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Exploring Changes in Functional Connectivity Associated with the Development of Cognitive Flexibility During Middle Childhood

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To the Graduate Council:

I am submitting herewith a thesis written by Meagan Smith entitled "Exploring Changes in Functional Connectivity Associated with the Development of Cognitive Flexibility During Middle Childhood." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Arts, with a major in Psychology.

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Exploring Changes in Functional Connectivity Associated with the Development of Cognitive Flexibility During Middle Childhood

A Thesis presented for the
Master of Arts
Degree
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Meagan Elizabeth Smith
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Dedication

I would like to dedicate this thesis to my family. Thank you for your endless support and for always encouraging me to pursue my dreams. To Tyler—you inspire me.

Acknowledgments

I would like to thank Dr. Aaron Buss, my graduate mentor, for everything he has done to help make this project possible. I am so grateful that Aaron welcomed me into his lab, for it has given me invaluable opportunities and learning experiences. He has taught me so much over the past few years and I would not be where I am today without his guidance. I would like to thank Dr. Anastasia Kerr-German for sharing data analysis protocols, as well as being an inspiration to me. She helped make functional connectivity analyses in this study possible. I would like to thank my lab members, Jessica Defenderfer, Kara Lowery, Kaleb Kinder, Rachel Eddings, Hollis Ratliff, and Bhoomika Nikam, for teaching me lab protocols, assisting with data collection, and always being there to provide moral support. I would also like to thank the members of my master's committee, Drs. Kalynn Schulz and Greg Reynolds, for the time they have invested in reviewing my work, providing me with feedback, and helping me improve as a researcher. I would also like to thank my family and my husband for their love and support throughout this journey.

Abstract

Cognitive flexibility is a subset of executive function that involves flexibly adapting one's behavior to meet the demands of a changing environment. In a cognitive task, this often entails shifts of attention between dimensions of a stimulus or flexibly changing response sets. This skill improves greatly throughout middle childhood and is supported by a frontal-parietal neural network. The level of synchrony in activation, or functional connectivity, between frontal and parietal regions has been reported to increase over development even after cognitive flexibility has stabilized. The current study aims to assess changes in functional connectivity across the age range when this ability most rapidly develops. fNIRS was used to measure synchrony in hemodynamic activation of the frontal and parietal cortices in children at age 5, 7 and 9. Functional connectivity was measured at a resting state and while children performed three tasks requiring cognitive flexibility. Task performance and connectivity strength were compared across age groups. Cognitive flexibility improved greatly with age, aligning with previous literature. Evidence was found for refinement of local connectivity within the frontal cortex, such that weaker connections decreased in strength with age and stronger connections increased in strength. Further, connectivity between frontal and parietal regions was greater for 9-year-olds when task demands increased, reflecting greater synchrony of this network with age. Understanding the neural dynamics associated with the development of flexibility promotes a better understanding of the brain-behavior relationship. This line of research can also allow us to make comparisons with atypically developing populations, such as those with Autism, who have impairments in this skill. By understanding how neural architecture develops to support executive function in typical populations, we can better understand how deficits arise from atypical trajectories.

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Section I:
INTRODUCTION

Executive function (EF) refers to three separable, yet interrelated, cognitive skills used to perform intentional, goal-directed behavior: working memory, inhibition, and cognitive flexibility (Diamond, 2014; Miyake et al., 2000). Cognitive flexibility (also referred to as switching or attention-shifting) involves flexibly adapting to meet the demands of a changing environment. This is often measured using tasks that require redirecting attention from one dimension of a stimulus to another or switching between response sets or task rules. This skill is important for developing higher-level reasoning and problem-solving abilities. Additionally, cognitive flexibility has important implications for academic success, as it has been linked to both math and reading performance in children (Yeniad et al., 2013), as well as creativity, occupational success and mental health in adulthood (Diamond, 2014; Shi et al., 2018). Deficits in cognitive flexibility, and EF more generally, have been identified in many mental and neurodevelopmental disorders such as ADHD and Autism (Diamond, 2014; Lai et al., 2017).

The executive dysfunction (EDF) hypothesis of Autism Spectrum Disorder (ASD) focuses on deficits in EF that underlie the behavioral symptoms associated with this disorder (Sanders et al., 2008). ASD is a neurodevelopmental disorder associated with a myriad of symptoms such as delays in language development, difficulty with social interaction, and the presence of restricted, repetitive behaviors (RRBs) (American Psychiatric Association, 2013). There is a large body of evidence to suggest that areas of EF such as cognitive flexibility, inhibition, planning, verbal and spatial working memory, are impaired in individuals with ASD (Lai et al., 2017; Ozonoff et al, 1999; Corbett et al., 2009; Yasumura et al., 2012; Yerys et al., 2009; Miller et al., 2015). Moreover, deficits in cognitive flexibility have been linked to the severity of RRB symptoms in this population, providing further support the EDF theory (Miller, 2015; Yerys et al., 2009).

Various therapies and interventions have been developed to reduce the symptomology of ASD and promote healthier behavior (Sharma et al., 2018). The development of new strategies is an active area of research (Maglione et al., 2012; Sharma et al., 2018). Understanding the neurocognitive mechanisms underlying the development of cognitive flexibility can provide insight as to how these processes are interconnected and influence one another in atypical development. By understanding general brain-behavior relationships and normative development patterns, we can better understand how developmental trajectories diverge from typical trajectories.

Typical Development of Cognitive Flexibility

In typical development, a foundation for cognitive flexibility is established during the preschool years (Hughes, 1998). For example, children at the age of three tend to perseverate on post-switch trials of the Dimensional Change Card Sort (DCCS) task but begin to succeed at the age of four (Zelazo, Müller, Frye and Marcovich, 2003). This task assesses cognitive flexibility by requiring children to sort bivalent cards to one of two locations based on its shape or color, and then switch to sorting cards by the other dimension. Successfully switching rules requires cognitive flexibility and is difficult for young children,

especially as rules become more complex. Anderson (2002) outlines a developmental trajectory of cognitive flexibility, highlighting six to nine years as the age range at which children experience the most improvements in this skill. Cognitive flexibility continues to develop through adolescence and adulthood, but becomes mostly stable by age 12 (Anderson, 2002).

Neuroimaging techniques have helped provide insight to the underlying neural processes associated with cognitive development. One method by which this has been achieved is by measuring evoked activity in particular regions of the brain in response to stimulus events in various tasks. Through this method, the initial emergence of cognitive flexibility in early childhood has been associated with increases in activation within frontal and parietal cortices (Buss and Spencer, 2018; Moriguchi and Hiraki, 2009, 2011). Numerous neuroimaging studies have also revealed that although cognitive flexibility stabilizes around age 12 (Anderson, 2002), the frontal-parietal network (FPN) supporting this skill continues to develop through adolescence and adulthood in both the strength of activation and the specific regions that are activated. For example, children and adolescents show different patterns of neural activation compared to adults during tasks that require cognitive flexibility. Morton and colleagues (2009) found that both children at age 11-13 and adults show increased activation of frontal and parietal regions in response to dimensional shifting in the DCCS task; however, age-related differences in activation were found. Children had greater activation of the right superior frontal cortex than adults, but adults had greater activation of the left superior parietal cortex (SPC) and right thalamus (Morton et al., 2009). These changes were unrelated to performance differences, as both groups performed comparably. Additionally, Rubia and colleagues (2006) measured neural activity with fMRI during a switching task in adolescents and adults, finding that adults showed greater activation of right inferior PFC, left parietal, anterior cingulate cortex (ACC) and putamen.

Altogether, these data suggest that the underlying neural structures supporting cognitive flexibility continue to develop after behavioral performance stabilizes, with parietal regions seemingly becoming more involved with age. This line of research also demonstrates how the neural bases of cognitive flexibility cannot be pinpointed to a single region. Rather, flexibly adapting behavior to changing environmental demands requires functional integration of a frontal-parietal network (FPN). In addition to measuring localized activity evoked in response to task demands, neuroimaging can be used to determine the degree of functional integration between brain regions, referred to as functional connectivity (FC). FC represents synchrony in activation between neural populations and is often computed as a correlation coefficient. Studies using this methodology have found that FC within and between nodes of the FPN also changes over development. For example, FC measured during a resting state (rsFC, or *task-negative* FC) between the left dlPFC and left intra-parietal sulcus (IPS), as well as between the left dorsal-frontal and left IPS, has been reported to increase from childhood (age 7-9) to adolescence (age 10-15) and adulthood (age 21-31) (Fair et al, 2007). Resting FC is informative because

it represents neural regions that are typically activated together. This suggests that developing a mature, adult-like attentional control network involves "segregation and integration processes", i.e. a decrease in short-range connectivity (segregation) accompanied by an increase in long-range connectivity (integration) (Fair et al, 2007). Abnormalities in this process are suggested to play a role in developmental disorders such as Autism (Fair et al., 2007).

FC can also be measured while completing tasks that measure executive function, referred to as *task-positive* (task+) connectivity. Similarly, Task+ connectivity of the FPN has been reported to change from childhood to adulthood. For example, O'Hare and colleagues (2008) found that frontal-parietal FC measured by fMRI increased from childhood (age 7-10) to adulthood (age 20-28) during a working memory task. Similarly, Mehnert et al. (2013) examined frontal-parietal FC using fNIRS while children (age 4-6) and adults completed a response inhibition task. They found stronger short-range connectivity and weaker long-range connectivity in children compared to adults, as well as poorer performance on the inhibition task. Additionally, Ezekiel, Bosma and Morton (2013) had children and adults complete the DCCS task while measuring neural activity with fMRI. Children at age 12 had lower FC between the lateral PFC, ACC, inferior parietal cortex and VTA than adults (Ezekiel, Bosma, & Morton, 2013). This research is consistent with the proposed segregation and integration hypothesis (Fair et al., 2007).

Brain-Behavior Relationships

While maturation of regions such as the frontal cortex are important for cognitive development, cognitive flexibility likely emerges through functional activation of many nodes within an executive control network. These specific nodes have been theorized to play particular roles in the process of attention-shifting. Flexibly switching rules during a task requires the individual to continually update the relevant rule in working memory, as well as suppress the irrelevant rule, largely involving nodes of the prefrontal cortex (PFC) (Dajani & Uddin, 2015; Crone et al., 2006). Parietal regions such as the posterior parietal cortex (PPC) are suggested to support attentional processing of visual information and integrate appropriate motor responses with incoming visual information (Dajani & Uddin, 2015). This region is thought to be involved in both top-down and bottom-up attentional control in response to rule-switches in order to orient to the appropriate features of the stimuli (Dajani & Uddin, 2015). Additionally, the pre-supplementary motor area (pre-SMA/SMA) is thought to be activated during rule-switching and is specifically more active when required to inhibit previously-used task rules that are no longer relevant to task completion (Crone et al., 2006). The more strongly these regions interact with one another and show functional integration may represent improvements in the cognitive operations that are necessary to successfully switch rules, including attentional control, rule representation, and inhibiting undesirable responses.

Task-Evoked Versus Resting Functional Connectivity

Research on the development of FPN connectivity associated with cognition has utilized both measures of FC at rest and during task performance. These methods have different implications and different versions of this methodology can be better suited for different types of questions. Synchrony in resting activity between neural populations is believed to reflect the regions that commonly interact with one another; thus, measures of rsFC have helped identify a number of neural *networks*, such as the FPN, that constitute an "intrinsic" neural architecture that is stable and present across all neural states (Rosazza & Ludovico, 2011). Regions of the brain that are engaged together during a task have been shown to maintain correlated activity at rest, leading many researchers rely on rsFC alone to study developing neural dynamics (Rosazza & Ludovico, 2011). However, differences in rsFC and task+ FC have been identified, suggesting that neural networks such as the FPN undergo reconfiguration in the presence of task demands.

Gonzalez-Castillo and Bandettini (2018) list a number of differences between task+ FC and rsFC. For example, connectivity between nodes of the same network is reportedly lower at rest than during task periods, while connectivity between nodes of different networks is higher at rest, reflecting global integration of neural communication (Gonzalez-Castillo & Bandettini, 2018). Conversely, within-network connections are suggested to be greater during tasks while between-network connections are lower (Gonzalez-Castillo & Bendettini, 2018; Di, Gohel, Kim, & Biswal, 2013). Moment-to-moment fluctuations in FC have also been reported to be more stable during task than at rest (Gonzalez-Castillo & Bandettini, 2018). These data suggest that rsFC may promote modularity of neural networks, while task+ FC may have lower intra-individual variability and involve greater cross-communication between neural networks. However, these differences in resting versus task-evoked FC have been shown to be subtle, as task+ FC has also been argued to consist primarily of intrinsic FC patterns (Cole et al., 2014). The differences in these measures are still unclear, making it difficult to determine which is better suited for studying the development of cognition. However, both of these methods have proven useful in detecting changes in neural dynamics associated with behavior.

It is also important to note that measures of FC are not equivalent to structural connectivity. Although structural changes such as increased myelination and synaptogenesis impact FC by permitting more efficient neural communication, FC can also occur between more distant brain regions that are indirectly connected. FC can be computed between nodes that are within the same region of the brain (short-range connectivity*)*, or between nodes of different brain regions (long-range connectivity*)*. Measures of FC are informative at the level of synchronized neural activity but cannot shed light on synaptic connections itself without structural neuroimaging.

Summary

In sum, these data provide evidence that the neural network supporting cognitive flexibility continues to develop through adolescence and adulthood in both strength and coordination of activation. The FPN seems to be increasingly recruited during task performance with age and the nodes that most contribute to performance change, such that there is greater involvement of parietal regions over time. Increases in long-range connectivity of this network with age have been found both during a resting state and while performing cognitive tasks, while short-range connectivity has been found to decrease.

However, differences in task-evoked in functional connectivity across the proposed critical period in middle childhood for developing cognitive flexibility has not been explored. This is necessary in order to track developmental changes in this network that are associated with the establishment of adult-like skills. If increases in functional integration of the executive control network reflect improvements in cognitive strategies used for performing such tasks, there should be evident increases in FC between frontal and parietal nodes across ages five to nine, when the greatest improvements in this skill have been reported.

Exploring this phenomenon in typical development would allow us to better understand which processes may be going awry in atypical populations such as those with ASD, which may be contributing to deficits in EF.

Cognitive Flexibility in Autism Spectrum Disorder

There is a large body of evidence to suggest that individuals with Autism Spectrum Disorder (ASD) have deficits in cognitive flexibility, as well as inhibition, planning, verbal and spatial working memory (Lai et al., 2017; Ozonoff et al, 1999; Corbett et al., 2009; Yasumura et al., 2012; Yerys et al., 2009; Miller et al., 2015). The primary symptoms of ASD are impairments in social interaction and communication. Individuals with an ASD diagnosis often have a narrow range of interests that they tend to become fixated on and engage in restricted and repetitive behaviors (RRBs) such as fidgeting and being extremely routine-oriented (American Psychiatric Association, 2013).

As previously mentioned, the executive dysfunction hypothesis of ASD suggests that deficits in EF underlie the behavioral symptoms of this disorder, possibly influenced by underlying abnormalities in the frontal-striatal and frontal-parietal networks (Sanders et al., 2008). For example, impairments in cognitive flexibility are commonly identified in individuals with ASD (Lai et al., 2017; Ozonoff et al, 1999; Corbett et al., 2009; Yasumura et al., 2012) and have been associated with RRB symptom severity (Yerys et al., 2009; Miller et al., 2015).

Neuroimaging has begun to be used as a tool to study the neural mechanisms that potentially underlie executive dysfunction and behavioral symptomatology of ASD. Research in this field first supported a general long-range cortical under-connectivity, or *hypoconnectivity*, theory of Autism, suggesting that individuals with this neurodevelopmental disorder have lower FC between canonical brain

networks such as the frontal-posterior network (Courchesne and Pierce, 2005; Schipul et al., 2011). Supporting evidence for this theory was found in research by Just and colleagues (2007), which examined FC of the FPN while adults with high-functioning autism performed a complex problem-solving task called the Tower of London. FC of the frontal-parietal network in adults with ASD was lower compared to TD adults, despite there being no performance differences. Additionally, Kana and colleagues (2007) found reduced FC between nodes the frontal and parietal cortices in Autistic adults while performing an inhibition task. Evidence of hypoconnectivity has also been found in the task-negative, default mode networks (DMN) of individuals with ASD, including the medial prefrontal cortex (mPFC), anterior cingulate cortex (ACC) and precuneus (PrC) (Assaf et al., 2010; Monk et al., 2009). Moreover, connectivity strength between these regions have been negatively associated with social and communication deficits in this population (Monk et al., 2009). Altogether, these studies provided evidence supporting a general hypoconnectivity hypothesis of Autism, suggesting that these individuals have a weaker integration of long-range brain networks.

This line of research involves adult subjects with ASD, rather than analyzing FC differences across different age groups. Uddin et al. (2013) suggested that a developmental perspective can be more informative when studying FC by incorporating age-related changes. Lynch et al. (2013) conducted whole-brain FC analyses using fMRI with Autistic children between the ages of 7 and 12 and found *hyper-connectivity* between several major brain networks that was also associated with severity of the RRB symptom.

Nomi and Uddin (2015) hypothesize that there is a general, widespread hyperconnectivity between several brain networks in children with ASD that then shifts to long-range under-connectivity in adulthood. They tested this by examining FC in three cohorts of individuals with ASD: children under 11 years, adolescents between ages 11 and 18, and adults over 18. They found widespread hyperconnectivity in Autistic children that decreased across development, with adults not showing hyperconnectivity.

The nature of atypical connectivity in Autism is therefore more complex than simply fewer connections between, or within, brain networks, as previously stated by the hypoconnectivity hypothesis. Specifically, individuals with ASD seem to deviate from the typical developmental pattern of decreased short-range connections and increased long-range connections outlined by Fair et al. (2007). This deviation seems to manifest in greater long-range and short-range connections that, over time, develop to be under-connected. Perhaps these neural networks in ASD undergo excessive pruning of synaptic connections over development in attempt to correct for hyperconnectivity that is noted in childhood, resulting in hypoconnectivity in adulthood. Although FC research with Autistic populations have begun to include children, no studies to date have examined task+ FC with individuals with ASD during middle childhood.

Current Study

In summary, cognitive flexibility is an important aspect of executive function that develops most rapidly between ages 6 and 9 in typical development. This ability is supported by a frontal-parietal network, which undergoes developmental change in both activity and connectivity through adolescence and adulthood. However, it is unclear how this network changes during task performance in order to support the rapid improvements in flexibility seen in middle childhood. Moreover, cognitive flexibility has been frequently reported to be impaired in those with ASD. Abnormalities in neurodevelopment have also been noted in this disorder, including widespread hyperconnectivity that transitions to hypoconnectivity later in development. Abnormalities in some of these networks have been linked to behavioral symptoms of the disorder.

In the current study, we used fNIRS to measure FC of the frontal-parietal network in children at ages five, seven, and nine while they perform a battery of tasks that probe cognitive flexibility. We also measured FC of this network during a resting state task. The goals of this study are to characterize how connectivity of the FPN changes during middle childhood to support the development of cognitive flexibility, as well as and identify channel-pairs at each age in which FC is contributing to task performance. Achieving this will allow future studies to compare these dynamics to those of Autistic children at this age in order to better understand how abnormalities in neurodevelopment contribute to executive dysfunction in this population.

We hypothesize that FC between the frontal and parietal cortices will increase with age, regardless of whether or not task performance differences are seen. We also hypothesize that performance on the cognitive flexibility tasks will improve with age. Specifically, we predict that the greatest differences in both connectivity strength and task performance will be between the ages of five and nine.

Section II:
METHOD

Participants

Children that were 5 years-old (n=20), 7 years-old (n=19) and 9 years-old (n=18) were recruited to participate in this study using the online participant database maintained by the Psychology Department. Experimental protocols and recruitment plans were approved by the Institutional Review Board (IRB) of the University of Tennessee Knoxville. Children were compensated by being allowed to select a toy of $5.00 value after participating.

Upon arrival, an informed consent document was explained verbally to the parent and signed prior to beginning the experiment. Assent forms were given to the children who were seven years of age or older and were explained to them in appropriate language. Parents then completed a demographics form, followed by a series of questionnaires assessing behavior that is characteristic of Autism Spectrum Disorders. The purpose of these documents was to provide an index of where typically-developing children in this age range fall on these scales in order to use this population as a comparison for an atypically-developing group with an Autism Diagnosis in a future study. These questionnaires were also correlated with performance scores on our task to determine whether or not Autistic traits were related to cognitive flexibility in our sample. These documents included the Autism Quotient – Child Version (AQ-Child), The Flexibility Scale (FS), and The Restricted-Repetitive Behavior Scale – Revised (RBS-R).

Measures

Autism Quotient – Child Version (AQ-Child)

The AQ-Child measures levels of Autistic traits for both typically and atypically-developing children (Auyeung et al., 2008). Parents are asked to rate the extent to which they agree or disagree with each of 50 statements about their child on a scale of zero to three ('definitely agree' to 'definitely disagree'). Items include statements such as "keeps going on and on about the same thing" and "can switch back after an interruption". The questionnaire is further broken down into 5 subscales: *social skills* (items 1, 11, 13, 15, 22, 36, 44, 45, 47, 48), *attention switching* (items 2, 4, 10, 16, 25, 32, 34, 37, 43, 46), *attention to detail* (items 5, 6, 9, 12, 19, 23, 28, 29, 30, 49), *communication* (items 7, 17, 18, 26, 27, 31, 33, 35, 38, 39) and *imagination* (items 3, 8, 14, 20, 21, 24, 40, 41, 42, 50). Scores are computed as the sum of all items, with some items reverse scored as necessary. Scores can fall between 0 and 150, with higher scores representing greater Autistic tendencies.

Restricted/Repetitive Behavior Scale-Revised (RBS-R)

The RBS-R scale assesses the nature of and severity of restricted and repetitive behaviors (RRBs) of children with ASD (Bodfish et al., 1999, 2000; American Psychological Association, 2013). It consists of 43 statements such as "*flaps hands, wiggles or flicks fingers, claps hands, shakes or waves arms…*" and parents are asked to rate both how frequently the behavior occurs and how problematic the behavior is for their child on a scale of on a scale of zero to three (0 = behavior does not occur, 1 = behavior occurs and is a mild problem, 2 = behavior occurs and is a moderate problem, 3 = behavior occurs and is a severe

problem). The scale can be broken down into 6 subscales: stereotyped behavior, self-injurious behavior, compulsive behavior, ritualistic behavior, sameness behavior, and restricted behavior. Scores on this questionnaire are calculated the sum of all items, with higher scores representing more restricted, repetitive behavior present.

Flexibility Scale (FS)

The FS (adapted from Strang et al., 2017) measures higher-order behavioral flexibility in social and verbal contexts. Parents rate 27 statements (e.g. *"does something special around bedtime,"* and *"can't shift gears even when told to do so."*) on a scale of zero to three, indicating the extent to which the statement applies to their child (*0 = no, 1 = somewhat, 2 = very much, 3 = always*). The FS can be broken down into 5 subscales: Routines/Rituals, Transitions/Change, Special Interests, Social Flexibility, and Generativity. Scores on this scale are computed as the sum of all items, with some items reverse-scored as necessary (*e.g. "shares toys, possessions"*).

Procedure and Design

The first task children completed was Raven's Colored Progressive Matrices (RCPM), which is a measure of non-verbal IQ and fluid intelligence for children between age 5-11. The test consists of three sets (set A, Ab and B) each containing 12 multiple choice items. Each item is a geometric design with a missing portion. Children are asked to choose from 6 possible answers the piece that completes the missing portion of the pattern. The purpose of this measure was to be used as a matching criterion in an exploratory analysis comparing a sample of children with ASD to our sample of TD children. Wechsler Intelligent Quotient tests have been criticized for under-estimating the intelligence of individuals with ASD, which is why we planned to use non-verbal IQ to match these participants in an exploratory analysis (Burack et al., 2004).

Following the RCPM, hemodynamic data was collected with fNIRS during a resting state task in which children watched a series of 5 videos lasting approximately 60 seconds each (e.g. Kerr-German, Buss and Tas, *under review*). After each video presentation, a black screen with a cross-hatch was presented until the researcher initiated the next video, as to allow the child's attention to be re-directed to the screen if necessary. Videos included stimuli that were aimed to both hold the interest of the child and promote relaxation, such as swimming fish, giraffes running, etc. Children were instructed to be calm and to not move or speak during the video presentation.

Following the resting state task, children completed a modified version of Dimensional Change Card Sort (DCCS) Task from the NIH toolbox (Zelazo et al., 2013). In this task, participants are presented with two adjacent sorting trays in which they are instructed to sort cards. Each sorting location contains a target card with an image of an either a fish or a house. Test cards then appear in the center of the screen above the sorting trays and children are instructed to sort the cards as fast as they can by pressing either

the left or right button on a Chronos® device corresponding to the sorting location (Psychology Software Tools, Pittsburgh, PA).

This adapted NIH Toolbox version of the DCCS consists of two practice trials, a pre-switch, post-switch, and mixed block (Figure 1). The researcher begins by giving the following instructions, "*We are going to play a card game. This is called the (color/shape) game! In the (color/shape) game, all of the yellow/fish) go here, and all of the (purple/houses) go here. You will press this button to put the (yellow/fish) here, and this button for to put the (purple/houses) here*." For the two practice trials, the researcher demonstrates sorting by either both colors or both shapes for the child by pressing the button for each appropriate sorting location for the first two cards that appear, with verbal instructions such as "*see, this one is yellow, so it will go here. This one is purple, so it will go here*." The researcher then tells the child is their turn to sort the cards, which initiates the pre-switch block. The pre-switch block includes five trials of sorting by the most recently-used rule in the practice trials. They are asked to sort test cards by one dimension (i.e. color) through instruction such as, "*Now we're going to play the color game! In the color game, all of the yellow cards go here, and all of the purple cards go here*." When they successfully sort 4 out of 5 cards in this block, they advance to the post-switch block. In this block, they are asked to sort the cards by the other dimension (i.e. shape) such that houses now go in one location and fish go to the other sorting location. For each trial, the word "shape" or "color" was also played auditorily from the computer speakers. When children successfully sort four out of five cards in this block, they proceed to the mixed block. The mixed block held 30 total trials, including "frequent/dominant" and "infrequent/nondominant" trials. The frequent trials were those that used the post-switch sorting dimension and the infrequent trials included the other dimension. Two-to-five frequent trials occurred between each infrequent trial in a semi-randomized manner. Each trial was initiated by the experimenter by pressing a space bar and each block of the task proceeded one after the other with no additional pauses or breaks.

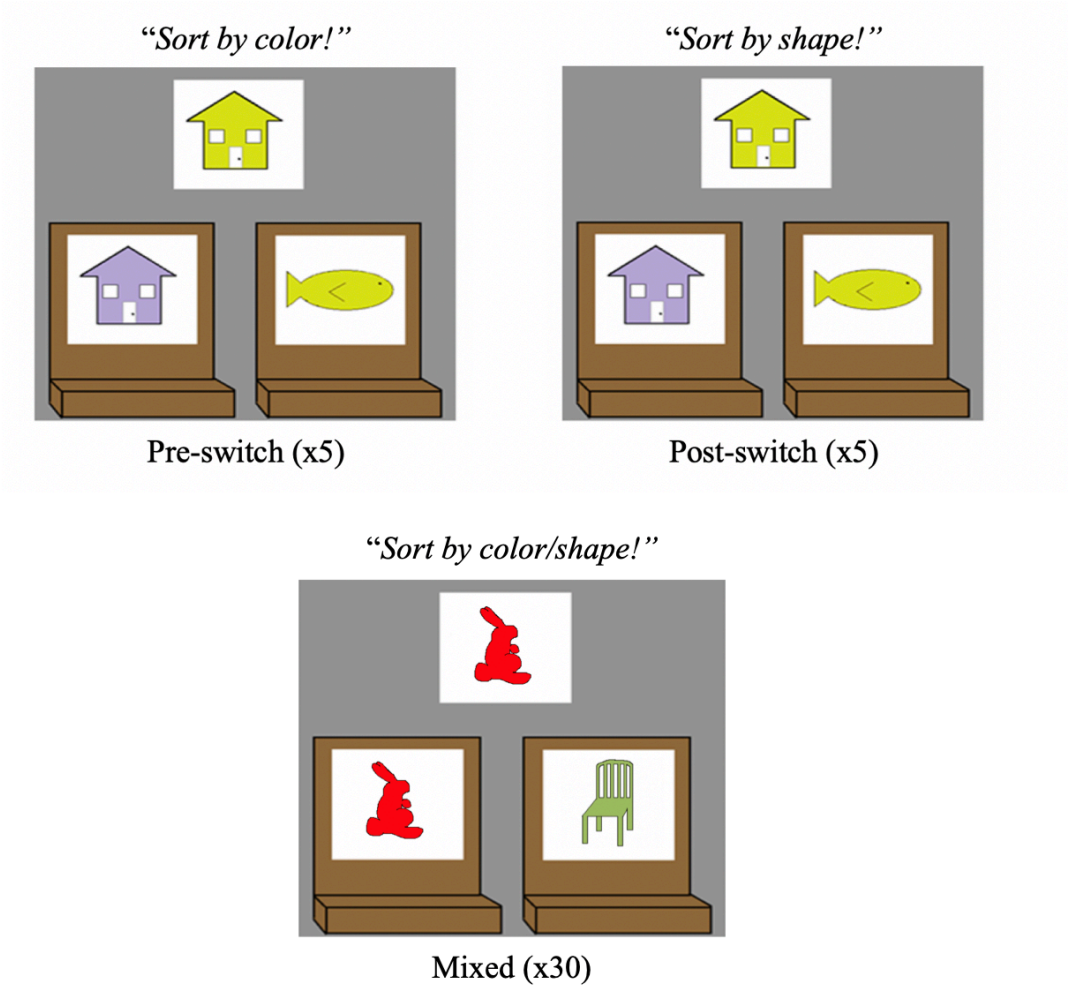

Figure 1. DCCS Task. The figure above displays the modified NIH Toolbox DCCS task (Zelazo et al., 2013). Children completed a pre-switch, post-switch and mixed block in this task.

Following the DCCS, children completed the *pTrails* and *Switcher* tasks from the Psychology Experiment Building Language Tests (PEBL) software (Mueller and Piper, 2014). The PEBL battery is made available to download in exchange for making a donation to their research program. pTrails is a digital version of the canonical "trail-making test" in which participants are asked to connect circles in ascending order by clicking one after the other as quickly as they can. We modified this task with a touch screen monitor to allowing children to simply touch the circles to connect them. This was done to allow the children to complete the task with minimal motor demands. Part A of the task requires children to connect the circles in ascending order by number as quickly as possible. They are then instructed to do so with letters. Part A of this task is generally used to obtain a measure of psychomotor speed, visuospatial scanning, and other task demands that do not involve cognitive flexibility. Part B then introduces cognitive flexibility demands. In this portion of the task, participants are presented with circles that have numbers and circles that have letters. They are asked to alternate between connecting a number to a letter in ascending order as quickly as they can (e.g. 1-A-2-B-3-C . . .) (Figure 2). When the correct ascending circle is selected, the number or letter becomes boldfaced and a line is automatically drawn from the previous circle to the circle that was selected. In this study, children completed part A and B twice. If children made an error during this task, they were corrected and guided by the experimenter and proceeded to finish the task. Errors do not affect scores other than adding to their overall completion time, which is recorded and used for scoring purposes. Timing for each trial did not begin until the first circle was clicked (which is always the circle labeled '1'). This task consisted of three rounds that were completed twice, yielding 6 total trials: part-A with numbers only, part A with letters only, and part-B (alternating numbers and letters).

Lastly, children completed the PEBL "switcher" task (Figure 3). In this computerized task, children were presented with several different shapes of various colors on the screen, each with a letter in the center of the shape. One of the shapes was circled and a rule cue was presented at the top of the screen—either the word "color," "shape," or "letter." The child was instructed to touch the item on the screen that is the same color/shape/letter as the one that is circled based on the given rule for that trial. The rule at the top of the screen was read aloud by the experimenter each time for the 5-year-old children due to the variability in reading skills of this age group.

This task consisted of three blocks with three sets each. Each set consisted of 12 trials in which the cue word, or rule, changed each time. After each set, the configuration of shapes on the screen changed. After each block, the instructions changed for the child. For example, in the first block, the same two selection rules alternate per set (e.g. color, shape, color, shape). The children were encouraged to try to remember the order of the rules so that they do not have to read the rule each time. In the second block, all three selection rules alternated in a consistent pattern, however, this pattern changed with each set. At this stage, the children were instructed again to try to remember the order of the rules so they can avoid

having to read the rule each time. In the last block, all three selection rules are presented in random order for each trial. In this block, the child is told that they will not know what rule will come next and must read the rule for each trial.

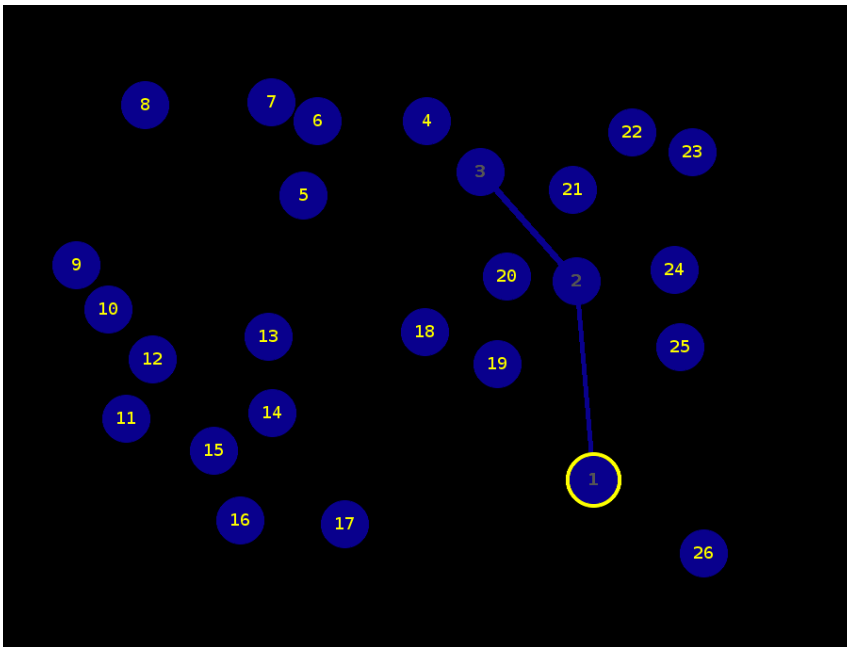

Figure 2. pTrails Task Image. The above figure is a screenshot of the pTrails task of the Psychology Experiment Building Language (PEBL) battery (Mueller & Piper, 2014).

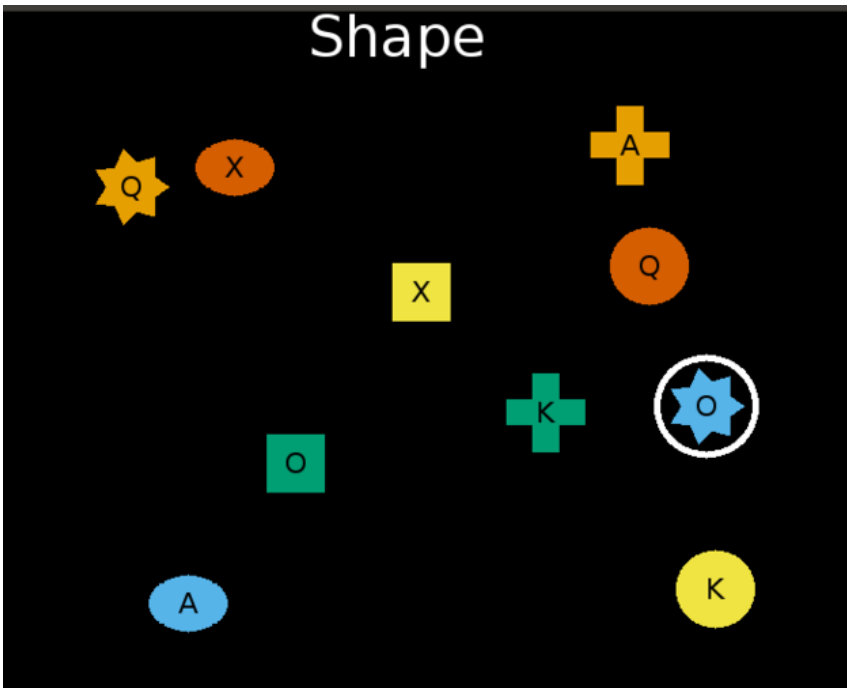

Figure 3. Switcher Task Image. The above figure is a screenshot of the Switcher task of the Psychology Experiment Building Language (PEBL) battery (Mueller & Piper, 2014).

Functional Near-Infrared Spectroscopy

While children completed the resting state and cognitive flexibility tasks, functional near-infrared spectroscopy (fNIRS) was used to measure hemodynamic changes in the cortex by monitoring changes in oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR). Data were collected at 25 Hz using a 24-channel TechEn Cw6 system with wavelengths of 830nm and 690nm. We used a custom-made probe with 24 channels to measure FC within and between nodes of the frontal and parietal cortices that have previously been implicated in dimensional attention shifting (Morton et al., 2009; Rubia et al., 2006; Zakanis et al., 2005; Kim et al., 2012) (Figure 4). Seven channels covered the left frontal cortex and five channels were placed over the left parietal cortex. Similarly, seven channels covered the right frontal and five covered the right parietal cortex. Specific areas targeted include the left precentral gyrus, left middle frontal gyrus, left superior frontal gyrus, left superior parietal cortex, left dorsolateral prefrontal cortex (dlPFC), right superior parietal lobule and right dlPFC.

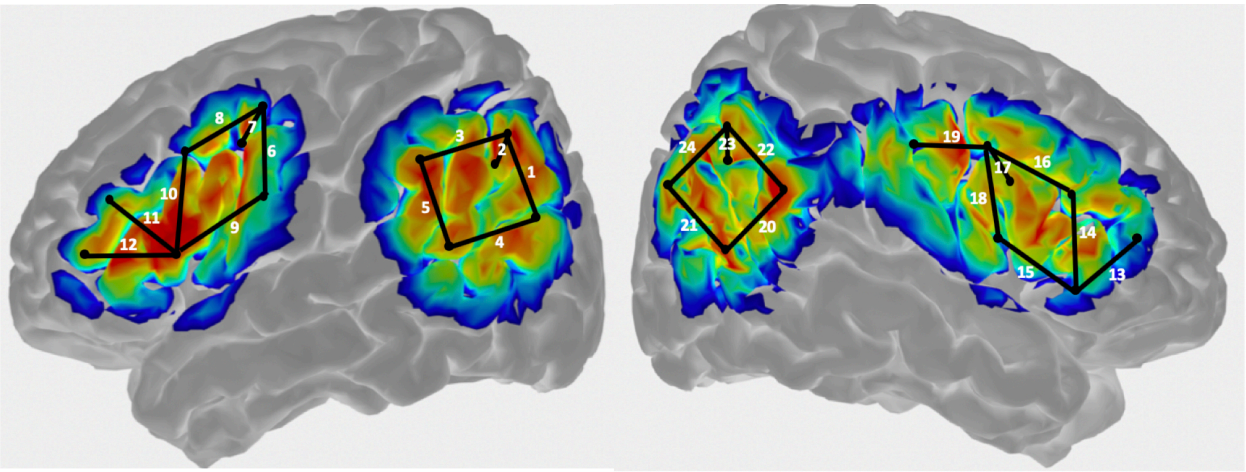

Figure 4. The figure above shows the sensitivity profile for the NIRS probe in the current study. The probe included 24 total channels covering the frontal and parietal cortices bilaterally. Channel numbers are included to indicate the brain region each channel is measuring hemodynamic changes from. The probe covers L precentral gyrus, L middle frontal gyrus, L superior frontal gyrus, L superior parietal cortex, L dorsolateral PFC, R superior parietal lobule, and R dorsolateral PFC.

Method of Analysis

DCCS Task

The DCCS was scored as an accuracy score plus a reaction time (RT) score for those participants that achieved 80% accuracy or better (e.g. Zelazo, 2013). First, accuracy scores were calculated as .125 times the number of correct responses on all trials in order to provide accuracy scores on a scale of 0 to 5 (5 points divided by 40 trials equals .125 points per accurate response). RT scores were then calculated and added to the participants' scores for those with high accuracy. The rationale for doing this is that younger children tend to have a greater speed-accuracy tradeoff, while older children tend to make slower responses, but have greater accuracy (Zelazo, 2013, 2014). Therefore, RT is better representative of switch costs for children who are achieve high accuracy. RT scores were based on the non-dominant trials of the mixed-block. These RTs were first truncated to include only those between 500 and 3,000ms, such that RTs between 3,000 and 10,000ms were set equal to 3,000ms, and those between 100 and 500ms were set equal to 500ms. RTs higher or lower than 100ms or higher than 10,000ms were considered outliers and were not used in determining performance. Next, participants' median RT on non-dominant trials of the mixed block was calculated. A log (base 10) transformation was applied to these values in order to normalize the distribution of scores. These values were then rescaled to a 0 to 5 scale rather than a log(500) to log(3000) scale. The rescaled scores were then reversed in order for lower RTs to be at the higher end of the scale and higher RTs to be at the lower end of the scale. This end value was then added to the accuracy score, yielding total performance scores on a scale of 0 to 10. To compare performance across age groups, an ANOVA was conducted with age as a between-subject factor and performance score as a within-subject factor. Follow-up paired comparisons were conducted for the tasks that had significant age effects.

pTrails Task

Completion times for each trial of the pTrails task were recorded. Number-only and letter-only trials were averaged to yield an average "Part A" completion time. The two switching trial completion times were also averaged. Overall scores on the task were calculated as a switch cost, defined as a Part B minus Part A difference score. Proportion scores were also calculated as [(Part B – Part A) / Part A]. Since five-year-olds were given a shorter version of the pTrails task, scores were normalized by dividing the trial completion times by the amount of responses required for each group (i.e. five-year-olds' scores were divided by 13, while seven and nine-year-olds' scores were divided by 26). pTrails Difference Scores were defined as the average completion time on part B trials minus the average completion time for part A trials. This score was also divided by the amount of responses required by the participant in order to normalize scores. To compare performance across age groups, an ANOVA was conducted with age as a between-subject factor and normalized time per response as the within-subject factor.

Switcher Task

The Switcher task was scored as average completion time for each trial per block of the task in milliseconds, which was then converted to seconds. A total task completion time was also recorded. To compare performance across age groups, an ANOVA was conducted with age as a between-subject factor and completion time as a within-subject factor. Follow-up paired comparisons were conducted for the tasks that had significant age effects.

fNIRS Data Acquisition and Data Processing

Experiment tasks were implemented using E-Prime (v 2.0 and v 3.0) software, as well as the PEBL 2.0 software (Mueller & Piper, 2014). Trial onsets were time-stamped with stimulus marks at the onset of each task, which were synchronized with fNIRS data. For the DCCS task, event-related analyses were performed to determine differences in regional activation. NIRS data were analyzed using MATLAB with original scripts as well as functions provided by the HomER2 software (Huppert, Diamond, Franceschini, and Boas, 2009). Raw signal intensities were de-meaned and data were converted to an optical density measure using HomER2. Motion artifacts were removed using the wavelet tool in EasyNIRS (iqr=.5). The data were then band-pass filtered to remove frequencies lower than 0.019 Hz and 2.0 Hz. To preserve high frequency fluctuations that could be due to motion, a low pass filter of 2 Hz was then used. Motion artifacts were considered changes in optical density that were greater than 0.3 units. Motion artifacts within 2s before the onset of a trial and more than 12s after the onset of a trial were removed from processing. Data were band-pass filtered again to only include frequencies between .016 and .5 Hz. The known extinction coefficients of oxygenated and deoxygenated hemoglobin and the modified Beer-Lambert Law were used to convert the data to concentration values (Boas et al., 2001). HbO and HbR are analyzed here with activation considered as a simultaneous increase in HbO and decrease in HbR. Mixed ANOVAs were then run to determine differences in HbO and HbR across task condition and age.

FC was measured for the remaining tasks (e.g. Kerr-German, Buss, & Tas, *under review)*. NIRS data pre-processing steps in EasyNIRS were similar for these analyses. Data were converted to an optical density measure using the Beer-Lambert Law. Channel-by-channel correlation matrices were then conducted at both the group and individual level for each task. This was done by comparing HbO concentrations for each channel with the concentrations for all other channels at each recorded point across a specified time window. For the resting state task, this time window was 45s per each 60s video recording. For pTrails and Switcher, time windows were specified by creating a matrix in MATLAB based on the participant's unique onset and completion time for each block of the tasks. Channel pairs that were significantly correlated at the $p < .001$ threshold were selected for further analyses. Correlation coefficients for each participant were extracted for those significant channel-pairs and used in further

statistical analyses for those groups. Correlation coefficients on significant channel-pairs were used as a score for the strength of FC between those two cortical regions or channels (i.e., channel-pairs).

A series of one-way ANOVAs were used to compare differences in FC across age during the resting state and pTrails task. Correlation coefficient values during Part A of the pTrails task were subtracted from the coefficients during Part B to obtain a "rho difference score" for each channel per participant. These tests included channel pairs that were significantly correlated for all age groups to determine whether or not FC strength increased or decreased between these channel pairs over development. A mixed ANOVA was run on FC values for each channel during the Switcher task with age as a between-subject factor and age as a within-subject factor. Channel pairs included here were those that were significantly correlated for any age group during any block in order to determine block-related and age-related differences in FC.

Section III:
RESULTS

Descriptive Statistics and Parent-Report Questionnaires

Fifty-seven children completed this experiment (28 females; (M=6.98 years, SD=1.64 years). Participants were broken up into three age groups: twenty five-year olds (M=5.07 years, SD=0.08 years), nineteen 7-year-olds (M=7.02 years, SD=0.09 years), and eighteen 9-year-olds (M=8.95 years, SD=0.09 years). Eight additional children were enrolled in the study but were excluded from further analyses: two were excluded due to technical difficulties, five were excluded due to experimenter error, and one was removed for fussiness/inability to complete the experiment or refusing to wear the NIRS hat. Two participants identified as African-American, two were American Indian, two identified as both Asian and Caucasian, and the remaining participants were Caucasian. Eleven participants had corrected-to-normal vision, while the remaining participants reported having normal vision. Six participants were left-handed, four were ambidextrous, and the remaining participants were right-handed.

A sample of our participants (n=45) had a mean score of 78.89 on the AQ-Child, which is intermediate of the TD sample (M=41.7) and ASD sample (M=103.0) reported in Auyeung et al. (2008). In order to determine if scores on the Autism trait questionnaires were related to performance on the cognitive flexibility tasks in our sample, we conducted Pearson correlations on these measures. The imagination subscale of the AQ negatively correlated with scores on the DCCS task, greater Autistic tendencies on this subscale were associated with poorer DCCS performance, $r(42)=-.332$, $p=.028$. Additionally, overall AQ scores were positively correlated with scores on the FS, $r(42)=.613$, $p<.001$, and the RBSR, $r(42)=.491$, $p=.001$ (Table 1).

Table 1.
Means, standard deviations, and correlations between questionnaires and behavioral performance

Variable	M	SD	1	1a	1b	1c	1d	1e	2	3	4	5	6	7	8
1. AQ Total	78.89	15.10													
1a. Social Skills	13.49	4.09	**.844****												
1b. Attention-switching	17.71	5.01	**.799****	**.681****											
1c. Attention to detail	19.98	4.39	**.492****	.240	.250										
1d. Communication	16.36	4.56	**.813****	**.692****	**.511****	.200									
1e. Imagination	11.36	3.5	**.503****	.291	.234	-.033	**.410****								
2. FS	20.84	9.6	**.613****	**.449****	**.748****	.236	**.416****	.207							
3. RBS-R	6.31	7.46	**.491****	**.412****	**.472****	.100	**.331***	**.402****	**.578****						
4. Raven's CPM	23.91	7.04	-.010	-.031	.003	.233	-.099	-.099	.200	-.009					
5. DCCS Scores	6.10	1.47	-.157	-.195	.031	.109	-.225	-.225	.238	-.027	**.681****				
6. pTrails Part B	3552.6	2216.3	.035	.079	.128	-.252	.066	.066	-.083	-.023	**-.612****	**-.616****			
7. pTrails Proportion Scores	1.00	.788	.041	.001	.008	.136	-.040	-.040	-.011	.091	.253	.303*****	-.070		
8. pTrails Difference Scores	1344.2	1307.4	-.092	-.047	-.144	-.018	-.133	-.133	-.189	.065	-.030	-.076	.222	**.743****	
9. Switcher Total	711.75	341.1	-.133	-.079	.009	-.255	-.066	-.066	-.049	.021	**-.555****	**-.556****	.089	**-.330****	.089

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

Cognitive Flexibility Task Performance

pTrails Task

To determine whether children performed better on the pTrails task with age, a one-way analysis of variance (ANOVA) was conducted on FC values for each channel-pair with age as the between-subject factor. A main effect of age was found for Part B of the pTrails task, $F(2,53)=18.965$, $p<.001$ (Figure 5). Follow-up pairwise comparisons using Tukey's HSD indicate that response times decreased between ages 7 (M=2982.7ms, SD=2489.2ms) and 9 (M=1791.6ms, SD=561.37ms), p=.001. There was no age effect on difference scores, $F(2,53)=2.186$, p=0.122. There was also not an age effect on proportion scores (part A average completion time subtracted from part B average completion time, divided by part A average completion time), although differences appear to be trending towards significance, $F(2,53)=2.72$, p=.075 (Figure 6).

Switcher Task

We ran one-way ANOVAs for the completion times for each block of the Switcher task as well as total completion time in order to determine age-related differences in performance. An age effect was found on scores for block one, $F(2,53) = 25.784$, $p< .001$, block two, $F(2,53) = 19.56$, $p< .001$, and block three, $F(2,53) = 18.84$, $p< .001$ (see Figure 7). Follow-up pairwise comparisons using Tukey's HSD indicate that average trial completion times during block 1 of the task decreased from age 5 (M=98.79s, SD=36.07s) to 7 (M=61.42s, SD=16.5s, $p< .001$) as well as 5 to 9 (M=43.4s, SD=10.98s, $p< 0.001$). No differences in block one completion times were found between ages 7 and 9 (p=.078), although differences were trending. Completion times for block 2 decreased from age 5 (M=115.6s, SD=50.2s) to 7 (M=73.9s, SD=21.8s, p=.001), as well as 5 to 9 (M=48.2s, SD=15.1s). Differences between ages 7 and 9 are trending (p=0.065). Finally, completion times for block 3 decreased from age 5 (M=109.1s, SD=41.7s) to 7 (M=73.9s, SD=18.0s, p= .001) as well as 5 and 9 (M=52.0s, SD=18.2s, $p< .001$). There were trending differences between ages 7 and 9 (p=.070).

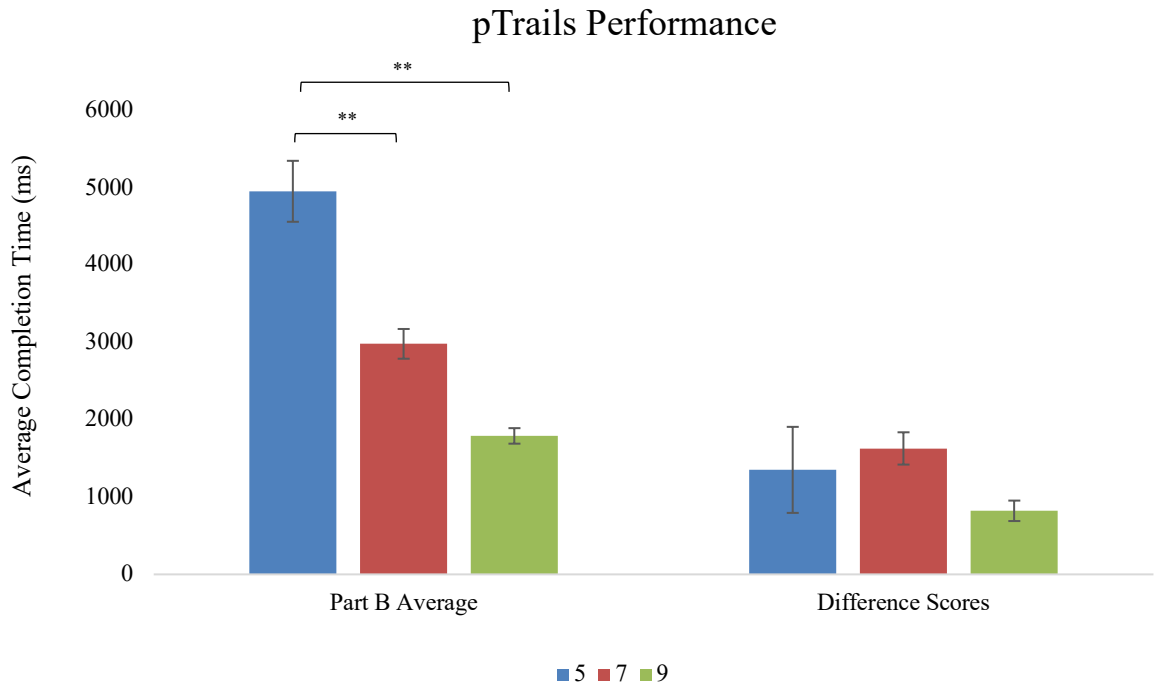

Figure 5. Average completion time for part B (requiring the participant to switch between connecting a letter and a number in sequential order) and difference scores (the difference in average completion times between part B and part A) for the pTrails task are depicted for each age group.
*** p< .01.*

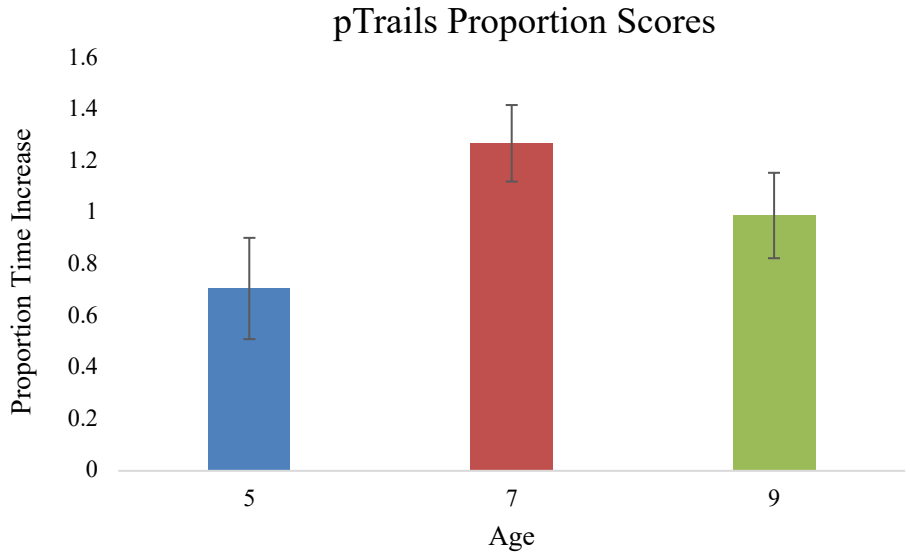

Figure 6. Proportion scores (part A average completion time subtracted from part B average completion time, divided by part A average completion time) are depicted for each age group.

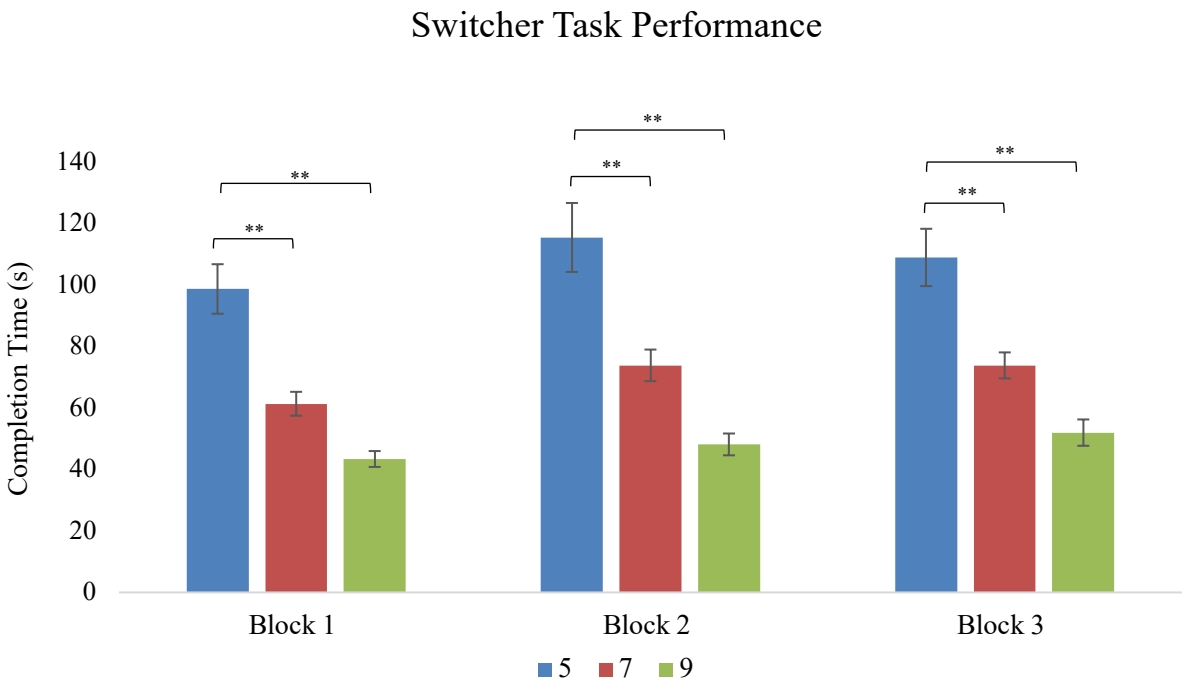

Figure 7. Average trial completion times for each block of the Switcher task are shown. ** $p < .01$.

An age effect was also found for total completion time, $F(2,53)=25.57$, $p<.001$ (see Figure 8). Follow-up pairwise comparisons using Tukey's HSD indicate that five-year-olds (M=970.2s, SD=348.6s) took significantly longer to complete the task than seven-year-olds (M=627.8s, SD=148.4s), p=.001, and nine-year-olds (M=430.9s, SD=125.4s), $p< .001$. Seven-year-olds also took significantly longer than nine-year-olds, p=0.04.

DCCS Task

We ran a one-way ANOVA with age as the independent, between-subject variable and performance scores as the dependent variable. DCCS performance differed with age, $F(2,54)=10.224$, $p< .001$. Follow-up Bonferroni-corrected pairwise comparisons indicated that five-year-olds (M=4.994, SD=1.10) had lower scores than seven-year-olds (M=6.485, SD=1.20, p=.002) and nine-year-olds (M=6.734, SD=1.57, $p< .001$) (Figure 9). There were no differences in scores between age seven and nine (p=1.00).

Raven's Colored Progressive Matrices

Scores on Raven's CPM were negatively correlated with total completion time on the Switcher task, $r(42)=-.555$, $p<.001$, as well as completion times on Part B of the pTrails task, $r(42)=-.612$, $p<.001$ (Table 1). Raven's scores were also positively correlated with performance on the DCCS task, $r(42)=.681$, $p<.001$. A one-way ANOVA indicated that scores on Raven's differed with age, $F(2,42)=20.017$, $p<.001$. Follow-up pairwise comparisons using Tukey's HSD revealed that five-year-olds (M=17.80, SD=4.78) scored lower than seven-year-olds (M=24.89, SD=5.48, p=.001) and nine-year-olds (M=30.55, SD=5.05, $p<.001$). Seven-year olds also scored lower than nine-year-olds, p=0.016.

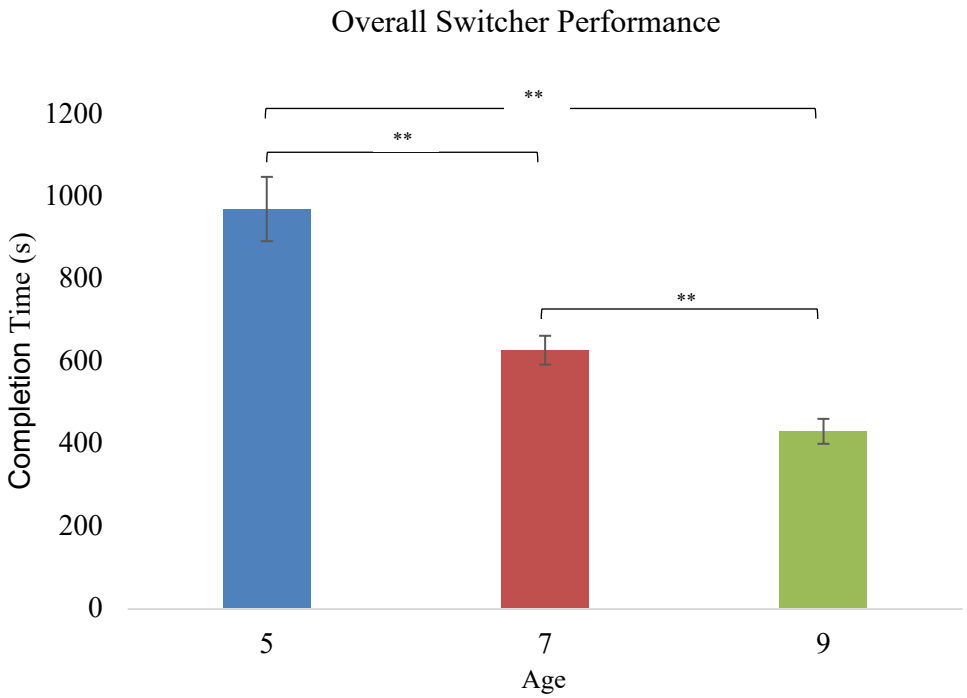

Figure 8. Total completion times (in seconds) for the Switcher task across age groups. ** $p < .01$.

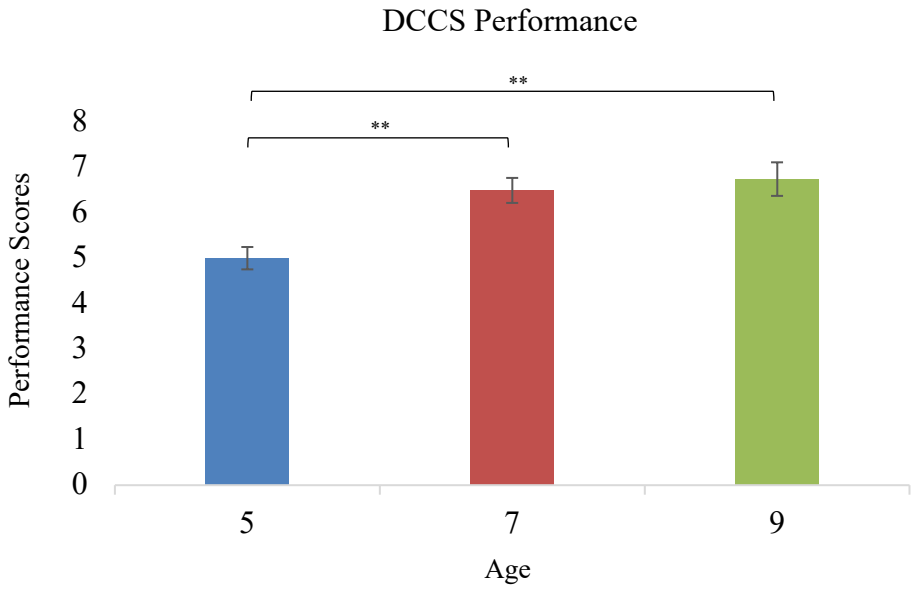

Figure 9. Average DCCS performance for each age group. RT scores were added to accuracy scores for participants with 80% accuracy or greater. ** $p < .01$.

fNIRS Analyses

Resting State Task

We ran multiple one-way ANOVAs with age as a between subject factor and the significantly correlated frontal-to-parietal channels that were common to all age groups as within-subject factors in order to determine whether the strength in rsFC between these channels changed with age. During the resting state task, FC between channels 16,21 (measuring from right frontal cortex to right parietal cortex) differed with age, $F(2,54)= 5.826$, $p=.005$. Follow-ups using Tukey's HSD indicated that FC significantly increased from age five ($M= -.070$) to nine ($M=.052$), $p=.005$. Differences in FC between ages 5 and 7 ($M=.016$) are trending ($p=.058$). No other age-related differences in long-range rsFC were found.

pTrails Task

In order to determine whether there were age-related differences in connectivity strength during the pTrails task, a series of one-way ANOVAs was conducted with age as a between subject factor and FC values for each channel pair as within subject-factors. This was done for each channel pair that was significantly connected in all age groups. There were no significant differences in FC strength with age for any of the channel pairs. However, an age related difference in FC was trending for channel pair 19-20 (covering the right frontal and right parietal cortex), $F(2,54)=3.109$, $p=.053$, appearing to decrease with age.

We then subtracted the functional connectivity correlation coefficient values during Part A from the coefficients during Part B to obtain a rho difference score for each channel per participant. The channel pairs included here were significantly connected in each age group. We ran multiple one-way ANOVAs with age as a between-subject factor and the rho difference scores as within-subject factors to determine if connectivity evoked by switching demands differed across age (Figure 10). An age effect was found for channel pair 4-6 (from left parietal to left frontal cortex), $F(2,52)=3.880$, $p=.027$. Follow-up pairwise comparisons using Tukey's HSD indicate an increase between age seven ($M= -.026$, $SD=.305$) and nine ($M=.193$, $SD=.185$), $p=0.034$. Differences between age five ($M=.002$, $SD=.270$) and nine were trending, $p=.071$. An age effect was also found for channel pair 4-8 (left parietal to left frontal cortex), $F(2,54)=5.070$, $p=.010$. Follow-up pairwise comparisons using Tukey's HSD showed differences between age seven ($M= -.098$, $SD=.374$) and nine ($M=.175$, $SD=.197$), $p=.010$. Differences between age five ($M= -.037$, $SD=.214$) and 9 were trending, $p=.053$. There were no differences between age 5 and 7, $p=.763$.

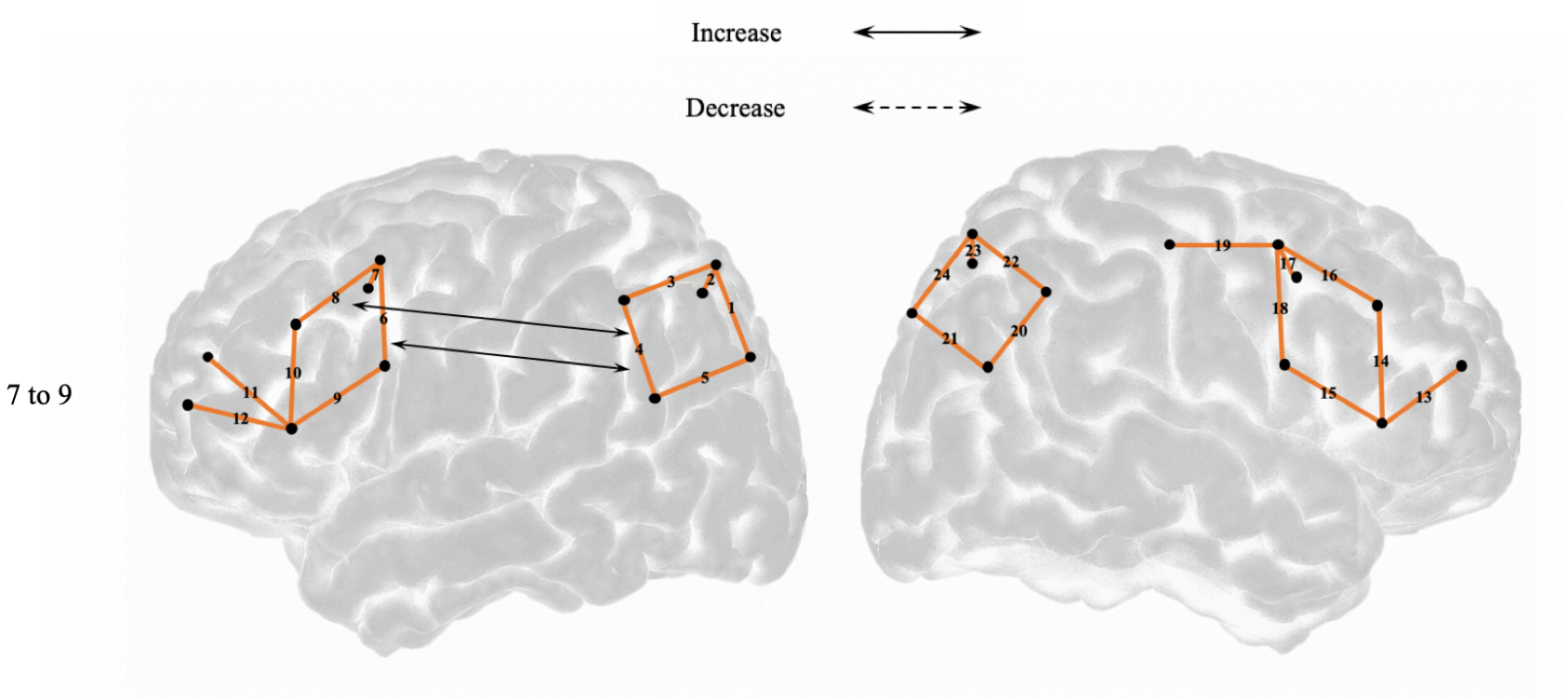

Figure 10. Age effects in "rho difference" values for the pTrails task. The figure above depicts the channel pairs in which task-evoked FC changed from ages 7 to 9.

Switcher Task

For each channel pair, we ran a repeated measures ANOVA with block as a within-subject factor and age as a between-subject factor. FC decreased from age 7 to 9 in several channel pairs within the left frontal cortex (Ch 6-10, 6-11, 6-12, 8-9, 8-10, 8-11, 8-12) and increased for one channel pair within the left frontal cortex (Ch 9-11) (Table 2, Figure 11). One channel pair within the right frontal cortex (Ch 14-16) increased from age 5 to 9 (Table 2, Figure 11). Main effects of block were found for channel pairs 5-11, 3-12, 18-24, 11-12, and 13-16 (Table 2). Two left frontal-parietal channel pairs increased in FC from block 1 to block 2, while one channel pair within the right frontal cortex and one from right frontal-parietal decreased in FC (Figure 12). Block x Age interactions were found for channel pairs 3-12, 8-12, 13-15, and 13-19 (Table 2). Specifically, FC within the left frontal cortex increased from block 1 to block 2 at age 5, while right frontal FC decreased at age 7, and FC between the left frontal and left parietal cortex increased at age 9 (Figure 13).

Lastly, we ran correlations between channel pairs that were significantly connected in each block with performance scores per block to determine channel pairs were associated with performance on the Switcher task. FC between channel pair 18-20 (right frontal to right parietal cortex) was negatively correlated with the average trial completion times on block 1 of the switcher task, such that greater connectivity was associated with faster completion times across all subjects (r=-.359, p=.007). FC strength between channel pair 6-11 (within left frontal cortex) was positively correlated with completion time on block 1, such that stronger connectivity was associated with slower completion times across subjects (r=.269, p=.045). When correlated with performance on block 2, the same patterns emerged with pair 18-20 (r=-.272, p=.043), while the pattern with pair 6-11 was trending (r=.259, p=.054). However, no correlations were found between FC strength at any channel pair and performance on block 3. We therefore decided to focus on blocks 1 and 2 alone, as block 3 appeared to be an outlier

Table 2. Summary of Switcher Task ANOVAs, follow-up tests, means and standard error

Channel Pair	Effect	F, p, η^2	Pairwise Comparison Correction	Follow-up Effect	p	M_1, M_2	SE_1, SE_2
6,10	Age	5.313, .008, .164		7, 9	.008	.287, .048	.051, .054
6,11	Age	3.984, .024, .129		7, 9	.025	.312, .102	.054, .056
6,12	Age	3.352, .042, .110		7, 9	.061	.264, .088	.053, .054
8,9	Age	3.383, .041, .111		7, 9	.051	.186, .013	.050, .052
8,10	Age	3.641, .033, .119	Tukey's HSD	7, 9	.027	.322, .092	.060, .062
8,11	Age	4.254, .019, .136		7, 9	.023	.258, .068	.049, .050
8,12	Age	4.715, .013, .149		7, 9	.010	.307, .102	.047, .048
9,11	Age	4.20, .020, .135		7, 9	.023	.623, .774	.039, .040
14,16	Age	3.509, .037, .115		5, 9	.042	.176, .395	.061, .064
5,11	Block	4.214, .045, .072		↑	.045	.178, .195	.030, .031
18,24	Block	7.204, .010, .118		↓	.010	.151, .132	.028, .026
11,12	Block	5.879, .019, .098		↑	.019	.850, .855	.023, .023
13,16	Block	8.463, .005, .135	N/A	↓	.005	.295, .277	.037, .037
3,12	Block	13.92, <.001, .205		↑	<.001	.089, .152	.029, .028
3,12	Block x Age Interaction	10.026, < .001, .271		9	<.001	-.032, .140	.051, .050
8,12	Block x Age Interaction	3.456, .039, .113		5	.026	.163, .201	.048, .046
13,15	Block x Age Interaction	3.438, .039, .113	Bonferroni	7	.007	.550, .520	.063, .064
13,19	Block x Age Interaction	3.848, .027, .125		7	.005	.371, .333	.057, .056

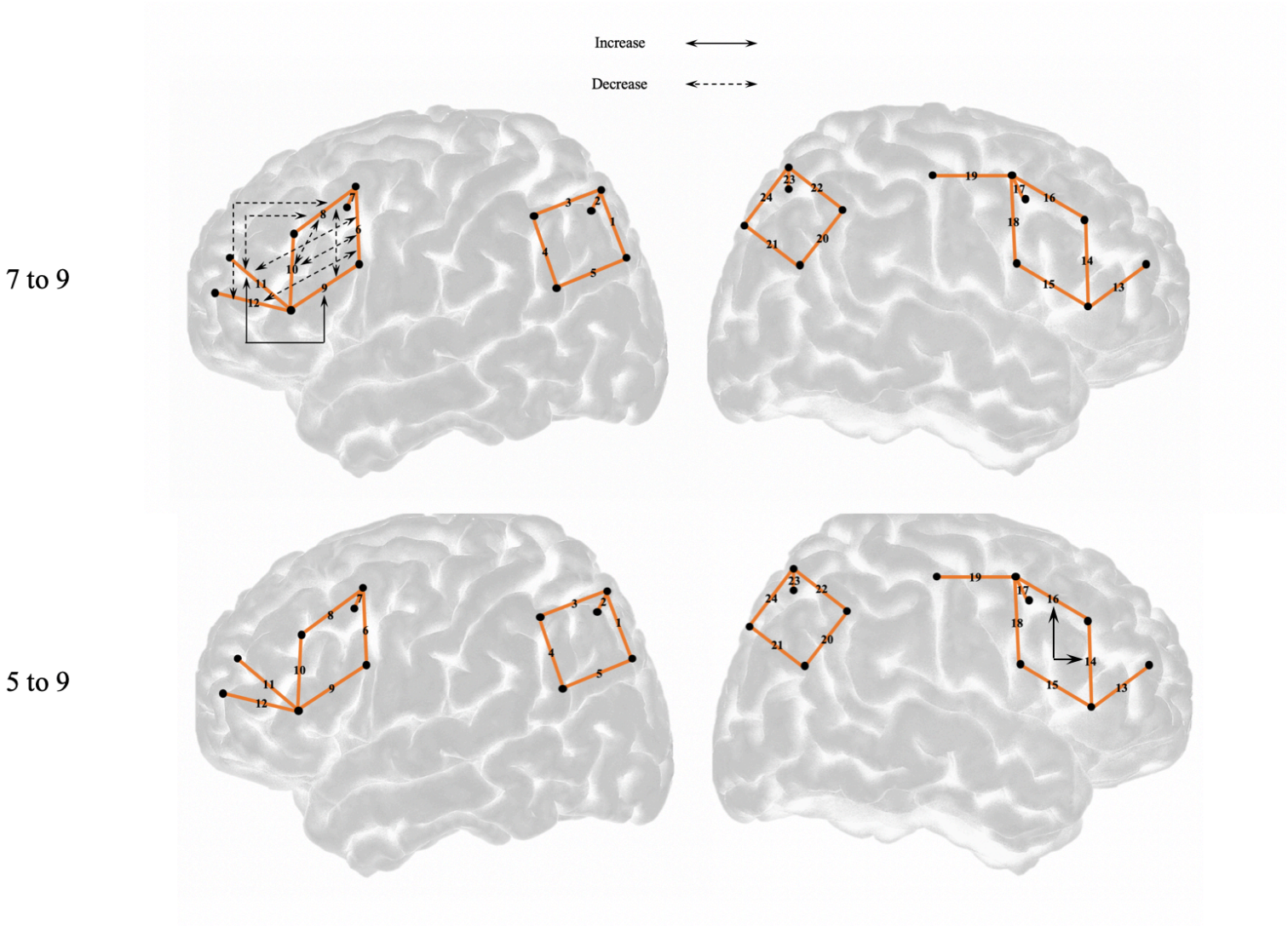

Figure 11. Age effects for the Switcher task. The figure above displays the channel pairs that changed in connectivity strength with age from ages 7 to 9 and from ages 5 to 9.

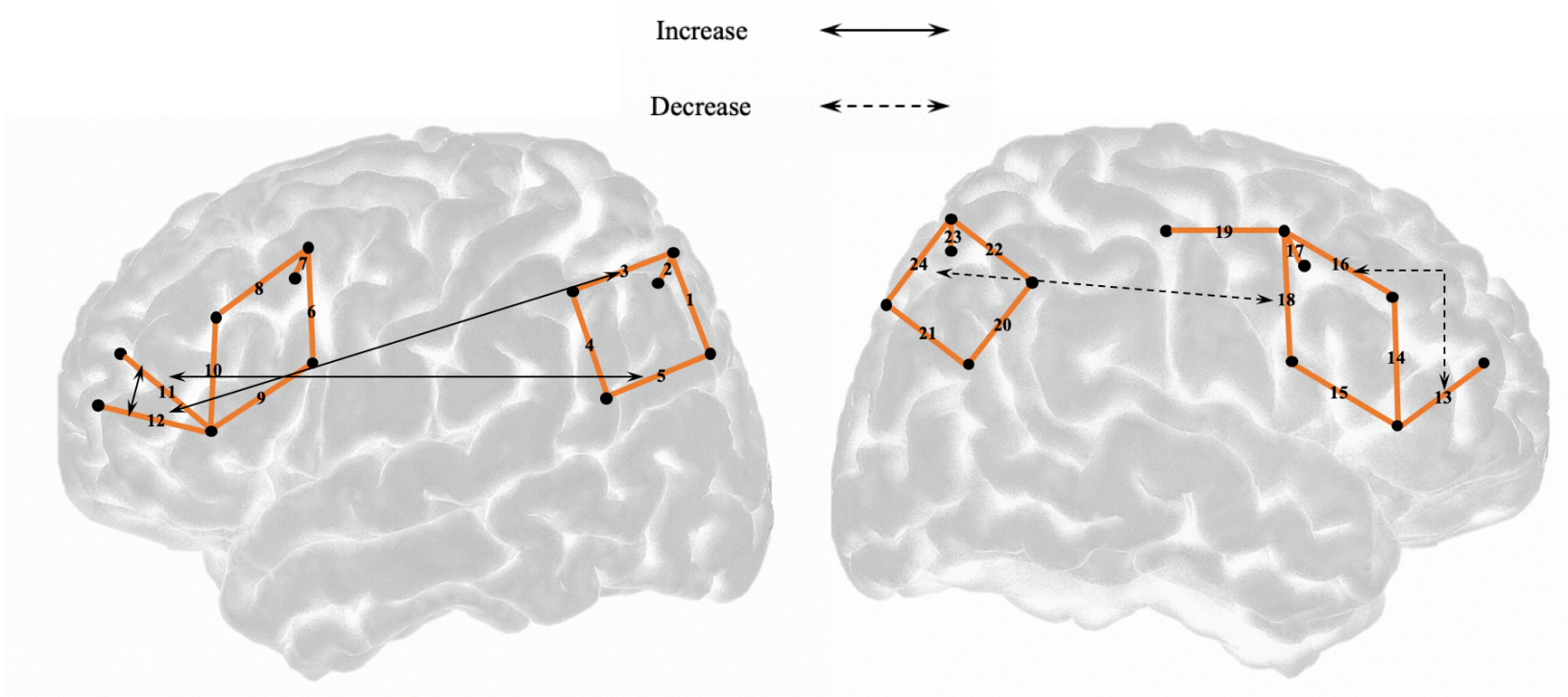

Figure 12. Channel pairs with a main effect of block for the Switcher task. Depicted above are the channel pairs that differed in FC from block 1 to block 2.

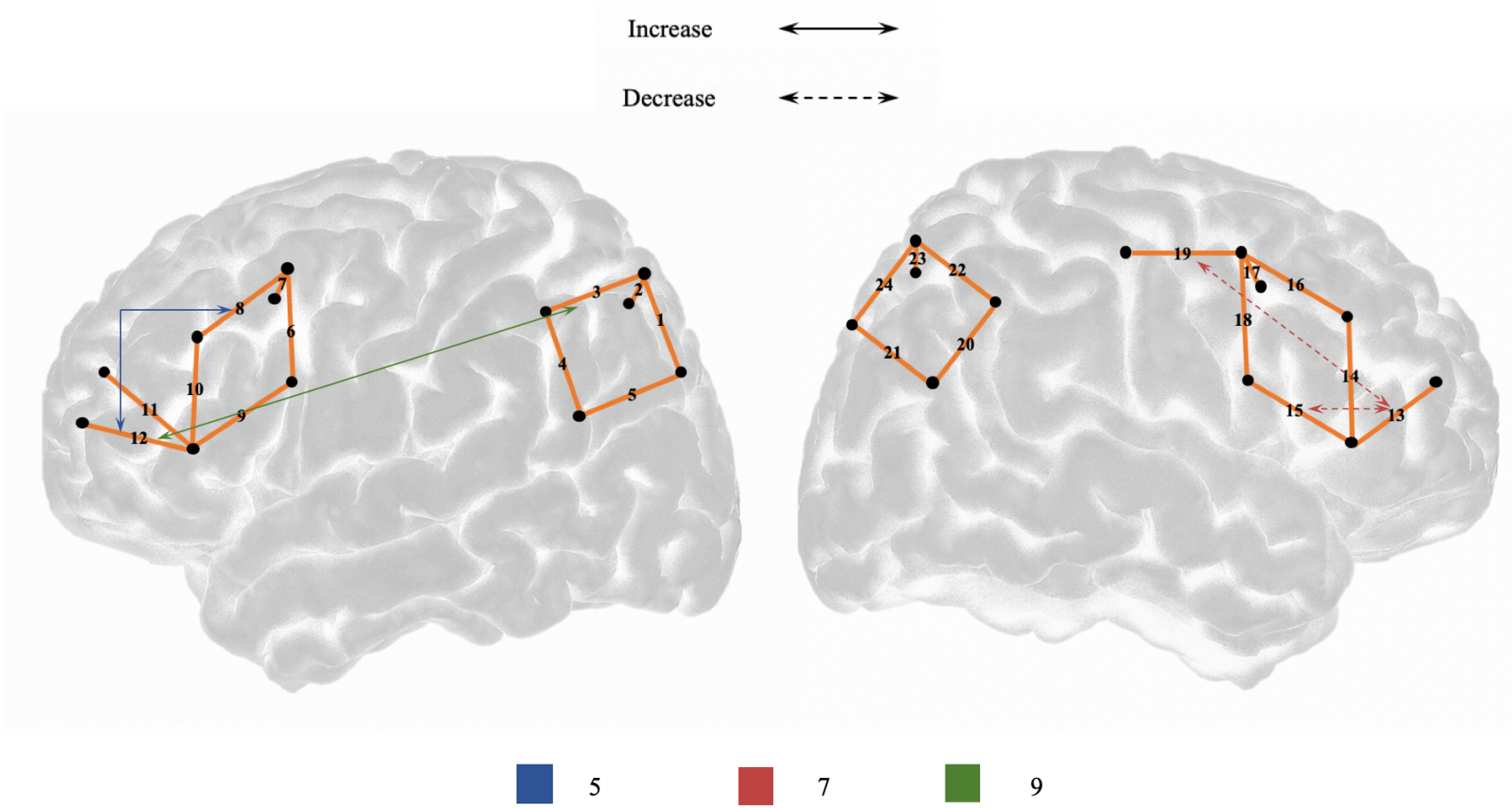

Figure 13. Block x Age interactions for the Switcher task. Depicted are the channel pairs that increased or decreased in strength from block 1 to block 2 for each age.

DCCS Task

We examined hemodynamic activation of the frontal parietal network between groups during the DCCS task using a 2x3x3 ANOVA (*oxy x phase x age*) that was conducted for each of the 24 channels. Main effects of oxy in these analyses indicate activation/deactivation and interactions with oxy indicate differences in activation across the other variables. An effect of oxy was found indicating deactivation at channel 1 (covering the left parietal cortex), such that HbO (M=-0.96, SE=0.045) was lower than HbR (M=0.027, SE=0.021), $F(1,108)=4.74$, $p=.034$, $\eta^2=.081$. An *oxy x phase x age* interaction was also found for channel 1, $F(4,108)=3.32$, $p=.013$, $\eta^2=.110$. Bonferroni corrected pairwise comparisons showed that during the pre-switch phase, HbR was greater for 5-year-olds than 7-year olds, $p=0.017$. During the post-switch phase, there was a trending difference in HbO between 5 and 7-year olds, such that HbO was higher. During the pre-switch phase, HbR was greater than HbO for 5-year-olds, $p=.021$. During the post-switch phase, HbR was greater than HbO for 7-year-olds, $p=.007$. An *oxy x phase x age* interaction was found for channel 3 as well, $F(4,104)=5.76$, $p<.001$, $\eta^2=.181$, which also covered the left parietal cortex. Bonferroni corrected pairwise comparisons showed that during the pre-switch phase, HbO was greater than HbR for 7-year-olds, $p=.035$. During the post-switch phase, HbR was greater than HbO for 7-year-olds, $p=.003$. Moreover, HbR was greater during the post-switch phase for 7-year-olds than during the pre-switch phase.

Section IV:
DISCUSSION

This study was the first to use fNIRS to measure both resting and task-evoked functional connectivity of the frontal-parietal network during the age range when this skill most rapidly develops. We compared task performance and connectivity strength of the FPN across children at age 5, 7, and 9 in order to determine if changes in connectivity support cognitive flexibility at this stage in development.

Autism Symptom Questionnaires

We assessed overall ASD symptoms as measured by the AQ-Child in order to compare our typically-developing sample to an atypically-developing group in a future exploratory study. Our participants' mean score on the AQ fell in-between the scores previously reported in TD and ASD groups by Auyeung et al. (2008). This indicates that our sample did not have clinically-significant levels of Autistic traits; however, may have fell on the higher range on this scale for TD children. Further, scores on the AQ were related to FS and RBS-R scores, which was expected given that these measures all measure the degree of Autistic traits. Interestingly, greater Autistic tendencies on the imagination subscale of the AQ were associated with poorer performance on the DCCS task. Items in this subscale included statements such as "he/she finds making up stories easy," and "if he/she tries to imagine something, he/she finds it very easy to create a picture in his/her mind". This finding may represent a link between creativity and flexibility in middle childhood. Further, greater fluid intelligence measured by Raven's CPM

Cognitive Flexibility

Average response times on the switching portion of the pTrails task differed with age; however, when completion times for non-switching trials were subtracted from these scores, there was no difference in switch costs across age groups. Additionally, switch costs measured as the proportion of time increase during switching trials did not differ across age groups. Therefore, there were no clear performance differences on this task. However, there were large performance differences on both the DCCS and Switcher task. Therefore, the results of the present study found increases in cognitive flexibility from age 5 to 7 as well as from age 7 to 9, aligning with previous research (Anderson, 2002). Further, greater fluid intelligence/NV-IQ as measured by Raven's CPM was associated with better performance on the flexibility tasks, and also increased with age.

Functional Connectivity and Activation

During the resting state, FC between the right frontal and right parietal cortices increased from age 5 to 9, providing support for our hypothesis that frontal-parietal connectivity at rest would increase with age. Additionally, the magnitude of connectivity increase that occurred in response to the demands of dimensional shifting differed with age. During the pTrails task, there was no difference in the overall connectivity strength during the switching trials (part B). However, when subtracting baseline connectivity strength measured during the non-switch trials, 9-year-olds showed greater task-evoked increases in FC between the frontal and parietal cortices. Although we have not yet used a statistical test

to compare FC on part A to part B, we plan to do so in the future. From observing group means, children at 9 years-old appear to have lower FC between frontal and parietal nodes during part A that increases to a greater degree when switching demands are introduced, whereas children at age 5 and 7 appeared to have higher levels of baseline task+ FC during part A, which in turn did not increase to as much of a degree during part B. This may reflect greater engagement of this network during non-switch trials for 5 and 7-year-olds, which in turn could represent greater cognitive involvement when connecting numbers and letters alone for these ages.

During the switcher task, we found that from age 7 to 9, seven channel pairs within the left frontal cortex decreased in connectivity strength, while one channel pair increased in connectivity strength. One channel pair within the right frontal cortex increased from age 5 to 9. A pattern that appears here is that those nodes that were less strongly connected (i.e. FC of .32 or weaker) decreased with age, while the nodes that were more strongly connected (i.e. FC of .62 or stronger) increased with age. We also noted overall task-evoked increases in FC between frontal and parietal channels when a third dimension/rule was introduced during block 2. Additionally, introducing a third rule during block 2 was associated with increases in left frontal cortex connectivity and decreases in right frontal cortex connectivity. Age-related changes in task-evoked FC from block one to block two were also found, such that frontal-parietal channels increased in FC for 9-year-olds, right frontal FC decreased for 7-year-olds, and left frontal FC increased for 5-year-olds.

Our assessment of FC during the switcher task suggests that frontal connections are being refined during this time, appearing to promote specialization and efficiency among the nodes within the prefrontal cortex that are more highly connected, while suppressing the connections that are less prominent. We believe this reflects mechanisms of the segregation process as discussed by Fair et al. (2007), as many short-range connections within the frontal cortex are decreasing with age here. The findings from this task are also consistent with that of the pTrails task in regard to 9-year-olds showing greater frontal-parietal connectivity in response to increasing task demands.

In addition to our connectivity analyses, we measured functional activation during the DCCS task. Our results showed mainly deactivation within the parietal cortex during this task. There was no sign of activation within the frontal cortex during this task, which was unexpected.

Limitations

There were several limitations to the current study. We had a relatively low sample size and did not include a population with ASD. Our NIRS probe was also limited to the specific *a-priori* regions of interest, which did not allow for between-network or whole-brain FC analyses. In the future, we hope to recruit more participants for this study in order to increase power. We also aim to replicate this experiment with an Autistic population and a typically-developing comparison group matched on age and

non-verbal IQ measured by Raven's CPM. This would allow us to make comparisons between these groups and draw conclusions about how neural architecture differs in ASD.

Additionally, there potentially confounding factors that could have impacted the results of this experiment, such as fatigue effects. In particular, the lengthiest task was the switcher task, which took place at the end of the experiment. Many times, children expressed boredom during this task. Therefore, it is unclear if completion time was the best measure of performance on this particular task. We hoped to assess errors on this task as an alternative measure of performance but were unable to do so. Due to completing the task on a touch screen computer, the task recorded an error any time the participant touched a portion of the screen that was not the correct shape for that trial. This led to many accidental errors that made this an unreliable measure. Video coding children's errors on this task in the future will allow us to record the number of perseverative errors on this task as well. Another possible confound is illiteracy. Many (but not all) five-year-old children seemed to struggle with the pTrails task due to being unable to recognize letters, which may have influenced their performance on this task. A recommendation for future studies using this task with this age group is implementing a letter recognition pre-test prior to completing the task.

Future Directions

Several future steps are planned for this study. The next steps in our analyses are to analyze FC during the DCCS task, which we have not yet included, as well as correlate rsFC with task+ FC for channel pairs between the frontal and parietal cortices to determine the relatedness between these measures. Our analyses up until this point have focused on long range frontal to parietal connectivity as well as short-range frontal connectivity. We would also like to assess short-range connectivity within the parietal cortex bilaterally during each of our tasks to determine if there are local connectivity changes in these regions with age, which we have not yet done. We hope to bolster our sample size in order to increase power in the current study. Furthermore, we would like to expand this study to include children in this age range that have been diagnosed with ASD or high-functioning Autism so that we can compare task performance between these groups, track changes in the neural dynamics of the FPN in this population and assess how neural dynamics differ in this group compared to typical development.

We suggest that future research on this topic include measurements of inter-network FC, such as between the default-mode network (DMN) and FPN. Increases in FC between the FPN and DMN have recently been linked to higher levels of creativity (Shi et al., 2018). Creativity is considered a form of divergent thinking that requires generating novel ideas that deviate from dominant, easily producible ideas—a process that requires cognitive flexibility. In the present study, greater difficulty with imagination as measured by the AQ-Child imagination subscale was associated with poorer DCCS performance, potentially representing a link between these two abilities. Since cognitive flexibility is also considered a form of divergent thinking, FC between these two networks could potentially increase across

middle childhood to support both creativity and cognitive flexibility. Perhaps those with better performance on the tasks have greater connectivity between these two networks. Because our probe was limited to the FPN, whole-brain FC analyses during this age range is an area in which this research can be expanded.

A replication of this study using fMRI would also be insightful, as much of the FC literature is conducted with this methodology. Comparisons could then be conducted between the two methodologies to establish if there are differences between these neuroimaging techniques. Conducting this study with fMRI would additionally allow for comparisons in structural connectivity that may accompany changes in FC during this age range. Anderson (2002) discusses how the increase in cognitive flexibility between ages 7 and 9 occur within the same time frame as the "second growth spurt" of the frontal lobe, suggesting that gains in task performance at this age range may be more dependent on short-range frontal dynamics than long-range dynamics. This may be why the majority of the changes in connectivity noted in the present study were identified within the frontal cortex; however, structural neuroimaging is required to determine this.

Conclusions

In conclusion, little neuroimaging work has been done to assess functional connectivity associated with the development of cognitive flexibility in middle childhood. To our knowledge, this was the first study to explore this phenomenon. Our results thus far support previous research that identified age 5-9 as a period in development when this skill immensely improves. Frontal cortex dynamics seem to be refined during this age range, promoting increases in connectivity among nodes that are more highly connected and suppressing connectivity strength between nodes that are less strongly connected. Older children showed increases in frontal-parietal connectivity in response to increasing switching demands, potentially supporting their performance on the tasks. These results shed light on potential neural mechanisms occurring during this period that may support the development of cognitive flexibility. However, further analyses are planned in the future to more clearly delineate these mechanisms. Furthermore, this project warrants replication in order to make definitive claims about this stage in development. Discovering the neural processes that may underlie the development of cognitive flexibility in neurotypical populations will allow us to better understand the brain-behavior relationship. This can also help us identify how atypical neural processes diverge from typical development and how this impacts executive function.

Section V:
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VITA

Meagan Smith was born in Greeley, Colorado and grew up in Danville, Kentucky. Meagan attended Jennie Rogers Elementary School, followed by Bate Middle School, and graduated from Danville High School in May of 2014. She attended Murray State University in Murray, Kentucky, where she received a Bachelor of Science Degree in both Psychology and Biology in May 2018. After graduation, Meagan joined the University of Tennessee Master's program in Experimental Psychology, with a concentration in developmental psychology. She has been a member of the ABC Lab under the supervision of Dr. Aaron Buss, and her research has focused on the neural markers associated with the development of executive function in children. She has also begun to study this phenomenon in children with Autism Spectrum Disorders. After graduating with a Master of Arts degree, Meagan plans to attend the University of Alabama where she will pursue her doctorate in Clinical Psychology with an emphasis in child psychology. She plans to focus her research on functional connectivity in Autism Spectrum Disorders and hopes to become a licensed clinical neuropsychologist in the future.