthreshold Elevation	-10.59	4.47	0.027*
	No Elevation	vs.	Clinical Elevation	-19.52	4.59	0.000**
	Subthreshold Elevation	vs.	Clinical Elevation	-8.93	4.31	0.051
Metacognition Index	No Elevation	vs.	Subthreshold Elevation	-13.17	3.26	0.000**
	No Elevation	vs.	Clinical Elevation	-20.77	3.35	0.000**
	Subthreshold Elevation	vs.	Clinical Elevation	-7.60	3.63	0.042*
Global Executive Composite	No Elevation	vs.	Subthreshold Elevation	-14.35	3.46	0.000**
	No Elevation	vs.	Clinical Elevation	-21.04	3.55	0.000**
	Subthreshold Elevation	vs.	Clinical Elevation	-6.69	3.83	0.089

* = $p<0.05$; ** = $p<0.01$; Red = statistically significant result.

When examining differences between ADHD-IV Hyperactivity severity groups on the BRIEF indices, there were no participants in the Clinical Elevation group. Thus, t-tests were used to examine differences between the No Elevation and Subthreshold Elevation groups; findings for group differences were nonsignificant on the Behavioral Regulation and Metacognition indices; however there were trends suggestive of differences between groups on the Self-Control, Flexibility, and Global Executive Composite indices (Figure 7, Table 9).

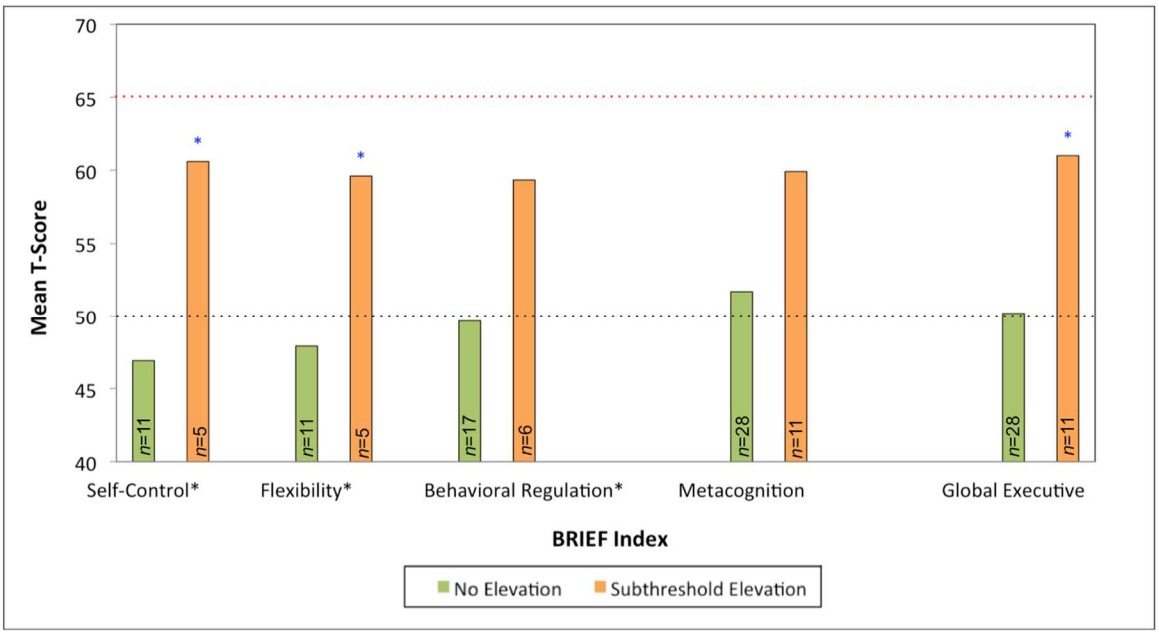

Figure 7. Comparison of BRIEF Indices Between ADHD-IV Hyperactivity Severity Groups

Mean T-scores for BRIEF indices between the No Elevation, Subthreshold, and Clinical Elevation groups on the ADHD-IV Hyperactivity Domain. Self-Control and Flexibility indices are only averaged for preschool-aged children (from BRIEF-Preschool measure only) and the Behavioral Regulation index is only averaged for school-aged children (from BRIEF-Parent measure only). The black dotted line indicates the mean score of the BRIEF (T=50). The red dotted line indicates the threshold for classifying clinical elevations; higher scores indicate more severe deficits. Note: a = post-hoc contrast between No Elevation and Subthreshold Elevation; b = post-hoc contrast between No Elevation and Clinical Elevation; c = post-hoc contrast between Subthreshold Elevation and Clinical Elevation. * = $p<0.05$; ** = $p<0.01$. Blue = trending result (statistical significance lost when corrected for multiple comparisons).

Table 9. BRIEF Index T-Score Differences Between ADHD-IV Hyperactivity Groups: T-Test Results

BRIEF Index	ADHD-IV Attention Severity				t	df	p	Mean Diff	d
	No Elevation		Subthreshold						
	Mean	(SD)	Mean	(SD)					
Self-Control	46.91	(10.44)	60.60	(12.36)	-2.303	14	0.037*	-13.691	1.20
Flexibility	47.91	(9.03)	59.60	(12.03)	-2.172	14	0.048*	-11.691	1.10
Behavioral Regulation	49.65	(9.60)	59.33	(15.29)	-1.818	21	0.083	-9.686	0.76
Metacognition	51.68	(12.41)	59.91	(10.78)	-1.929	37	0.061	-8.231	0.71
Global Executive	50.18	(12.25)	61.00	(11.76)	-2.508	37	0.017*	-10.821	0.90

Note: Only 1 participant with Clinical Elevation; not included in this analysis.
* = $p<0.05$; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

3.2.2.3 Comparison of Performance and Parent Report Outcomes

One-way ANOVAs and t-tests revealed a general lack of consistency between performance- and parent-based measures of attention and executive functioning skills. Specifically, there were no significant differences in neuropsychological composite scores between ADHD-IV Attention severity groups (Table 10) nor Hyperactivity severity groups (Table 11).

Table 10. Composite Score Differences Between ADHD-IV Attention Groups: One-Way ANOVA Results

NP Composite	ADHD-IV Attention Severity						df (Between, Within)	F	p	η^2
	No Elevation		Subthreshold		Clinical					
	Mean	(SD)	Mean	(SD)	Mean	(SD)				
Attention	-1.78	(1.03)	-1.35	(0.85)	-1.10	(1.06)	2, 21	0.93	0.411	0.08
Working Memory	0.00	(1.22)	-0.61	(0.66)	-0.41	(0.92)	2, 36	1.36	0.270	0.07
Verbal Retrieval	-0.28	(0.91)	-1.03	(1.03)	-0.70	(0.59)	2, 37	2.61	0.087	0.12
Inhibitory Control	-0.96	(1.04)	-1.84	(1.10)	-1.58	(1.13)	2, 36	2.43	0.103	0.12
Flexibility/Shifting	-1.13	(0.58)	-0.34	(1.37)	-0.89	(0.38)	2, 18	1.33	0.290	0.13
Plan/Organize	-2.02	(0.77)	-1.09	(1.36)	-1.85	(1.08)	2, 17	1.35	0.287	0.14
Processing Speed	-0.59	(1.38)	-1.09	(0.88)	-1.32	(0.98)	2, 37	1.49	0.238	0.07

Table 11. Composite Score Differences Between ADHD-IV Hyperactivity Groups: T-Test Results

NP Composite	ADHD-IV Hyperactivity Severity				t	df	p	Mean Difference	d
	No Elevation		Subthreshold						
	Mean	(SD)	Mean	(SD)					
Attention	-1.31	(0.99)	-1.33	(0.79)	0.04	21	0.965	0.02	0.02
Working Memory	-0.21	(0.89)	-0.34	(1.28)	0.36	36	0.724	0.13	0.12
Verbal Retrieval	-0.53	(0.79)	-0.77	(1.18)	0.74	37	0.463	0.24	1.29
Inhibitory Control	-1.28	(1.18)	-1.54	(0.94)	0.64	36	0.529	0.26	0.24
Flexibility/Shifting	-0.58	(0.93)	-1.16	(1.07)	1.16	18	0.260	0.58	0.59
Plan/Organize	-1.45	(1.12)	-2.07	(1.20)	0.96	17	0.348	0.62	0.53
Processing Speed	-0.85	(1.05)	-1.00	(1.40)	0.37	37	0.715	0.15	0.12

Note: Only 1 participant had clinical elevation and was dropped from analysis

Pearson correlational analyses between parent report on the Global Executive Composite (GEC) Index of the BRIEF and the Executive Functioning composite performance test scores revealed significant negative correlations between the GEC and the Verbal Retrieval composite as well as the Processing Speed composite but the remaining domains (Working Memory, Inhibitory Control, and Flexibility/Shifting) were nonsignificant (i.e., children who were classified by their parents as having more significant problems with overall executive functioning did not perform worse than children with less parent-reported problems; Figure 8, Table 12).

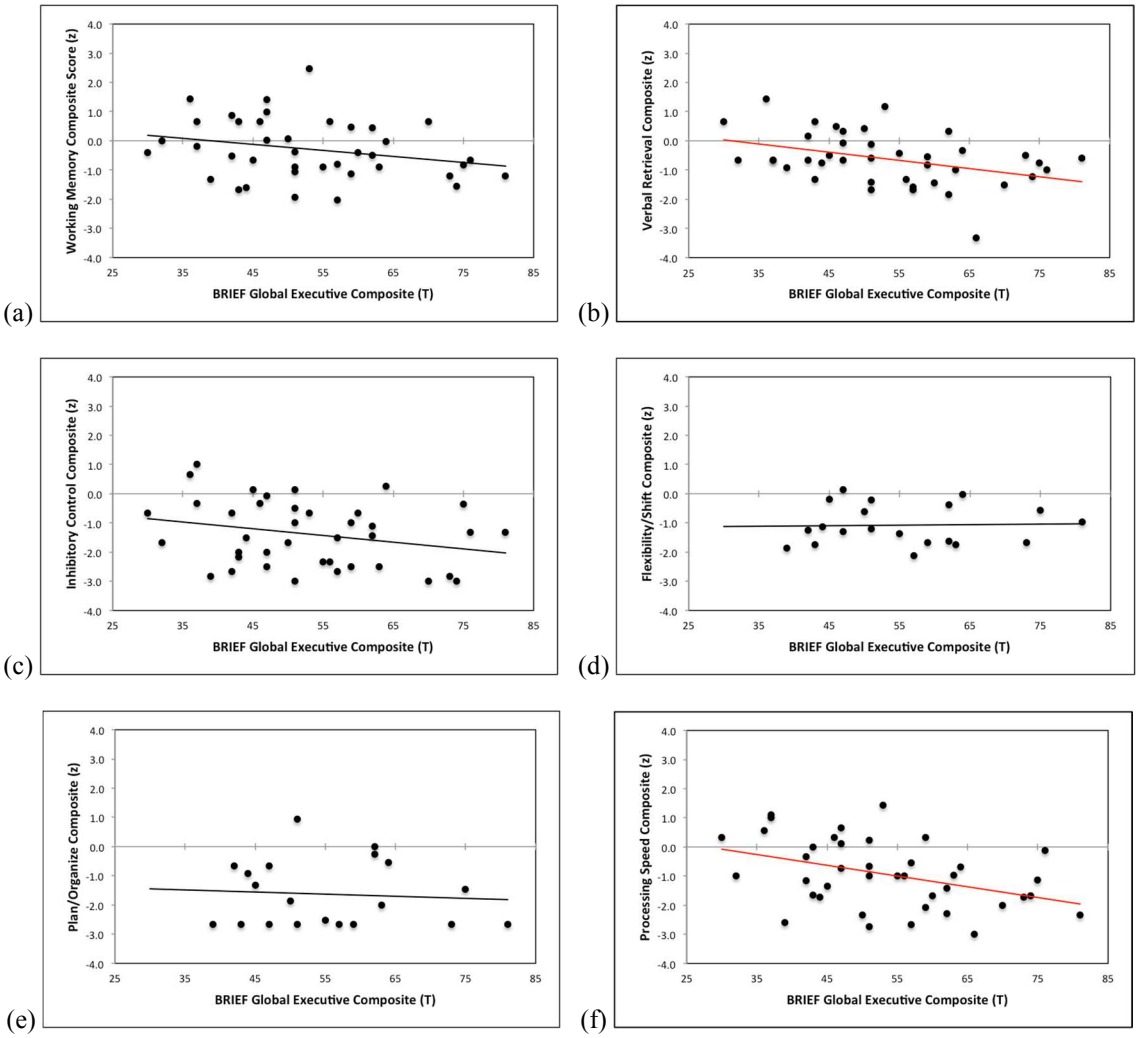

Figure 8. Correlations Between BRIEF GEC and Executive Functioning Composite Scores

Scatter plots showing each participant's BRIEF GEC score and composite score for each EF domain. (a) Working Memory Composite (*n*=39); (b) Verbal Retrieval Composite (*n*=40); (c) Inhibitory Control Composite (*n*=39); (d) Flexibility/Shift Composite (*n*=21); (e) Plan/Organize Composite (*n*=20); (f) Processing Speed Composite (*n*=40). Flexibility/Shifting, and Plan/Organize domains are comprised of only the school-aged participants, as these domains were not calculable for preschool participants. Red slope = statistically significant result.

Table 12. Pearson Correlation Results for BRIEF GEC and Executive Functioning Composite Scores

		BRIEF GEC	
EF Composite	**N**	**r**	**p**
Working Memory	39	-0.26	0.110
Verbal Retrieval	40	-0.40	0.011*
Inhibitory Control	39	-0.26	0.106
Flexibility/Shifting	21	-0.03	0.902
Plan/Organize	20	-0.08	0.752
Processing Speed	40	-0.41	0.009**

* = p<0.05; ** = p<0.01; Red = statistically significant result.

Together, these findings suggested that parent report did not typically align with performance-based testing. As a result, parent report was not incorporated into the composite scores of the appropriate domains, but instead was considered separately from the performance-based test composites.

3.3 Effects of Demographic, Lesion, and Clinical Factors on Cognitive Performance

The following are results based on demographic, lesion, and clinical characteristics.

3.3.1 Age

Pearson correlational analyses revealed a statistically significant negative relationship between age and the Working Memory Composite (i.e., increasing age is related to poorer working memory skills) and a trend towards negative correlations between age and the Processing Speed Composite (i.e., increasing age is related to poorer processing speed skills). No relationships were identified between age and IQ or the remaining functional composites/domains: Attention, Verbal Retrieval, Inhibitory Control, Flexibility/Shifting, and Plan/Organize (Figure 9, Table 13).

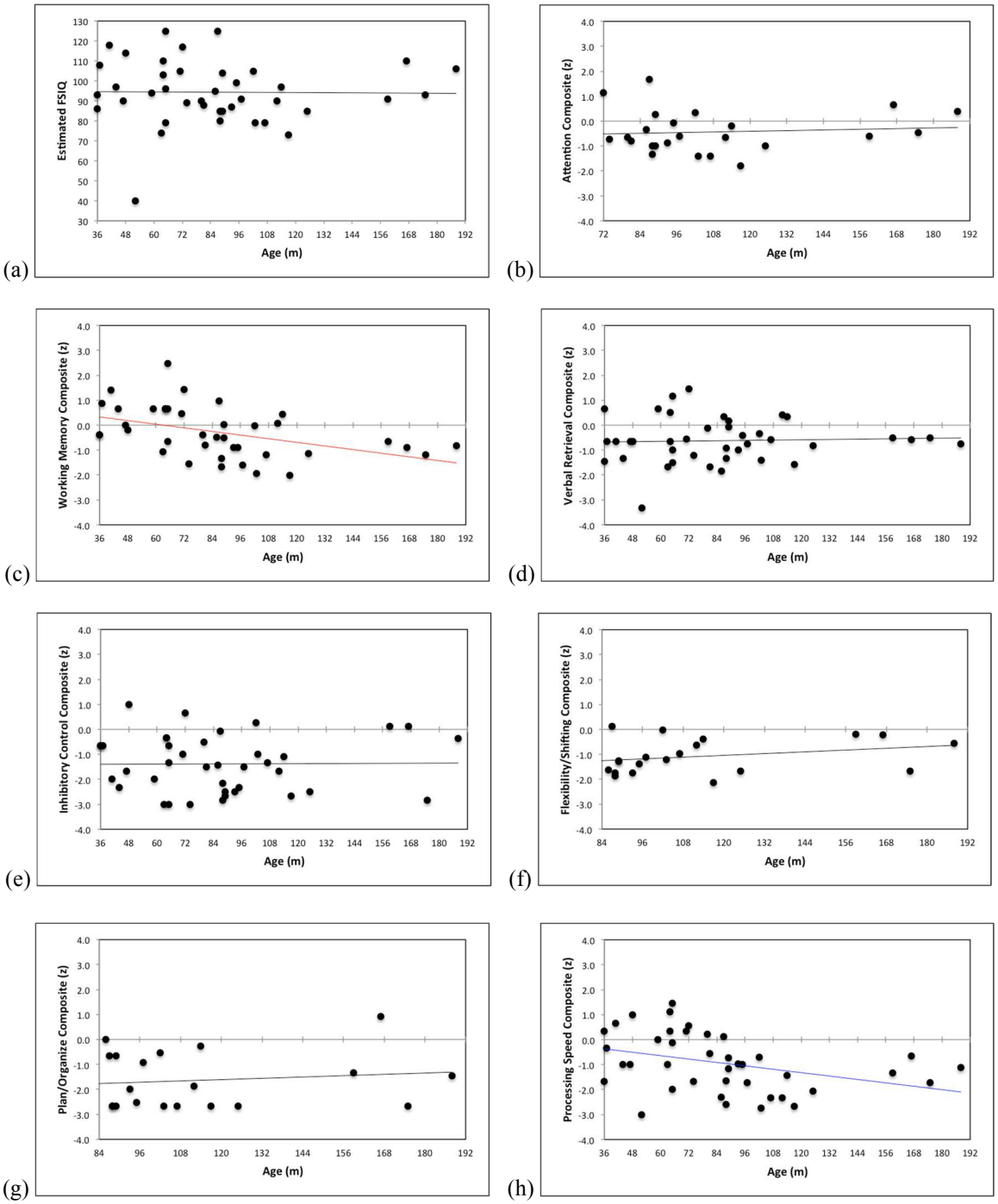

Figure 9. Correlations Between Age and IQ, Composite Scores

Scatter plots showing each NAIS participant's age and composite score for each neuropsychological domain. (a) FSIQ (*n*=40); (b) Attention (*n*=24) (c) Working Memory Composite (*n*=39); (d) Verbal Retrieval Composite (*n*=40); (e) Inhibitory Control Composite (*n*=39); (f) Flexibility/Shift Composite (*n*=21); (g) Plan/Organize Composite (*n*=20); (h) Processing Speed Composite (*n*=40). Attention, Flexibility/Shifting, and Plan/Organize domains are comprised of only the school-aged participants, as these domains were not calculable for preschool participants. Red slope = statistically significant result; Blue slope = trending result (statistical significance lost when corrected for multiple comparisons).

Table 13. Pearson Correlation Results for Age and IQ, Neuropsychological Composite Scores

		Age	
NP Domain	**N**	**r**	**p**
IQ	40	-0.01	0.936
Attention	24	0.05	0.813
Working Memory	39	-0.45	0.004**
Verbal Retrieval	40	0.04	0.788
Inhibitory Control	39	0.01	0.945
Flexibility/Shifting	21	-0.09	0.690
Plan/Organize	20	0.13	0.599
Processing Speed	40	-0.37	0.020*

* = p<0.05; ** = p<0.01; Red = statistically significant result; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

Pearson correlational analyses assessing age and parent-reported BRIEF index scores revealed no significant findings but there were negative correlational trends suggesting that increased age was more likely to result in higher T-scores (i.e., more severe symptoms) in both metacognitive and global executive functioning domains (Figure 10, Table 14).

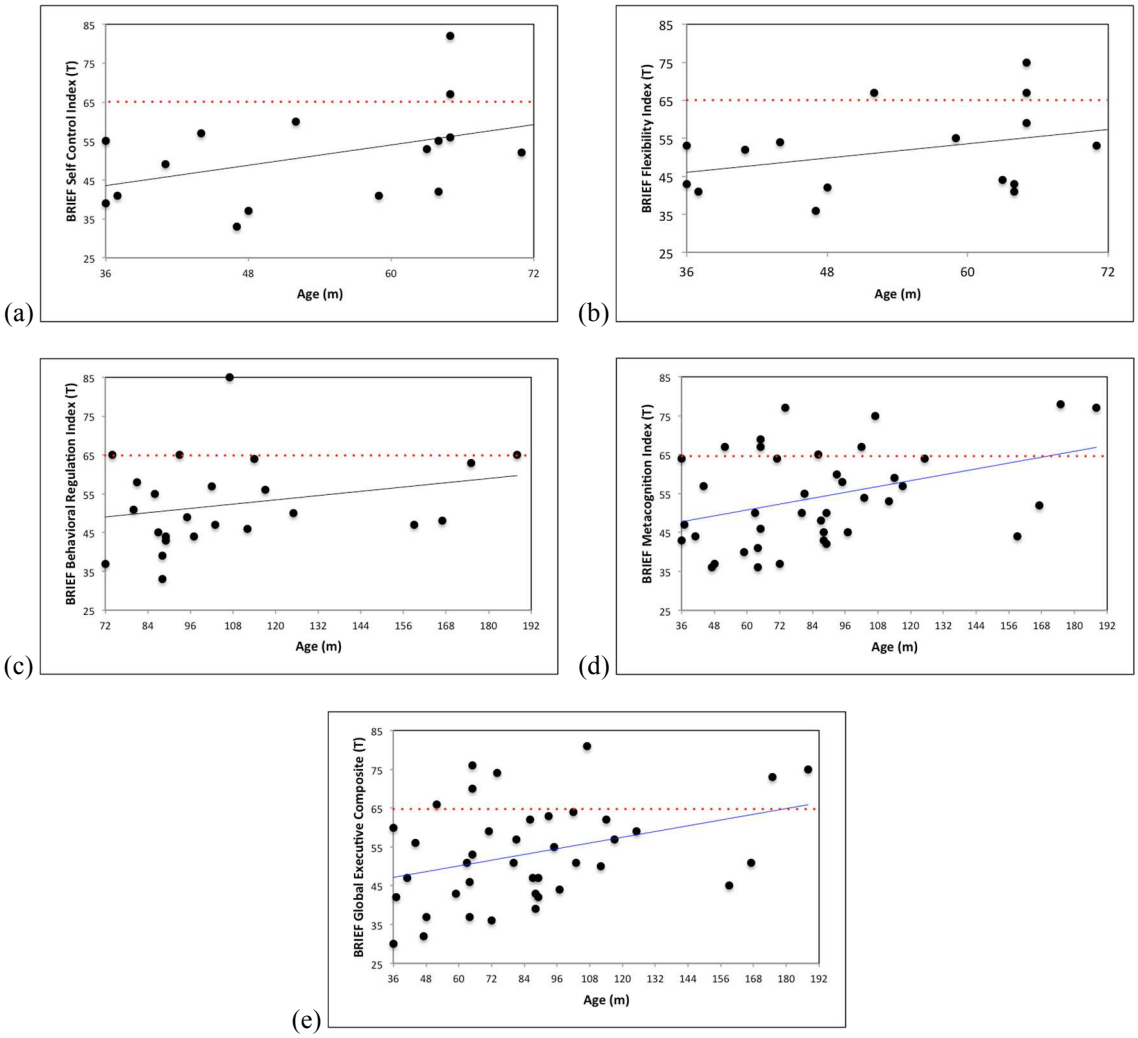

Figure 10. Correlations Between Age and BRIEF T-Scores

Scatter plots showing each NAIS participant's age and BRIEF index scores. (a) Self-Control (*n*=16); (b) Flexibility (*n*=16); (c) Behavioral Regulation (*n*=24); (d) Metacognition (*n*=40); (e) Global Composite (*n*=40). Self-Control and Flexibility are comprised of only preschool children and BRI is comprised of only school-age children, due to differences in administration forms. The red dotted line indicates the threshold for classifying clinical elevations; higher scores indicate more severe deficits. Blue slope = trending result (statistical significance lost when corrected for multiple comparisons).

Table 14. Pearson Correlation Results for Age and BRIEF Index Scores

		Age	
BRIEF Index	**N**	**r**	**p**
Self-Control	16	0.43	0.099
Flexibility	16	0.34	0.192
Behavioral Regulation	24	0.26	0.222
Metacognition	40	0.39	0.014*
Global Executive	40	0.36	0.022*

* = $p<0.05$; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

In contrast to performance test results on attention measures, a one-way ANOVA assessing parent report on the ADHD-IV indicated statistically significant differences in age between attention severity levels. Post-hoc results showed that children with no elevation on the Attention scale were significantly younger than children with clinical elevations; no differences existed between no elevation and subthreshold groups nor between subthreshold and clinically elevated groups. Hyperactivity was not notable for any significant findings impacted by age, which aligns with the nonsignificant finding for the relationship between age and behavioral regulation on the BRIEF (Figure 11, Table 15).

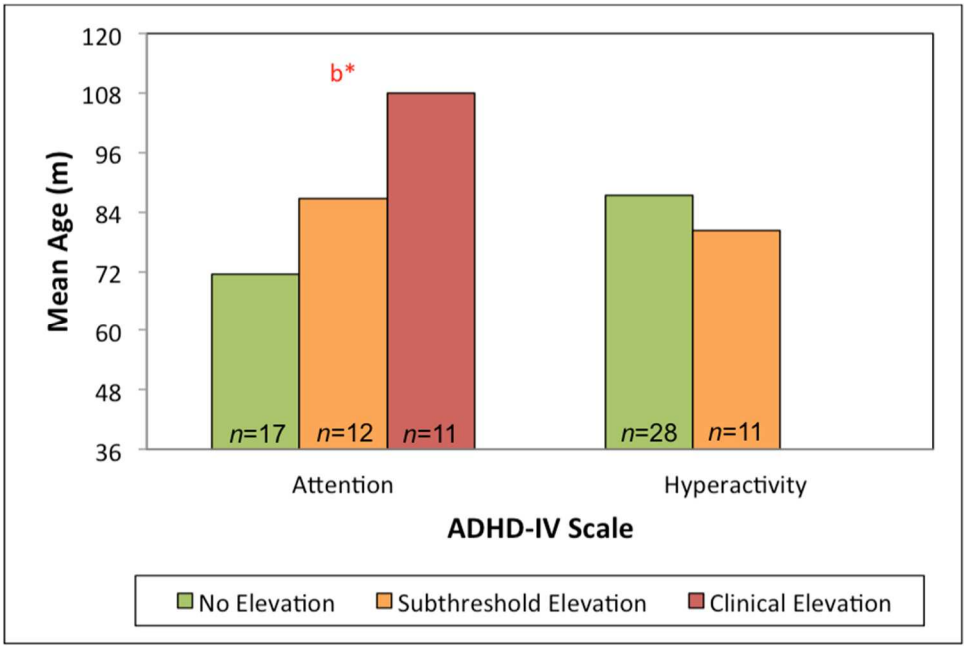

Figure 11. Age Differences Between ADHD-IV Groups

Bar graphs showing average age of participants classified as having no elevation, a subthreshold elevation, or a clinical elevation on the Attention and Hyperactivity scales of the ADHD-IV. Note: a = post-hoc contrast between No Elevation and Subthreshold Elevation; b = post-hoc contrast between No Elevation and Clinical Elevation. * = $p<0.05$. Red = statistically significant result.

Table 15. Age Differences Between ADHD-IV Groups: One-Way ANOVA Results

ADHD-IV Scale	No Elevation		Subthreshold		Clinical		df (Between, Within)	F	p	η^2
	Mean	(SD)	Mean	(SD)	Mean	(SD)				
Attention	71.53	(33.16)	86.75	(28.60)	108.00	(44.08)	2, 37	3.57	0.038*	0.16
Hyperactivity	87.32	(42.78)	80.27	(20.33)	-	-	1, 37	0.27	0.606	0.01

* = p<0.05; Red = statistically significant result.
Attention Post-hoc Analyses: significant difference between no elevation and clinical elevation (p = 0.011).

Subsequent to the finding that age was negatively correlated with the Working Memory Composite, we completed a post hoc exploratory analysis to examine parent report of this individual variable on the BRIEF. This revealed the same pattern (i.e., significant correlations between increasing age and worsening Working Memory scores on the BRIEF). Thus, while working memory did not result in a statistically significant problem area for the PAIS group as a whole, both parent and performance data indicate that this domain is an increasing problem as children with PAIS age. That is, age was significantly negatively correlated with the working memory composite (r = -0.45, p = 0.004) as well as with the working memory subdomain of the BRIEF (r = -0.38, p = 0.016). Findings are summarized in Figure 12.

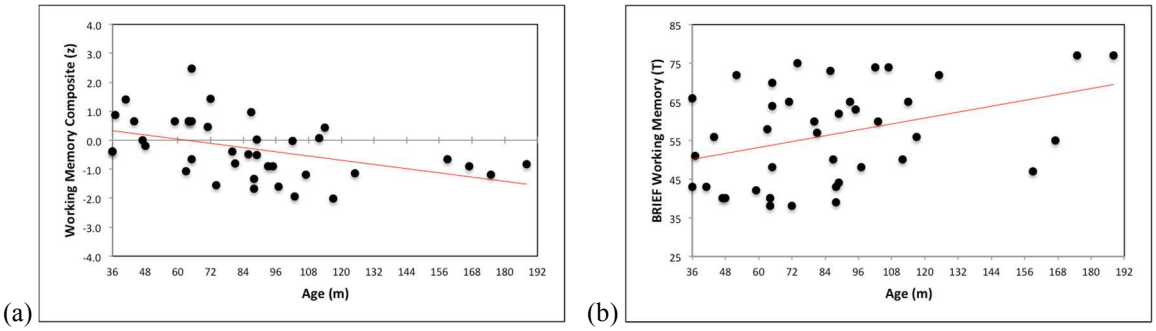

Figure 12. Correlations Between Age and Working Memory
Scatter plots showing correlations between (a) participants' ages and Working Memory Composite scores (n=39); and (b) participants' ages and BRIEF Working Memory T-scores (n=40).

3.3.2 Sex

There was no significant difference or noteworthy trend pertaining to sex on any measures of intellectual or attention and executive functioning outcomes, as determined by performance measures (i.e., domain composites, Table 16). There were also no significant effects of sex found in parent report of executive functioning (Table 17). However, males had significantly more inattentive and hyperactive symptoms of ADHD than females in parent report of ADHD symptoms (Figure 13, Table 18). Of note, once sex specific norms were applied to the data and analyzed for differences in severity, the overall impact of sex became non-significant (Fisher's Exact Test for Attention: p = 0.558, V = 0.18; Hyperactivity: p = 0.842, V = 0.17).

Table 16. Neuropsychological Composite T-Test Results for Sex

NP Domain	Sex				t	df	p	Mean Diff	d
	Male (*n*=23)		Female (*n*=17)						
	Mean z	(SD)	Mean z	(SD)					
IQ	-0.57	(1.16)	-0.12	(0.87)	-1.33	38	0.190	-0.45	0.43
Attention	-1.24	(1.12)	-1.57	(0.77)	0.82	22	0.424	0.33	0.34
Working Memory	-0.32	(1.00)	-0.24	(1.08)	-0.24	37	0.814	-0.08	0.08
Verbal Retrieval	-0.80	(1.01)	-0.38	(0.70)	-1.46	38	0.153	-0.42	0.48
Inhibitory Control	-1.47	(1.15)	-1.27	(1.11)	-0.55	37	0.583	-0.20	0.18
Flexibility/Shifting	-0.48	(1.12)	-1.10	(0.53)	1.51	19	0.147	0.61	0.71
Plan/Organize	-1.65	(1.09)	-1.61	(1.25)	-0.06	18	0.949	-0.03	0.03
Processing Speed	-1.18	(1.15)	-0.61	(1.13)	-1.58	38	0.123	-0.58	0.50

Table 17. BRIEF T-Test Results for Sex

BRIEF Index	Sex				t	df	p	Mean Diff	d
	Male (*n*=23)		Female (*n*=17)						
	Mean T	(SD)	Mean T	(SD)					
Self-Control	54.50	(13.95)	45.67	(7.74)	1.41	14	0.180	8.83	0.78
Flexibility	53.50	(12.88)	48.33	(7.37)	0.89	14	0.388	5.17	0.49
Behavioral Regulation	55.62	(13.81)	48.45	(6.92)	1.56	22	0.133	7.16	0.66
Metacognition	56.70	(13.24)	50.53	(10.12)	1.60	38	0.117	6.17	0.52
Global Executive	56.65	(13.86)	48.82	(9.85)	1.98	38	0.054	7.83	0.65

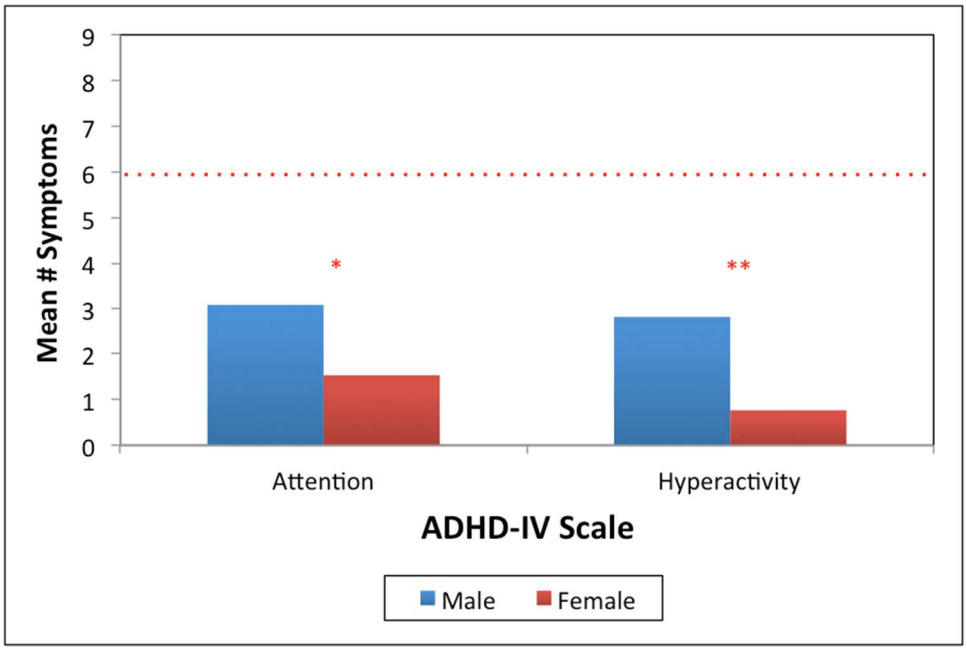

Figure 13. Effect of Sex on ADHD-IV Symptom Counts

Bar graphs showing the mean ADHD symptom count for each ADHD-IV Scale (Attention and Hyperactivity), contrasted between males (*n*=23) and females (*n*=17). The red dotted line indicates the threshold for diagnosing ADHD; higher symptom counts indicate more severe deficits. Note: * = p<0.05; ** = p<0.01. Red = statistically significant result.

Table 18. ADHD-IV Symptom Count T-Test Results for Sex

ADHD-IV Scale	Sex				t	df	p	Mean Diff	d
	Male (*n*=23)		Female (*n*=17)						
	Mean	(SD)	Mean	(SD)					
Attention	3.09	(2.89)	1.53	(1.77)	2.10	36.93	.042*	1.558	0.65
Hyperactivity	2.83	(2.35)	0.76	(1.15)	3.66	33.68	.001**	2.061	1.12

* = p<0.05; ** = p<0.01; Red = statistically significant result;

3.3.3 Stroke Laterality

Only one participant presented with a bilateral stroke and therefore this category was excluded from group comparisons. In comparing left- (*n*=32) and right (*n*=7) hemisphere strokes, there was no significant effect or noteworthy trend related to stroke laterality on intellectual outcome or attention and executive functioning outcome, both as determined by performance measures (i.e., domain composites, Table 19) and parent report (Tables 20 and 21).

Table 19. Neuropsychological Composite T-Test Results for Stroke Laterality

NP Domain	Stroke Hemisphere				t	df	p	Mean Diff	d
	Left (*n*=32)		Right (*n*=7)						
	Mean z	(SD)	Mean z	(SD)					
IQ	-0.69	(0.60)	-0.33	(1.14)	-0.80	37	0.431	-0.36	0.40
Attention	-1.51	(1.18)	-1.44	(0.89)	-0.14	21	0.891	-0.07	0.07
Working Memory	-0.37	(0.95)	-0.28	(1.06)	-0.19	36	0.847	-0.08	0.09
Verbal Retrieval	-0.40	(0.79)	-0.68	(0.95)	0.74	37	0.466	0.28	0.32
Inhibitory Control	-1.36	(1.12)	-1.44	(1.12)	0.17	36	0.867	0.08	0.07
Flexibility/Shifting	-0.55	(0.94)	-0.81	(1.01)	0.46	18	0.652	0.26	0.27
Plan/Organize	-1.97	(0.55)	-1.62	(1.25)	-0.83	12.1	0.426	-0.35	0.36
Processing Speed	-0.86	(1.38)	-0.96	(1.15)	0.22	37	0.830	0.11	0.08

Table 20. ADHD-IV Fisher's Exact Test Results for Stroke Laterality

ADHD-IV Scale	Group	Percentage of Participants with Elevation			p	V
		No Elevation	Subthreshold	Clinical		
Attention	Left	40.6	34.4	25.0	0.852	0.17
	Right	57.1	14.3	28.6		
Hyperactivity	Left	68.8	31.3	0.0	0.186	0.36
	Right	71.4	14.3	14.3		

Table 21. BRIEF T-Test Results for Stroke Laterality

BRIEF Index	Stroke Hemisphere				t	df	p	Mean Diff	d
	Left (*n*=32)		Right (*n*=7)						
	Mean T	(SD)	Mean T	(SD)					
Self-Control	52.57	(12.80)	41.50	(0.71)	-1.19	14	0.255	-11.07	1.22
Flexibility	52.07	(11.56)	48.00	(9.90)	-0.47	14	0.645	-4.07	0.38
Behavioral Regulation	51.89	(12.84)	53.00	(7.78)	0.18	21	0.857	1.11	0.10
Metacognition	54.88	(12.69)	48.57	(8.90)	-1.24	37	0.222	-6.30	0.58
Global Executive	53.84	(13.55)	49.43	(8.75)	-0.82	37	0.417	-4.42	0.39

3.3.4 Stroke Volume

Of the 28 children who had NAIS strokes (i.e., presented acutely in the newborn period), only 25 had modASPECTS scores to utilize for statistical analyses; the remaining three did not have MRI or CT scans available for scoring. Pearson correlational analyses revealed a trend towards negative correlations between stroke volume and IQ (i.e., larger strokes were more likely to have lower FSIQ scores) and statistically significant strong, negative correlations between stroke volume and Verbal Retrieval, Inhibitory Control, and Processing Speed (i.e., larger strokes were correlated with greater difficulties in these cognitive domains). Nonsignificant correlations existed between stroke volume and Attention, Working Memory, Flexibility/Shifting, and Plan/Organize domains (Figure 14, Table 22).

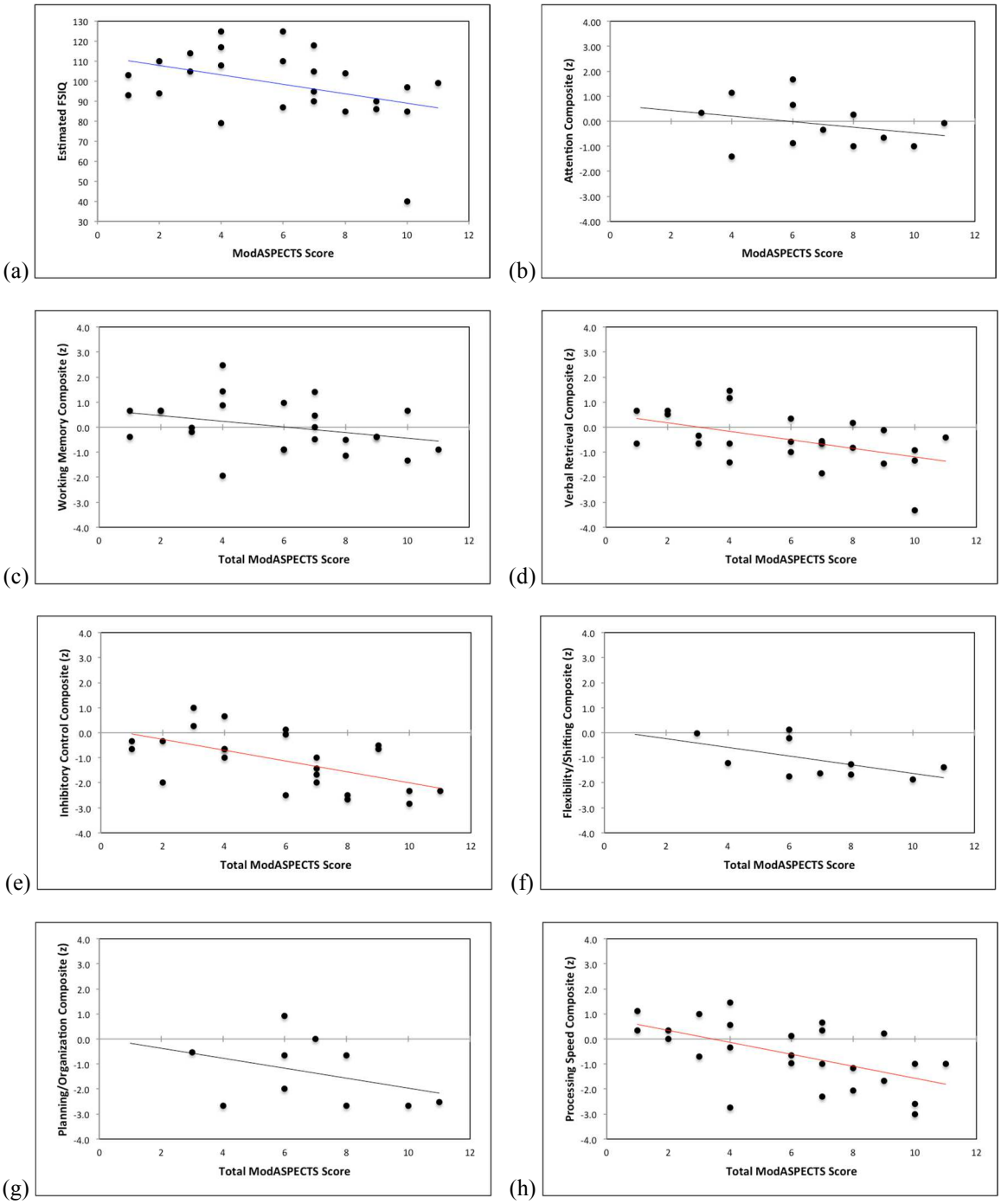

Figure 14. Correlations Between ModASPECTS Score and IQ, Composite Scores

Scatter plots showing each NAIS participant's total modASPECTS score and composite score for each neuropsychological domain. (a) FSIQ (*n*=25); (b) Attention (*n*=12); (c) Working Memory Composite (*n*=24); (d) Verbal Retrieval Composite (*n*=25); (e) Inhibitory Control Composite (*n*=24); (f) Flexibility/Shift Composite (*n*=10); (g) Plan/Organize Composite (*n*=10); (h) Processing Speed Composite (*n*=25). Attention, Flexibility/Shifting, and Plan/Organize domains are comprised of only the school-aged participants, as these domains were not calculable for preschool participants. Red slope = statistically significant result; Blue slope = trending result (statistical significance lost when corrected for multiple comparisons).

Table 22. Pearson Correlation Results for Stroke Volume and IQ, Neuropsychological Composite Scores

		Total ModASPECTS Score	
NP Domain	**N**	**r**	**p**
IQ	25	-0.40	0.047*
Attention	12	-0.24	0.451
Working Memory	24	-0.33	0.117
Verbal Retrieval	25	-0.51	0.009**
Inhibitory Control	24	-0.58	0.003**
Flexibility/Shifting	10	0.15	0.670
Plan/Organize	10	-0.37	0.288
Processing Speed	25	-0.57	0.003**

* = $p<0.05$; ** = $p<0.01$; Red = statistically significant result; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

Pearson correlational analyses were also used to assess relationships between stroke volume and parent-reported BRIEF index scores. Results indicated no significant findings for Self-Control, Flexibility, or Behavior Regulation indices, but there were positive correlational trends suggesting that larger strokes were more likely to result in higher T-scores (i.e., more severe symptoms) in both the Metacognitive and Global Executive functional domains (Figure 15, Table 23).

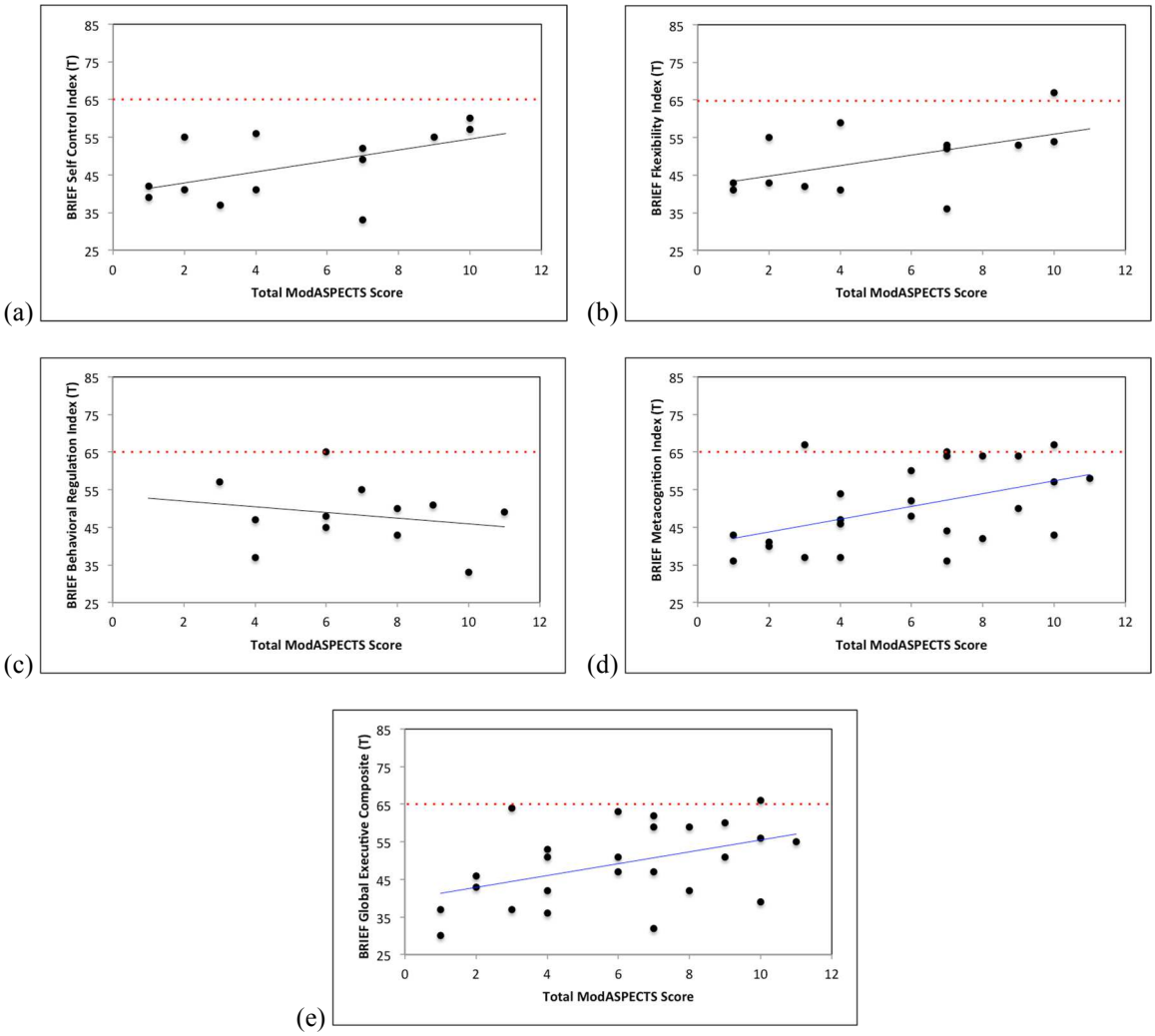

Figure 15. Correlations Between ModASPECTS Score and BRIEF T-Scores

Scatter plots showing each NAIS participant's total modASPECTS score and BRIEF index scores. (a) Self-Control (*n*=13); (b) Flexibility (*n*=13); (c) Behavioral Regulation (*n*=12); (d) Metacognition (*n*=25); (e) Global Composite (*n*=25). Self-Control and Flexibility are comprised of only preschool children and BRI is comprised of only school-age children, due to differences in administration forms. The red dotted line indicates the threshold for classifying clinical elevations; higher scores indicate more severe deficits. Blue slope = trending result (statistical significance lost when corrected for multiple comparisons).

Table 23. Pearson Correlation Results for Stroke Volume and BRIEF Index Scores

		Total ModASPECTS Score	
BRIEF Index	**N**	**r**	**p**
Self-Control	13	0.54	0.055
Flexibility	13	0.53	0.065
Behavioral Regulation	12	-0.22	0.494
Metacognition	25	0.48	0.015*
Global Executive	25	0.45	0.024*

* = $p<0.05$; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

In contrast to performance results on attention measures, a one-way ANOVA assessing parent report on the ADHD-IV indicated statistically significant differences in total modASPECTS scores between attention severity levels. Post-hoc results showed that children with no elevation on the Attention scale had lower total modASPECTS scores (i.e., smaller strokes) than children with subthreshold elevations as well as children with clinical elevations; no differences existed between the subthreshold and clinically elevated groups. Hyperactivity was not notable for any significant findings impacted by stroke volume, aligning with the nonsignificant finding for the relationship between stroke volume and behavioral regulation on the BRIEF (Figure 16, Table 24).

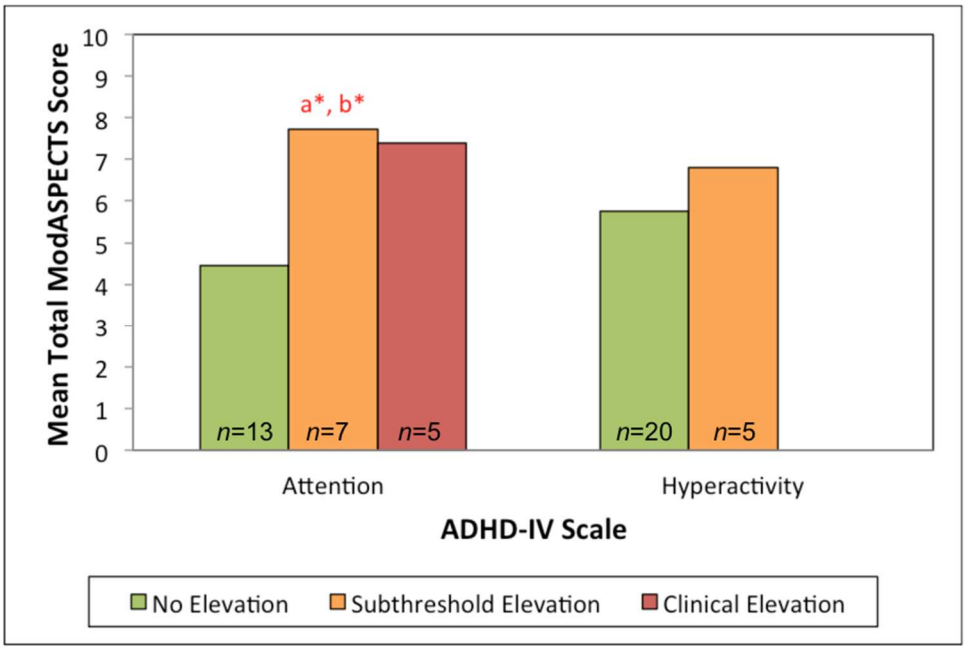

Figure 16. ModASPECTS Score Differences Between ADHD-IV Groups

Bar graphs showing average total modASPECTS scores for participants classified as having no elevation, a subthreshold elevation, or a clinical elevation on the Attention and Hyperactivity scales of the ADHD-IV. Note: * = $p<0.05$. Red = statistically significant result.

Table 24. ModASPECTS Score Differences Between ADHD-IV Groups: One-Way ANOVA Results

ADHD-IV Scale	No Elevation		Subthreshold		Clinical		df (Between, Within)	F	p	η^2
	Mean	(SD)	Mean	(SD)	Mean	(SD)				
Attention	4.46	(2.93)	7.71	(2.06)	7.40	(2.70)	2, 22	4.26	0.027*	0.28
Hyperactivity	5.75	(3.11)	6.80	(2.77)	-	-	1, 23	0.47	0.499	0.02

* = p<0.05; Red = statistically significant result.
Attention Post-hoc Analyses: significant difference between no elevation and subthreshold (p = 0.017) and no elevation and clinical elevation (p = 0.049).

3.3.5 Stroke Location

Only 3 participants presented with a subcortical-only stroke and therefore this category was excluded from group comparisons. In comparing cortical-only (i.e., cortical and subjacent white matter; n=11) and cortical+subcortical (i.e., combination of cortical structures, thalamus, and/or basal ganglia involvement; n=26) strokes, there was no significant effect or noteworthy trend related to cortical involvement on intellectual outcome or attention and executive functioning outcome, both as determined by performance measures (i.e., domain composites, Table 25) and parent report (Tables 26 and 27).

Table 25. Neuropsychological Composite T-Test Results for Stroke Location

NP Domain	Stroke Location				t	df	p	Mean Diff	d
	Cortical (*n* = 11)		Cortical+Subcortical (*n* = 26)						
	Mean z	(SD)	Mean z	(SD)					
IQ	-0.15	(0.85)	-0.53	(1.14)	1.01	35	0.318	0.39	0.38
Attention	-1.35	(1.12)	-1.39	(0.98)	0.07	21	0.945	0.03	0.04
Working Memory	-0.14	(1.19)	-0.42	(0.98)	0.72	34	0.474	0.27	0.26
Verbal Retrieval	-0.23	(0.83)	-0.81	(0.94)	1.76	35	0.087	0.58	0.65
Inhibitory Control	-1.05	(1.06)	-1.61	(1.06)	1.46	34	0.155	0.56	0.53
Flexibility/Shifting	-0.82	(0.36)	-0.70	(1.15)	-0.24	18	0.811	-0.12	0.14
Plan/Organize	-1.49	(1.02)	-1.62	(1.22)	0.23	17	0.822	0.13	0.12
Processing Speed	-0.56	(1.25)	-1.20	(1.09)	1.56	35	0.128	0.64	0.55

Table 26. ADHD-IV Fisher's Exact Test Results for Stroke Location

ADHD-IV Scale	Group	Percentage of Participants with Elevation			p	V
		None (<80th %ile)	Subthreshold (80-90th %ile)	Clinical (≥93rd %ile)		
Attention	Cortical	45.5	9.1	45.5	0.174	0.31
	Cortical + Subcortical	38.5	38.5	23.1		
Hyperactivity	Cortical	63.6	27.3	9.1	0.455	0.26
	Cortical + Subcortical	73.1	26.9	0.0		

Table 27. BRIEF T-Test Results for Stroke Location

BRIEF Index	Stroke Location				t	df	p	Mean Diff	d
	Cortical (*n* = 11)		Cortical + Subcortical (*n* = 26)						
	Mean T	(SD)	Mean T	(SD)					
Self-Control	52.00	(18.07)	53.44	(9.25)	-0.20	12	0.844	-1.44	0.10
Flexibility	54.60	(13.74)	52.11	(10.35)	0.38	12	0.707	2.49	0.20
Behavioral Regulation	58.67	(6.83)	50.59	(12.45)	1.50	21	0.149	8.08	0.80
Metacognition	55.82	(14.99)	54.42	(11.36)	0.31	35	0.758	1.40	0.11
Global Executive	55.91	(15.77)	53.54	(11.63)	0.51	35	0.614	2.37	0.17

3.3.6 Epilepsy

10 of our 40 participants (25%) developed epilepsy after perinatal stroke. This is comparable with reports of post-PAIS epilepsy prevalence rates in previous studies, which have ranged from 15% to 54% (Kirton et al., 2008; Ricci et al., 2008;

Wanigasinghe et al., 2010). Children with comorbid epilepsy not only had a significantly lower FSIQ (FSIQ = 78 vs. 100) but also performed more poorly on five of the seven cognitive domains: Working Memory, Verbal Retrieval, Inhibitory Control, Plan/Organize, and Processing Speed. Attention and Flexibility/Shifting were not significantly impacted (Figure 17, Table 28).

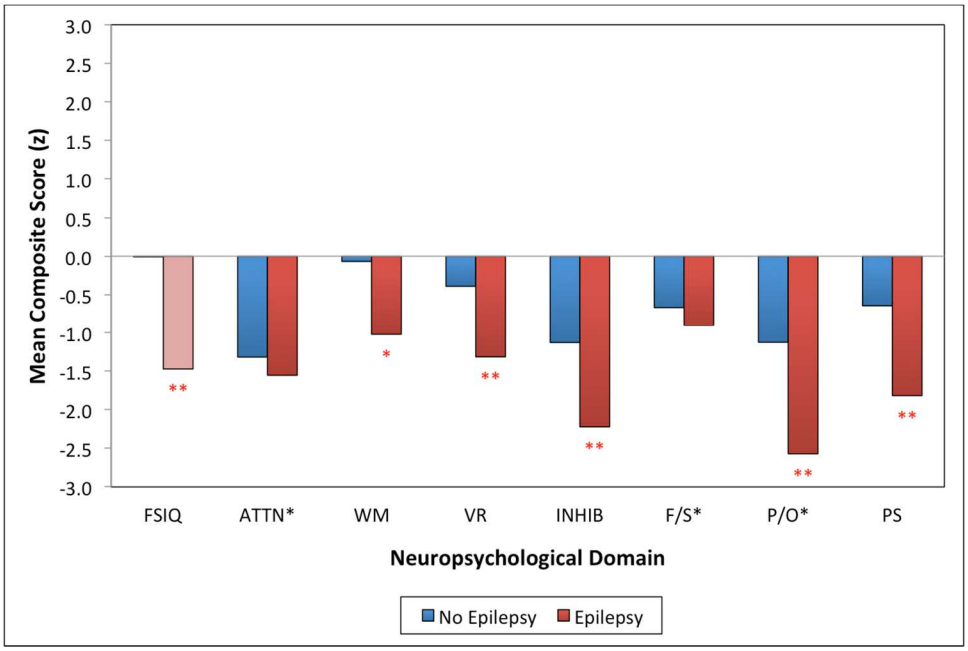

Figure 17. Effect of Epilepsy on Attention and Executive Functioning Composites

Bar graphs showing the mean composite score for each neuropsychological domain tested, contrasted between children with (*n*=10) and without (*n*=30) comorbid epilepsy. FSIQ = Full-Scale IQ; ATTN = Attention; WM = Working Memory; VR = Verbal Retrieval; INHIB = Inhibitory Control; F/S = Flexibility/Shifting; P/O = Plan/Organize; PS = Processing Speed. Attention, Flexibility/Shifting, and Plan/Organize domains are comprised of only the school-aged participants, as these domains were not calculable for preschool participants. Note: * = $p<0.05$; ** = $p<0.01$. Red = statistically significant result.

Table 28. Neuropsychological Composite T-Test Results for Comorbid Epilepsy

NP Domain	Diagnosis				t	df	p	Mean Diff	d
	No Epilepsy (*n* = 10)		Epilepsy (*n* = 30)						
	Mean z	(SD)	Mean z	(SD)					
IQ	-0.01	(0.80)	-1.47	(1.00)	4.70	38	0.000**	1.46	1.61
Attention	-1.32	(1.03)	-1.56	(0.84)	0.53	22	0.600	0.24	0.26
Working Memory	-0.07	(0.96)	-1.02	(0.88)	2.66	37	0.011*	0.96	1.03
Verbal Retrieval	-0.39	(0.81)	-1.32	(0.86)	3.08	38	0.004**	0.93	1.11
Inhibitory Control	-1.13	(1.12)	-2.22	(0.65)	3.68	23.6	0.001**	1.09	1.19
Flexibility/Shifting	-0.67	(0.99)	-0.91	(0.93)	0.53	19	0.599	0.24	0.25
Plan/Organize	-1.13	(1.10)	-2.57	(0.25)	4.52	14.2	0.000**	1.44	1.81
Processing Speed	-0.64	(1.11)	-1.82	(0.85)	3.05	38	0.004**	1.18	1.19

* = $p<0.05$; ** = $p<0.01$; Red = statistically significant result.

Parent report of attention and executive functioning did not statistically differ between children who had comorbid epilepsy and those did not (Figure 18, Tables 29 and 30). However, there was a notable trend suggesting that children with comorbid epilepsy also have more significant symptoms of hyperactivity. Although there were no statically significant differences in parent-reported attention problems between the non-epilepsy and epilepsy groups, a closer examination suggests that epilepsy increases a child's risk factor for attention problems. That is, whereas PAIS children without comorbid epilepsy were equally likely to have no elevated concerns with attention as they are to have either a subthreshold or clinical elevation, those with comorbid epilepsy had a much larger chance of having elevated attention problems (a 4:1 ratio in our cohort; Figure 18).

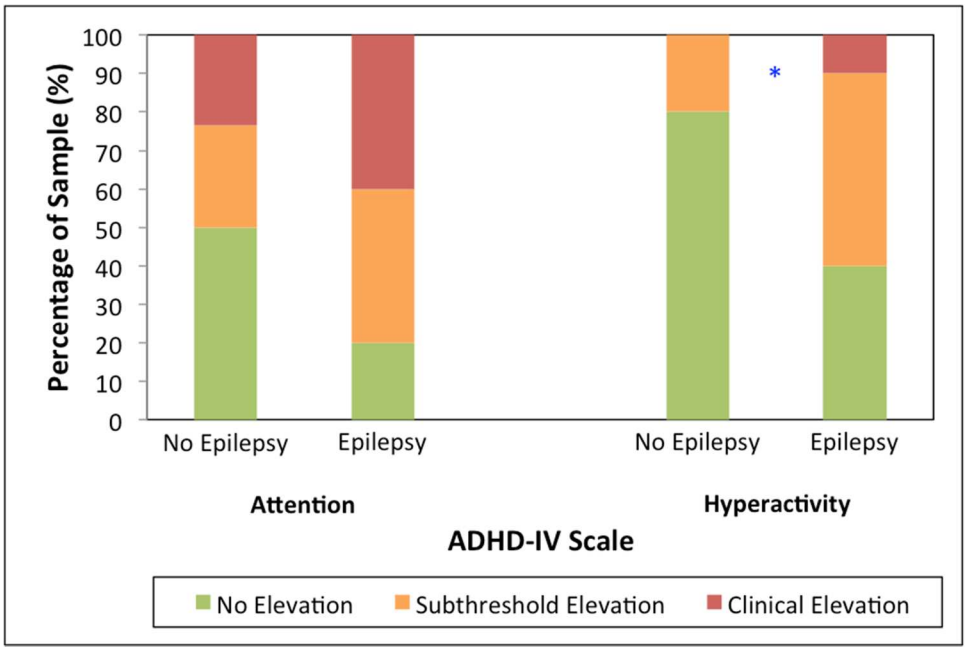

Figure 18. Effect of Epilepsy on ADHD-IV Scores

Bar graphs showing percentage of participants classified as having no elevation, a subthreshold elevation, or a clinical elevation on the Attention and Hyperactivity scales of the ADHD-IV, comparing children with (*n*=10) and without (*n*=30) comorbid epilepsy. Note: * = p<0.05. Blue = trending result (statistical significance lost when corrected for multiple comparisons).

Table 29. ADHD-IV Fisher's Exact Test Results for Comorbid Epilepsy

ADHD-IV Scale	Group	Percentage of Participants with Elevation			p	V
		No Elevation	Subthreshold	Clinical		
Attention	No Epilepsy	50.0	26.7	23.3	0.248	0.26
	Epilepsy	20.0	40.0	40.0		
Hyperactivity	No Epilepsy	80.0	20.0	0.0	0.034*	0.42
	Epilepsy	40.0	50.0	10.0		

* = p<0.05; Blue = trending result (statistical significance lost when corrected for multiple comparisons).

Table 30. BRIEF T-Test Results for Comorbid Epilepsy

BRIEF Index	Diagnosis				t	df	p	Mean Diff	d
	No Epilepsy (*n* = 10)		Epilepsy (*n* = 30)						
	Mean T	(SD)	Mean T	(SD)					
Self-Control	49.92	(13.57)	56.67	(3.51)	-0.83	14	0.419	-6.74	0.68
Flexibility	50.77	(11.38)	55.00	(11.53)	-0.58	14	0.572	-4.23	0.37
Behavioral Regulation	51.18	(9.77)	55.14	(15.64)	-0.76	22	0.457	-3.97	0.30
Metacognition	54.93	(12.93)	58.40	(11.69)	-0.75	38	0.458	-3.47	0.28
Global Executive	50.30	(12.94)	55.50	(8.62)	-1.18	38	0.245	-5.20	0.47

3.4. Summary of Demographic, Lesion, and Clinical Findings

Table 31 summarizes all findings related to demographic and medical variable analyses within the current study.

Table 31. Summary of Demographic, Lesion, and Clinical Findings

Variable		Demographic Characteristics		Lesion Characteristics			Clinical Characteristics
		Age	Sex	Laterality	Volume	Stroke Location	Epilepsy
IQ					Larger < Smaller		Yes < No
NP Composite	Attention*						
	Working Memory	Older < Younger					Yes < No
	Verbal Fluency				Larger < Smaller		Yes < No
	Inhibitory Control				Larger < Smaller		Yes < No
	Flexibility/Shifting*						
	Plan/Organize*						Yes < No
	Processing Speed	Older < Younger			Larger < Smaller		Yes < No
ADHD-IV	Attention	Older < Younger	Male < Female		Larger < Smaller		
	Hyperactivity		Male < Female				Yes < No
BRIEF Indices	Self-Control						
	Flexibility						
	Behavioral Regulation						
	Metacognition	Older < Younger			Larger < Smaller		
	Global Executive	Older < Younger			Larger < Smaller		

White = No differences within the given variable
Dark Red = Statistically significant finding
Light Red = Statistical trend (statistical significance lost when corrected for multiple comparisons)

4. DISCUSSION

4.1 Findings and Implications

This study sought to determine whether children exhibit deficits in the domains of attention and executive functioning following PAIS and whether specific demographic, lesion, and/or clinical factors significantly impact cognitive outcome in these domains.

Convincing support was obtained suggesting that children with PAIS perform significantly lower on neuropsychological performance measures than normative populations. As predicted, mean composite scores on the performance-based neuropsychological tests of the PAIS group were significantly lower than normative population means on measures of general cognitive ability, attention, verbal retrieval inhibitory control, flexibility/shifting, planning/organization, and processing speed. Falling approximately 1.5 standard deviations below the normative mean, the most severe deficits were observed in inhibitory control for all children, with the added burden of deficits in both planning/organization and attention in older children (these domains were not measured in younger children). Moderate issues (i.e., falling approximately 0.75 to 1 standard deviations below the normative mean) were identified in processing speed across the group as well as in flexibility/shifting among older children and the most mild issues (i.e., falling approximately 0.5 standard deviations below the normative mean) were found in verbal retrieval skills across the group. Group differences were not significant on measures of working memory; however, as will be discussed, this finding may be an underestimate of impairment, with deficits not becoming apparent until later in development.

Additionally, as captured by parent report, children with PAIS demonstrated an

increased rate of ADHD symptoms—especially inattention—compared to the normal population. In contrast to the estimated 5% of children that meet criteria for ADHD in the general population (APA, 2013), 27.5% had clinical symptoms of inattention (and an additional 30% with subthreshold symptoms), aligning with previous studies (Everts et al., 2008; Max et al., 2002; Max, et al., 2003), and supporting our hypothesis that these symptoms are more prevalent in the PAIS population. We also examined the group for family history of ADHD, as this has been shown to be a risk factor in the development of the disorder. The three (7.5%) of our participants with a family history of ADHD in a first degree relative, all had elevated attention problems on the ADHD-IV rating scale (two with subthreshold elevations; one clinically elevated), suggesting that family history is an additional important consideration.

Moreover, children with clinically elevated parent-reported attention problems were significantly more impaired in certain parent-reported executive functioning domains including self-control, flexibility, behavioral regulation, metacognition, and overall global functioning compared to those with no elevations (on parent-based attention measures). Similar findings have been reported in prior work (Max et al., 2002; Mahone, et al., 2002; Pratt et al., 2000, cited in Gioia, Isquith, Guy, & Kenworthy, 2000b; Toplak, Bucciarelli, Jain, & Tannock, 2009). Our findings suggested that once children reach the subthreshold level of symptom elevation, they are at a similar risk of impairment in executive domains as those whose symptoms are considered to be in the range of clinical elevation.

While performance in the composite domains was correlated with FSIQ scores, Dennis et al. (2009) provide rationale for why IQ should not be a matching variable or a

statistical covariate in investigations of neurocognitive outcomes: doing so produces overcorrected, anomalous, and counterintuitive findings about neurocognitive functions. They argue that that IQ does not represent an independent domain of "intelligence," but rather represents the intersection (and perhaps union) of many different cognitive abilities, potentially including the cognitive faculty being tested by the experimental paradigm. Covarying for IQ therefore increases the risk of a Type II error. They also explain that, in the context of early brain insult and neurodevelopmental disorders, IQ is always confounded by the condition and cannot be separated from the effects of it. In line with this notion, our findings suggest that a slightly lower IQ is a consequence of PAIS (and hence connected to the disorder itself). Subsequently, controlling for IQ would reduce the impact and significance of PAIS as the independent variable, as has been reported as a limitation in other studies (e.g., Lee, Yeatman, Luna, & Feldman, 2011). Thus, as with cognitive studies preceding ours, we did not control for this variable in our analyses.

With regard to predictors of cognitive outcome, comorbid epilepsy, stroke volume, and age were associated both with poorer performance on standardized attention and executive functioning measures as well as greater functional problems reported by parents. Given that larger stroke volumes represent a greater insult to the brain, these findings are not surprising. Others have demonstrated a significant association between larger lesion volume and poor cognitive outcome in PAIS (Golomb et al., 2009; Hajek et al., 2013; Lee et al., 2005), and the literature is rich with examples of lesion volume negatively impacting cognitive outcomes in childhood stroke (as reviewed earlier). Such deficits are consistent with current models of executive functioning that suggest a wide

neural network support these skills (Gogtay et al., 2004; Stuss et al., 2002; Stuss et al., 1998), and also with findings of neuroimaging studies demonstrating that these neural networks are particularly diffuse in the immature brain (Tamm et al., 2002). Thus, larger lesions will inherently disrupt a wider network of neural connections, resulting in more negative cognitive outcomes and adversely affecting functional brain organization (Bava, Archibald, & Trauner, 2007).

The detrimental effects of epilepsy are also congruent with those documented in earlier studies (Ballantyne et al., 2008; Brinckman & Krivitzky, 2014; Chabrier et al. 2011; Golomb et al., 2009; Ricci et al., 2008; Wanigasinghe et al., 2010) and support the notion that the presence of seizures limits the brain's plasticity (and ability to compensate for the injury), resulting in a significantly altered course of cognitive development (Ballantyne et al., 2008). It is difficult to determine whether the observed differences between epilepsy and non-epilepsy groups are the result of the seizures themselves, anti-epileptic drugs (AED), or a combination thereof. However, only half of the epilepsy group (5/10 participants) were on medications at the time of testing, and comparison of outcomes between those medicated to those unmedicated revealed nonsignificant differences. Thus, the differences noted in the present study are likely (at least in part) related to the epilepsy itself rather than to medications used for treatment of seizures. With the added burden of a comorbid neurological condition that has been shown to have its own harmful effects on neuropsychological functioning (Bailet & Turk, 2000; Berg et al., 2008; Carreño Mar, Donaire Antonio, & Sánchez-Carpintero Rocío, 2008; Dam 1990; Kernan et al., 2012), the findings are not surprising. Yet, this study is the first to thoroughly examine the impact of epilepsy specifically on attention and executive

functioning (compared to global cognitive skills, i.e., IQ) in the PAIS population and suggests that children whom develop this diagnosis should be carefully monitored and screened for neurocognitive deficits.

Aside from the clear negative impact of neurological insult caused by larger strokes and epilepsy, findings from this study suggest that age is an influential factor in cognitive outcomes of PAIS. That is, children with a history of PAIS appear to "grow into" their deficits, regardless of what lesion or clinical risk factors they possess. While six of the seven domains did not show any effects of age, "real-world" parent-reported data revealed notable trends of increasing problems with inattentive symptoms, metacognition, and overall executive functioning skills with age. This finding may indicate that, regardless of age, children with PAIS exhibit global deficits in attention and executive functioning skills that might not be discovered (or become problematic) in everyday settings until they begin to grow older and have higher expectations placed upon them by parents and teachers. Similar findings have been reported in other clinical pediatric populations (Walsh et al., 2013).

Also notable is that, of the seven cognitive domains assessed via performance testing, working memory was the only one significantly impacted by age effects. While this domain did not result in a statistically significant problem area for the PAIS group as a whole, both parent and performance test data indicated that this domain is an increasing problem as children with PAIS age. Thus, it is possible that the Working Memory Composite score "washes out" problems in this domain when examined as a group mean and does not necessarily reflect the changes over time. In contrast, the other six domains appear to be impacted across the cohort overall and not necessarily by age.

One empirically supported explanation is that executive functioning demonstrates a prolonged developmental course with different skills emerging at different points in development. Working memory, specifically, becomes increasingly differentiated over the course of development, as evidenced by significant correlations between these measures in 6-year old children that were not evident in 9-year-old children (Tsujimoto, Kuwajima, & Sawaguchi, 2007). Further, while school-aged children are expanding the metacognitive ability to consciously monitor and control their own thinking processes (as well as experience an increased demand for these skills in their environment as discussed above), preschool-aged children have yet to develop these skills (Flavell, 1979; Flavell, Green, & Flavell, 1995) and therefore do not exhibit delayed skills in this particular domain, as such skills are not yet expected of them.

Ultimately, these results highlight the importance of informing teachers, families, and health professionals about the cognitive and behavioral manifestations of early brain lesions. In particular, findings emphasize that specific risk factors should be taken into consideration and that deficits may go undetected until the child reaches the appropriate age when specific skills typically mature or become more important in a child's environment. Moreover, given the range of cognitive challenges they may face following PAIS, children with a history of PAIS (especially those with one or more of the risk factors above) should undergo neuropsychological assessment (ideally including parent report, teacher report, and behavioral measures) to ensure implementation of appropriate interventions and environmental adjustments as early as possible.

4.2 Performance Testing Versus Parent Report

The relationship between parent report of attention and executive functioning and performance measures was somewhat complex, as evidenced in our exploratory analyses. While children with PAIS were broadly found to have difficulties in attention and executive functioning on both parent report and performance measures, few significant correlations were found when these two types of measures were directly compared. Similar null findings have been reported in other studies using different performance-based tasks of executive function (see McAuley, Chen, Goos, Schachar, & Crosbie, 2010 for a summary of studies with null findings). This is why we chose not to combine parent-report scores with performance test scores when calculating composite scores.

At present, reasons for the dissociation between parent ratings and scores on performance tasks of attention executive function are not fully understood. One interpretation is based on the premise that these measures assess different aspects of the same underlying construct. That is, performance tasks may assess underlying skills whereas parent questionnaires assess the application of those skills at home and/or school in a more functional way. It may be the case that environmental variables mediate this relationship, which would explain why children's scores on performance tasks do not necessarily correspond to parent ratings on the ADHD-IV and BRIEF; however this has not yet been addressed in the literature.

Another interpretation is that performance-based tasks of executive function lack ecological validity due to the manner in which they are typically administered. Testing usually occurs in environments that are designed to minimize distractions, maximize support, and provide individuals with a high degree of structure (e.g., clear instructions,

well-specified goals). Because these conditions bear little resemblance to the ones in which we typically function, it has been suggested that performance-based tasks do not engage the same set of skills that are required in naturalistic settings (Burgess, 1997).

It may also be the case that parents underestimate or underreport their child's deficits. Prior research has demonstrated difficulties with consistency in reporting executive functioning skills across settings. For example, parent report of attention and behavioral regulation has been shown to be inconsistent (in terms of symptom type and severity) with teacher report of these skills in studies of other clinical pediatric populations (Mares, McLuckie, Schwartz, & Saini, 2007; McCann, Rider, Weiss, Litman, & Baron, 2014; Scott, Taylor, Fristad, Klein, & Espy, 2012). It has been suggested that these inconsistencies may arise as a result of parent bias and/or differing levels of expectation and amount of supports provided in different settings (i.e., home vs. school/formal settings; Walsh et al., 2015; Wochos, Semerjian, & Walsh, 2014).

Ultimately, findings thus far (including our own) suggest that behavioral ratings may provide different information than performance measures, and that multiple sources of informant-based (i.e., both parent and perhaps teacher) and performance-based data are needed in order to make more accurate conclusions about functioning in these domains.

4.3 Limitations

Although this is the first study to thoroughly examine attention and executive functioning outcomes in children after PAIS as well as the impact of various medical and neurophysiological factors on these outcomes, there are some limitations to acknowledge. First, this study did not include an age and demographically matched control group.

Consequently, we compared the cognitive outcome of our study sample with child-specific, psychometrically robust age-standardized norms.

Another potential limitation is that, while our sample size is comparable to—or larger than—those of previous studies of children with PAIS, it was challenging to create proportionate subgroups for the examination of the medical variables, as these factors were difficult to control when recruiting. This limitation likely limited the power of group comparisons. Although many findings approached significance and suggested that different demographic, lesion, and clinical factors influence cognitive outcome in children with PAIS, larger subgroup sizes may have allowed for more clearly discernable effects. That said, our sample is representative of the typical population of children with PAIS (with respect to the distribution across demographic, lesion, and clinical variables). Further, whereas other studies have included a mixed population of various congenital and acquired brain injury, ours is comprised of a pure population of PAIS (that excludes hemorrhages and sinovenous thrombosis) with timing ascertained and no comorbid conditions. Although future studies with larger samples may have the power to more thoroughly explore these variables, they will likely require multi-center efforts to achieve the numbers to support these goals.

Additionally, although we intended to, we did not have a calculable Attention composite for children who were administered the preschool battery (ages 3-5), preventing us from being able to fully assess this domain in younger children. Related to this assessment issue, given the range of ages included in this study, we did not have neuropsychological measures that could be used across the entire cohort. This is expected, however, as younger children are not developmentally expected to have

developed the same skill set as older children. Subsequently, as much as possible, age-appropriate measures were utilized to assess equivalent skills in both age groups.

Finally, as previously discussed, the modASPECTs procedure can only be applied to the NAIS subgroup of the PAIS population whom have available acute scans. This is because the scoring system has only been validated on MRI with acute, diffusion-weighted imaging (DWI; imaging that is used to confirm a diagnosis of stroke within the preceding 7-10 days). Children with PPAIS do not have these sequences completed because their (presumed) stroke is "old" (i.e., beyond the 7-10 day window). Thus, as it stands modASPECTS scoring cannot be completed for PPAIS, hindering our ability to examine stroke volume as a risk factor in this group as well as preventing the comparison of stroke volume between PPAIS and NAIS subgroups. This is particularly limiting, as stroke volume appears to be a significant risk factor for cognitive outcome in PAIS.

Despite the above limitations, the results of the present study allow careful and well-reasoned statements about attention and executive functioning outcome after stroke.

4.4 Future Research and Directions

While the current study provides initial clues about the complex and subtle patterns attention and executive functioning deficits that exist in the PAIS, more research is needed to further refine our knowledge about outcomes in this population.

In addition to addressing the limitations discussed above, it would be useful to investigate the long-term cognitive effects of PAIS. Because many studies to this point (including the current one) have been cross-sectional, we can only generalize how age impacts cognitive functioning by comparing age groups. Moreover, there remain unanswered questions regarding how children with varying levels of cognitive outcomes

progress over time and how individual factors (i.e., the medical factors studied in the present study) impact an individual's development. Thus, longitudinal studies are needed to assess PAIS at multiple time points and provide insight into the long-term prognosis of perinatal stroke survivors.

Additionally, while the purpose of our study was to thoroughly assess attention and executive functioning outcomes after PAIS, future studies should examine outcomes in other important neuropsychological domains such as learning, memory, and visual-spatial skills, as these skills may be differentially affected. Formal (i.e., paper/pencil) testing of these skills may be particularly informative, given that parent report is not always a reliable *standalone* measure of cognitive skills (as this and other studies have found; discussed and cited above) and parents may be underreporting or fail to identify other neurocognitive deficits critical to development. Similarly, it will be important to examine how cognitive functioning translates into academic performance and functional impairment in other areas (e.g., social) in order to design effective remediation interventions, both in the home and academic settings. This is especially important, as recent studies suggest children may exhibit deficits in the classroom that are not observed on standardized tests (De Schryver et al., 2000), and therefore may be overlooked.

Finally, given the range of cognitive and behavioral challenges children may face following PAIS, development of effective interventions is necessary. Although intervention and rehabilitation studies for children with stroke are currently lacking, some insight can be gained from translational animal studies which have demonstrated that increased physical, social, and environmental stimulation can facilitate recovery in brain injured rats (Kolb et al., 2010). Moreover, Kolb et al. (2010) found that after one month

of increased environmental and tactile stimulation, injured rats exhibited improvements in cognitive, motor, and social functioning. The rats also exhibited signs of neurological recovery including increases in brain volume, synapses, and astrocytes. Based on these findings, Kolb et al. (2010) posited that because brain injury disrupts connections in neural networks, specific rehabilitation strategies (e.g., a combination of behavioral and physical therapy) may help repair or create new connections, leading to improved cognitive and behavioral outcomes. Subsequently, it has been suggested that intensive post-stroke physical therapy and massage may be viable translations of such "enriched environments" and "tactile stimulation" for humans (Kolb et al., 2010).

Similarly, studies of pediatric traumatic brain injury (TBI) suggest that the combination of behavioral, physical, psychological, and academic supports is advantageous post-injury. For example, family emotional and social support, large social networks, and physical activities seem to positively influence the course of functional recovery (Chapman & McKinnon, 2000). Additionally, interventions with speech/language therapists, physical therapists, and occupational therapists can help foster recovery following TBI. Adapted educational programming and academic support has also been shown to help this population of children adapt and cope with cognitive difficulties and learning problems (Lansing et al., 2004). Further, psychological counseling and behavioral therapy appears to facilitate recovery and alleviate stress for parents and children during the process (Chapman & McKinnon, 2000). While effective in pediatric TBI, it is unknown whether these findings can be generalized across the diverse population of children with PAIS. Thus, future research is needed to develop appropriate interventions tailored specifically for this population of children.

List of References

Alderson, R. M., & Mullins, L. L. (2011). Theoretical and clinical implications of using an ADHD framework to understand attention, concentration, and executive functioning deficits in pediatric cancer survivors. *Pediatr Blood Cancer, 57*(1), 4-5.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th Edition*. Washington, DC: American Psychiatric Association, 2013.

Armstrong-Wells, J., Johnston, S. C., Wu, Y. W., Sidney, S., & Fullerton, H. J. (2009). Prevalence and predictors of perinatal hemorrhagic stroke: results from the kaiser pediatric stroke study. *Pediatrics, 123*(3), 823-828.

Baddeley, A. D., & Hitch, G. J. (1974). *Working Memory*. In G. Bower (Ed.), The Psychology of Learning and Motivation (Vol. 8, pp. 47-90). New York: Academic Press.

Bailet, L. L., & Turk, W. R. (2000). The Impact of Childhood Epilepsy on Neurocognitive and Behavioral Performance: A Prospective Longitudinal Study. *Epilepsia*, *41*(4), 426-431.

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

Barkley, R. A. (2006). *Attention-deficit hyperactivity disorder: A handbook for diagnosis and treatment* (3rd ed.). New York: The Guilford Press.

Bava, S., Archibald, S. L., & Trauner, D. A. (2007). Brain structure in prenatal stroke: quantitative magnetic resonance imaging (MRI) analysis. *J Child Neurol, 22*(7), 841-847.

Berg, A. T., Langfitt, J. T., Testa, F. M., Levy, S. R., DiMario, F., Westerveld, M., & Kulas, J. (2008). Global cognitive function in children with epilepsy: A community□based study. *Epilepsia*, *49*(4), 608-614.

Beslow, L. A., Vossough, A., Dahmoush, H. M., Kessler, S. K., Stainman, R., Favilla, C. G., . . . Smith, S. E. (2012). Modified Pediatric ASPECTS Correlates with Infarct Volume in Childhood Arterial Ischemic Stroke. *Front Neurol, 3*(122), eCollection 2012. doi: 10.3389/fneur.2012.00122.

Braun, C. M., Montour-Proulx, I., Daigneault, S., Rouleau, I., Kuehn, S., Piskopos, M., . . . Rainville, C. (2002). Prevalence, and intellectual outcome of unilateral focal cortical brain damage as a function of age, sex and aetiology. *Behavioural Neurology, 13*(3-4), 105-116.

Brinckman, D., & Krivitzky, L. *The Impact of Epilepsy on Intellectual, Executive, and Behavioral Functioning in Pediatric Stroke*. Poster to be presented at the 2014 conference of the National Academy of Neuropsychology, Fajardo, PR.

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

Cappa, S. F., Papagno, C., & Vallar, G. (1990). Language and verbal memory after right hemisphere stroke: a clinical-CT scan study. *Neuropsychologia 28*(5), 503-509.

Carreño Mar, M. D., Donaire Antonio, M. D., & Sánchez-Carpintero Rocío, M. D. (2008). Cognitive Disorders Associated with Epilepsy: Diagnosis and Treatment. *The Neurologist*, *14*(6 Suppl 1), S26-S34.

Chabrier, S., Husson, B., Dinomais, M., Landrieu, P., & Nguyen The Tich, S. (2011). New insights (and new interrogations) in perinatal arterial ischemic stroke. *Thromb Res, 127*(1), 13-22.

Chadehumbe, M. A., Khatri, P., Khoury, J. C., Alwell, K., Szaflarski, J. P., Broderick, J. P., . . . Kleindorfer, D. O. (2009). Seizures are common in the acute setting of childhood stroke: a population-based study. *J Child Neurol, 24*(1), 9-12.

Chapman, S. B., Max, J. E., Gamino, J. F., McGlothlin, J. H., & Cliff, S. N. (2003). Discourse plasticity in children after stroke: age at injury and lesion effects. *Pediatr Neurol, 29*(1), 34-41.

Chapman, S. B., & McKinnon, L. (2000). Discussion of developmental plasticity: factors affecting cognitive outcome after pediatric traumatic brain injury. *J Commun Disord, 33*(4), 333-344.

Cnossen, M., Aarsen, F., Van Den Akker, S., Danen, R., Appel, I., Steyerberg, E., & Catsman-Berrevoets, C. (2010). Paediatric arterial ischaemic stroke: Functional outcome and risk factors. *Developmental Medicine and Child Neurology, 52*(4), 394-399.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences (2nd ed.).* Hillsdale, NJ: Erlbaum.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155-159.

Culbertson, W., & Zillmer, E. A. (2005). *TOL-DX Tower of London-Drexel University* (2nd ed.). Toronto, Ontario: Multi-Health Systems.

Dam, M. (1990). Children with epilepsy: the effect of seizures, syndromes, and etiological factors on cognitive functioning. *Epilepsia*, *31*(Suppl 4), S26-29.

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

De Schryver, E. L., Kappelle, L. J., Jennekens-Schinkel, A., & Boudewyn Peters, A.C. (2000). Prognosis of ischemic stroke in childhood: a long-term follow-up study. *Dev Med Child Neurol, 42*(5), 313-318.

deVeber, G. A., MacGregor, D., Curtis, R., & Mayank, S. (2000). Neurologic outcome in survivors of childhood arterial ischemic stroke and sinovenous thrombosis. *J Child Neurol, 15*(5), 316-324.

DuPaul, G. J., Power, T. J., Anastopoulos, A. D., & Reid, R. (1998). *ADHD Rating Scale IV: Checklists, norms, and clinical interpretation*. New York: Guilford.

Earley, C. J., Kittner, S. J., Feeser, B. R., Gardner, J., Epstein, A., Wozniak, M. A., . . . Buchholz, D. (1998). Stroke in children and sickle-cell disease: Baltimore-Washington Cooperative Young Stroke Study. *Neurology, 51*(1), 169-176.

Estan, J., & Hope P. (1997). Unilateral neonatal cerebral infarction in full term infants. Arch Dis *Child Fetal Neonatal Ed, 76*(2): F88-93.

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

Flavell, J. H. (1979). Metacognition and cognitive monitoring: A new area of cognitive-developmental inquiry. *American Psychologist, 34*(10), 906-911.

Flavell, J. H., Green, F. L., & Flavell, E. R. (1995). Young children's knowledge about thinking. Monographs of the Society for Research in Child Development 60(1), Serial No. 243.

Flavell, J. H., Green, E L., Flavell, E. R., & Grossman, J. B. (1997). The development of children's knowledge about inner speech. *Child Development, 68*(1), 39-47.

Fox, C. K., Glass, H. C., Sidney, S., Lowenstein, D. H., & Fullerton, H. J. (2013). Acute seizures predict epilepsy after childhood stroke. *Ann Neurol*. [Epub ahead of print].

Ganesan, V., Hogan, A., Shack, N., Gordon, A., Isaacs, E., & Kirkham, F. J. (2000). Outcome after ischaemic stroke in childhood. *Dev Med Child Neurol, 42*(7), 455-461.

Ganesan, V., Prengler, M., McShane, M. A., Wade, A. M., & Kirkham, F. J. (2003). Investigation of risk factors in children with arterial ischemic stroke. *Ann Neurol, 53*(2), 167-173.

Gaub, M., & Carlson, C. L. (1997). Gender differences in ADHD: a meta-analysis and critical review. *J Am Acad Child Adolesc Psychiatry, 36*(8), 1036-1045.

Gerring, J. P., Brady, K. D., & Chen, A., (1998). Premorbid prevalence of ADHD and development of secondary ADHD after closed head injury. *J Am Acad Child Adolesc Psychiatry, 37*(6), 647-654.

Gerring, J., Brady, K., & Chen, A. (2000). Neuroimaging variables related to development of secondary attention deficit hyperactivity disorder after closed head injury in children and adolescents. *Brain Inj, 14*(3), 205-218.

Gioia, G. A., Espy, K. A., & Isquith, P. K. (2003). *The Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P).* Odessa , FL: Psychological Assessment Resources.

Gioia, G.A., & Isquith, P.K. (2004). Ecological assessment of executive function in traumatic brain injury. *Developmental Neuropsychology, 25*(1&2), 135-158.

Gioia, G. A., Isquith, P. K., Guy, S. C., Kenworthy, L. (2000a). *The Behavior Rating Inventory of Executive Function-Parent Form (BRIEF)*. Odessa, Fl: Psychological Assessment Resources.

Gioia, G.A., Isquith, P.K., Guy, S.C., & Kenworthy, L. (2000b). *The behavior rating inventory of executive function. Professional manual*. Lutz, FL: Psychological Assessment Resources.

Giroud, M., Lemesle, M., Gouyon, J. B., Nivelon, J. L., Milan, C., & Dumas, R. (1995). Cerebrovascular disease in children under 16 years of age in the city of Dijon, France: a study of incidence and clinical features from 1985 to 1993. *J Clin Epidemiol, 48*(11), 1343-1348.

Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., . . . Thompson, P. M. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci USA, 101*(21), 8174-8179.

Golomb M. R. (2009). Outcomes of perinatal arterial ischemic stroke and cerebral sinovenous thrombosis. *Semin Fetal Neonatal Med, 14*(5), 318-322.

Golomb, M. R., MacGregor, D. L., Domi, T., Armstrong, D. C., McCrindle, B. W., Mayank, S., & deVeber, G. A. (2001). Presumed pre- or perinatal arterial ischemic stroke: risk factors and outcomes. *Ann Neurol, 50*(2), 163-168.

Goodman, R., & Yude, C. (1996). IQ and its predictors in childhood hemiplegia. *Developmental Medicine and Child Neurology, 38*(10), 881-890.

Gordon, H. W. (1986). The cognitive laterality battery: Tests of specialized cognitive function. *International Journal of Neuroscience, 29*(3-4), 223-244.

Hajek, C. A., Yeates, K. O., Anderson, V., Mackay, M., Greenham, M., Gomes, A., & Lo, W. (2013). Cognitive Outcomes Following Arterial Ischemic Stroke in Infants and Children. *J Child Neurol.* [Epub ahead of print].

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform, 42*(2), 377-381.

Hartel, C., Schilling, S., Sperner, J., & Thyen, U. (2004). The clinical outcomes of neonatal and childhood stroke: review of the literature and implications for future research. *Eur J Neurol, 11*(7), 431-438.

Hetherington, R., Tuff, L., Anderson, P., Miles, B., & deVeber, G. (2005). Short-term intellectual outcome after arterial ischemic stroke and sinovenous thrombosis in childhood and infancy. *J Child Neurol, 20*(7), 553-559.

Herskovits, E. H., Megalooikonomou, V., & Davatzikos, C. (1999). Is the spatial distribution of brain lesions associated with closed-head injury predictive of subsequent development of attention-deficit/hyperactivity disorder? Analysis with brain-image database. *Radiology, 213*(2), 389-394

IBM Corp. Released 2013. IBM SPSS Statistics for Mac OS, Version 22.0. Armonk, NY: IBM Corp.

Kernan, C. L., Asarnow, R., Siddarth, P., Gurbani, S., Lanphier, E. K., Sankar, R., & Caplan, R. (2012). Neurocognitive profiles in children with epilepsy. *Epilepsia*, *53*(12), 2156-2163.

Kirton, A. & deVeber, G. (2006). Cerebral palsy secondary to perinatal ischemic stroke. *Clinics in Perinatology, 33*(2), 367-386.

Kirton, A. & deVeber, G. (2013). Life After Perinatal Stroke. *Stroke, 44*(11), 3265-3271.

Kirton, A., deVeber, G., Pontigon, A. M., Macgregor, D., & Shroff, M. (2008). Presumed perinatal ischemic stroke: vascular classification predicts outcomes. *Ann Neurol, 63*(4), 436-443.

Kolb, B., & Gibb, R. (2007). Brain plasticity and recovery from early cortical injury. *Dev Psychobiol, 49*(2), 107-118.

Kolk, A., Ennok, M., Laugesaar, R., Kaldoja, M. L., & Talvik, T. (2011). Long-term cog□nitive outcomes after pediatric stroke. *Pediatr Neurol, 44*(2), 101-109.

Korkman, M., Kirk, U., & Kemp, S. (2007). *NEPSY: Second Edition (NEPSY-II)*. San Antonio, TX: Pearson.

Lansing A. E., Max, J. E., Delis, D. C., Fox, P. T., Lancaster, J., Manes, F. F., & Schatz, A. (2004). Verbal learning and memory after childhood stroke. *J Int Neuropsychol Soc, 10*(5), 742-752.

Lee, J., Croen, L. A., Lindan, C., Nash, K. B., Yoshida, C. K., Ferriero, D. M., . . . Wu, Y. W. (2005). Predictors of outcome in perinatal arterial stroke: a population-based study. *Ann Neurol, 58*(2), 303-308.

Lee, J. C., Lin, K. L., Wang, H. S., Chou, M. L., Hung, P. C., Hsieh, M. Y., . . . Wong, A. M. (2008). Seizures in childhood ischemic stroke in Taiwan. *Brain Dev, 31*(4), 294-299.

Lee, E. S., Yeatman, J. D., Luna, B., & Feldman, H. M. (2011). Specific language and reading skills in school-aged children and adolescents are associated with prematurity after controlling for IQ. *Neuropsychologia, 49*(5), 906-913.

Long, B., Anderson, V., Jacobs, R., Mackay, M., Leventer, R., Barnes, C., & Spencer-Smith. M. (2011). Executive function following child stroke: the impact of lesion size. *Dev Neuropsychol, 36*(8), 971-987.

Lynch, J. K., Hirtz, D. G., deVeber, G., & Nelson, K. B. (2002). Report of the National Institute of Neurological Disorders and Stroke workshop on perinatal and childhood stroke. *Pediatrics, 109*(1), 116-123.

Mahone, M. E., Cirino, P. T., Cutting, L. E., Cerrone, P. M., Hagelthorn, K. M., Hiemenz, J. R., . . . Denckla, M. B. (2002). Validity of the behavior rating inventory of executive function in children with ADHD and/or Tourette syndrome. *Archives of Clinical Neuropsychology*, *17*(7), 643-662.

Mares, D., McLuckie, A., Schwartz, M., & Saini, M. (2007). Executive function impairments in children with attention-deficits hyperactivity disorder: Do they differ between home and school environments?. *The Canadian Journal of Psychiatry, 52*(8), 527-534.

Max, J. E., Arndt, S., Castillo, C. S., Bokura, H., Robin, D. A., Lindgren, S. D., . . . Mattheis, P. J. (1998). Attention-deficit hyperactivity symptomatology after traumatic brain injury: a prospective study. *J Am Acad Child Adolesc Psychiatry, 37*(8), 841-847.

Max, J. E., Lansing, A. E., Koele, S. L., Castillo, C. S., Bokura, H., Schachar, R., . . . Williams, K.E. (2004). Attention deficit hyperactivity disorder in children and adolescents following traumatic brain injury. *Dev Neuropsychol 25*(1-2),159-177.

Max, J. E., Mathews, K., Lansing, A. E., Robertson, B. A., Fox, P. T., Lancaster, J. L., . . . Smith, J. (2002). Psychiatric disorders after childhood stroke. *J Am Acad Child Adolesc Psychiatry, 41*(5), 555-562.

Max J. E., Mathews, K., Manes, F. F., Robertson, B. A., Fox, P. T., Lancaster, J. L., . . . Collings N. (2003). Attention deficit hyperactivity disorder and neurocognitive correlates after childhood stroke. *J Int Neuropsychol Soc, 9*(6), 815-829.

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

McCann, J. P., Rider, G. N., Weiss, B. A., Litman, F. R., & Baron, I. S. (2014). Latent mean comparisons on the BRIEF in preterm children: parent and teacher differences. *Child Neuropsychol, 20*(6), 737-751.

McGoey, K. E., DuPaul, G. J., Haley, E., & Shelton, T. L. (2007). Parent and Teacher Ratings of Attention-Deficit/Hyperactivity Disorder in Preschool: The ADHD Rating Scale-IV Preschool Version. *J Psychopathol Behav Assess, 29*(4), 269-276.

McLinden, A., Baird, A. D., Westmacott, R., Anderson, P. E., & deVeber, G. (2007). Early cognitive outcome after neonatal stroke. *J Child Neurol, 22*(9), 1111-1116.

Muir-Broaddus, J. E., Rosenstein, L. D., Medina, D. E., & Soderberg, C. (2002). Neuropsychological test performance of children with ADHD relative to test norms and parent behavioral ratings. *Arch Clin Neuropsychol, 17*(7), 671-689.

Muter, V., Taylor, S., & Vargha-Khadem, F. (1997). A longitudinal study of early intellectual development in hemiplegic children. *Neuropsychologia, 35*(3), 289-298.

Nelson, K. B., & Lynch, J. K. (2004). Stroke in newborn infants. Lancet Neurol, 3(3), 150-158.

Pavlovic, J., Kaufmann, F., Boltshauser, E., Capone Mori, A., Gubser Mercati, D., . . . Steinlin, M. (2006). Neuropsychological problems after paediatric stroke: two year follow-up of Swiss children. *Neuropediatrics, 37*(1), 13-9.

Pfefferbaum, A., Mathalon, D. H., Sullivan, E. V., Rawles, J. M., Zipursky, R. B., & Lim, K. O. (1994). A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. Arch Neurol, 51(9), 874-887.

Pickering S. J., & Gathercole S. E. (2001). *Working Memory Test Battery for Children (WMTB-C)*. London: The Psychological Corporation, 2001.

Reitan, R. M. (1958). Validity of the Trail-Making Test. *Perceptual and Motor Skills*, 8, 271-276.

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

Sandberg, S. (2002). *Hyperactivity and attention disorders of childhood* (2nd ed.). Cambridge, England: Cambridge University Press.

Scott, M. N., Taylor, H. G., Fristad, M. A., Klein, N., Espy, K. A., Minich, N., & Hack, M. (2012). Behavior Disorders in Extremely Preterm/Extremely Low Birth Weight Children in Kindergarten: *Journal of Developmental & Behavioral Pediatrics*, *33*(3), 202-213.

Singh, R. K., Zecavati, N., Singh, J., Kaulas, H., Nelson, K. B., Dean, N. P., . . . Carpenter, J. (2012). Seizures in acute childhood stroke. *J Pediatr, 160*(2), 291-296.

Studer, M., Boltshauser, E., Capone Mori, A., Datta, A., Fluss, J., Mercati, D., . . . Steinlin, M. (2014). Factors affecting cognitive outcome in early pediatric stroke. *Neurology, 82*(9), 784-792.

Stuss, D., Alexander, M., Floden, D., Binns, M., Levine, B., McIntosh, A. R., . . . Hevenor, S. J. (2002). Fractionation and localization of distinct frontal lobe processes: Evidence from focal lesions in humans. In D. Stuss & R. Knight (Eds.), *Principles of frontal lobe function* (pp. 392-407). New York, NY: Oxford University Press.

Stuss, D., Alexander, M., Hamer, L., Palumbo, C., Dempster, R., Binns, M., . . . Izukawa, D. (1998). The effects of focal anterior and posterior brain lesions in verbal fluency. *Journal of the International Neuropsychological Society*, *4*(3), 265-278.

Tamm, L., Menon, V., & Reiss, A. L. (2002). Maturation of brain function associated with response inhibition. *Journal of the American Academy of Child and Adolescent Psychiatry*, *41*(10), 1231-1238.

Tillema, J. M., Byars, A. W., Jacola, L. M., Schapiro, M. B., Schmithorst, V. J., Szaflarski, J. P., & Holland, S. K. (2008). Reprint of "Cortical reorganization of language functioning following perinatal left MCA stroke" [Brain and Language 105 (2008) 99-111]. *Brain Lang, 106*(3), 184-194.

Toplak, Bucciarelli, Jain, & Tannock. (2009). Executive functions: performance-based measures and the behavior rating inventory of executive function (BRIEF) in adolescents with attention deficit/hyperactivity disorder (ADHD). *Child Neuropsychol, 15*(1), 53-72.

Tsujimoto, S., Kuwajima, M., & Sawaguchi, T. (2007). Developmental fractionation of working memory and response inhibition during childhood. *Exp Psychol, 54*(1), 30-37.

U.S. Census Bureau. (2014). *Educational Attainment of the Population 25 Years and Over, by Selected Characteristics: 2014*. Retrieved from http://www.census.gov/hhes/socdemo/education/data/cps/2014/tables.html.

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

Vriezen & Pigott. (2002). The relationship between parental report on the BRIEF and performance-based measures of executive function in children with moderate to severe traumatic brain injury. *Child Neuropsychol, 8*(4),296-303.

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

Wanigasinghe, J., Reid, S. M., Mackay, M. T., Reddihough, D. S., Harvey, A. S., & Freeman, J. L. (2010). Epilepsy in hemiplegic cerebral palsy due to perinatal arterial ischaemic stroke. *Dev Med Child Neurol, 52*(11), 1021-1027.

Wechsler, D. (2011). *Wechsler Abbreviated Scale of Intelligence—Second Edition (WASI-II)*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2012). *Wechsler Preschool and Primary Scale of Intelligence—Fourth Edition (WPPSI-IV)*. Bloomington, MN: Pearson.

Westmacott, R., MacGregor, D., Askalan, R., & deVeber, G. (2009). Late emergence of cognitive deficits after unilateral neonatal stroke. Stroke, 40(6), 2012-2019.

Westmacott, R., Askalan, R., MacGregor, D., Anderson, P., & deVeber, G. (2010). Cognitive outcome following unilateral arterial ischaemic stroke in childhood: effects of age at stroke and lesion location. *Dev Med Child Neurol, 52*(4), 386-393.

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

Wu, Y. W., Lynch, J. K., & Nelson, K.B. (2005). Perinatal arterial stroke: understanding mechanisms and outcomes. *Semin Neurol, 25*(4), 424-34.

Wulfeck, B. B., Trauner, D. A., & Tallal, P. A. (1991). Neurologic, cognitive, and linguistic features of infants after early stroke. *Pediatr Neurol, 7*(4), 266-269.

Wusthoff, C. J., Kessler, S. K., Vossough, A., Ichord, R., Zelonis, S., Halperin, A., . . . Smith, S. E. (2011). Risk of later seizure after perinatal arterial ischemic stroke: a prospective cohort study. *Pediatrics, 127*(6), e1550-e1557.

Danielle D. Bosenbark, M.S.

787 Reading Court, West Chester, PA 19380
Phone: (215) 895-5854 • danielle.bosenbark@gmail.com

EDUCATION

Sept 2011 – Present	**Drexel University**, Philadelphia, PA Doctoral Program in Clinical Psychology Clinical Neuropsychology, Major Area of Study M.S. Clinical Psychology, October 2013 *"An fNIRS Study of the Effects of Medication on Cognitive Functioning and Cerebral Hemodynamics in Adults with Attention-Deficit/Hyperactivity Disorder"* Anticipated Graduation Date: June 2016 Mentors: Maria Schultheis, Ph.D., Jennifer Gallo, Ph.D.
Aug 2005 – May 2009	**The Pennsylvania State University**, University Park, PA B.S., *with High Distinction*, Science, Life Science Option, May 2009 Minors: Neuroscience, Psychology GPA: 3.97

ACADEMIC HONORS & AWARDS

2014	Philadelphia Neuropsychology Society & Clinical Neuropsychology Associates John E. Gordon Dissertation Award *$1,500 awarded for dissertation research.*
2011 – 2013	Drexel University Dean's Fellowship
2009	Eberly College of Science Student Marshal of the Science Major *Awarded to graduating Science major with the highest cumulative GPA.*
2008	Dunning Scholarship in Science
2008	Ruth E. Duffy Endowment Scholarship
2007 – 2009	National College Scholars Honor Society
2007 – 2009	Karl K. and Anna M. Gottshalk Memorial Scholarship
2005 – 2009	Dean's List (all semesters)
2005	The President's Freshman Award *Awarded to freshman students with 4.0 GPA.*

CLINICAL EXPERIENCE

July 2013 – May 2015 **Clinical Psychology Extern**
Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE
Supervisor: Rochelle Glidden, Psy.D.

- Administration and scoring of neurodevelopmental, neuropsychological, and psychological evaluations for children and adolescents aged 5-16
- Integrative report writing
- Intake and feedback sessions with parents and children and adolescents

July 2013 – May 2015 **Clinical Psychology Extern**
Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE
Supervisor: Erica Sood, Ph.D.

- Psychological consultation and therapy for children and adolescents (ages 5-16) with a variety of behavior- and mood disorders
- Development of treatment plans to improve referring problem
- Regular follow-up with children/adolescents and their families to maintain and adjust interventions

July 2013 – June 2014 **Neuropsychology Extern**
Jefferson Hospital for Neuroscience, Philadelphia, PA
Supervisors: Joseph Tracy, Ph.D., ABPP-CN; Jennifer Tinker, Ph.D.
Administered neuropsychological test batteries to adults aged 18-80 in both outpatient and inpatient settings. Scored and interpreted test results, wrote integrated reports, progress notes, observed intake interviews and feedback sessions. Also attended weekly case conferences focused on pre-surgical epilepsy patients.

- Administration and scoring of neuropsychological evaluations for adolescents and adults aged 16-80
- Integrative report writing
- Intake and feedback sessions with patients and families
- Weekly case conferences focused on pre-surgical epilepsy patients

July 2012 – June 2013 **Neuropsychology Extern**
The Children's Hospital of Philadelphia, Philadelphia, PA
Supervisor: Lauren Krivitzky, Ph.D., ABPP-Cn
Administered neuropsychological test batteries to children aged 4-18 in an outpatient setting. Scored and interpreted test results, wrote integrated reports, progress notes, observed intake interviews and feedback sessions.

- Administration and scoring of neuropsychological tests for children with medical conditions
- Integrative report writing
- Intake and feedback sessions with parents and children and adolescents
- Weekly case conferences focused on pediatric stroke
- Weekly pediatric neuropsychology seminars

Oct 2009 – June 2011 **Psychology Technician/Clinical Assistant**
The National Institute of Neurological Disorders and Stroke,
The National Institutes of Health, Bethesda, MD
Supervisor: Edythe Wiggs, Ph.D.

- Administration and scoring of clinical functional evaluations and neuropsychological tests for research participants (ages 2-80) with deficits in cognitive functioning participating in a variety of NIH protocols
- Brief research report writing
- Consultation with Neurology and pre-surgical teams
- Conducted Wada testing

RESEARCH EXPERIENCE

Doctoral Dissertation	**Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke** Investigating and describing the profile of attention and executive functioning in children following perinatal stroke; examining the influence of medical and demographic factors on attention and executive functioning outcomes in children following perinatal stroke. Proposal of Dissertation: May 2014 (completed) Committee Chair: Maria T. Schultheis, Ph.D. Committee Members*:* Jennifer Gallo, Ph.D., Lauren Krivitzky, Ph.D., ABPP-CN, Lori Billinghurst, M.D., Brian Daly, Ph.D. Dissertation Status: IRB approved; Ongoing data collection
Master's Thesis	**An fNIRS Study of the Effects of Medication on Cognitive Functioning and Cerebral Hemodynamics in Adults with Attention-Deficit/Hyperactivity Disorder** Compared differences in cognition and neurophysiology between adults with ADHD (when unmedicated) and healthy controls; compared differences in cognition and neurophysiology between medicated and unmedicated states in adults with ADHD. Investigated the potential application of fNIRS as an assessment tool for both diagnostic and monitoring purposes. Defense of Thesis: October 2013 (completed) Committee Chair: Maria T. Schultheis, Ph.D. Committee Members*:* Jennifer Gallo, Ph.D., Anna Rodriquez, Ph.D., Edward Moss, Ph.D.
Sept 2011 – Present	**Graduate Research Assistant** **Applied Neuro-Technologies Laboratory** **Drexel University, Philadelphia, PA** Supervisors: Maria Schultheis, Ph.D. and Jennifer Gallo, Ph.D. • Data collection, data analysis, supervision of research assistants, development of research projects, and manuscript preparation
June 2009 – June 2011	**Research Coordinator/Associate Investigator** **The National Human Genome Research Institute, Genetics Disease Research Branch, Human Development Section** **The National Institutes of Health, Bethesda, MD** Supervisors**:** Leslie Biesecker, M.D.; Julie Chevalier Sapp, ScM, CGC • Coordination of recruitment, enrollment, consent, neuropsychological testing, DNA and tissue acquisition, and database management of multiple research studies involved in comparison of clinical, neuropsychological, genetic, and neuroimaging data in patients with various genetic syndromes • Participation in the development, start-up, and data collection phases of a new protocol • Manuscript preparation

May 2008 – May 2009 **Research Assistant**
The Penn State Brain Development Laboratory
The Pennsylvania State University, State College, PA
Supervisor: Rick Gilmore, Ph.D.

- EEG technician
- Administration of vision screens and computerized visual tasks to research participants for studies focused on motion contrast in vision
- Supervision and training of junior research assistants
- Data collection, coding, and analysis
- Manuscript preparation

May 2007 – Aug 2008 **Research Assistant**
The Unit for Experimental Psychiatry
The University of Pennsylvania School of Medicine, Philadelphia, PA
Supervisor: David Dinges, Ph.D.

- EEG and EOG technician
- Administration of computerized simulations, reaction time measures, and cognitive tasks for a variety of research protocols involved in sleep deprivation and it's effect on cognition, motor skills, and emotion
- Supervision and training of junior research assistants
- Data collection, coding, and analysis

PEER-REVIEWED MANUSCRIPTS

Keppler-Noreuil, K. M., Blumhorst, C., Sapp, J. C., **Brinckman, D.**, Johnston, J., Nopoulos, P. C., & Biesecker, L. G. (2011). Brain tissue- and region-specific abnormalities on volumetric MRI scans in 21 patients with Bardet-Biedl syndrome (BBS). *BMC Medical Genetics, 12*(1), 101-109. doi:10.1186/1471-2350-12-101.

Fesi, J. D., Yannes, M. P., **Brinckman, D. D.**, Norcia, A. M., Ales, J. M., & Gilmore, R. O. (2011). Distinct cortical responses to 2D figures defined by motion contrast. *Vision Research*, *51*(19), 2110-2120. doi:10.1016/j.visres.2011.07.015

Brinckman, D. D., Keppler-Noreuil, K. M., Blumhorst, C., Biesecker, L. G., Sapp, J. C., Johnston, J. J., & Wiggs, E. A. (2013). Cognitive, sensory, and psychosocial characteristics in patients with Bardet-Biedl syndrome. *Am J Med Genet A, 61*(12), 2964-2971. doi: 10.1002/ajmg.a.36245.
Featured publication in AJMG sequence article 2013 43:123.

Daly, B. P., Nicholls, E. G., Patrick, K., **Brinckman, D. D**., & Schultheis, M. T. (2014). Driving Behaviors in Adults with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, *44*(12), 3119-3128.

Osipowicz, K., **Bosenbark, D.,** & Patrick, K. (2015). Cortical Changes Across the Autism Lifespan. *Journal of Autism Research.* doi: 10.1002/aur.1453.

Schultheis, M. T., Sunderaraman, P., Patrick, K., **Bosenbark, D.**, & Vickers, K. (submitted) Examination of Driving in Young Adults After Concussion. *Neurology.*

PEER-REVIEWED MANUSCRIPTS IN PREPARATION

Bosenbark, D. D. & Schultheis, M. T. An fNIRS Study of the Effects of Medication on Cognitive Functioning and Cerebral Hemodynamics in Adults with Attention-Deficit/Hyperactivity Disorder. *Journal of Attention Disorders.*

Bosenbark, D. D., Schultheis, M. T., Weisser, V., & Merzagora, A. Diurnal Rhythms and fNIRS: Does The Time of Day Matter? An Exploratory Study. *Neurorehabilitation*.

Keppler-Noreuil, K. M., **Bosenbark, D.**, Wiggs, E., Blumhorst, C., Sapp, J.C., Johnston, J., Nopoulos, P. C., & Biesecker, L. G. Characteristic Brain Abnormalities Correlate with Neurodevelopmental Findings in 29 patients with Bardet-Biedl Syndrome. *BMC Medical Genetics.*

Manning, K. J., Gallo, J. L., Williams, R., Seligman, S., **Bosenbark, D. D.**, & Moberg, P. J. Impact of Subjective Cognitive Impairment on Neuropsychological Performance and Cognitive Decline in Older Adults Without Dementia: A Meta-Analysis.

Schultheis, M. T., **Bosenbark, D.**, & Patrick, K. Reliability of a Virtual Reality Driving Simulator for Neurological Populations. *Cyberpsychology*.

Vickers, K., **Bosenbark, D.**, & Schultheis, M. T. What Virtual Reality Can Teach Us About Driving Fitness After TBI. *The Journal of Head Trauma Rehabilitation*.

BOOK CHAPTERS

Krivitzky, L., & **Bosenbark, D.** (in preparation). Behavioral and Emotional Functioning. In H. Atkinson, K. Nixon-Cave, & S. Smith (Eds.), *Pediatric Stroke Rehabilitation: An Interprofessional and Collaborative Approach*. Thorofare, NJ: SLACK Incorporated.

PUBLISHED ABSTRACTS

Brinckman, D., Schultheis, M. T., Ehrhart, L. Weisser, V., Medaglia, J., & Merzagora, A. (2012). Demonstration of Diurnal Patterns of Brain Activity Using fNIRS. *Archives of Clinical Neuropsychology, 27*(6), 575. Presented at the 32nd annual conference of the National Academy of Neuropsychology, Nashville, TN.

Iampietro, M., Krivitzky, L. & **Brinckman, D.** (2013). Memory functioning in Pediatric Stroke Survivors. *Journal of the International Neuropsychological Society, 19*(S1), 23. Presented at the 41st Annual Conference of the International Neuropsychological Society, Waikoloa, HI.

Brinckman, D., Ayaz, H., & Schultheis, M. T. Working Memory Performance and fNIRS Activation: Does ADHD Make a Difference? (2013). *Archives of Clinical Neuropsychology, 28*(6), 435. Presented at the 33rd Annual Conference of the National Academy of Neuropsychology, San Diego, CA.

Schultheis, M. T., Whipple, E., & **Brinckman, D**. (2014). Cognition and driving in multiple sclerosis. *Journal of the International Neuropsychological Society, 20*(S1). Presented at the 42nd Annual Meeting of the International Neuropsychological Society, Seattle, WA.

Brinckman, D. D. & Schultheis, M.T. (2014). An fNIRS study of the effects of medication on cognitive functioning and cerebral hemodynamics in adults with Attention-Deficit Hyperactivity Disorder. *The Clinical Neuropsychologist.* Presented at the 12th Annual Conference of the American Academy of Clinical Neuropsychology, New York, NY.

Brinckman, D. & Krivitzky, L. (2014). The Impact of Epilepsy on Intellectual, Executive, and Behavioral Functioning in Pediatric Stroke. *Archives of Clinical Neuropsychology, 29*(6), 553-554. Presented at the 34th Annual Conference of the National Academy of Neuropsychology, Fajardo, PR.

Patrick, K. E., Agate, F. T., **Bosenbark, D. D.,** Hurewitz, F., & Schultheis, M. T. (2015). Driving behaviors of young adults with autism spectrum disorder. *Journal of International Neuropsychology Society, 21*(S1). Poster presented at the 43rd Annual Conference of the International Neuropsychology Society, Denver, CO.

Krivitzky, L. & **Bosenbark, D. D.** (2015). Pediatric Stroke: A Prime Example of the Challenge of Studying EF Skills in Heterogeneous Pediatric Disorders. *Journal of International Neuropsychology Society, 21*(S1). Poster presented at the 43rd Annual Conference of the International Neuropsychology Society, Denver, CO.

Bosenbark, D.D., Krivitzky, L., Jastrzab, L., Ichord, R., & Billinghurst, L. (2015). Impact of Epilepsy on Attention, Intellectual, and Executive Functioning in Children with Perinatal Arterial Ischemic Stroke. Poster presented at the 44th Annual Meeting of the Child Neurology Society, Washington, DC.

WORKSHOPS AND SYMPOSIA

Keppler-Noreuil, K. M., **Brinckman, D.**, Wiggs, E., Blumhorst, C., Sapp, J. C., Johnston, J., Nopoulos, P. C., & Biesecker, L. G. (2011). *Brain abnormalities on volumetric MRI scans in 21 patients with Bardet-Biedl syndrome (BBS) correlate with neurodevelopmental findings*. Platform presentation at the 2011 David W. Smith Workshop on Malformations and Morphogenesis, Lake Arrowhead, CA.

CONFERENCE PRESENTATIONS (NON-ARCHIVED)

Yannes, M., **Brinckman, D.,** Klemencic, J., Fesi, J. D., & Gilmore, R. O. (2009). *The Use of SSVEP in Understanding Motion Form*. Poster presented at the 2009 Undergraduate Research Exhibition, The Pennsylvania State University, State College, PA.

McGrath, M. C. Irani, F., Rodriguez Merzagora, A. C., **Brinckman, D.**, & Schultheis, M. T. (2012). *Examining Resting State Functional Activity in the Medial Prefrontal Cortex Using fNIRS: A "Proof-of-Concept" Study*. Poster presented at the 2012 Conference of Functional Near Infrared Spectroscopy, London, UK.

Schultheis, M. T., Nicholls, E., **Brinckman, D.**, & Daly, B. P. (2013). *Driving Behaviors in Individuals with Autism Spectrum Disorders*. Poster presented at the 15th Annual Conference of Rehabilitation Psychology, Jacksonville, FL.

Keppler-Noreuil, K. M., **Brinckman, D.**, Wiggs, E., Blumhorst, C., Sapp, J. C., Johnston, J., Nopoulos, P.C., & Biesecker, L.G. (2013). *Characteristic Brain Abnormalities Correlate with Neurodevelopmental Findings in 29 patients with Bardet-Biedl Syndrome*. Poster presented at the 2013 Annual Conference of the American College of Medical Genetics, Phoenix, AZ.

OTHER PUBLICATIONS/EDITOR-REVIEWED ARTICLES

Brinckman, D. (2013). Just Keep Swimming: Aquatic Advice For Coping with Amnesia. [Review of the Film Finding Nemo, 2003]. Retrieved from http://www.neuropsyfi.com/6/post/2013/04/finding-nemo.html.

GRANTS SUBMITTED

Year	Title	Organization	Amount
2013	**Young Scientist Research Fund Awards** Project Title: "An fNIRS Study of the Effects of Medication on Cognitive Functioning and Cerebral Hemodynamics in Adults with Attention-Deficit/Hyperactivity Disorder"	Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)	$5000
2014	**2014 Thesis and Dissertation Awards** Project Title: "Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke"	Division 40: Society for Clinical Neuropsychology	$1000
2014	**The Emily Reid O'Connor Memorial Endowed Fellowship Fund** Project Title: "Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke"	Drexel University Department of Psychology	$5000
2014	**APA Dissertation Research Award** Project Title: "Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke"	The American Psychological Association (APA)	$1000
2014	**2015 Thesis and Dissertation Awards** Project Title: "Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke"	Division 40: Society for Clinical Neuropsychology	$1000
2014	**SSCP Dissertation Grant Award**	Society for a Science of	$500

	Project Title: "Attention and Executive Functioning Profiles in Children Following Perinatal Arterial Ischemic Stroke"	Clinical Psychology	

PROFESSIONAL MEMBERSHIPS

2014 – Present	Association for Psychological Science (APS)
2013 – Present	Society for a Science of Clinical Psychology (SSCP)
2012 – Present	American Psychological Association (APA) Division 40: Neuropsychology/Society for Clinical Neuropsychology (SCN) American Psychological Association of Graduate Students (APAGS)
2012 – Present	International Neurological Society (INS)
2012 – Present	Association of Neuropsychology Students in Training (ANST)
2011 – Present	National Academy of Neuropsychology (NAN)
2011 – Present	Philadelphia Neuropsychology Society (PNS)
2011 – Present	Acquired Brain Injury Network of Pennsylvania (ABIN-PA)

PROFESSIONAL SERVICE

Leadership Roles

July 2014 – June 2015 **Interest Group Representative**
Association of Neuropsychology Students in Training (ANST), Drexel University Chapter

Sept 2012 – June 2015 **Neuropsychology Major Area of Study, Graduate Student Representative**
Drexel University, Clinical Psychology Ph.D. Program

Journal Review

January 2014 **Ad-Hoc Reviewer**
Neuropsychological Rehabilitation

Conference Volunteer

November 2014 **Student Member Volunteer**
2014 Conference of the National Academy of Neuropsychology (NAN), Fajardo, Puerto Rico.

November 2012 **Student Member Volunteer**
2012 Conference of the National Academy of Neuropsychology (NAN), Nashville, TN.

TEACHING EXPERIENCE

Graduate Level

Sept 2011 – Dec 2012 **Teaching Assistant**
PSY530: Principles of Neuroscience, Drexel University
Supervisor: Maria Schultheis, Ph.D.

Undergraduate Level

Sept 2011 – June 2012 **Teaching Assistant**
PSY 340: Psychological Testing and Assessment, Drexel University
Supervisor: Jennifer Gallo, Ph.D.

PSY 410: Neuropsychology, Drexel University
Supervisor: Kristen Begosh, Ph.D.

PSY 330: Cognitive Psychology, Drexel University
Supervisor: John Kounios, Ph.D.

PSY 111: Preprofessional General Psychology, Drexel University
Supervisors: Maureen Gibney, Ph.D. and Tamara Medina, Ph.D.

PSY 480: Technology & Psychology, Drexel University
Supervisor: Maria Schultheis, Ph.D.

REFERENCES

Research Advisors, Drexel University

Maria Schultheis, Ph.D. (Drexel University Advisor)
Associate Professor
Psychology Department and School of Biomedical Engineering, Sciences, and Health Systems
Drexel University
Phone: 215-895-6105; E-mail: schultheis@drexel.edu

Jennifer Gallo, Ph.D. (Drexel University Advisor)
Assistant Teaching Professor
Department of Psychology
Drexel University
Phone: 215-895-2805; E-mail: jlg37@drexel.edu

Clinical Supervisors

Lauren Krivitzky, Ph.D., ABPP-CN
Pediatric Clinical Neuropsychologist
Department of Child and Adolescent Psychiatry and Behavioral Sciences
The Children's Hospital of Philadelphia
Phone: 215-590-7064; E-mail: krivitzkyl@email.chop.edu

Rochelle Glidden, Psy.D.
Pediatric Psychologist
Division of Pediatric Behavioral Health
Department of Pediatrics
Alfred I. DuPont Hospital for Children
Phone: 302-651-4525; Email: rochelle.glidden@nemours.org