DISSERTATION

PHASES OF SYSTEMATIC BRAIN PROCESSING DIFFERENTIALLY RELATE TO COGNITIVE CONSTRUCTS OF ATTENTION AND EXECUTIVE FUNCTION IN TYPICALLY-DEVELOPING CHILDREN: A LATENT VARIABLE ANALYSIS

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In partial fulfillment for the requirements

For the Degree of Doctor of Philosophy

Colorado State University

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Summer 2017

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ABSTRACT

PHASES OF SYSTEMATIC BRAIN PROCESSING DIFFERENTIALLY RELATE TO COGNITIVE CONSTRUCTS OF ATTENTION AND EXECUTIVE FUNCTION IN TYPICALLY-DEVELOPING CHILDREN: A LATENT VARIABLE ANALYSIS

The series of studies presented in this dissertation examines the complex interrelationships between brain measures, cognitive abilities, and simple behaviors in typically-developing children. Much recent research has been dedicated to understanding the interaction between neural processing and behaviors across development. However, the field continues to rely on simplistic statistical approaches (e.g., correlations, *t* tests, ANOVAs), which 1) are unable to simultaneously examine multiple interrelationships among variables of interest, and 2) are easily confounded by sources of measurement error. The result is weak relationships between brain and behavioral measures. In this series of studies, we progressively demonstrate how more sophisticated statistical approaches, namely structural equation modeling (SEM) techniques, can be utilized in order to improve researchers' ability to detect brain-behavior relationships in children. All three of the present studies utilize event-related potential (ERP) and behavioral data collected from a sample of typically-developing children ages of 7- to 13-years-old during two separate sessions.

In *Study 1*, we explore the interrelationships between the E-wave component of an ERP, two trait behavioral measures of attentional processing, and simple reaction time (RT) measures during the ERP task. Whereas simple bivariate correlations indicated that the E-wave and RT only shared 7.9 – 9.6% of their variance, a latent variable approach using E-wave and trait

attention measures successfully predicted 47.7% of the variance in RT. However, the predictive coefficient from brain-to-behavior was still weak (β = .23), suggesting that there may be neural influences in addition to the E-wave that contribute to the variance in RT.

Thus, in *Study 2* we elaborated on this model and explored whether the full time-course of an averaged ERP could be conceptualized as a sequence of phases that represents stimulus-to-response decision-making processes. Specifically, we tested a latent variable path model in which one ERP component predicted the next in chronological order, with the full stream of neural processing ultimately predicting RT during the task (N1 → P2 → N2 → P3 → E-wave → RT). Age served as a control variable on each phase of processing and on RT. Results indicated strong predictive relationships from one component to the next (β's = .59 - .86), with the full stream of processing significantly predicting RT (β = .45). The model was fully-mediated, underscoring the importance of the full time-course of the ERP for understanding behaviors during the task. In addition, there were significant age effects on the N2, P3, and RT latent variables (β =.28, -.48, & -.42 respectively). Given the nature of path analyses, the findings suggested that "age" was likely a multifaceted construct representing maturation within multiple domains of cognitive or motor functioning.

Study 3 explored the differential relationships between two developmentally-sensitive cognitive constructs and each of the phases of neural processing, effectively replacing "age" with more substantive definitions of maturational effects in the model. The two cognitive constructs captured aspects of attention and executive function processing. Indeed, the findings indicated that each phase of neural processing was differentially influenced by each of the two cognitive constructs. The data suggested that children with better, more matured abilities within a specific cognitive domain tended to have smaller amplitude ERP components from the N1 through the

P3, and larger amplitude E-wave components. Conceptually, children with more matured cognitive abilities were able to process the ERP task more efficiently (or with less effort), and engaged in greater anticipatory processing leading to the task behavior when compared to children with less matured cognitive abilities. Of note, the full model did still significantly predict RT during the task, and to a much greater extent than was found in *Study 2* ($\beta = .92$).

The series of investigations in this dissertation demonstrate the utility of SEM approaches for understanding brain-behavior relationships in typically-developing children. Namely, the studies showed that 1) latent variable approaches are helpful in reducing measurement error in ERP and behavioral data, which may impede the detection of brain-behavior relationships when using more simplistic statistical approaches; 2) conceptualizing the full time-course of an ERP preceding a task behavior is not only *helpful*, but *necessary* to successfully predict behaviors; and 3) we can further elucidate unique influences of maturation on neural processing within multiple cognitive domains when we embrace advanced statistical approaches like SEM. Implications of the findings and import to the field are discussed in the final chapter.

ACKNOWLEDGEMENTS

I would like to begin by thanking my committee members, Drs. William Gavin, Patricia Davies, Carol Seger, and Lauren Shomaker, for supporting me throughout my graduate degree. Each of you has contributed to my knowledge and understanding of the field, and I could not have completed this effort without your help. You each see the world, and consequently research, with such a unique lens. Thank you for taking the time to share your views, and for challenging me to broaden my own perspective as a researcher.

I owe a special thanks to Drs. William Gavin and Patricia Davies. When I started my graduate degree, I was a bit lost, dreaming big but thinking small, and I think you both knew that. You somehow managed to simultaneously give me the freedom to explore my own interests, yet still keep me grounded. You guided and structured my thinking in order to help me grow as a researcher and meet my goals. You knew how to challenge me to push the limits of my own knowledge and abilities. At times I felt overwhelmed by both the breadth and depth of training I was receiving… You know very well that I shed more than a couple of tears during my graduate degree, but that never stopped you from challenging me to be my best. It never stopped me from striving to exceed your expectations, either. Thank you for understanding me, for teaching me, and for helping me transform from “student” to “colleague”.

I’d also like to thank all of the students in the Brainwaves Research Lab. I have had the pleasure of working with over two dozen students during my time in the lab, and each member has helped me to learn and grow. So many of you have helped me with my own research over the years, with conducting literature reviews, collecting and preprocessing data, and even performing statistical analyses. Your efforts were tremendously helpful, and I cannot imagine completing this dissertation effort (let alone my other projects in the lab) without your continued support over the years. You also gave me plenty of opportunities to exercise my skills as a mentor. I appreciated having the chance to work with so many eager, motivated students. You were also a very a forgiving audience as I learned how to teach, so thank you for that.

Of course, none of this would have been possible without the unending love and support from my family. To my parents, Sheryl and David Cabral, you have pushed me to pursue my goals, whatever they may be, for as long as I can remember. You never stopped supporting my dreams, even when I decided to get a degree in Psychology – sorry dad, this girl just isn’t an engineer! Through my entire educational career, you celebrated my accomplishments, commiserated with my frustrations, and always made sure that I got back up after I fell. Thank you for continually supporting me, and for helping me to achieve this milestone in my life. I love you both and I could not have done this without you.

Last but certainly not least, I need to thank my incredible husband, Jon Taylor. You, above all others, made sure that I met this goal, and I love you all the more for your dedication to my dreams. You’ve made incredible sacrifices over the last few years to ensure that I would be able to stay in school and continue pursuing my educational goals. You put my needs and desires above your own, even when I asked you not to. You kicked me into gear when I needed to be pushed, and you held my hand when I needed help. You always knew exactly what I needed to keep going. I cannot thank you enough for your love and support as I’ve worked to meet my goals, and I’m so excited to share this accomplishment with you and our sweet Lily. Thank you for all that you are and all that you do. You are an incredible person, and I can’t imagine getting here without you. I love you.

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CHAPTER I

The prevalence of neurological and developmental disorders among children is on the rise in the United States. For example, the Centers for Disease Control and Prevention (CDC; 2015a, 2015b) currently report that 1 in 68 children receive a diagnosis of autism spectrum disorder (ASD), and as many as 1 in 10 children receive a diagnosis of attention-deficit/hyperactivity disorder (ADHD; Visser, Zablotsky, Holbrook, Danielson, & Bitsko, 2015). Such disorders commonly impact cognitive systems that are critical to everyday functioning. Dysfunction in cognitive systems leads to the manifestation of observable behavioral deficits that are the premise of standard diagnostic tools like the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychological Association, 2013) and the International Statistical Classification of Disease and Related Health Problems (ICD-10; World Health Organization, 2015).

For decades, diagnostic labels have been binary classifications; one must meet a full criterion of symptoms in order to be diagnosed with any specific disorder. For example, in order to receive a diagnosis of ASD, one must show several deficits in the categories of “social communication and interaction,” and “restricted, repetitive patterns of behavior” (American Psychological Association, 2014). Within each of these categories, the DSM-5 provides a list of more specific symptoms (e.g., deficits in developing and maintaining relationships). An individual must express a certain number of symptoms in each category to be diagnosed with ASD.

Although many individuals do receive a diagnosis of ASD given these criteria, there are many children who receive no diagnosis because they do not cross the threshold for the number of specific symptoms required by the DSM-5. For example, in the CDC study which established that 1 in 68 children have ASD, only 82% of those children identified had previously received a formal diagnosis (Christensen, 2016). Roughly translated, the study results suggested that nearly 1 in 5 individuals who *should have* received a diagnosis of ASD had not been formally diagnosed. Without a diagnosis, children are unable to receive special education and therapeutic services despite presenting a constellation of behavioral deficits that impair everyday functioning. Given the limitations of the current binary categorization, the National Institutes of Health (NIH), and primarily the National Institute of Mental Health (NIMH), have proposed a new framework for understanding mental disorders: the Research Domain Criteria (RDoC).

Research Domain Criteria

The RDoC offers a framework for moving away from blunt categorization of disorders and instead emphasizes the need to understand spectra of individual differences and symptoms measured from multiple levels. More specifically, RDoC represents a paradigmatic shift toward understanding mental disorders and psychopathology in terms of a confluence of translational genetic, neuroscience, and behavioral research (Insel et al., 2010; Morris & Cuthbert, 2012; NIMH, 2011). Although the overarching goal is to move toward a more fluid diagnostic system based in biologically- and behaviorally-based individual differences, RDoC is currently used primarily for research purposes.

The RDoC framework organizes observable symptoms and biological measures into a matrix of rows and columns (Cuthbert & Insel, 2013; Cuthbert & Kozak, 2013). Rows are comprised of different constructs (e.g., attention), and columns represent units of analysis for measuring the level of functioning within a particular construct (e.g., physiology). Cells of the matrix offer examples of measures one might explore in order to understand the level of functioning in a behavioral construct, like measures of the brain's electrical activity during a specific task (NIMH, 2011). Among the numerous constructs NIMH has defined for RDoC, attention (see Figure 1.1) and cognitive control (see Figure 1.2) are two constructs that are commonly impaired in children with neurological and developmental disorders.

Attention

Attention is a construct that is widely recognized in the literature, though there are varying definitions. In general, attention is described as the ability to select and focus on a target, and maintain focus on that target in the midst of distractors (e.g., Petersen & Posner, 2012; Posner & Petersen, 1990). Some researchers define attention as a series of systems that *regulate* cognitive processing and behaviors, serving a critical role in human functioning (Cicerone & Maestas, 2014; Posner & Rothbart, 2007). For the purpose of RDoC, NIMH developed the following definition:

> "Attention refers to a range of processes that regulate access to capacity-limited systems, such as awareness, higher perceptual processes, and motor action. The concepts of capacity limitation and competition are inherent to the concepts of selective and divided attention" (NIMH, 2011, pp. 3-4).

From this definition, it is clear that attention plays an important role in everyday functioning. Without the ability to decipher what aspects of information processing are salient from moment-to-moment, and without proper resources dedicated to those neural processes, individuals struggle to successfully engage in and complete context-appropriate behaviors.

Researchers have commonly defined several subtypes of attention, each of which serves a different purpose and is shown to have different neural circuitry. Although the naming scheme varies throughout the literature, three subtypes of attention are commonly noted: selective attention, switching attention, and sustained attention (Manly et al., 2001; Petersen & Posner, 2012; Posner & Petersen, 1990).

Selective Attention. Selective attention is the ability to focus and enhance processing of a particular stimulus regardless of where it occurs in space (Manly et al., 2001), and resembles Petersen and Posner's (2012) frontoparietal executive control system of attention. The selective attention network is believed to play a key role in the initiation and adjustment of behaviors in real-time based on start-cue signals (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Dosenbach et al., 2007; Petersen & Posner, 2012). The neural circuitry of selective attention has been localized to lateral frontal and parietal regions of the brain (Petersen & Posner, 2012).

It is noteworthy that Petersen and Posner describe an additional opercula network that is encompassed in the broader "executive attention" system. The opercular network is similar to Posner and Petersen's (1990) originally-proposed "target detection" system, which is involved in the sustained, stable maintenance of overall task performance. The system has roots in the medial frontal lobe, the anterior cingulate cortex, and the bilateral insula (Dosenbach et al., 2008; Dosenbach et al., 2007; Petersen & Posner, 2012).

Switching Attention. Switching attention, or attentional control, allows an individual to change focus from one task or mental process to another (Manly et al., 2001). Other researchers' definitions encompass the process of prioritizing incoming sensory stimuli and orienting to one sensory modality while ignoring another, as is described in Petersen and Posner's (2012) orienting system. In particular, the orienting system is key in determining *where* a stimulus will occur. The switching attention network is a fronto-parietal network involving large portions of the parietal lobes, and parts of the frontal lobes including the dorsolateral prefrontal cortex (DLPFC) and frontal eye fields (FEF; Snyder & Chatterjee, 2006). Interactions with the temporo-parietal junction and the ventral frontal cortex have also been shown to be involved in the process of switching attention (Sestieri, Shulman, & Corbetta, 2012; Shulman & Corbetta, 2012). The system is heavily influenced by cholinergic systems of the basal forebrain (Fan et al., 2009).

Sustained Attention. Sustained attention, also termed the alerting system (Petersen & Posner, 2012; Posner & Petersen, 1990), or vigilance (Niendam et al., 2012; Warm, 1984), is responsible for maintaining focus on a task and responding to rare or novel stimuli in a relatively uneventful environment (Hilti et al., 2013; Manly et al., 2001; Matchock & Mordkoff, 2009). In particular, sustained attention processes are shown to be key in determining *when* a stimulus will occur (Petersen & Posner, 2012). Functional magnetic resonance imaging (fMRI) studies show that sustained attention processing is heavily lateralized to the right hemisphere with activations in frontal areas and dorsal parietal areas (Goldman, Shapiro, & Nelson, 2004; Petersen & Posner, 2012). Although it seems to overlap with the localization of switching attention, sustained attention networks have been shown to be uniquely independent of switching attention networks (Fan et al., 2009) Additionally, animal models have shown that sustained attention systems are particularly influenced by norepinephrine systems of the brain (Beane & Marrocco, 2004; Davidson & Marrocco, 2003).

Units of Analysis for Measuring Attention. Researchers have used a myriad of measures, both biological and behavioral, to understand the complexity of attention. Based on the current body of literature the RDoC matrix provides examples of measures for assessing an individual's attention abilities (see Figure 1). Much of the research exploring attention has focused on behavioral assessments such as the Teat of Everyday Attention for Children (TEA-Ch; Manly et al., 2001). The assessment consists of nine game-like subtests that purport to measure the three previously-described subtypes of attention. In addition to behavioral measures, the RDoC matrix includes a unit of analysis called “physiology” which subsumes a number of electrophysiological measures of brain processing.

Electroencephalography and event-related potentials. With electroencephalography (EEG), researchers and clinicians can non-invasively measure the electrical activity of the brain using small metal sensors placed on the scalp (Stern, Ray, & Quigley, 2001). A major advantage of EEG is its temporal resolution, which allows researchers to examine neural processing with millisecond-precision. Researchers have found that certain electrical signals of the brain are likely representations of sensory, cognitive, and motor processing in the brain. Because it is relatively risk-free, EEG has been used to study neurally-based cognitive processing across the lifespan, including attentional processing (e.g., Goldman et al., 2004; Segalowitz & Davies, 2004).

One method of studying the electrophysiology of attention is through the use of event-related potentials (ERPs). ERPs represent the brain’s electrical response time-locked to a specific event, like the presentation of a stimulus. Researchers create an averaged ERP for an individual by averaging together the brain’s response to that specific event over multiple presentations during a computerized paradigm. Many of these paradigms require some behavioral response of the participant, like a simple button press following a stimulus. The resulting averaged ERP consists of a number of positive and negative voltage deflections called components, each of which has been related to specific aspects of sensory, cognitive, or motor processing relevant to decision-making (for a complete review, see Kappenman & Luck, 2012).

Two main features of ERP components are commonly measured by researchers: the amplitude and the latency of the component. Amplitude refers to the degree of voltage deflection, typically measured in microvolts (μV), and has been interpreted as a representation of the intensity of neural processing as well as the amount of neural resources dedicated to processing an event within a specific sensory, cognitive, or motor domain (Walhovd, Rosquist, & Fjell, 2008). Latency, measured in milliseconds, refers to the time at which an ERP component reaches its maximum amplitude, and has been associated with the temporal efficiency of processing within a sensory, cognitive, or motor domain. Many ERP components are named based on the polarity of their voltage deflection (i.e., positive versus negative), and their latency (e.g., the P300, or P3, is a positivity occurring approximately 300 milliseconds following a stimulus).

Researchers have been interested in understanding the functional associations of ERP components for several decades. Through experimental manipulations of cognitive demands during a paradigm, and through correlations with validated behavioral assessments, a number of ERP components have been described as representations of attention. Thus, the RDoC matrix lists several ERP components as potential physiologic measures of an individual's attentional abilities (NIMH, 2011).

ERP measures of attention.

N1. One prominently studied ERP component that is believed to represent aspects of attentional processing is the N1. The N1 component is a negativity that occurs approximately 100ms following the presentation of an auditory stimulus, or 170ms following the presentation of a visual stimulus. Research has shown that the amplitude of the N1 is sensitive to features of the stimulus, including intensity (i.e., volume) and luminance (brightness), which has lead scientists to believe that the component represents aspects of sensory processing in the brain. Interestingly, the N1 also seems to be influenced by the individual's attention to the stimulus such that the amplitude of the N1 to attended stimuli is larger than the amplitude to unattended stimuli (Kappenman & Luck, 2012).

Studies exploring the neural generators of the N1 component have indicated a number of dispersed brain regions. For instance, examinations of the visually-evoked N1 component suggest origins in lateral extrastriate cortex and inferior occipitotemporal cortex (Hopf, Vogel, Woodman, Heinze, & Luck, 2002; Kappenman & Luck, 2012). Other studies have shown that the anterior cingulate and supplementary motor areas of the prefrontal cortex may also contribute to the N1 (Kappenman & Luck, 2012; Picton & Taylor, 2007).

P2. The P2 is a positive voltage deflection occurring approximately 150-250ms following the presentation of a stimulus, and has been generically described as an indication of early stimulus processing (Kappenman & Luck, 2012; Polich, 1993). Interestingly, the P2 has not been studied as heavily as other ERP components, though researchers have still hypothesized about its functional associations. Like the N1 component, researchers have found that the P2 is sensitive to stimulus characteristics such as the frequency and intensity of auditory stimuli, even during very simple tasks that do not require any behavioral responses (Davies & Gavin, 2007). Because of its sensitivity to sensory information, researchers have sometimes described the P2 component as a representation of sensory registration processes (Davies, Chang, & Gavin, 2010; Davies & Gavin, 2007).

Interestingly, much like the N1 component, the P2 also seems to be representative of early attentional processing. Recent work by Adams, Popovich, and Staines (2017) indicated that the P2 component elicited to visual stimuli is modulated by attention to a task. Participants were presented with visual, vibrotactile, or a combination of stimuli and asked to respond to one specific stimulus modality. The researchers found that the P2 component elicited by visual stimuli was significantly larger on trials in which the visual stimulus was attended compared to trials in which the visual stimulus was ignored. Thus, attention to the task seems to be a relevant contributor to the morphology of the P2 component, at least for visual stimuli (Adams et al., 2017).

P3. The P3 is an ERP component that has captured the attention of numerous researchers, and has been studied in a myriad of cognitive contexts. The P3 component is a robust positivity that typically occurs around 250-500ms following the presentation of an attended stimulus. It is noteworthy that the P3 does not present following unattended stimuli, at least in neurotypical adult samples (Polich, 1993; Segalowitz & Davies, 2004). Thus, many scientists believe that the P3 is chronologically the first component in an ERP that represents controlled attention during a task (Kappenman & Luck, 2012; Segalowitz & Davies, 2004). Researchers two different P3 components: the P3a, and the P3b, each of which presents under different cognitive demands and with a different scalp topography.

Both the P3a and the P3b can be elicited within a single, three-stimulus variant of a commonly utilized task called the oddball paradigm (Bachiller et al., 2015; Polich, 2007; Segalowitz & Davies, 2004). In the task, which is typically auditory in nature, participants are presented with three different types of tones. One tone is a rare target stimulus to which the participant is instructed to respond, often with a simple button press. Another tone is a frequently-presented standard stimulus to which the participant does not need to attend. The third type of tone is a rare, novel stimulus (i.e., each presentation is different) to which the participant does not respond. Some researchers refer to the novel tone as a distractor stimulus (e.g., Bachiller et al., 2015; Polich, 2007). In neurotypical adults, a P3 is prominent in response to both the novel and the rare types of stimuli, but not to the standard stimuli.

The P3a is an early, frontally-maximal positivity that seems to reflect a quick orienting response to novel stimuli (Polich, 2007; Segalowitz & Davies, 2004). In turn, the P3b presents in a later timeframe with a more posterior scalp distribution. Because it is present in response to rare target stimuli, researchers believe that the P3b represents a deeper, higher-order processing of the attentional demands of the task (Segalowitz & Davies, 2004).

Researchers have developed a number of theories in an attempt to explain the functional meaning of the P3 components. One theory, the context updating theory, suggests that following the presentation of a stimulus, the brain must process whether the stimulus was different from the previous, thus engaging in a working memory-based comparison. When the comparison decision is that the stimulus was different, attentional processes in the brain must update the current stimulus representation, which coincides with the presentation of a P3 (Kappenman & Luck, 2012; Polich, 2007). Another theory is that the P3 represents an index of attentional resource allocation such that more attentionally-demanding tasks will be marked by a smaller-amplitude and a longer-latency P3 component (Kappenman & Luck, 2012; Polich, 2007). Because of the implications for attentional processing, some researchers have examined the P3 in individuals with attention difficulties including schizophrenia (Bachiller et al., 2015), ADHD (Janssen, Geladé, van Mourik, Maras, & Oosterlaan, 2016), and autism (Cui, Wang, Liu, & Zhang, 2016).

For example, Janssen et al. (2016) conducted a study in which children with and without ADHD (age 7-to-14 years; $N = 85$; $n = 36$ with ADHD) completed a two-stimulus (rare target and frequent standard) auditory oddball task while high-density EEG data were recorded. The researchers also collected parent- and teacher-reports of the children's ADHD symptoms and behaviors. The data indicated that children with ADHD had significantly smaller P3 amplitudes compared to their typically-developing peers. Source localization of the EEG data indicated multiple sources of activation during the time frame of the P3 in the frontal and temporoparietal regions mainly in the left hemisphere. Children with ADHD had reduced activation in the middle- and superior-frontal gyri, as well as in the temporoparietal junction, angular, middle temporal, and superior temporal gyri. Additionally, P3 amplitudes were negatively correlated with teacher-reported inattention, and teacher-reported hyperactivity/impulsivity scores among children with ADHD (Janssen et al., 2016). The researchers suggested that children with ADHD exhibited altered functionality within specific attention systems including the cinguloopercular and ventral attention networks, specifically in the time window of the P3 component.

Contingent Negative Variation (CNV). Another event-related potential component that has been related to attentional processing is the contingent negative variation (CNV). The CNV is a slow negative drift in voltage that presents between two stimuli, typically a warning/cue stimulus and an imperative stimulus like those presented in a delayed-response Go/No-Go task (Segalowitz & Davies, 2004; Taylor, Gavin, & Davies, 2016; Walter, Winter, Cooper, McCallum, & Aldridge, 1964).

In this type of task, participants are first presented with a cue stimulus that informs them as to whether they should respond to the following stimulus (i.e., Go or No-Go trial). On a Go trial, the participant is asked to respond to the upcoming imperative stimulus, often by pressing a button. There is a fixed amount of time between the presentation of the cue and imperative stimuli. The participant does not respond to the imperative stimulus during a No-Go trial. The event-related potential time-locked to the cue stimulus follows a standard pattern of positive and negative voltage deflections that would be expected in a simple cognitive task through the P3 component on both Go and No-Go trials. However, on Go trials following the P3, the voltage of the ERP continues to drift negatively and builds in amplitude leading to the presentation of the imperative stimulus. It is this negative drift in voltage that characterizes the CNV. Interestingly, there is no negative drift following the P3 on No-Go trials; the voltage returns to baseline levels for the remainder of the trial.

Because the CNV is only visible on Go trials, a number of researchers have suggested that the CNV is representative of sustained attention processing (Segalowitz & Davies, 2004; Taylor et al., 2016; Walter et al., 1964). That is to say the CNV represents the additional attentional processing that must occur in order to adequately anticipate and prepare for the upcoming imperative stimulus and response. Without the need to attend to the stimulus (i.e., a No-Go trial), the ERP voltage simply returns to baseline indicating that there is no further, consistent processing of the trial leading to the presentation of the imperative stimulus. Magnetoencephalography (MEG) and fMRI studies have isolated the neural generators of the CNV to primarily the dorsolateral prefrontal cortex (Bareš, Rektor, Kanovsky, & Streitová, 2000; Bareš, Rektor, Kaňovský, & Streitová, 2003). Additional neural influences have been noted in the supplementary motor cortex, primary motor cortex, anterior cingulate cortex, basal ganglia, thalamus, and orbitofrontal cortex (Bareš et al., 2000; Bareš et al., 2003).

Researchers have further investigated the CNV component and found that it is comprised of two unique phases of processing: an early orienting phase, and a late expectancy phase. The early phase of the CNV, termed the O-wave, is considered to be an orienting response to the cue stimulus (Giard, Perrin, Pernier, & Bouchet, 1990; Rohrbaugh, Newlin, Varner, & Ellingson, 1984; Zimmer & Demmel, 2000). In contrast, the expectancy phase of the CNV, termed the E-wave, is believed to be more representative of the anticipation of the upcoming imperative stimulus (Basile, Ballester, de Castro, & Gattaz, 2002; Bender, Resch, Weisbrod, & Oelkers-Ax, 2004; Knott et al., 1991). Although not clearly distinguishable from the total CNV in an averaged ERP, the O-wave and E-wave have been isolated from each other using principle components analysis (PCA). Bender et al. (2004) showed that even in children, the O-wave and E-wave could be separated into orthogonal components that presented in different timeframes and were stronger at different scalp sites.

Investigations using high spatial-resolution techniques and source-localization methods have indicated that the neural generators of the two components also differ from one another. The O-wave can be attributed to activity in areas of the prefrontal and frontal cortex, sharing many of the same generators as the total CNV (Falkenstein, Hoormann, Hohnsbein, & Kleinsorge, 2003; Giard et al., 1990; Rohrbaugh et al., 1984). In turn, the E-wave seems to be more dispersed with generators spanning prefrontal, frontal, and parietal cortices with the more posterior regions contributing more to the generation of the E-wave component (Basile et al., 2002; Bender et al., 2004; Falkenstein et al., 2003; Knott et al., 1991).

Cognitive Control/Executive Functioning

Cognitive control, more commonly termed "executive function" in developmental literature, is a complex construct that has stirred a number of debates among researchers and clinicians. Executive function is conceptualized as an umbrella term encompassing a number of cognitive processes that aid in goal-directed behaviors. Researchers describe executive functions as *modulatory* systems, changing the way that humans process information and behave; however, there is variability in the definition of executive functions from field-to-field. For example, in the field of developmental psychology, Carlson (2005) defined executive function as "higher order, self-regulatory, cognitive processes that aid in the monitoring and control of thought and action" (p. 595). Additionally, in the Occupational Therapy literature, executive function has been defined as a set of component processes required for successful engagement (Cramm, Krupa, Missiuna, Lysaght, & Parker, 2013). In an attempt to define the term for RDoC, NIMH developed the following definition:

> "Cognitive control [or executive function] involves multiple subcomponent processes, including the ability to select, maintain, and update goal representations and performance monitoring and other forms of adaptive regulation. The implementation of these processes includes mechanisms such as response selection and inhibition or suppression" (NIMH, 2011, p. 12).

There is much confusion and disagreement over which cognitive constructs comprise executive function (Barkley, 2012). Some of the more commonly agreed-upon processes include inhibition, working memory, performance monitoring, and planning and organizing (Gioia, Isquith, Retzlaff, & Espy, 2002; Glozman & Shevchenko, 2014; Miyake, Friedman, Emerson, Witzki, & Howerter, 2000). The inherent ambiguity in the term "executive function" has left researchers with myriad definitions, and combinations of over 30 cognitive abilities included in the umbrella term in any given study (Eslinger, 1996).

Nonetheless, researchers have pursued the study of executive function and have shown evidence that specific brain regions are implicated in executive processes. The frontal lobes, and primarily prefrontal cortex, have long been studied as the central hubs for executive functioning (Barkley, 2012; Chung, Weyandt, & Swentosky, 2014). Research has shown that individuals with prefrontal lesions and dysfunctions often show deficits in performance on executive functioning measures (Hernandez et al., 2002; Kertesz, 1994; Powell & Voeller, 2004). Additionally, functional neuroimaging evidence has localized neural processing of executive tasks to specific frontal brain regions including anterior cingulate cortex and dorsolateral prefrontal cortex (for a review see Jurado & Rosselli, 2007). More recent views suggest that rather than housing all executive functioning abilities, prefrontal cortex may serve as a mediator in a complex network of brain regions necessary to complete executive tasks (Jacobs, Harvey, & Anderson, 2011; Wilson, Gaffan, Browning, & Baxter, 2010). Indeed, psychophysiological evidence suggests that executive functions originate from a diffuse network of brain regions (e.g., Church et al., 2009; Gratton et al., 2016).

Units of analysis for measuring executive function. As noted with respect to the construct of attention, the RDoC matrix consists of a number of units of analysis for assessing executive functions. Much of the literature examining executive functions in children focuses on a combination of behavioral assessments (e.g., the Stroop task, the Wisconsin Card Sorting Task; WCST; Golden, 1978; Heaton, 2003, respectively) and parent- or teacher-report measures (e.g., the Behavior Rating Inventory of Executive Functions; BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000). However, more recent literature has turned to physiological measures, namely ERPs, to better understand the neural processing associated with executive functions.

ERP measures of executive function.

N2. The N2 component is a negative voltage deflection occurring approximately 250-350ms after the presentation of a stimulus (Kappenman & Luck, 2012). Researchers abound describe the role of the N2 as a representation of executive control processes including discrimination and inhibition (Heil, Osman, Wiegelmann, Rolke, & Hennighausen, 2000; Patel & Azzam, 2005). In fact, researchers have utilized unique paradigms in order to elicit specific subtypes of the N2 component that may represent more specific executive function abilities.

One subtype of the N2 is termed the mismatch negativity (MMN) and is elicited during oddball tasks (as described previously for eliciting P3 components). When an individual is presented with a rare stimulus, the N2 component is actually larger in amplitude when compared to the N2 following a frequent stimulus (Cheour, Leppänen, & Kraus, 2000; Patel & Azzam, 2005). The disparity in N2 amplitudes between rare and frequent stimuli is the MMN component. Researchers argue that the MMN is a representation of executive discriminatory processes in response to the unexpected, rare stimulus. Interestingly, the MMN does appear in an averaged ERP even if the participant was not attending to the stimulus, thus researchers have suggested that the MMN is more a representation of executive processes than attentional processes, and that the MMN may be indicative of novelty-detection as well (Patel & Azzam, 2005).

In addition to the MMN, researchers have noted a different subtype of N2 component elicited during Go/No-Go tasks termed the inhibitory N2 (Cid-Fernández, Lindín, & Díaz, 2014; Heil et al., 2000; Patel & Azzam, 2005). In a traditional Go/No-Go task, participants are presented with two conditions of stimuli: a frequent "Go" stimulus, and a rare "No-Go" stimulus. Participants are instructed to respond to Go stimuli (e.g., by pressing a button) and to withhold their response to No-Go stimuli (for examples, see Grammer, Carrasco, Gehring, & Morrison, 2014; Lamm et al., 2014). Researchers have noted that the N2 response to No-Go stimuli is larger than the N2 response to Go stimuli, thus researchers have suggested that the N2 may represent some unique inhibitory processes in addition to executive discrimination (Lamm et al., 2014; Patel & Azzam, 2005).

P3. Although the P3 component is frequently described as a representation of attentional processing, some researchers have provided evidence that the P3 may also be linked to executive functioning and other higher-order cognitive processes. For example, a number of studies have indicated that the P3 is sensitive to working memory, a cognitive skill that is frequently identified as an executive function ability (e.g., Morgan, Klein, Boehm, Shapiro, & Linden, 2008; West, Bowry, & Krompinger, 2006). West et al. (2006) studied the effects of simple declarative working memory load on the amplitude of the P3 component in a sample of healthy young adults. Participants completed a 1-back and a 3-back task, thereby manipulating the amount of information that needed to be maintained in working memory to be successful. The data indicated that participants' P3 amplitudes were significantly larger under the lower working memory load condition (West et al., 2006). Further evidence suggests that neurotypical individuals with better working memory abilities tend to have larger P3 amplitudes than individuals with poorer working memory abilities, including those with clinical diagnoses like mild cognitive impairment (Cid-Fernández et al., 2014; Dong, Reder, Yao, Liu, & Chen, 2015).

Based on findings with working memory load (in addition to novelty oddball manipulations), researchers have suggested the context-updating theory to explain the sensitivity of the P3 component. Polich (2007) explained that the brain quickly learns and has set expectations about what stimuli to expect next; in other words, the brain develops a mental schema of the environment. When a new stimulus is detected, the brain must update its schema to process and integrate the new information.

Other newer theories of the P3 suggest that the component may be reflective of neural inhibition processes (Polich, 2007). More specifically, researchers have suggested that the P3 reflects inhibition of ongoing neural activity that is extraneous to the current stimulus-response task demands. By reducing the amount of peripheral neural activity during a task, the brain may be able to more efficiently process the information necessary to activate appropriate behavioral responses.

Furthermore, some researchers have suggested that the P3 is an important component in mediating early stimulus processing and later behavioral responses (Verleger, Jaśkowski, &

Wascher, 2005). In their study, Verleger et al. (2005) indicated that the P3 was a critical component occurring between early stimulus perception during an auditory task and later indicators of response initiation, like the lateralized readiness potential. The researchers suggested that the P3 component may be conceptualized as a representation of monitoring processes that serve to evaluate a decision. In other words, Verleger et al. (2005) suggested that the P3 is an indication of ongoing stimulus-response processing mechanisms that ensure that the appropriate behavioral response is being initiated given the preceding stimulus information.

Current Limitations in Brain-Behavior Relationship Research

Research in the field of brain-behavior relationships has dramatically expanded in the last few decades; however, the field is arguably still in its infancy. Researchers continue to uncover weak, variable relationships between neural processing measures and behaviors (e.g., Brydges, Fox, Reid, & Anderson, 2014; Foti et al., 2016), especially among populations that are inherently more variable in their brain activity and performance, such as children and clinical populations.

One hindrance to progress in the field has been the reliance on simplistic, univariate statistical methods to evaluate brain-behavior relationships. Because univariate methods evaluate only the variation of a single random variable, they may be limiting the field’s ability to better understand the brain’s dynamic structure and function. Recent work has begun to apply more advanced modeling methodologies such as graph theory (e.g., Bullmore & Sporns, 2009; Park & Friston, 2013), dynamic causal modeling (e.g., Friston, Harrison, & Penny, 2003), and Granger causality (e.g., Brovelli et al., 2004). These methodologies work well for understanding the *structure* of neural systems, but are still limited in showing how brain activity relates to dynamic *function*. Furthermore, these techniques do not lend themselves well to modeling how several equally important variables simultaneously relate to one another while accounting for individual differences.

Rather than examining individual ERP components or single, simple behaviors, it may be more meaningful to explore the *system* of neural processing that relates to complex behaviors. A systems-based approach to understanding brain-behavior relationships may be more representative of the true nature of neural processing. That is to say examination of a single ERP component in relation to a single behavioral measure may not be an accurate representation of the complex nature of brain processing in context. By including systems of neural processing measures, multiple task behavior measures, and even trait measures of cognitive abilities, researchers may be better able to understand individual differences that contribute to clinical diagnoses, cognitive development, and more. Interestingly, Landa, Krpoun, Kolarova, and Kasparek (2014) describe ERP components as representations of complex neural network activity. In other words, ERP components may be better viewed as systematic phases of neural processing rather than isolated events that represent a single aspect of cognitive or motor abilities. The idea that ERPs may represent full systems of neural activity is in support of decades of advancements in dynamic systems theory and connectionist theory.

Dynamic Systems Theory

Dynamic systems theory posits that for any given individual, his ability to function is the product of complex, transactional interactions among many levels of the individual and his environment (Spencer, Austin, & Schutte, 2012). That is to say from micro-level units of analysis (e.g., genes, molecules) to the macro-level contextual factors of the individual (e.g., family, culture), factors within each level are continually interacting and evolving across the individual’s life course. Those interacting factors comprise a dynamic system that shapes and defines the individual (Schöner, 2008; Van Leeuwen, 2005). Using dynamic systems theory, researchers aim to develop models for understanding the individual in context, including understanding how individual differences in experience and history manifest in cognition and behavior (Schöner, 2008).

Dynamic systems theory has several main assumptions that help guide the development of models of individual differences. Within any system, researchers can consider a number of relevant parameters referred to as a time set (Van Leeuwen, 2005). Order parameters are variables that specify the state of the system. Considering the brain as the system of interest, examples of order parameters may include behavioral patterns, maturation of the brain, or even overall health, though this is not an exhaustive list. In turn, control parameters are variables that are external to the system, but can influence the functioning of the system (Van Leeuwen, 2005). Order and control parameters interact and evolve over time, changing the state of the system. Researchers often try to model the evolution of a system through a series of equations referred to as the trajectory of the system. However, every system has an attractor state, or a baseline state, in which the system is in equilibrium. Although order and control parameters are continually evolving and dynamically interacting, the system is always lured toward achieving its attractor state (Schöner, 2008; Van Leeuwen, 2005).

Dynamic systems theory has been widely used in a number of scientific fields because it provides a broad but rich perspective for understanding the individual in context. The basic principles described in dynamic systems theory can be molded to describe functioning in nearly any domain. However, in the fields of cognitive and behavioral neuroscience, dynamic systems theory may not be adequate. In the domain of neuroscience, researchers are working to understand finite neural mechanisms and how brain structure and function relate to cognitive and behavioral outcomes. Dynamic systems theory can account for neural mechanisms as order parameters within a system, but it fails to describe how those neural mechanisms actually function as a system of their own. Thus, using the principles of dynamic systems theory as a foundation, researchers developed connectionist theory to better describe the systematic functioning of neurons distributed throughout the brain (McNaughton & Nadel, 1990).

Connectionist Theory

Connectionist theory has spurred rich discussion in the field of neuroscience since its beginnings in the 1940's with Hebb's (1949) work on the formulation of short-term memory. From simpler processes like basic sensation, to the more complex cognitive and behavioral realms of attention and language, the field has embraced the lens of connectionist theory as a means of understanding multifaceted neural processing patterns (e.g., Bear & Cooper, 1990; Hebb, 1949; Laufs et al., 2003; Lowe et al., 2016; Raftopoulos, 1997).

In addition to the principles outlined by dynamic systems, connectionist theory includes assumptions that help researchers more directly address the complexity of neural processing and organization in the brain. One new principle that aims to better describe neural processing is that of phase sequences, which are neural state trajectories underlying sensory-motor events (Hebb, 1949; McNaughton & Nadel, 1990). In essence, phase sequences are cascades of neural activity spurred by the attractor state of the system, which expects that populations of neurons will activate in certain patterns in order to produce a specific cognitive or behavioral response. Neurons, their inputs (e.g., sensory information), and their outputs (e.g., motor responses) are all dynamically-interacting parameters that form systems of cognitive and behavioral functioning called neural networks (McNaughton & Nadel, 1990; Raftopoulos, 1997).

Recent research has made great strides in computationally modeling abstracted, computerized neural networks capable of mimicking human behaviors (e.g., Liljenström, 2010; Raftopoulos, 1997). Neural networks are comprised of multiple, hierarchically organized layers of information processing units that can be trained in order to produce more advanced cognitive and behavioral outcomes. Additional hidden units allow the network to systematically store and re-reference previously-experienced activation states in order to inform new patterns of activation that may foster appropriate learning and behavior.

For example, Raftopoulos (1997) developed a neural network capable of processing language. First, the lowest-level units of the network were trained to recognize basic vocabulary in the absence of grammar. The researcher then tested the vocabulary-trained network on its ability to process grammar, and the network failed to produce adequate performance. However, by adding another level of information processing to the network and training grammatical rules, the network was able to feed forward its previous experience with simple vocabulary and incorporate the new training to successfully integrate words and grammar (Raftopoulos, 1997). The researcher also noted that without the early foundational training in simpler information processing, the network was unable to attain higher-level abstractions like grammatical rules. The dynamic neural system was able to integrate experiences from the environment (i.e., the introduction of grammatical rules) and its own prior knowledge (i.e., training in vocabulary) to produce a more complex outcome, a prime example of the application of connectionist theory. Although in the past it has been more common to develop computerized models of neural networks, the advent of affordable neuroimaging technologies has brought about a new wave of research in mapping neural networks in the human brain.

ERPs as Dynamic Systems

To date, ERP components have been almost entirely viewed as isolated instances of stimulus and response processing. Few researchers have considered the interrelationships between components of a single averaged ERP. However, with the advent of research exploring neural networks, scientists have suggested that ERPs may also be viable measures for understanding systems of neural processing. Landa et al. (2014) actually describe ERPs and their components as representations of complex neural systems activations that are important in new stimulus detection and discrimination, and the resulting behavioral responses of individuals. Indeed, when considering the functional associations of individual components as described in the literature, it is reasonable to consider that an ERP is a representation of a continuous stream of stimulus-to-response processing. Processing begins with basic sensory processing and early attention to the stimulus (N1), followed by detection and discrimination processes (P2 and N2) in order to make a decision about how to appropriately respond. The decision is then evaluated, incorporating prior knowledge and updating the contextual information contributing to the individual's cognitive processing (P3). Then, sustained attention, anticipation, and motor preparation processes engage (CNV/E-wave) in order to execute a behavioral response.

Despite the logical progression of stimulus-to-response processing exhibited in an ERP, researchers have yet to show the interrelationships between components and effectively map the system of processing. In general, research tends to focus on single ERP components in an attempt to understand how brain processing relates to simple behaviors. Scientists often struggle to detect stable, strong brain-behavior relationships using such techniques. In fact, even studies attempting to show relationships between ERP components and task-specific behaviors (e.g., reaction time and accuracy in the ERP paradigm) yield weak and variable results despite the logical notion that *brain processing* during a task should relate to *behaviors* during a task. The challenges associated with detecting brain-behavior relationships using ERPs may be rooted in the inadequately-managed variance comprising the measures of interest. Indeed, an averaged ERP and each of its components are comprised of multiple sources of variance, many of which are unrelated to the effect of the stimulus – the primary focus of most ERP investigations.

Gavin and Davies (2008) suggested that psychophysiological measurements (PM), including ERPs, are compilations of variance from a number of sources that can be expressed in an equation (equation 1 reprinted from Gavin & Davies, 2008, p. 428):

$$\text{PM} = \text{Effect}_{\text{STIMULUS}} + \text{Effect}_{\text{STATE}} + \text{Effect}_{\text{TRAIT}} + \text{Effect}_{\text{PM\_PROCESSING}} + \text{Measurement Error} \quad (1)$$

The equation suggests that any PM, including an ERP, encompasses aspects of the individual that may alter his neural processing patterns. For example, $\text{Effect}_{\text{STATE}}$ could include anxiety or other emotional states of the individual. Researchers have consistently shown that altering an individual's emotional state can affect features of ERP components (e.g., Grillon & Ameli, 1994; Meyer, Weinberg, Klein, & Hajcak, 2012; Rossi & Pourtois, 2012). However, $\text{Effect}_{\text{STATE}}$ can also include aspects of the individual that are more difficult for the researcher to manage. State features such as hunger (Baldeweg, Ullsperger, Pietrowsky, Fehm, & Born, 1993; Stockburger, Schmälzle, Flaisch, Bublatzky, & Schupp, 2009) and lack of sleep (Hoedlmoser et al., 2011; Molfese et al., 2013) can also affect the individual's neural responses during a visit to the lab.

In addition to state, trait effects of the individual can also affect his neural responses. Traits may include biological characteristics of the individual such as sex or maturation (Gavin & Davies, 2008). Researchers have shown that sex and age often interact, particularly during puberty, to affect ERPs (e.g., Brumback, Arbel, Donchin, & Goldman, 2012; Davies, Segalowitz, & Gavin, 2004). Of course, traits go beyond simple biological measures of age and sex and can include cognitive and affective characteristics of the individual. For example, trait anxiety (Aarts & Pourtois, 2010; Sadeh & Bredemeier, 2011) and attentional abilities (Spronk, Jonkman, & Kemner, 2008) are known to affect features of ERPs. To further complicate the issue, effects of biological, affective, and cognitive traits can be additive and create unique effects on ERPs (e.g., Omura & Kusumoto, 2015). Systematic work exploring the effects of age and clinical diagnosis, both of which are considered to be traits, have shown that not only do children have more variable ERPs than adults, but children with clinical diagnoses have more variable ERPs than children without clinical diagnoses (e.g., Davies & Gavin, 2007; Gavin et al., 2011).

An important feature of Gavin and Davies' (2008) equation is that an ERP is not just a result of individual differences from participants; researchers must also consider their own influence on the resulting ERP. The term $\text{Effect}_{\text{PM\_PROCESSING}}$ refers to the manner in which researchers process their data and extract an ERP. Aspects of electrophysiological data reduction that are common practice for deriving ERPs such as bandpass filtering (Chang, Gavin, & Davies, 2012) and artifact removal or rejection techniques (Junghöfer, Elbert, Tucker, & Rockstroh, 2000) can affect the resulting ERP.

Combined, the various effects contributing to the variance of an ERP can obscure researchers' interpretations of their findings, which are often attempting to understand the effect of a particular stimulus or event (i.e., $\text{Effect}_{\text{STIMULUS}}$) on neural processing signatures. In fact, many researchers fail to control for these numerous effects, thus Gavin and Davies (2008) suggested a second equation to better represent how ERPs are typically conceptualized in literature (equation 2 from Gavin and Davies, 2008, p. 428):

$$\text{PM} = \text{Effect}_{\text{STIMULUS}} + \text{Measurement Error} \tag{2}$$

In sum, failing to control for multiple sources of variance resulting from processing techniques and individual differences compounds the measurement error term in the equation. Standard analyses like bivariate correlations, *t* tests, and ANOVA designs are often confounded by the multiple sources of variance, which likely increases type II error rates. In other words, traditional analysis techniques are unable to effectively manage multiple sources of variance, which can muddle the interpretation of systems of neural processing critical in understanding brain-behavior relationships, developmental changes, and diagnostic indicators. Schonbein (2005) stated that in order to computationally model neural systems of communication, researchers must effectively manage the inherent ubiquity of noise in neural signals.

With an increasing emphasis on developing diagnostic and intervention tools based on brain-behavior relationships, there is a need to adopt different statistical techniques that can better manage sources of variance, thus allowing researchers to better detect stable brain-behavior relationships. One statistical technique, structural equation modeling (SEM), may prove to be a viable option for managing sources of variance in order to better model systems of neural processing represented by ERPs.

Structural Equation Modeling

SEM is an advanced statistical technique that can efficiently model complex multivariate relationships while simultaneously managing sources of variability, including measurement error. Variables can be modeled via path analyses in order to demonstrate causal, predictive relationships between measures. For instance, a recent longitudinal investigation explored the interrelationships of an ERP component amplitude measure collected at two time points (four years apart) and a self-report measure of symptoms in middle-aged patients diagnosed with schizophrenia, also measured at two time points (Foti et al., 2016). The model was able to demonstrate moderate reliability of the ERP component measure and the self-report measure over the four-year time period. Additionally, the model indicated that the ERP component measure at time one was a significant predictor of the self-report measure at time two, though the relationship was weak ($\beta = .20$). The investigation by Foti and colleagues (2016) is one of few attempts to understand brain-behavior relationships using SEM techniques, and the selected approach was still fairly simplistic. It is possible that researchers could achieve stronger predictions between brain measures and clinical measures (e.g., self-reports, behavioral assessments) by utilizing more advanced approaches.

In particular, latent variable analyses define complex, sometimes abstract constructs like “attention” or “anticipation” by utilizing the common variance of multiple items of measured data, also termed manifest variables (Iacobucci, 2010; Wolf, Harrington, Clark, & Miller, 2013). Because the latent construct is comprised of only the common variance among manifest variables, the resulting latent construct is free of measurement error. Thus, latent variable models of ERP components may be able to better represent the $\text{Effect}_{\text{STIMULUS}}$ portion of the variance that researchers are often interested in understanding.

Although the current literature sparse, some researchers have begun to explore the utility of latent variable analysis in understanding ERP components. For example, Brydges et al. (2014) examined whether the N2 and P3 components of an ERP could predict executive function abilities in seven-to-nine year-old children. Three manifest variables, the N2 and P3 amplitudes, and the P3 latency were used to create three latent variables in order to remove the measurement error of each variable. The latent variables defined by neural processing were then used to predict a latent variable of executive function, which was defined by a combination of eight different behavioral assessments which have been validated as measures of executive functioning. The data indicated that the N2 and P3 amplitudes were significant predictors of executive function, though the predictive coefficients were weak (β_{N2} = -.27, β_{P3} = .17). P3 latency was not a significant predictor of executive function (Brydges et al., 2014). The interrelationships between the N2 and P3 components were not included in the model; rather, the components were viewed as entirely separate constructs.

Using SEM to Address Connectionist Theory

Examination of individual ERP components in isolation ignores the key principles of connectionist theory, a perspective which has quickly gained credibility in the neuroscience literature. It is possible that SEM could be applied in a more advanced manner in order to better model the concept of phase sequences: dynamically-interacting phases of stimulus-to-response processing beginning with sensory inputs and ending in observable behavioral outputs (Hebb, 1949; McNaughton & Nadel, 1990; Raftopoulos, 1997). For example, one might use a path analysis to model the sequence of ERP components in chronological order leading to task-specific behaviors, N1 → P2 → N2 → P3 → CNV → task behaviors (e.g., reaction time, accuracy). In this simple path, one ERP component successively predicts the next, culminating in the observable task behavior.

Furthermore, the simple path model noted above could be refined by removing measurement error from the ERP components and task behaviors of interest by employing latent variables in the analysis. Latent variables can be utilized in more complex analyses, like latent path analyses which allow the calculation of cause-effect predictive paths from one latent construct to another. Thus, using latent variable path analysis could allow researchers to effectively remove measurement error from ERP components, and *then* systematically map the progression of stimulus-to-response processing in the brain leading to behaviors (i.e., phase sequences). By modeling the full system of decision-making in the brain, researchers can better account for variance in successive ERP components, thereby creating a more comprehensive view of brain processing as it relates to behaviors.

Summary and Purpose

The purpose of the following three studies is to develop and test models of systematic brain-behavior relationships in children. The models established in this series of studies with typically-developing children will set the foundation for future work examining brain-behavior relationships in clinical samples.

Study 1

The first study will begin with simple examinations of brain-behavior relationships in children using traditional, univariate statistical techniques. The goal of the study will be to examine relationships between a specific ERP component, namely the E-wave component of the CNV, task-specific reaction times, and trait measures of attention. The study will first examine simple correlations between measures in order to serve as an anchor to traditional statistical methods present in the literature. Then, the study will progress through more advanced statistical techniques, employing path analyses and latent variable models in order to determine whether SEM can improve our ability to detect simple brain-behavior relationships among children.

Study 1 research questions.

1. To what extent are the E-wave and task-specific reaction times related to one another among children performing a simple Go-NoGo task?
2. How do the E-wave and reaction times relate to trait measures of attention?

3. Can SEM techniques improve our ability to detect brain-behavior relationships compared to univariate statistical techniques?

Study 2

In the second study, ERP and behavioral data that are specific to the ERP task (i.e., reaction times of button presses to stimuli) will be examined. Specifically, data from a large sample of children will be used to develop a model of systematic neural processing wherein one phase of neural processing defined by ERP components successively predicts the next in a chronological order. The full stream of processing will be used to predict task-specific behaviors. Model fit statistics and the strength of predictive coefficients will be used to determine the viability of the model.

Study 2 research questions.

1. Can the components of event-related potentials (ERPs) be modeled as a systematic phases of neural processing (see Figure 1.1 for the hypothesized model)?

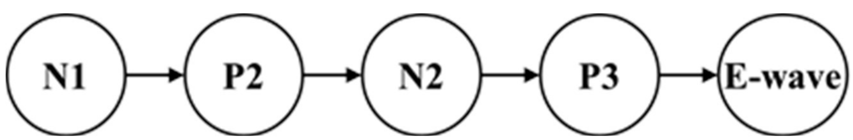

Figure 1.1. Phases of neural processing successively predicting each other in chronological order.

2. Does the full time course of an ERP predict task-specific behaviors (i.e., reaction time; see Figure 1.2 for the hypothesized model)?

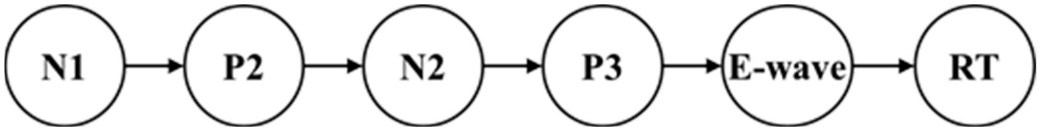

Figure 1.2. The full stream of neural processing predicting task-specific behaviors in a fully-mediated model.

Study 3

The final study tests a cohesive biobehavioral model of decision-making behaviors in children. The study will begin by establishing the factor structure of developmentally-sensitive cognitive constructs defined by behavioral assessments that purport to measure aspects of attention and executive function abilities. Based on the literature, I hypothesize that the data will separate into a three-factor structure: Control Attention, Sustained Attention, and Executive Function (EF). The study will then build on the model established in *Study 2*, which examines the full stream of neural processing leading to task behaviors. The study will give conceptual labels based in the literature to each phase of brain processing in order to better capture the cognitively-based nature of the ERPs that comprise the latent variables. The purpose of the study is to determine to what extent developmentally-sensitive cognitive constructs can differentially relate to each phase of neural processing. The first model will examine how each cognitive construct relates to each phase of neural processing in order to provide the most holistic view of brain-behavior relationships. Then, a reduced model will assess only hypothesized relationships between each cognitive construct and the different phases of brain processing based on assertions in the literature.

Study 3 research questions.

1. What cognitive constructs can be derived from a battery of behavioral assessments that purport to measure aspects of attention and executive function in typically-developing children?
2. Do the obtained cognitive constructs differentially relate to phases of stimulus-to-response neural processing during decision-making behaviors (see Figure 1.3 for the models to be tested)?

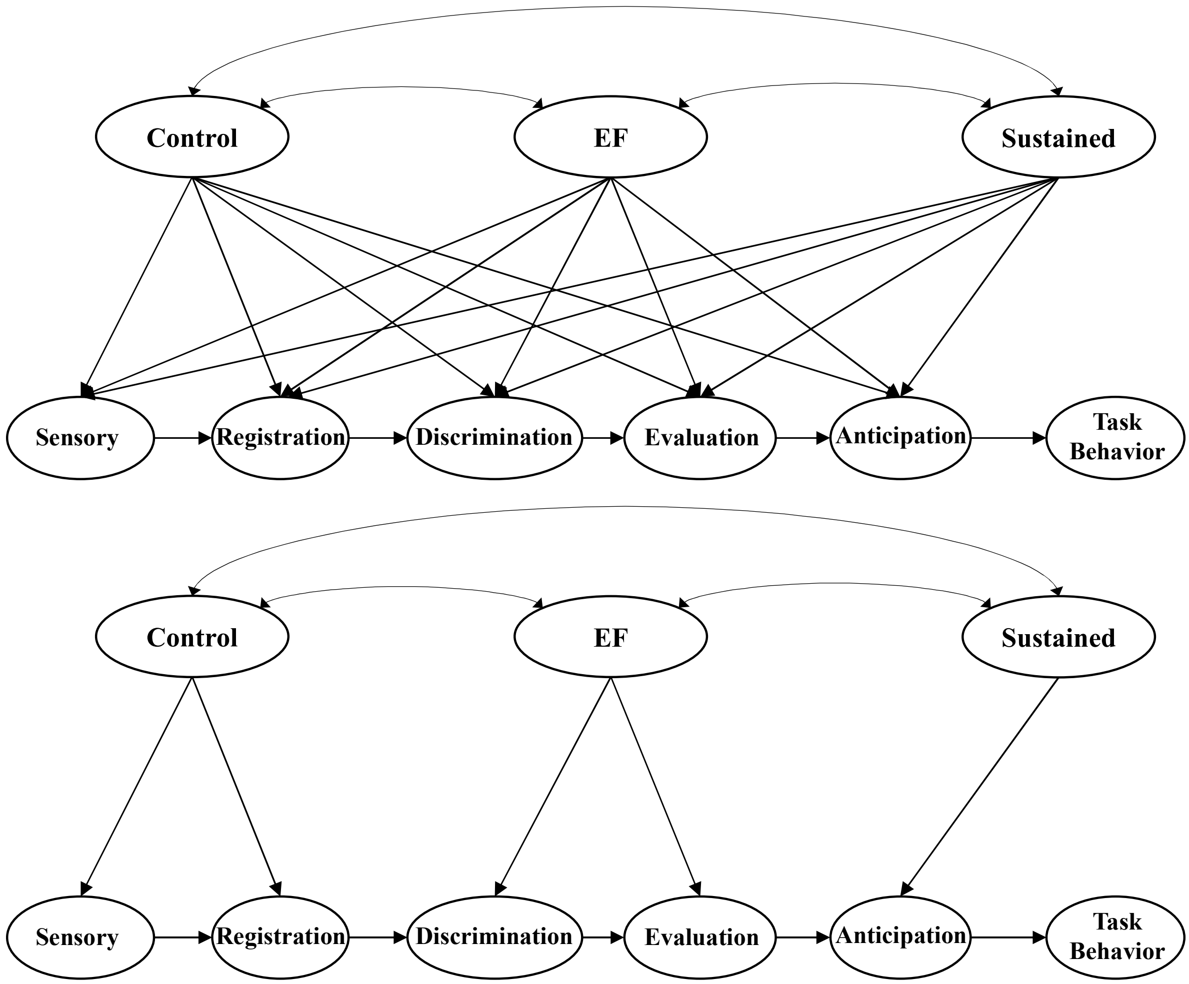

Figure 1.3. Latent phases of neural processing being predicted by developmentally-sensitive cognitive constructs of Control Attention, Sustained Attention, and Executive Function (EF). Top: The full model in which each cognitive construct predicts each phase of brain processing; Bottom: The reduced model with only the hypothesized relationships between cognitive constructs and phases of brain processing.

CHAPTER II – STUDY 1

For over two decades now, brain imaging technologies have been applied to the study of cognitive development and neurological disorders in children. Although great progress has been made, past research has relied heavily on univariate statistical methods for exploring the relationships between brain activity and human behaviors measured in a variety of ways. Some researchers focus more on simple task behaviors, such as reactions times within the task used to elicit the neural activity (e.g., Brunner et al., 2015; Jongen, Smulders, & Van Breukelen, 2006). Other researchers have tried to establish more complex relationships between brain and behavior, attempting to relate neural processing to clinical behavioral assessments which are believed to test trait measures of cognitive functioning (e.g., Brydges et al., 2014; Foti et al., 2016).

Because univariate methods evaluate only the variation of a single random variable, they may be limiting the field's ability to better understand the brain's dynamic structure and function. Recent work has begun to apply more advanced modeling methodologies, such as graph theory (e.g., Bullmore & Sporns, 2009; Park & Friston, 2013), dynamic causal modeling (e.g., Friston et al., 2003), and Granger causality (e.g., Brovelli et al., 2004). These methodologies work well for understanding the *structure* of neural systems, but are still limited in showing how brain activity relates to dynamic *function*. Furthermore, these techniques do not lend themselves well to modeling how several equally important variables simultaneously relate to one another while accounting for individual differences. This article attempts to demonstrate the value of multivariate analyses, in particular, structural equation modeling (SEM), to better interpret event-related potentials (ERPs) obtained from electroencephalography (EEG) recordings. This demonstration builds on the fundamental model suggested by Gavin and Davies

(2008) for understanding the individual differences that participants bring to an EEG/ERP session.

In the Gavin and Davies (2008) model, any given psychophysiological measure (PM), such as the amplitude of an ERP component, can be conceptualized as the combined effect of (1) the *stimulus processing* involved in eliciting the component; (2) the *state* of the individual participant during measurement such as current mood or sleepiness; (3) the *trait* characteristics of the individual such as general attention abilities or maturation level; (4) the *signal processing techniques* employed to calculate the ERP component including filtering and averaging of EEG signals; and (5) *measurement error* (ME), which is any other unaccounted-for variance (see equation 1 below, reprinted from Gavin & Davies, 2008, p. 428).

Such a model can be simply written as

$$PM = Effect_{STIMULUS} + Effect_{STATE} + Effect_{TRAIT} + Effect_{PM\_PROCESSING} + ME \qquad (1)$$

and this type of model allows for the use of multiple regression techniques to understand the variation of brain activity across individuals performing a given task. This is in contrast to univariate statistical techniques that compare group means of only the stimulus processing effect and ignore other sources of individual variability that contribute to an ERP component measure. As this model suggests, when researchers fail to account for one or more of these other potential sources of individual differences that are contributing to an ERP component measure, the researchers are compounding the unaccounted-for individual effects into the ME term (see equation 2 below reprinted from Gavin and Davies, 2008, p. 428). Larger measurement error may result in spurious effects or even missed effects (type II error). For example, if investigators wish to test whether or not a given physiological measure successfully relates to or predicts a functional behavior (FB), then this effort may be modeled in its simplest form as shown in equation 3.

$$PM = Effect_{STIMULUS} + ME_{TOTAL} \tag{2}$$

$$Effect_{STIMULUS} + ME_{TOTAL} \rightarrow FB \tag{3}$$

Equation 3 shows that if a significant statistical relationship between a physiological measure and a functional behavior is found, this relationship could be explained by either the stimulus effect *or* the undefined measurement error. Thus, it is important to reduce the amount of measurement error in analyses by accounting for variance of factors that are often folded into the measurement error, especially in populations that are inherently more variable, such as children, if the study's conclusions are to be as unambiguous as possible.

Although the use of univariate statistics may be appropriate for asking about simple aspects of brain activity in college-aged adults, it may not be adequate for studying the development of dynamic brain activity in neurotypically-developing children. If researchers rely on more simplistic, univariate statistical analyses, like ANOVA designs and bivariate correlations, the results may be more likely to be confounded by measurement error as these traditional analysis techniques in ERP literature frequently fall short of controlling for the variety of sources of individual variability that comprise an ERP component measure. The present studies demonstrate how the use of more sophisticated statistical techniques may better account for individual differences and allow for modelling the relationship between multiple variables. Specifically, this work demonstrates how the use of structural equation modeling (SEM) techniques may lead to insights on the relationship of brain activity represented by an ERP component and functional behaviors during a simple visual Go/No-Go task (Taylor et al., 2016).

The E-wave component of the contingent negative variation (CNV) is a slow negative drift in ERPs resulting from attentional anticipation between two stimuli (Bender et al., 2004; Segalowitz & Davies, 2004; Walter et al., 1964). Specifically, the E-wave is believed to represent aspects of sustained attention processing. Researchers have shown alterations to CNV E-wave amplitudes in different attentional states, like wakeful, conscious activity versus sleep (Yasuda, Ray, & Cote, 2011). Additionally, research has shown that in adult samples, larger (more negative) E-wave amplitudes are related to faster reactions times during Go/No-Go ERP tasks using simple bivariate correlations and ANOVA designs (Brunner et al., 2015; Connor & Lang, 1969; Jongen et al., 2006). To the best of our knowledge, researchers have yet to formally establish the construct validity of the E-wave and continue to assume that the component represents sustained attention based on these simple analyses.

Interestingly, a previous study involving children indicated that across two assessment sessions conducted one-to-two weeks apart, CNV E-wave amplitudes became more negative despite consistent behavioral performance, suggesting that the children were attentive and successfully completing the task during each session (Taylor et al., 2016). Although the E-wave is known to become more negative across development (e.g., Hämmerer, Li, Müller, & Lindenberger, 2010; Jonkman, 2006; Jonkman, Lansbergen, & Stauder, 2003; Taylor et al., 2016), it is unlikely that developmental changes occurred over such a short period of time. Prior research suggests that changes in ERP amplitudes after practicing a task, even without notable improvement in task performance, may indicate shifts in cognitive strategies as a result of practice (Pauli et al., 1994; Romero, McFarland, Faust, Farrell, & Cacace, 2008). Thus, Taylor et al. (2016) suggested that the shift in amplitude across sessions may have been the result of a shift in attentional strategies as the children practiced the task used to elicit the E-wave.

The present studies aim to expand on the findings from Taylor and colleagues (2016) to better understand the shift in children's E-wave amplitudes across sessions as they practiced a simple visual Go/No-Go task. In order to both examine our findings in relation to previous literature and to better account for individual variability in E-wave amplitude measures and task behavior measures, we use a combination of analysis techniques. Specifically, we begin our analyses using more traditional methods (*t*-tests and correlations), and then we employ SEM techniques, which can better manage individual variability and minimize measurement error. *Study 1.1* investigates whether the E-wave is related to task-specific reaction times using a variety of statistical techniques that differentially manage sources of variability stemming from individual differences within and between individuals during each session. *Study 1.2* permeates further and explores whether E-wave or reaction time measures can be related to trait measures of attention assessed by a valid, clinical behavioral assessment once we have effectively removed measurement error from the variables of interest.

Study 1.1

Rationale and Purpose

The first study in this investigation examined a variety of methods for understanding individual differences in neural processing and task-specific behaviors, namely reaction times, in a sample of neurotypical children. This investigation expands on the work presented in Taylor et al. (2016), which showed that children's average E-wave amplitudes became significantly larger (more negative) across sessions despite consistent task performance, at least as measured at the group level. It is possible that we may be able to detect subtleties in neural processing and task performance at the individual level if: (1) we include additional measures that better represent individual differences, namely standard deviations of E-wave amplitudes and reaction times, and

(2) we utilize more advanced statistical techniques that effectively examine the interrelationships between multiple variables while simultaneously managing measurement error.

We specifically included both mean and standard deviation measures of the E-wave and of reaction times on the basis that *typical* performance (i.e., means) and *intra-individual variability* in performance (i.e., standard deviations) are known to measure independent aspects of an individual's abilities (Kievit, Davis, Griffiths, Correia, & Henson, 2016). Measures of intra-individual variability in brain processing and behavioral performance are not frequently studied in the literature, though several recent investigations suggest that there is much to learn from exploring indices of variability. For example, Kievit et al. (2016) showed that measures of brain structure differentially predicted means versus standard deviations of reaction times, which in turn differentially predicted measures of fluid intelligence. Another study using time frequency analysis of EEG data showed that less intra-individual variability in phase-locking relative to the onset of a stimulus was related to better general intelligence (Euler, Weisend, Jung, Thoma, & Yeo, 2015). Overall, the literature suggests that intra-individual variability in behavioral performance and in neural processing are important, unique measures of an individual's abilities (for a complete review, see MacDonald, Nyberg, & Bäckman, 2006).

In this study, we first replicated the findings from Taylor et al. (2016) by examining the test-retest reliability of E-wave and task performance measures, as well as group differences across sessions. Then, we employed a simple path analysis to examine whether E-wave measures could predict reaction time measures during each session after controlling for age. We expected to find a significant predictive relationship between brain and behavioral measures based on previous findings. Finally, we examined whether moving to latent variable models could strengthen brain to behavior relationships due to the reduction in measurement error that occurs when the latent variables of interest are created. We hypothesized that removing measurement error would result in a stronger relationship between E-wave measures and reaction times.

Methods

Participants. Data were collected from a total of 91 neurotypical children between the ages of 7 and 13 years during two sessions scheduled one-to-two weeks apart. Eighteen children were excluded due to poor performance, as described in detail in the results. The final sample included 73 children (34 males; *M* = 10.40 years, *SD* = 1.54). The sample is comprised of data collected in two separate waves. Fifty-one of the included children were assessed in Wave 1 (previously published sample; see Taylor et al., 2016), and 22 children were assessed in Wave 2. Procedural differences in data collection procedures between the two waves are described in detail below. Participants had no reported neurological or developmental diagnoses, nor were they currently taking any psychopharmaceutical medications, as reported by parents. Parents of children signed informed consent forms, and child participants signed assent forms. Children received their choice of a t-shirt or cocoa mug after completing their first visit, and their choice of a t-shirt, cocoa mug, or $10 after their second visit. All procedures were approved by the local university institutional review board.

Procedure. Participants completed two EEG recording sessions scheduled one or two weeks apart with the second session being at the same time and day of the week as the first session. Participants were seated in a comfortable chair at a table in front of a computer screen. Two research assistants placed the EEG cap and sensors on the participant. For each participant, the same EEG cap was used for each session, and measurements were performed to assure proper placement each time. Next a research assistant gave participants a brief training on how to reduce production of artifacts from eye blinks and muscle movements. Then, three minutes of eyes-opened resting EEG were recorded while participants stared at a fixation point on the screen. Participants then performed a total of four EEG paradigms lasting approximately one hour. Only the Go/No-Go paradigm, which was the third paradigm, will be discussed in this study. Participants were given a short break of 2 to 4 minutes between each paradigm. Following EEG data collection, children completed a battery of behavioral assessments of attention and executive function abilities which will not be discussed further in *Study 1.1*. In total, each session lasted approximately two hours.

Visual Go/No-Go paradigm. During each trial of the task, children saw a sequence of two stimuli. First, a circle, either red or green, was displayed in the center of the screen for 250ms. Then the screen went blank for 1750ms before a picture of a car appeared in the center of the screen with a duration of 250ms. If the circle at the beginning of the trial was green, children were instructed to press a button in front of them as quickly as possible after the car appeared on the screen (i.e., a Go trial). However, if the circle was red, the children were instructed not to press the button (i.e., a NoGo trial). The task consisted of 40 Go and 40 NoGo trials presented in a pseudorandom order. The same task was performed during both sessions.

Electrophysiological recording. EEG recordings were obtained using the BioSemi ActiveTwo system with an Active Two Lycra head cap (BioSemi, Inc., Amsterdam, The Netherlands). For children in Wave 1, active EEG was recorded from 32 Ag-AgCl sintered electrodes based on the American Electroencephalographic Society nomenclature guidelines (1994) with an additional pin-type Ag/AgCl electrode placed at FCz for a total of 33 scalp sites. EEG data recorded from the additional 22 children in Wave 2 were collected using a 64-channel BioSemi ActiveTwo system with Ag/AgCl sintered electrodes. Scalp electrodes were positioned according to a modified 10-20 system (American Electroencephalographic Society nomenclature guidelines, 1994). For both waves of data collection, there were additional common mode sense (CMS) and driven right leg (CRL) sensors, which served as reference and ground, respectively. An additional six sensors were placed on the face (on the left supra- and infra-orbital regions, and on the left and right outer canthi) and both the left and right earlobes to record eye movements and provide sites for offline re-referencing. Data were sampled at a rate of 1024Hz. Electrode offsets were maintained at ±20mV throughout each session.

Electrophysiological data reduction. Using BrainVision Analyzer 2.0 software (www.brainproducts.com), data from the continuous EEG recording were re-referenced to the averaged voltage of the two earlobe electrodes, filtered with a .03 to 30Hz bandpass filter (12dB/octave), and then segmented from 200ms prior to the conditional stimulus onset to 2250ms after the conditional stimulus onset. Only correct Go trials were examined in this study. Correct Go trials were any trials in which a green circle appeared before the car, and the button was pressed after the car appeared. Baseline correction was performed on each segment using the EEG data from -200 – 0ms relative to the conditional stimulus onset. A regression procedure used to remove eye blinks was applied to retained segments (Segalowitz, 1996). Following the regression procedure, segments were baseline corrected again using the -200 to 0ms window and then underwent an artifact rejection procedure to remove segments with voltages exceeding ±100µV. An averaged ERP was calculated for each participant and for each session using the Go segments retained after data reduction.

The E-wave was measured as the averaged amplitude in the 200ms window directly preceding the onset of the imperative stimulus on Go trials for each session based on prior research (e.g., Kropp et al., 2000; Taylor et al., 2016). All measurements were performed at scalp site Cz. The averaged amplitude and the standard deviation of the amplitude were calculated for each individual to understand typical neural processing and variability in neural processing during each session. Reaction times for each correct Go trial were calculated as the time in milliseconds from the imperative stimulus onset to the time of the button press. The mean and standard deviations of reaction times were calculated for each individual to better understand typical performance as well as variability in performance during each session.

Data analysis. Analyses began with basic descriptive statistics for each dependent measure. We also completed a series of paired-samples *t*-tests and Pearson product-moment correlations to confirm the effects described in Taylor et al (2016) in our larger sample. Namely, we assessed any changes across sessions in the dependent measures, and we examined each variable's test-retest reliability. All initial descriptive and confirmatory analyses were completed using SPSS version 23.

Following confirmation, we developed a simple path model to examine the interrelationships between all dependent measures simultaneously. The model included means and standard deviations of E-wave amplitudes and reaction times for each session. Session 1 variables were modeled as predictors of session 2 variables, and E-wave measures were modeled as predictors of behavior measures within each session. Additionally, the mean and standard deviation of a single measure (e.g., mean and standard deviation of session 1 reaction time) were correlated. Age was used as a control variable on all measures. All parameters were freely estimated.

After the simple path model, we moved to a latent variable path analysis. Latent variables are derived from the common variance of multiple manifest variables, essentially removing any measurement error from the resulting latent variable (i.e., any variance that is not common among the manifest variables is removed). We defined a latent variable by the combination of the two sessions of each dependent measures (e.g., session 1 and session 2 mean E-wave amplitudes combined into a latent variable). In order to allow all manifest variables loadings to be freely estimated, we identified each latent variable by its mean (set to 0) and variance (set to 1). The latent variable model was designed with E-wave latent variables as predictors of reaction time latent variables, just as we established in the simpler model. Again, age served as a control on all latent variables. All structural equation modeling was performed using Mplus version 7.3.

Results and Discussion

Descriptive and confirmatory statistics. A total of eighteen children were excluded from analyses due to having too few segments remaining for either session after data reduction procedures (i.e., < 12 correct Go segments). Using data from the remaining 73 participants, a series of paired samples *t*-tests and Pearson product-moment correlations were used to examine mean differences and test-retest reliability of five different variables across sessions: mean and standard deviation of the E-wave amplitude, mean and standard deviation of reaction times, and the total number of correctly performed Go trials. Descriptive statistics and results are reported in Table 2.1.

Table 2.1.
Descriptive statistics, differences, and test-retest reliability for E-wave amplitudes and Go/No-Go task behaviors during each session.

	Session 1	**Session 2**	**Difference**	**Reliability**
Measure	*M* (*SD*)	*M* (*SD*)	*t*	*r*
E-wave$_M$ (μV)	-1.76 (4.65)	-3.32 (5.15)	2.71**	.50***
E-wave$_{SD}$	22.62 (19.17)	23.31 (13.48)	-.26	.10
RT$_M$ (ms)	289.51 (92.48)	293.02 (121.60)	-.34	.69***
RT$_{SD}$	115.39 (89.84)	149.20 (152.97)	-1.73	.13
Number Correct	33.68 (3.80)	32.73 (5.37)	1.65	.46***

* $p < .05$, ** $p < .01$, *** $p < .001$
Note: RT = reaction time; *M* = mean; *SD* = standard deviation

The data indicate that mean E-wave amplitudes were moderately reliable across sessions despite becoming significantly more negative in session 2, suggesting a systematic group shift from session 1 to session 2 in accordance with Taylor et al. (2016). However, standard deviations of E-wave amplitudes were not reliable, nor did they significantly differ across visits. Thus, the data suggest that means and standard deviations of the E-wave component amplitude are affected differently as children performed the Go/No-Go task across the two sessions.

Children's task behaviors, including means and standard deviations of reaction times, and accuracy on the Go/No-Go task, did not significantly differ across sessions. Interestingly, average reaction time was reliable, whereas standard deviation of reaction time was not. Again, the data indicate differential effects on average performance versus variability of performance during each session.

Modeling brain and behavior. In order to better understand the relationships between E-wave and reaction time measures in children, we examined the correlations between measures. The intercorrelations between brain and behavioral measures are reported in Table 2.2.

Table 2.2.
The intercorrelations between means and standard deviations of E-wave (µV) and reaction time (ms) measures during both sessions, and mean age (years).

	RT_{M1}	RT_{M2}	RT_{SD1}	RT_{SD2}	Age
E-wave$_{M1}$	$.28^{*}$	.11	.16	.042	$-.24^{*}$
E-wave$_{M2}$	$.31^{**}$	$.28^{*}$	.18	.15	$-.27^{*}$
E-wave$_{SD1}$	.17	.18	.082	.067	-.12
E-wave$_{SD2}$	.11	.038	.16	.036	$-.23^{*}$
Age	$-.51^{***}$	$-.53^{***}$	$-.40^{***}$	$-.39^{**}$	–

* $p < .05$, ** $p < .01$, *** $p < .001$
Note: RT = reaction time; M_1 = mean session 1; M_2 = mean session 2; SD_1 = standard deviation session 1; SD_2 = standard deviation session 2

Although the effects were small, correlations indicated significant positive associations between average E-wave amplitudes and average reaction times (see Table 2.2). Thus, the data in the present investigation were in accordance with prior literature with adult samples showing that individuals with larger (more negative) average E-wave amplitudes tended to have faster average reaction times (Brunner et al., 2015; Connor & Lang, 1969). The correlations indicated that mean E-wave amplitudes and mean reaction times shared 7.84% of their variance in session 1, and 9.61% of their variance in session 2. Standard deviations of E-waves and reaction times were not significantly correlated with any measures other than Age.

Next, we used SEM techniques to evaluate a simple path model in order to further understand the interrelationships of brain processing and task behavior measures during each session. The model yielded good model fit, $\chi^2(12) = 19.01$, $p = .09$, RMSEA = .09, 90% CI (< .001, .16), CFI = .96, SRMR = .05, indicating that the model adequately explained the correlational structure present in the data (see Figure 2.1).

Model results for the E-wave. With respect to averaged amplitudes of the E-wave, the model indicated expected relationships based on prior literature (e.g., Taylor et al., 2016). Specifically, the mean amplitude of the E-wave in session was related to age, such that children who were older also had larger (more negative) E-wave amplitudes. Additionally, session 1 averaged amplitudes significantly predicted session 2 amplitudes, as was expected based on the test-retest reliability of the ERP component. The model corroborates evidence that the shift in ERP amplitudes over time was systematic within and between participants. Importantly, there was no additional significant effect of age on session 2 averaged amplitudes *above and beyond* what was already accounted for in session 1. These data support the notion that children had not significantly matured over the one-to-two week period, thus the shift in E-wave averaged amplitudes over time cannot be simply explained by maturation.

The standard deviation of the E-wave amplitudes indicated a different pattern compared to the averaged amplitudes. Session 1 standard deviations indicated no significant relationship with age, nor was there a significant prediction to session 2 standard deviations. However, there was a significant age effect on session 2 standard deviations, such that older children had less variability in their E-wave amplitudes than younger children. The model suggests that children's overall variability in neural processing patterns was changing over time as they learn the task, but the effect was stronger for older children.

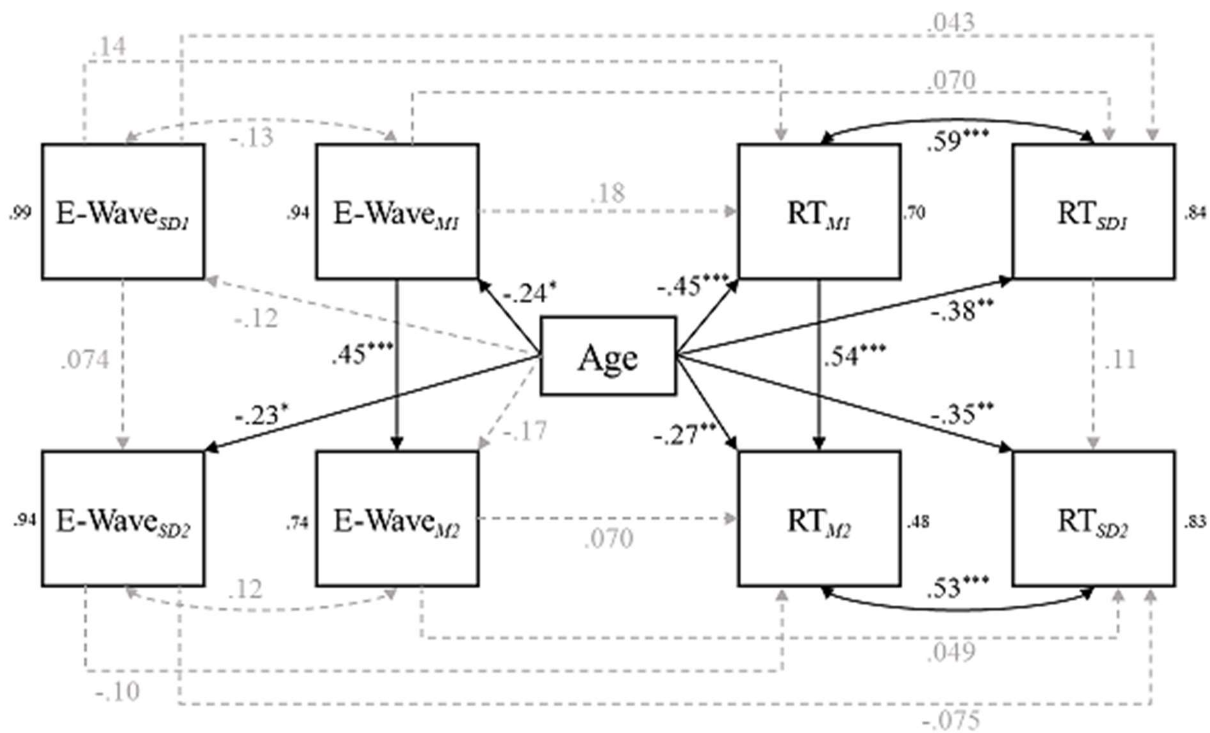

*Figure 2.1. The structural model exploring interrelationships between means and standard deviations of E-wave amplitudes, and means and standard deviations of reaction times (RT) during Go trials for both sessions. Note: All reported coefficients are standardized. Residual variances are reported next to each manifest variable in small font. Non-statistically significant relationships are shown as gray, dotted lines. Statistical significance is indicated as follows: * p < .05, ** p < .01, *** p < .001. Note: RT = reaction time;* M_1 *= mean session 1;* M_2 *= mean session 2;* SD_1 *= standard deviation session 1;* SD_2 *= standard deviation session 2*

The associations between averaged amplitudes and standard deviations of amplitudes was not significant for either session. In combination with the differential effects of age and session, these data suggest that E-wave amplitudes and standard deviations may represent unique aspects of neural processing.

Model results for reaction times. Considering average reaction times, session 1 significantly predicted session 2, which was in accordance with the previously-reported test-retest reliability (see Table 2.1). There was a significant effect of age on session, such that older children tended to be faster than younger children. Interestingly, session 2 average reaction time had an additional age effect above and beyond what was already accounted for in session 1. The results indicated that although older children tended to be faster than younger children in the first session, the effect was further exaggerated in session 2. The effect was present in spite of any significant group differences in average reaction times across sessions (see Table 2.1).

Standard deviations of reaction times were not related across sessions, which was again in accordance with the previously established test-retest reliability. However, both sessions had a significant effect of age, such that older children were less variable in their response speed compared to younger children. Correlations between averages and standard deviations of reaction times indicated significant, positive relationships for each session. Specifically, the data indicated that children who were typically faster also tended to be less variable in their response times.

Can brain measures predict behavior? The model indicated that none of the E-wave measures significantly predicted any of the reaction time measures (see Figure 2.1). The result was surprising given the previously-noted correlations between average E-wave amplitudes and average reaction times (see Table 2.2). Additionally, prior literature examining adults has also reported correlations between average E-wave amplitudes and reactions times such that individuals with more negative E-wave amplitudes tend to have faster responses (Brunner et al., 2015; Connor & Lang, 1969). However, the simple path model indicated large residual variances for most of the measures, indicating that much of the variance was not explained by the simple correlations and predictive relationships. To further reduce the influence of measurement error in E-wave amplitude and reaction time measures, we employed a more sophisticated form of SEM: a latent variable path analysis.

Latent variable modeling. We first attempted to develop a four-latent variable model in which the two sessions of each measure (e.g., mean of E-wave amplitude) were combined into a latent variable. Age was used as a control variable, and E-wave latent variables were predictors of reaction time latent variables. However, the model did not converge. The non-convergence was not surprising given that the standard deviations of E-wave amplitudes and reaction times were not related across sessions, thus their latent variables were poorly-defined. We then simplified the model to include only the latent variables defined by average E-wave amplitudes and reaction times. The resulting model yielded good model fit, $\chi^2(3) = 5.12$, $p = .16$, RMSEA = .10, 90% CI (< .001, .24), CFI = .98, SRMR = .03, indicating that the model adequately accounted for the correlational structure of the data (see Figure 2.2).

The latent variables were both well-defined by their contributing manifest variables, with all measures significantly contributing to the definition of their respective latent constructs. Additionally, the effect of age remained significant in the latent variable model, indicating that older children tended to have larger (more negative) average E-wave amplitudes, and faster reaction times. Because the effect of age was statistically significant for both latent variables, the model suggests that the effect of age on reaction times was unique, and could not be entirely accounted for by the effect of age on E-wave amplitude.

Interestingly, even after enforcing better control of measurement error by creating latent variables, brain measures still did not significantly predict behavior measures. The predictive relationship from the E-wave latent variable to the reaction time latent variable was small, though still in the expected direction given prior research and the previously-established

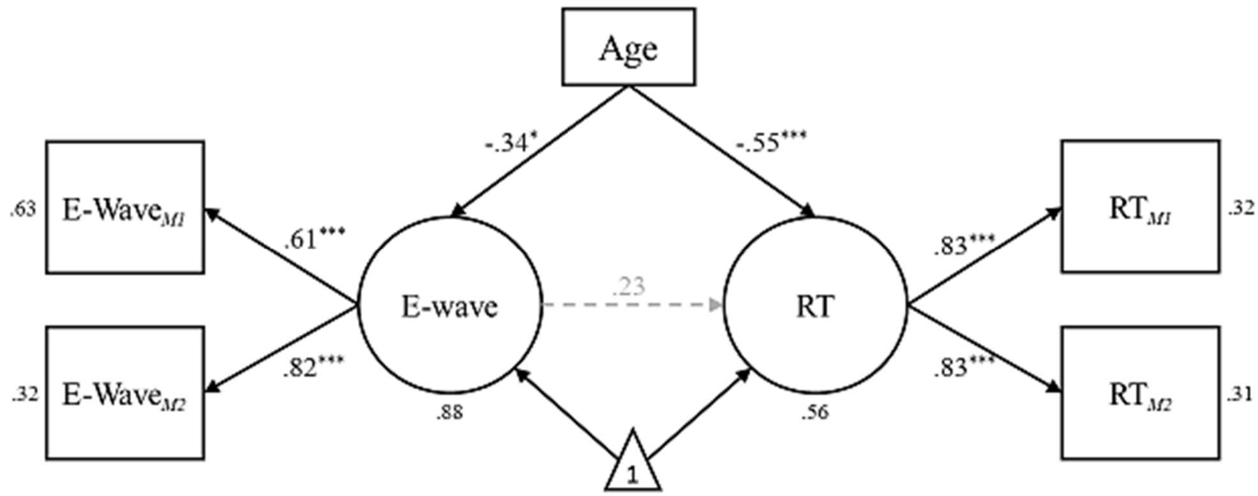

*Figure 2.2. The latent variable model exploring interrelationships between means of E-wave amplitudes and reaction times (RT) during Go trials for both sessions. Note: All reported coefficients are standardized. Residual variances are reported next to each manifest variable, and disturbances are reported below latent variables in small font. Non-statistically significant relationships are shown as gray, dotted lines. Statistical significance is indicated as follows: * p < .05, ** p < .01, *** p < .001. Note: RT = reaction time;* M_1 *= mean session 1;* M_2 *= mean session 2;* SD_1 *= standard deviation session 1;* SD_2 *= standard deviation session 2*

correlations (β = .23, *p* = .10; see Table 2.1). It was surprising to find that the association was not statistically significant given the previously established bivariate correlations, which *were* significant when the individual variables were contaminated with multiple sources of variance (e.g., age effects, individual differences across sessions). In total, the model accounted for only a small proportion of the variance in E-wave measures, $R^2 = .18$, $p = .21$, but explained a significant proportion of the variance in reaction times, $R^2 = .44$, $p < .001$.

Summary

The progression of models in the present study revealed interesting patterns in the brain and task-specific behavioral data across sessions in children. Using a simple path model (Figure 2.1), we simultaneously summarized our previously-established univariate findings (e.g., reliability of the mean E-wave amplitude) while exploring individual differences in neural processing and task performance via standard deviation measures. The model indicated no significant relationships between brain and behavior measures, though there were a number of unique age effects in each session. The multitude of developmental effects may suggest that children relied on different cognitive resources to process and perform the task across sessions. For example, children may have engaged in different types of attention processing, various executive control processes, and differential motor control mechanisms as they practiced the task and developed a strategy for optimal performance (e.g., Pauli et al., 1994; Romero et al., 2008).

Examination of the latent variable model further indicated unique effects for brain versus behavior (see Figure 2.2). There was still no significant relationship between brain and behavior even after we effectively removed measurement error, including differences in state effects between sessions, from E-wave and reaction time measures. Notably, each latent variable had a unique age effect. The latent variable model suggests that perhaps E-wave and reaction time are representations of different underlying constructs such as executive function or motor control. Further work is needed to better understand the cognitive processes that may be contributing to E-wave and reaction time variability.

Study 1.2

Rationale and Purpose

The E-wave component has been described as a representation of sustained attention processing in the brain for a number of reasons, one of which is the finding that E-wave amplitudes are related to within-task reaction times (Brunner et al., 2015; Connor & Lang, 1969). However, to the best of our knowledge neither E-wave amplitudes nor within-task reaction time have been definitively related to validated behavioral assessment measures of attentional abilities. Behavioral assessment measures are often conceptualized as indicators of an individual's trait-based cognitive abilities, which should be relatively stable.

The purpose of the present study was to establish whether the E-wave or reaction times during the visual Go/No-Go task could be related to a behavioral assessment of attention in children designed for clinical use. We specifically focused on the Test of Everyday Attention for Children (TEA-Ch; Manly et al., 2001; Manly, Robertson, Anderson, & Nimmo-Smith, 1999), which purports to measure three different types of attention: selective, switching, and sustained attention. The tripartite factor structure of the TEA-Ch has only been validated in a sample of 6- to 16-year-old Australian children, thus we began our investigation by first exploring the factor structure of the TEA-Ch in a younger sample of neurotypical children in the United States. We then examined (1) whether the different types of attention measured by the TEA-Ch were related to the E-wave, and (2) whether the E-wave or the TEA-Ch factors were better predictors of reaction times during the Go/No-Go task. Based on prior literature, we hypothesized that both the E-wave and reaction time would have the strongest relationships with *sustained* attention as measured by the TEA-Ch. Additionally, we expected that reaction times may be better-related to trait measures of attention defined by the TEA-Ch compared to the E-wave based on the weak predictive relationship established previously in *Study 1.1*.

Methods

Participants. In order to first validate the factor structure of the TEA-Ch in young, neurotypical children in the United States, we employed data from a larger sample of children who had completed the TEA-Ch in our lab. Data were collected from a total of 130 neurotypical children between the ages of 6 and 13 years (63 males; $M = 9.34$ years, $SD = 1.86$), who each participated in two sessions of data collection. Of the total sample, 73 were included in the *Study 1.1* description above, and an additional 57 children completed the TEA-Ch as part of other ongoing research studies. Participants had no neurological or developmental diagnoses, nor were they currently taking any psychopharmaceutical medications, as reported by parents. All parents of participants signed informed consent forms, and all children signed assent forms. Participants received their choice of a t-shirt or cocoa mug after their first visit, and their choice of a t-shirt, cocoa mug, or a small cash prize ($10-15 depending on the study) following their second visit. Procedures for all studies were approved by the local university institutional review board.

Procedure. Regardless of what study each child participated in, all participants completed approximately one hour of EEG testing prior to completing behavioral assessments. For children who completed the Go/No-Go task (i.e., the 73 children included in *Study 1.1*), the TEA-Ch was completed following the second session of EEG testing. In some studies, the TEA-Ch was completed following EEG testing on the first visit. Behavioral tests were administered by a trained research assistant in a quiet room.

TEA-Ch. The TEA-Ch consists of a battery of nine game-like subtests that purport to measure three types of attention: selective, switching, and sustained attention (Manly et al., 2001; Manly et al., 1999). Children are asked to perform auditory and visual tasks, such as counting the number of sounds on an audio clip or finding matching pairs of space ships in the midst of distractor stimuli on a large sheet. The assessment is normed for children ages 6 to 16 years, providing standardized scores for each subtest ranging from 1 to 20. With respect to standard scores, a score of 10 is an average score for a child of a particular sex and age, and larger scores are indicative of better attention abilities relative to other children of the same sex and age. Manly et al. (2001) demonstrated that, using standard scores, the TEA-Ch subtests result in a three-factor structure representing the three different types of attention in 6 to 16 year-old Australian children.

Data analysis. All analyses were conducted using Mplus version 7.3. We began by validating the TEA-Ch in our larger sample of children. Using the same techniques previously reported in Manly et al. (2001), we defined a three-factor model of attention using the nine TEA-Ch subtests. Each latent variable was identified by the first-listed manifest variable in accordance with Manly et al (2001). Once a viable model was established in the larger sample of children, factor loadings for the manifest variables were retained and fixed for the following analysis.

To examine the interrelationships between E-wave, reaction time, and TEA-Ch factors, we established a final latent variable model to investigate the relationship between a behaviorally-measured trait (TEA-Ch measures of attention), measures of brain activity (E-wave), and task performance. Specifically, the TEA-Ch was defined using the fixed factor loadings obtained from the larger sample (as described above). All other TEA-Ch model parameters, including means, variances, and the correlation between factors, were allowed to freely vary. We then added in the E-wave and reaction time latent variables, which were freely estimated in this model (i.e., not fixed based on prior findings). This was specifically to allow parameters of interest to vary as we added in trait measures of attention. E-wave and reaction time latent variables were established as described in *Study 1.1*, again using age as a control variable. The E-wave was correlated with TEA-Ch attention factors. Then, the E-wave and all TEA-Ch attention factors were used as predictors of reaction time.

Results and Discussion

Validation of the TEA-Ch. Using the sample of 130 children, we first tried to directly replicate the factor structure described by Manly and colleagues (2001). Specifically, we attempted to model a three-factor structure of Selective, Sustained, and Switching attention using the nine subtests of the TEA-Ch. Although the model yielded good fit statistics, $\chi^2(24) = 33.66$, $p = .09$, RMSEA = .06, 90% CI (< .001, .10), CFI = .94, SRMR = .06, there were two key problems with the resulting structure: (1) none of the manifest variables defining Sustained attention significantly loaded onto the latent variable; and (2) there was a high correlation between Selective and Switching attention ($\varphi = .93$, $p < .001$), which could cause problems with further analysis due to multicollinearity between these two latent variables. Further examination using exploratory factor analysis indicated that a two-factor structure in which the subtests defining the Selective and Switching attention variables were collapsed into a single factor would be the most parsimonious structure given the data. Additionally, the manifest variable for the subtest *Score!*, which is the simplest of the nine subtests, did not significantly load onto either factor. We attempted to fit two variations of the two-factor model: the first included the *Score!* manifest variable in the Sustained attention latent variable in accordance with Manly et al. (2001), and the second excluded *Score!* from the analysis entirely. When *Score!* was included, once again, none of the manifest variables were significantly loading onto the Sustained attention latent variable. However, removing *Score!* from the analysis produced a good-fitting model,

$\chi^2(19) = 19.32$, $p = .44$, RMSEA = .01, 90% CI (< .001, .08), CFI = .99, SRMR = .04, in which all manifest variables significantly contributed to their respective latent variable definitions. Additionally, the correlation between the resulting latent variables, which we termed Control Attention and Sustained Attention, was reasonable for further analysis, $\varphi = .69$, $p < .001$. The factor loadings from this model, which was established with the larger sample of children, were retained and fixed in the following analysis, which only included the 73 children from *Study 1.1* who had the E-wave and reaction time data from the Go/No-Go task (Note: the fixed TEA-Ch parameters can be viewed in Figure 2.3).

Connecting traits, brain measures, and simple task behaviors. Next, we attempted to model the interrelationships between the two obtained TEA-Ch latent variables of attention, the E-wave, and reaction times. Specifically, we defined a model in which Control and Sustained attention and the E-wave latent variable were correlated and served as predictors of the reaction time latent variable. Age was a control variable on the E-wave and reaction time latent variables; the control variable was not necessary for the attention latent variables because they were defined using standard scores, which are already free of developmental effects. Although the Control and Sustained attention factor loadings were fixed, all other TEA-Ch parameters, the E-wave, reaction time, and age parameters (e.g., factor loadings, correlations, means, variances) were all free to vary. The intent was to allow the brain and task behavior parameters to adequately shift once trait measures of attention were included, thereby better representing the full effects of the trait measures above and beyond what was established in *Study 1.1*. The model yielded good model fit statistics, $\chi^2(64) = 66.13$, $p = .40$, RMSEA = .02, 90% CI (< .001, .07), CFI = .99, SRMR = .08, indicating that the model was viable (see Figure 2.3).

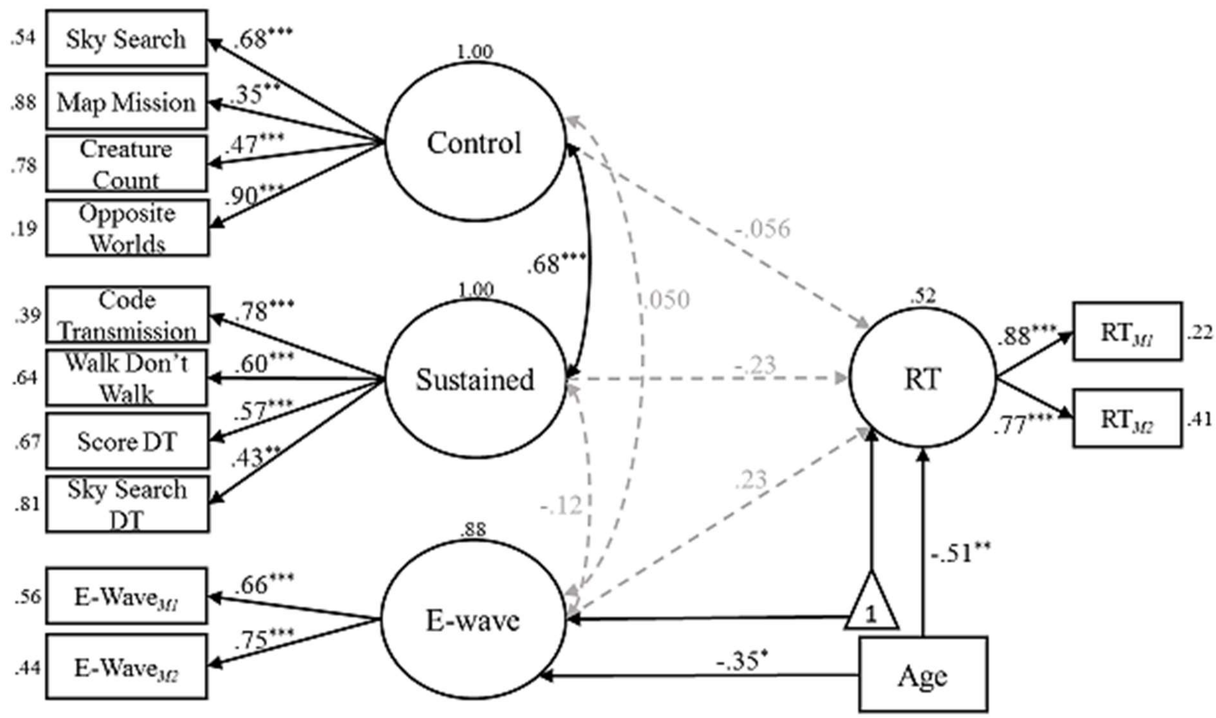

*Figure 2.3. The latent variable model exploring interrelationships between TEA-Ch attention factors, the E-wave, and reaction time (RT). Note: All reported coefficients are standardized. Residual variances are reported next to each manifest variable, and disturbances are reported above the latent variables in small font. Non-statistically significant relationships are shown as gray, dotted lines. Statistical significance is indicated as follows: * $p < .05$, ** $p < .01$, *** $p < .001$. Note: RT = reaction time; M_1 = mean session 1; M_2 = mean session 2; SD_1 = standard deviation session 1; SD_2 = standard deviation session 2*

Model results for the E-wave. Despite abundant literature purporting that the E-wave is at least in part a representation of attentional abilities, the model indicated no significant relationships between the E-wave latent variable and either attention variable. That is to say, whatever variance in the averaged E-wave amplitudes that was common across sessions was not significantly related to the trait abilities of either Control or Sustained attention as measured by the TEA-Ch.

Although we failed to show a significant relationship to trait measures of attention, the model did indicate a significant age effect on the E-wave latent variable. The finding was in accordance with previous literature indicating that older children tend to have a larger (more negative) average E-wave amplitude compared to younger children (e.g., Hämmerer et al., 2010; Jonkman et al., 2003; Taylor et al., 2016). Although it was a significant effect, age did not account for a significant proportion of the variance in the E-wave latent variable, $R^2 = .13$, $p = .17$, suggesting that other variables may better explain the variability in averaged E-wave amplitudes that is consistent across sessions.

Model results for reaction time. The model explored whether Control attention, Sustained attention, or E-wave amplitude latent variables could predict the reaction time latent variable. Interestingly, none of the three predictors had statistically significant effects. Considering the trait attention measures, both Sustained and Control attention indicated a negative relationship with reaction time, suggesting that individuals with better trait attention tended to have faster reaction times. Sustained attention had a stronger predictive relationship to reaction time than Control attention, but again, neither prediction was statistically significant. Regardless, the model may suggest that Sustained attention is contributing to reaction times to a greater extent than Control attention, at least with respect to reaction times in the Go/No-Go task.

Considering the E-wave as a predictor, the results indicated a positive, though non-statistically significant prediction, such that children with larger (more negative) E-wave amplitudes tended to have faster reaction times. The general finding was in accordance with the literature, and matched the results of *Study 1.1*.

The only significant predictor of reaction time was age, indicating that older children tended to have faster reaction times than younger children. The effect of age remained significant even after accounting for the effects of the E-wave (along with its own age effects) as well as trait measures of Control and Sustained attention. Based on these findings, one might conclude that reaction time is not entirely explained by either the E-wave or trait measures of attention, and its variance contains unique developmental effects that may be better explained by other abilities and cognitive constructs, such as motor control or executive function. In total, the model explained a significant proportion of the variance in reaction time, $R^2 = .48$, $p < .001$, though there was still a large amount of variance that is not explained by E-wave amplitudes, trait attention, or age.

Summary

Validation of the TEA-Ch factor structure indicated that, at least in the present sample of young, neurotypically-developing children in the United States, a two-factor solution was the most parsimonious in contrast to Manly et al.'s (2001) three-factor model, established in a sample of Australian children ages 6 to 16 years-old. Specifically, Selective and Switching attention measures were collapsed into a single factor which we termed Control attention. The finding was interesting given recent work by Petersen and Posner (2012), who suggested that the neural networks responsible for Switching attention (termed "orienting" in their paper) and Selective attention (termed "executive control" in their paper) may not be differentiated in childhood. That is to say children do not necessarily engage unique neural networks to perform Switching versus Selective attention tasks the way that adolescents and adults do, which may explain why our younger sample yielded only a two-factor model of attention. Further work is needed to confirm the neural mechanisms underlying the obtained attention factors in this study.

Interestingly, the trait measures of attention were not significantly related to either the E-wave or reaction time during the Go/No-Go task (see Figure 2.3). It is possible that with a larger sample, the predictive relationships from the E-wave ($\beta = .23$, $p = .13$) and from Sustained attention ($\beta = -.23$, $p = .27$) to reaction time may be statistically significant, though the effects are relatively weak. Weaker still were the correlations between the E-wave and both of the trait attention measures, despite over 50 years of researchers claiming that CNV E-waves represent aspects of sustained attention processing (Bender et al., 2004; Segalowitz & Davies, 2004; Walter et al., 1964). Given the findings from the present study, it seems more likely that the E-wave and reaction time may be better explained by other cognitive constructs and abilities. For instance, Perchet and Garcia-Larrea (2005) suggested that the E-wave may be a representation of executive control processes and motor preparation in the brain, rather than simple sustained attention. Other researchers have suggested a greater influence of motor control processes on the E-wave, like energization (Brunner et al., 2015). It is clear that the field requires more rigorous testing in order to appropriately validate both brain and task behavior measures if we hope to move toward more applied work, such as clinical diagnostics and intervention development.

Discussion

In the present investigations, we have demonstrated how advanced statistical modeling techniques, namely SEM, can (1) effectively manage sources of variance resulting from individual differences, thereby allowing researchers to better examine potential brain-behavior relationships, and (2) allow for the simultaneous examination of a constellation of complex interrelationships, which is likely more representative of neural processing than traditional univariate analyses. The two studies yielded a number of interesting findings, each of which contributes to our understanding of simple brain-behavior relationships.

From these data, it became clear that the variance defining a given measure, E-wave or reaction time, may be comprised of more unique, distinct constructs than researchers had previously suggested. For instance, we demonstrated that E-wave and reaction times measures each had unique age effects, even after removing measurement error by employing latent variable analysis. Where many researchers are quick to think of “age” as a single, non-changing construct (for a review, see(Johnson & de Haan, 2011), these findings suggested that “age” may be indicative of unique maturation within different constructs (e.g., motor control, executive function, attention), each of which may have a differential effect on our simple brain and behavioral measures. Such effects would not have been easy to detect via simple univariate analyses. Moving to a multivariate approach allowed us to simultaneously model multiple effects and better understand how each of our variables of interest, both brain and functional behavior, related to one another as well as other important variables like maturation (age). Thus, the multivariate approach afforded us a more complete, cohesive depiction of brain-behavior relationships in children than we could have detected with more simplistic univariate analyses.

When we expanded our model to include trait attention measures, we were unable to validate either the E-wave or reaction time measures as indicators of attentional processing. However, by examining all potential relationships simultaneously, we gained a clearer perspective on how the assorted measures may be interacting. For instance, although not all statistically significant, age, the E-wave, and the trait factor of Sustained attention were the strongest predictors of reaction time, indicating that they collectively accounted for at least a portion of the variance in task behavior (48% of the variance in the latent variable RT). However, “age” being the only significant predictor suggests that there is some unique developmental effect underlying children’s task performance that is not explained by the E-wave or trait attention abilities. The findings have important implications for future work looking to understand brain-behavior relationships.

It is possible that the simplistic relationship we tried to establish between a single cognitive construct (attention), a single ERP component, and a single task behavior measure was insufficient for explaining what is clearly a complex phenomenon. Researchers may need to consider additional measures to effectively map brain-behavior relationships. In other words, to better understand the complexities of neural processing and trait abilities that lead to functional output behaviors, we must introduce additional variables into our models that help us to understand the complete process.

In the case of CNV E-waves, the E-wave is only one phase of the complete CNV component. Researchers have described the CNV as a biphasic component comprised of an early orienting phase, the O-wave (Giard et al., 1990; Rohrbaugh et al., 1984; Zimmer & Demmel, 2000), and a late expectancy phase, the E-wave (Basile et al., 2002; Bender et al., 2004; Knott et al., 1991). It is possible that including both phases of the CNV as predictors of functional behaviors in the model may provide a more comprehensive picture of brain-behavior relationships. Additionally, including a more complete picture of the neural processing leading to task behaviors may better address Gavin and Davies' (2008) equation of individual differences (see equation 1 above). Unfortunately, we were unable to measure the O-wave in the present study due to the children's overwhelming P3 response, which obscured the O-wave component (for similar discussion, see Jonkman et al., 2003; Taylor et al., 2016). However, future investigations may examine both the O-wave and E-wave in samples of older children in which both ERP components are more likely to be measurable.

Each phase of neural processing, like the phases of the complete CNV component, may have unique measurement variance that contributes to the prediction of behavioral outcomes. Even with our simplistic models including simple trait attention measures, a single ERP component and a single task behavior, we were able to account for 48% of the variance in functional behavior after removing measurement error. This far supersedes the small amount of variance explained by simple bivariate correlations between an ERP component and a reaction time (e.g., in our study: mean E-wave and RT measures shared 7.84% of their variance in session 1; see Table 2.2). By including additional neural processing measures, researchers may effectively reduce the ME term further, yielding stronger, more definitive predictions of brain-behavior relationships. If the field ever hopes to reliably use ERP components as biomarkers or measures of intervention efficacy, we must first be able to effectively manage ME in the data and indicate strong, stable brain-behavior relationships.

CHAPTER III – STUDY 2

Recently, researchers have been motivated to detect strong, stable brain-behavior relationships that can be used as viable indicators of development or clinical disorders. In consequence of the non-invasive and relatively inexpensive nature, many researchers have turned to electroencephalography (EEG) and event-related potential (ERP) techniques to examine brain and behavior in a number of populations, including children with and without clinical diagnoses. Despite notable growth in research on brain-behavior relationships in the last few decades, the field is arguably still in its infancy. Researchers continue to uncover weak, variable relationships between neural processing measures and behaviors (e.g., Brydges et al., 2014; Foti et al., 2016), especially among populations that are inherently more variable in their brain activity and performance, such as children and clinical populations. For example, Brydges et al. (2014) found only small predictive relationships between ERP component measures and behavioral assessments of executive functions in a sample of typically-developing children with β values ranging from -.27 to .17.

Such weak effects are inadequate for use in diagnostics, or for measuring development over time. In fact, in order to be relevant for such use, many researchers agree that the psychometric properties of a measure being used as a dependent variable should include test-retest reliability coefficients upwards of r = .80, though greater than .90 is preferred (for reviews, see Clayson & Miller, 2017; Hopkins, Stanley, & Hopkins, 1990; McCauley & Swisher, 1984; Salvia & Ysseldyke, 1981). However, a growing body of evidence indicates that the test-retest reliability of ERP components commonly used in brain-behavior relationship research is moderate at best in groups of interest for developmental and clinical investigations, including neurotypical children and individuals with neuropsychological diagnoses (e.g., Foti et al., 2016; Meyer, Bress, & Proudfit, 2014; Segalowitz & Barnes, 1993; Taylor et al., 2016). Inadequate stability of dependent measures may explain, at least in part, why researchers have struggled to identify viable brain-behavior relationships in such groups.

To conceptualize why a psychophysiological measure (PM) may have low test-retest reliability, Gavin and Davies (2008) suggested that any PM, including an ERP component, is comprised of the combined variance from multiple sources: (1) the *stimulus processing* involved in eliciting the component; (2) the *state* of the individual participant during measurement such as current mood or sleepiness; (3) the *trait* characteristics of the individual such as general attention abilities or maturation level; (4) the *signal processing techniques* employed to calculate the ERP component including filtering and averaging of EEG signals; and (5) *measurement error* (ME), which is any other unaccounted-for variance (see equation 1 below, reprinted from Gavin & Davies, 2008, p. 428).

$$PM = Effect_{STIMULUS} + Effect_{STATE} + Effect_{TRAIT} + Effect_{PM\_PROCESSING} + ME \qquad (1)$$

When researchers submit ERP measures to simple univariate analyses, like *t* tests or correlations, they fail to account for individual differences that may be contributing to the ERP component, like state-specific effects. Thus, the individual effects are compounded into the ME term (see equation 2 below reprinted from Gavin & Davies, 2008, p. 428). The larger the ME term, the greater the likelihood of spurious effects (i.e., type I errors) or missed effects (i.e., type II errors). In order produce unambiguous, stable results it is important to reduce the ME term as much as possible. For example, part of the Gavin & Davies chapter (2008) focuses on ways to implement behavioral controls to reduce or minimize the contribution of variance due to differences in the state of children within a group or between sessions for an individual child.

$$PM = Effect_{STIMULUS} + ME_{TOTAL} \quad (2)$$

To explore statistical methods for controlling for state effects ($Effect_{STATE}$) in ERP components, *Study 1* used structural equation modeling techniques to establish a simple model of brain-behavior relationships between latent variables. Specifically, the study explored whether a latent variable defined by combining the E-wave component of an ERP from two sessions could be used to predict reaction times to the ERP task, also defined as a latent variable derived from two sessions. The latent variable approach significantly improved the amount of variance explained in reaction times beyond what was accounted for using univariate analyses. However, the effect was still small and failed to reach statistical significance ($\beta = .23$, $p = .10$). It is possible that examining a single ERP component in isolation may not be sufficient for explaining task behaviors. That is to say, earlier phases of neural processing represented by other ERP components that occur before the E-wave may be important contributors to behavioral performance.

Connectionist theory suggests the concept of sequenced processing of a stimulus through to production of a response: i.e., cascades of neural activity in which neuronal populations activate in certain patterns to trigger specific cognitive or behavioral responses (Hebb, 1949; McNaughton & Nadel, 1990; Raftopoulos, 1997). Furthermore, Landa et al. (2014) describe ERPs and their components as representations of complex neural system activations that are important in new stimulus detection and discrimination, and the resulting behavioral responses of individuals. Based on these theoretical perspectives, we believe it is reasonable to conceptualize the full time course of an ERP as a phase sequence, giving credence to each phase of systematic stimulus-to-response processing being represented by one or more ERP components preceding a task behavior. When considering that a traditional cognitive ERP consists of a stereotypical succession of components (N1, P2, N2, and P3; Kappenman & Luck, 2012), it is reasonable to consider an ERP as a continuous stream of phases of stimulus-to-response processing. During tasks requiring a delayed response, like a two-stimulus Go/No-Go task, other components such as the E-wave follows the P3 (Kappenman & Luck, 2012; Segalowitz & Davies, 2004). Given the predictable morphology of the cognitive ERP, it is possible that the full time course of the ERP can be modeled as a continuous path (i.e., a phase sequence), where one component predicts the next in chronological order leading to a behavioral response (i.e., N1 → P2 → N2 → P3 → E-wave → task behavior).

In the present study, we investigate whether the full time-course of an ERP, from the N1 through the behavioral response, can be modeled as a sequence of related phases each significantly predicting the next phase. Specifically, we employ structural equation modeling (SEM) techniques in order to establish a model depicting the full stream of stimulus-to-response processing in a sample of typically-developing children. We first establish the validity of the phase sequence conceptualization by assessing two variations of simple path models using manifest-level variables: one representing just the stream of neural processing during "Go" trials of a delayed response Go/No-Go task, and one representing the stream of neural processing *predicting the required task behavior (i.e., button press)*. We expect to find statistically significant predictions from one component to the next representing the full stream of processing, which in turn significantly predicts the task behavior. Next, we establish two *latent variable models* of the phase sequence: one representing just the stream of neural processing, and one in which the stream of neural processing predicts simple task behaviors. We hypothesize that by using latent variables, and thus effectively controlling the "state" sources of measurement error (i.e., the $\text{Effect}_{\text{STATE}}$ specified in equation 1 above defining variances in a physiological measure), we will establish stronger predictive relationships between ERP component measures, and a stronger prediction to task behavior.

Methods

Participants

Data were collected from a total of 101 neurotypical children between the ages of 7 and 13 years (46 males; *M* = 10.19 years, *SD* = 1.54) during two sessions scheduled one-to-two weeks apart (note: this is an extension of the sample in *Study 1.1*; Wave 1 = 57, Wave 2 = 44). Unlike in *Study 1.1*, no participants were excluded based on performance due to the use of estimation procedures in our statistical software. Details are described below. Participants had no neurological or developmental diagnoses, nor were they currently taking any psychopharmaceutical medications, as reported by parents. Parents of children signed informed consent forms, and child participants signed assent forms. Children received their choice of a t-shirt or cocoa mug after completing their first visit, and their choice of a t-shirt, cocoa mug, or $10 after their second visit. All procedures were approved by the local university institutional review board.

Procedure

The complete procedure is described in *Study 1.1*. For clarity of this study, we include some information on the procedure below. During each session, electroencephalographic (EEG) data were collected while children performed a simple, visual Go/No-Go task on a computer. During each trial of the task, children saw a sequence of two stimuli. First, a circle, either red or green, was displayed in the center of the screen for 250ms. Then the screen went blank for 1750ms before a picture of a car appeared in the center of the screen with a duration of 250ms. If the circle at the beginning of the trial was green, children were instructed to press a button on a response pad placed on the table in front of them as quickly as possible after the car appeared on the screen (i.e., a Go trial). However, if the circle was red, the children were instructed not to press the button (i.e., a NoGo trial). The task consisted of 40 Go and 40 NoGo trials presented in a pseudorandom order. The same task was performed during both sessions. Following EEG data collection, children completed a battery of behavioral assessments of attention and executive function abilities which will not be discussed further in this study.

Electrophysiological Recording

Details of the EEG recording equipment and procedures for the 57 children in Wave 1 are reported in Taylor et al. (2016, pp. 165-166), and in *Study 1.1*. EEG data recorded from the additional 44 children in Wave 2 were collected using a 64-channel BioSemi ActiveTwo system with Ag/AgCl sintered electrodes. Scalp electrodes were positioned according to a modified 10-20 system (American Electroencephalographic Society nomenclature guidelines, 1994) with additional common mode sense (CMS) and driven right leg (DRL) sensors, which served as reference and ground, respectively. An additional six sensors were placed on the face (on the left supra- and infra-orbital regions, and on the left and right outer canthi) and both the left and right earlobes to record eye movements and provide sites for offline re-referencing. Data were collected at a sampling rate of 1024Hz.

Electrophysiological Data Reduction

EEG data were reduced using previously established methods (*see Study 1.1*, Taylor et al., 2016). Following data reduction, only averaged ERPs depicting brain processing during correct Go trials were analyzed further. Correct Go trials were defined as any trial in which a green circle appeared before the car, and the participant pressed the button after the car appeared on the screen. Separate averaged ERPs were derived for each session.

The averaged ERPs were processed using a Matlab routine which allows for automatic scoring and visual inspection of ERP components, and, when necessary, allows for manual marking of components. All ERP component measurements were reviewed by one trained research assistant. Baseline-to-peak amplitudes for the N1, P2, N2, and P3, and the averaged amplitude in the time window of the E-wave were measured via the Matlab routine. All components were measured at site Cz. The N1 was defined as the most negative amplitude in the 70-170ms window, P2 as the most positive peak in the 150-300ms window N2 window as the most negative amplitude in the 250-400ms window, and P3 as the post positive peak in the 400-650ms window. The E-wave was measured as the averaged amplitude in the 1800-2000ms window. All ERP component time windows were selected based on prior research, and modified to accommodate the variability inherent in data collected from children (e.g., Hämmerer et al., 2010; Kappenman & Luck, 2012; Kropp et al., 2000; Taylor et al., 2016).

In addition to ERP component measures, averaged reaction times (RT) were derived for correct Go trials for each participant. RTs were calculated by the amount of time between the onset of the imperative stimulus (i.e., the car) and the participant’s button press for each trial. Then, an average RT was computed for each session separately, for each individual participant.

Data Analysis

Missing values. If a child had fewer than 12 correct Go segments (i.e., fewer than 30% of possible Go trials) remaining following EEG data reduction procedures, ERP component amplitudes were not measured for that session. Measuring ERPs comprised of relatively few trials could potentially introduce additional confounds into the data, including a poor signal-to-noise ratio in the data. It is noteworthy that all children did perform the task well enough to be included in the study (i.e., all children correctly performed more than 12 Go trials each session).

For participants that had less than 12 trials in the ERP, the loss of data was simply due to movement artifacts (e.g., eye blinks). A total of 11 children in session 1, and 12 children in session 2 received null values for their ERP component measures. Missing values were estimated in Mplus version 7.3 using full-information maximum likelihood (FIML) procedures.

Descriptive statistics. Analyses began with basic descriptive statistics for each dependent measure, including ERP component amplitudes as well as average RTs during the task. We also completed a series of paired-samples t-tests and explored test-retest reliability via Pearson product-moment correlations to examine any changes in the measures across sessions in accordance with prior literature (*Study 1.1;* Taylor et al., 2016). The analyses were also meant to demonstrate and confirm the inherent variability present in ERP data collected from children. In addition, we performed Pearson product-moment correlations to examine the interrelationships among the measures of interest (ERP component amplitudes, RTs, and age) to set the foundation for building models of brain processing and task behavior. All initial descriptive analyses were completed using SPSS version 24.

Manifest level path models. Following descriptive analyses, we developed two simple path models that represented the stream of neural processing in the averaged ERPs for each session. In both models, a single ERP component amplitude was used to predict the next in chronological order such that N1 → P2 → N2 → P3 → E-wave. Age was used as a control variable on each ERP component. All parameters were freely estimated. Once the structure of the models of brain processing during Go trials was established, we pursued the second variation of path analyses. Specifically, we added in average RT as the final outcome variable in each model, such that N1→ P2 → N2 → P3 → E-wave → RT. Age was also used as a control variable on

RT. The goal was to determine whether the full stream of neural processing, modeled with manifest variables, could successfully predict simple task behaviors.

Latent variable path models. After the manifest variable path models, we moved to latent variable path analyses. Latent variables are derived from the common variance of multiple manifest variables, and the resulting latent variable is free of any measurement error (i.e., any variance that is not common among the manifest variables is removed). Thus, the latent variable definition should also remove state-specific effects (i.e., $\mathrm{Effect}_{\mathrm{STATE}}$) in the data that varied across sessions. We defined a latent variable by the combination measurements from each of the two sessions for each dependent measures (e.g., session 1 and session 2 N1 amplitudes combined into a latent “N1”variable). Each latent variable was identified by the first session manifest variable (e.g., $\mathrm{N1}_{\mathrm{S1}}$). All other parameters were freely estimated. Before modeling the path of neural processing, we examined the reliability of each individual latent variable by calculating the ratio of explained variance to total variance (i.e., the factor rho coefficient: $\hat{\rho} = \frac{(\Sigma\hat{\lambda}i)2\hat{\Phi}}{(\Sigma\hat{\lambda}i)2\hat{\Phi}+\Sigma\hat{\theta}ii}$; Kline, 2011; Raykov, 1997, 2004). Each reliability coefficient was derived based on the freely-estimated latent variable with age as a control variable in order to best represent the latent variables used in the following models.

The latent variable paths were modeled similarly to the manifest variable paths. In the first latent variable path analysis, each latent variable derived from a set of ERP components predicted the next in chronological order (N1 → P2 → N2 → P3 → E-wave) to model the full stream of neural processing represented in an averaged ERP. The second latent variable model added in the simple task behavior component at the end of the stream of processing, wherein an RT latent variable was derived from the averaged RTs of both sessions. Age was used as a control variable on all latent variables. All modeling was performed using Mplus version 7.3.

In building the models in which brain processing predicts reaction times, both manifest-level and latent variable-level models, we began with just the E-wave predicting RT, then added in the P3, then the N2, and etcetera. At each step, we examined the models for direct and indirect effects in order to determine whether other ERP components may also predict RT. In all cases, there were no significant direct effects from any other ERP component predicting RT. Thus, only the fully-mediated models representing the complete path from N1 through RT are presented in the results section.

All models were examined for model fit. To evaluate overall model fit, we used the model fit criteria suggested by Hu and Bentler (1999), including comparative fit index (CFI) > .95, root mean square error of approximation (RMSEA) < .06, and standardized root mean square residual (SRMR) < .08. We also examined the chi-square test of model fit, where a non-statistically significant test indicates perfect fit of the model to the data. In all cases, only the best-fitting models are reported.

Results

Descriptive Statistics

Means and standard deviations, paired-samples *t* tests, and test-retest reliability indices of ERP component amplitude measures and average RTs are shown in Table 3.1. The data indicated that the N1, P2, and N2 ERP component amplitudes, and RTs were similar across sessions. The P3 component was significantly larger (more positive) in session 1 than in session 2, and the E-wave was significantly larger (more negative) in session 2 than in session 1. With respect to test-retest reliability, all components and RTs were moderately reliable across sessions. The findings related to E-wave and RT test-retest reliabilities are in accordance with previous work (*Study*

1.1; Taylor et al., 2016). The intercorrelations among ERP component amplitude measures, age, and RTs within a given session are shown in Tables 3.2 and 3.3.

Development of Brain and Behavior

Examination of the grand averaged ERPs and RTs separated by age group showed developmental trends from 8-to-12 years of age (see Figure 3.1). The ERP morphology was generally more organized with less variability in older children compared to younger children.

Table 3.1.
Means and standard deviations of baseline-to-peak Go trial ERP component amplitudes (µV), and averaged reaction times (RT; ms) for each session.

	Session 1	**Session 2**	**Difference**	**Test-retest Reliability**
	M (SD)	*M (SD)*	*t*	*r*
N1	-6.68 (4.75)	-6.23 (4.44)	-.63	$.59^{***}$
P2	9.30 (5.00)	8.60 (5.61)	.86	$.57^{***}$
N2	-6.11 (6.80)	-7.01 (6.57)	1.92	$.51^{***}$
P3	10.47 (5.65)	8.80 (5.20)	3.09^{*}	$.43^{***}$
E-wave	-2.11 (4.78)	-3.54 (5.22)	2.48^{*}	$.49^{***}$
RT	298.87 (97.03)	308.21 (128.05)	-.85	$.76^{***}$

Note: $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$

Table 3.2.
Intercorrelations of baseline-to-peak ERP component amplitudes (µV), average reaction times (RT; ms), and age (years) for session 1 Go trials.

	N1	**P2**	**N2**	**P3**	**E-wave**	**RT**	**Age**
N1	–						
P2	$.25^{*}$	–					
N2	$.40^{***}$	$.37^{***}$	–				
P3	$.23^{*}$	$.51^{***}$	$.40^{***}$	–			
E-wave	$.23^{**}$	$.44^{***}$	$.38^{***}$	$.48^{***}$	–		
RT	.057	.078	.013	.028	$.34^{**}$	–	
Age	.087	-.14	.15	-.19	$-.25^{*}$	$-.49^{***}$	–

Note: $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$

Table 3.3.
Intercorrelations of baseline-to-peak ERP component amplitudes (μV), average reaction times (RT; ms), and age (years) for session 2 Go trials.

	N1	P2	N2	P3	E-wave	RT	Age
N1	–						
P2	$.30^{**}$	–					
N2	$.44^{***}$	$.42^{***}$	–				
P3	.11	$.31^{**}$	$.31^{**}$	–			
E-wave	.20	$.24^{*}$	$.34^{**}$	$.41^{***}$	–		
RT	.075	-.090	-.031	.053	$.26^{*}$	–	
Age	.14	-.038	.042	$-.27^{*}$	$-.27^{*}$	$-.50^{***}$	–

Note: $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$

In general, the magnitude of the voltage deflections from one ERP component to the next seemed to decrease with age. Additionally, the 12-year-old children seemed to have earlier, narrower P3components compared to the younger children in the sample, and also had the most negative (adult-like) E- wave components out of all age groups. Younger children's E-wave components were much less negative with many tracings resting near baseline, especially in the first session.

With respect to RTs, older children tended to have a narrower distribution that clustered closer to the onset of the imperative stimulus when compared to younger age groups (see Figure 3.1). In contrast, the younger children had much more dispersed distributions of average RTs. The data suggest a developmental trend such that older children tended to perform more consistently, and more quickly than younger children in this sample.

Manifest Variable Path Model Results

Model fit statistics were examined for each of the established path models. With the simple path structure of neural processing (N1 → P2 → N2 → P3 → E-wave) using age as a control variable on all ERP component measures, model fit statistics did not meet the criteria set by Hu and Bentler (1999). For example, chi square *p* values were <.001 and .001, RMSEA

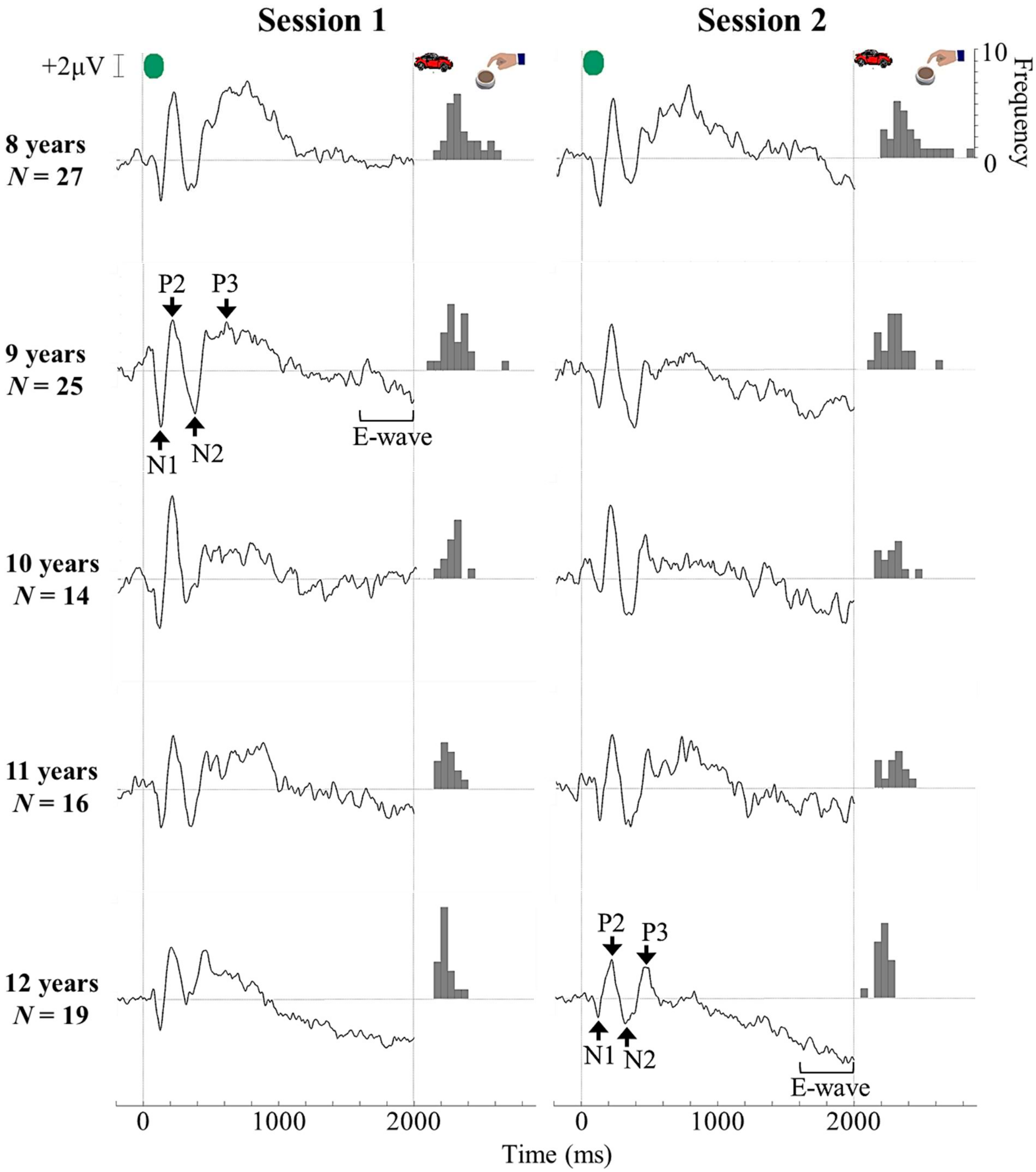

Figure 3.1. The grand averaged event-related potentials (ERPs) for session 1 and session 2 Go trials separated by age group. All ERP images were derived at site Cz. The frequency distribution of average reaction times for each session and age group is shown to the right of each ERP. Note: there were very few children that were 7- or 13-years-old, and those children's data were grouped with the 8- and 12-year-olds' data, respectively.

values were .14 and .24, CFI values were .69 and .80, and SRMR values were .10 and .13 for session 1 and session 2 models, respectively. Thus, we utilized the modification indices (MODINDICES) command in Mplus to determine additional relationships to include in the models in order to improve model fit. Based on the suggestions, we added correlations between all positive deflections (e.g., P2 with P3), and between all negative deflections (e.g., N2 with E-wave), which significantly improved model fit for both the session 1 and session 2 models, with and without the final prediction to simple task behaviors (i.e., RTs). It is noteworthy that the parameter estimates in the models did not significantly change following the addition of the correlations, thus the conclusions drawn regarding the structure of the models were the same before and after including the modification indices with the added benefit that the fit statistics were greatly improved. Although not all model fit indices were in the excellent range each of the established models (see Table 3.4), we chose to keep the model structures identical for ease of interpretation rather than continuing to add in correlations that saturated the models.

Table 3.4.
Model fit statistics for each of the established manifest variable path models after including the correlations suggested as modification indices.

	Chi Square	**RMSEA**	**CFI**	**SRMR**
Go Session 1	$\chi^2(2) = 7.87$ $p = .02$	RMSEA = .18 90% CI [.06, .32] $p = .22$	CFI = .94	SRMR = .05
Go Session 2	$\chi^2(2) = 1.10$ $p = .58$	RMSEA = .00 90% CI [.00, .19] $p = .64$	CFI = 1.00	SRMR = .02
Go Session 1 + RT	$\chi^2(6) = 13.20$ $p = .04$	RMSEA = .11 90% CI [.02, .19] $p = .10$	CFI = .95	SRMR = .05
Go Session 2 + RT	$\chi^2(6) = 8.28$ $p = .22$	RMSEA = .06 90% CI [.00, .16] $p = .36$	CFI = .98	SRMR = .05

Manifest variable model of session 1 brain processing. The model for session 1 Go trials indicated that beginning with the N1, each component significantly predicted the following component in chronological order all the way through to the E-wave (see Figure 3.2a). All predictive coefficients were positive, suggesting that having a larger (i.e., farther from baseline) ERP component amplitude at one point in the stream of neural processing predicted a smaller (i.e., closer to baseline) amplitude at the next component.

Considering age, only two ERP component amplitudes showed statistically significant effects of age: the N2 and the P3. There was a significant positive effect of age on the N2 amplitude, indicating that older children tended to have smaller (less negative) N2 amplitudes. In turn, there was a significant negative effect of age on the P3, again indicating that older children tended to have smaller (less positive) P3 amplitudes. The findings suggest that older children may have required less intense processing at the later stages of decision-making during session 1 Go trials.

Manifest variable model of session 2 brain processing. The model for session 2 Go trials was similar to that of session 1 Go trials. In the path model, each ERP component amplitude significantly predicted the next in chronological order through the entire stream of processing, from the N1 through the E-wave (see Figure 3.2b). Again, the predictive coefficients were all positive.

Interestingly, the pattern of age effects differed between session 1 and session 2 Go trial models. For session 2, there was only one statistically significant age effect, indicating that older children tended to have smaller P3 amplitudes than younger children. The finding was in contrast to the session 1 model, which indicated an age effect on the N2 component in addition to the P3.

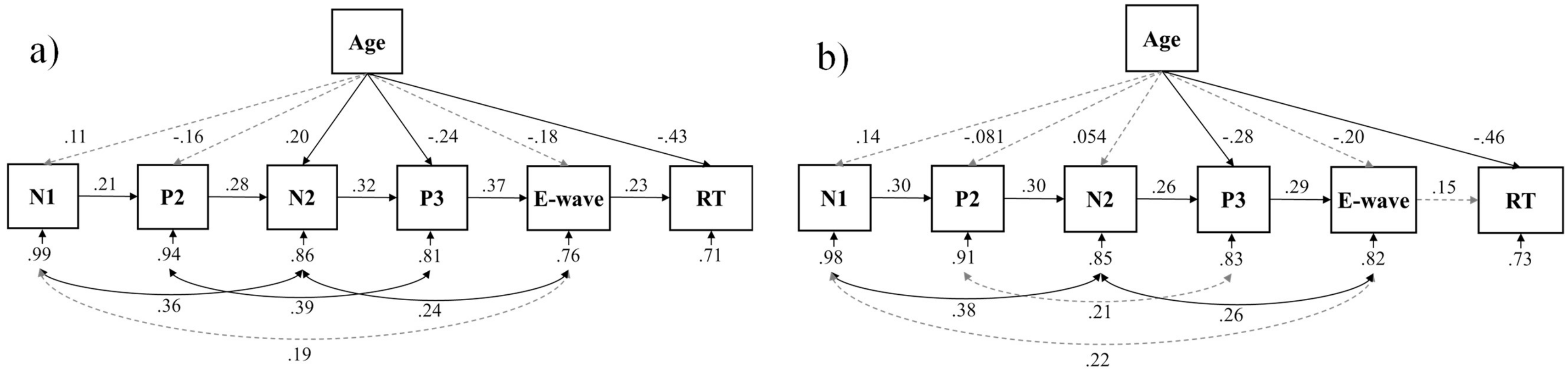

*Figure 3.2. The two established models of neural processing predicting simple task behaviors (average reaction times) where **a**) Session 1 Go trials; and **b**) Session 2 Go trials. Gray dotted arrows indicate non-statistically significant relationships at the p < .05 level. Residual variances are reported below each variable. All reported coefficients are standardized. Note: the model structures, including all predictive coefficients, correlations, and residual variances, did not differ for the neural processing portion of the model (i.e., N1 → P2 → N2 → P3 → E-wave) before and after adding in the prediction to reaction time, thus only the completed models are shown here.*

The data suggest that older and younger children may process Go trials more similarly in session 2 than they did in session 1 up through the N2 component. However, younger children continue to engage in more intensive neural processing than their older peers during the P3 component in session 2.

Manifest variable models of brain processing predicting task behavior. To examine whether the models of brain processing could be helpful in understanding simple task behaviors, we explored whether the full stream of processing could predict average RTs during each session. Considering the model for session 1, the full stream of processing did significantly predict average RT, though the effect was small ($\beta = .21$, $p = .01$; see Figure 3.2a). The data suggested that children with a larger (more negative) E-wave tended to have faster RTs, which is in accordance with prior literature. The effect of age on RT was moderate in size ($\beta = -.43$, $p < .001$), and indicated that older children tended to have faster RTs.

Interestingly, the pattern of effects differed for the session 2 model. Specifically, the predictive coefficient from the E-wave to RT was not statistically significant for the session 2 model ($\beta = .15$, $p = .17$; see Figure 3.2b). However, age was still a significant predictor of RT in session 2 such that older children tended to have faster average RTs than younger children ($\beta = -.46$, $p < .001$).

It is noteworthy that in each established manifest-level path model, the manifest variables showed only small effects, and had large residual variances. The data suggest that a large proportion of the variance in neural processing was not being explained in the models. It is possible that a more refined statistical approach that could better manage the variance in the data may yield a clearer view of the stream of neural processing, and its relationship to simple task behaviors.

Latent Variable Path Model Results

In order to better manage sources of variance in the data, including state-specific effects that may vary across sessions, we developed a latent variable model to examine the stream of neural processing. Each latent variable was derived from the combination of the two sessions of a single ERP component measure (e.g., N1 latent variable = $N1_{S1}$ and $N1_{S2}$). Thus, the latent variable was comprised of only the variance in the N1 measure that was common across both sessions, removing the influence of measurement error and state-specific effects that varied across sessions. The reliability of the latent variables was in the moderate-to-strong range (ρ_{N1} = .77; ρ_{P2} = .72; ρ_{N2} = .67; ρ_{P3} = .57; $\rho_{E\text{-}wave}$ = .63; ρ_{RT} = .81), which was an improvement over the test-retest reliability of the manifest-level variables (see Table 3.1).

Latent variable model of brain processing. Similar to our previous models using only the manifest-level variables, model fit statistics for the latent variable path were initially below the established criteria ($\chi^2(59) = 232.29$, $p < .001$, RMSEA = .17, 90% CI [.15, .19], $p < .001$; CFI = .55; SRMR = .14). Thus, we utilized the modification indices command in Mplus to determine additional relationships to include in the model in order to improve fit. Based on the suggestions, we added correlations between the residual variances of the manifest variables. Specifically, we added correlations between an ERP component and its chronological successor in the opposite session (e.g., $N1_{S1}$ with $P2_{S2}$; $N1_{S2}$ with $P2_{S1}$). The additional correlations resulted in excellent model fit ($\chi^2(28) = 40.27$, $p = .06$; RMSEA = .07, 90% CI [.00, .11], $p = .25$; CFI = .95; SRMR = .06), and did not change the conclusions drawn from the original model. All manifest variables significantly and strongly loaded onto their respective latent variables, with both sessions of data loading relatively equally. The findings suggested that the latent variables were well-defined and captured variance from both sessions of neural processing during the Go/No-Go task.

The data indicated statistically significant predictions from one latent variable to the next through the full stream of neural processing (see Figure 3.3). The weakest prediction, which was from N1 → P2, was moderate in size (β = .56, *p* = .001), still larger than any effect achieved in either manifest-level model (see Figures 3.2 and 3.3). All other predictive relationships between ERP components were strong, reaching clinically desirable levels (β's = .80 - .88, all *p*'s < .001). Both the N2 and the P3 latent variables showed significant age effects. In both instances, the data suggested that older children tended to have smaller amplitude ERP components compared to younger children. The finding matched the conclusions drawn from the manifest-level models.

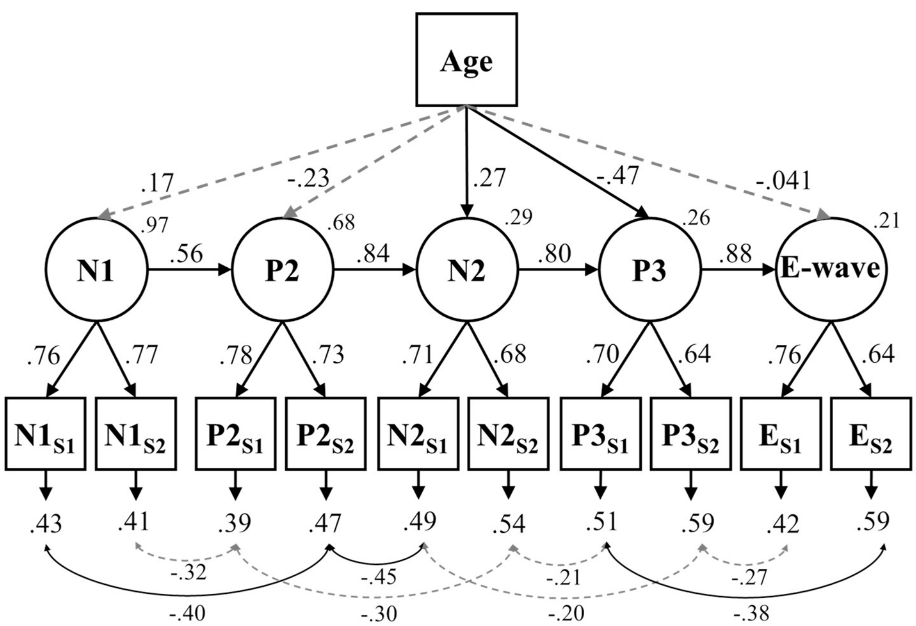

Figure 3.3. The established latent variable model of neural processing. Gray dotted arrows indicate non-statistically significant relationships at the p < .05 level. Residual variances are reported below each manifest variable, and disturbances are reported at the upper right of each latent variable. All reported coefficients are standardized. Note: S1 = session 1 measure, S2 = session 2 measure; E_{S1} *= E-wave amplitude in session 1,* E_{S2} *= E-wave amplitude in session 2.*

Latent variable model of brain processing predicting task behavior. Using this latent variable path model structure, we examined whether the full stream of neural processing could successfully predict simple task behavior. We began by simply adding the prediction from the E-wave latent variable to the RT latent variable, with age as a control on RT. However, the model fit did not meet the established criteria ($\chi^2(55) = 113.10$, $p < .001$; RMSEA = .10, 90% CI [.08, .13], $p = .002$; CFI = .85; SRMR = .09). We again utilized the modification indices command in Mplus to determine additional relationships that would improve fit. Interestingly, we only needed to add a correlation between the P2 and RT latent variables. The resulting model yielded excellent fit ($\chi^2(46) = 56.88$, $p = .13$; RMSEA = .05, 90% CI [.00, .09], $p = .50$; CFI = .97; SRMR = .06).

The path of neural processing from the N1 through the E-wave was very similar to the prior model, with each component significantly predicting the next (see Figure 3.4). Again, the model indicated moderate-to-large effects between ERP component latent variables. The full stream of neural processing significantly predicted the RT latent variable with a moderate effect size ($\beta = .45$, $p = .02$), larger than either predictive value achieved in the manifest-level models (see Figure 3.2). In addition to the predictive relationships, the P2 latent variable was significantly correlated with the RT latent variable ($\varphi = -.50$, $p = .03$). The data suggested that children with larger P2 amplitudes tended to have faster RTs. The result was surprising given that simple bivariate correlations indicated little-to-no relationship between the P2 amplitude and RT during either session (see Tables 3.2 and 3.3). Age was significantly related to the N2, P3, and RT latent variables. Like in previous models, the data suggested that older children tended to have smaller N2 and P3 ERP component amplitudes. Additionally, older children tended to have faster RTs ($\beta = -.42$, $p < .001$).

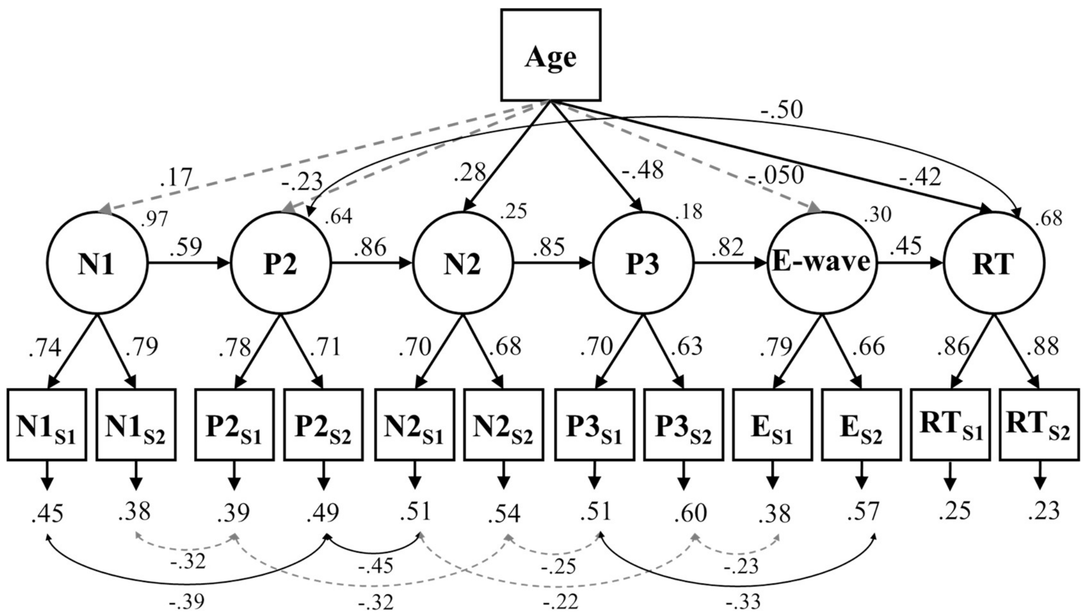

Figure 3.4. The established latent variable model of neural processing predicting simple task behaviors (i.e., reaction times). Gray dotted arrows indicate non-statistically significant relationships at the p < .05 level. Residual variances are reported below each manifest variable, and disturbances are reported at the upper right of each latent variable. All reported coefficients are standardized. Note: S1 = session 1 measure, S2 = session 2 measure, E_{S1} *= E-wave amplitude in session 1,* E_{S2} *= E-wave amplitude in session 2.*

Discussion

The current investigation presented a unified view of ERP components as systematic phases of stimulus-to-response processing that can predict the task behavior in neurotypical children. We first showed that even using simple, manifest-level variables, ERP components can be modeled as a continuous stream of processing in which one component predicts the next in chronological order beginning with the N1 and ending with the E-wave (see Figure 3.2). The effects were replicable across sessions. We then showed that the full stream of neural processing could be used to predict average RTs, though the predictive relationship was only statistically significant for the session 1 model.

All predictive coefficients were small, and the ERP component and RT measures had large residual variances, suggesting that the influence of measurement error may have been obscuring our ability to detect strong relationships between brain and behavior. The findings supported the ideas presented by Gavin and Davies (2008), namely that all psychophysiological measures, including ERP components, are comprised of multiple sources of variance. When those sources of variance are not controlled, the resulting variance is compounded into the measurement error term. For instance, state-specific effects that may have varied across sessions (e.g., strategies used to perform the task, fatigue, mood, etc.) could have confounded the measurements, thus leading to large residual variances and low predictive power.

The Benefits of a Latent Variable Approach

In order to remove the confound of measurement error and reveal the true nature of brain-behavior relationships in the data, we utilized a latent variable approach. Latent variables were comprised of the common variance among the same ERP component or RT measure obtained during two separate sessions. Thus, the latent variables effectively removed any state-dependent effects that may have varied across sessions, as well as any other sources of measurement error. In accordance with Gavin and Davies' (2008) models of psychophysiological measures, the resulting latent variables can be conceptualized as shown in equation 3 below:

$$PM_{LATENT} = Effect_{STIMULUS} + Effect_{TRAIT} + Effect_{PM\_PROCESSING} \tag{3}$$

Using the latent variables, we were able to establish a strong, stable path of predictive coefficients in which one latent variable representing an ERP component measure predicted the next in chronological order from the N1 through the E-wave (see Figure 3.3). The effects were much stronger than those obtained using simple manifest-level variables during either session (see Figures 3.2 and 3.3). Importantly, the stream of neural processing in the first 1000ms following the stimulus (i.e., N1 → P2 → N2 → P3) significantly, strongly predicted neural processing nearly 1000ms later in the task (i.e., the E-wave) with $\beta = .82$.

The full stream of latent variables (i.e., neural processing) was able to predict task behavior to a greater extent than any one latent variable or manifest-level variable on its own. The significant, moderate prediction to RT in the present study ($\beta = .45$) was larger than any one bivariate correlation between RT and an ERP component using manifest-level variables (see Tables 3.2 and 3.3). The effect was also an improvement over prior work showing only weak predictive ability from brain to task behavior (see *Study 1.1 and 1.2*). The findings suggest that ERP components leading up to the task behavior can, in fact, be conceptualized and modeled as phase sequences of neural processing in accordance with connectionist theory (Hebb, 1949; Landa et al., 2014; McNaughton & Nadel, 1990; Raftopoulos, 1997). To the best of our knowledge, this is the first investigation to model ERPs as a full stream of systematic neural processing leading to task behavior. The latent variable path analysis revealed strong significant predictive coefficients from one phase of processing to the next, with dependent measures (i.e., the latent variables) that were much more stable than traditional measurements (i.e., the manifest-level variables) obtained from neurotypical children.

Another advantage to the latent variable path approach was the ability to further examine additional effects that are present in the data. For example, we found a statistically significant correlation between the P2 and RT latent variables, a relationship that would have otherwise not been revealed had we relied on simple bivariate correlations (see Tables 3.2 and 3.3, Figure 3.4). It is reasonable to consider that the P2 may be related to RT during a task. Researchers have argued that the P2 component is related to stimulus encoding and perceptually-based matching in implicit memory processes, especially with visually-based tasks (Bahramali, Gordon, Li, Rennie,

& Wright, 1998; Curran & Dien, 2003; Sprondel, Kipp, & Mecklinger, 2011). However, investigations examining whether the P2 amplitude is related to task behaviors via simple correlations in adult samples, including reaction times and accuracy during a task, revealed no significant relationships (e.g., Bahramali et al., 1998; Curran & Dien, 2003). Thus, one might conclude that using a latent variable approach in which state-dependent effects and measurement error are removed from the measures may provide a unique new view of the nature of brain-behavior relationships.

Understanding Development from a New Perspective

Using simple bivariate correlations, the data indicated a significant relationship between age and the E-wave component and RT in session 1, and between age and the P3, the E-wave, and RT in session 2 (see Tables 3.2 and 3.3). However, a path analysis approach, both at the manifest variable and latent variable levels, revealed a slightly different pattern of age effects. Specifically, it was the N2 and P3 components along with RT that were significantly related to age (see Figures 3.2, 3.3, and 3.4). Despite what our bivariate correlations showed, and despite what prior work by other research groups has shown (e.g.,Hämmerer et al., 2010; Jonkman, 2006; Jonkman et al., 2003; Segalowitz & Davies, 2004; Taylor et al., 2016), there was no significant effect of age on the E-wave component (i.e., a subcomponent of the contingent negative variation) in our current modeling.

The path analysis takes into account the variability of the prior components, including their unique age effects. It is possible that the developmental effect that researchers previously identified in the E-wave is actually accounted for (i.e., mediated) by the developmental effects present in prior phases of neural processing. Thus, the path analyses in the present study showed no additional significant effect of age on the E-wave *above and beyond* what was already explained in the chronologically earlier components of the ERP, specifically, the N2 and P3 components.

Interestingly, the significant age effects in path models also indicate that there were unique developmental effects that account for variance in N2 and P3 components, and in RT. The data suggest that the age effects were not accounted for by prior phases of neural processing and may actually represent several different aspects of cognitive and behavioral maturation. In fact, Johnson and de Haan (2011) argue that "age" may not be a single, non-changing construct; rather, the researchers suggest that "age" can be conceptualized as unique maturation within a number of constructs, such as attention, motor control, and executive function. Thus, any single "age" effect present in the path models may indicate development of any number of cognitive and behavioral abilities that are otherwise unaccounted for in the present models.

Functional associations in the literature. Prior literature has indicated that different ERP components have specific functional associations related to cognitive processing, especially in the domains of attention and executive function. For instance, the N1 is often associated with early selective attention to the stimulus, and is shown to be sensitive to the sensory characteristics of the stimulus (Hillyard, Hink, Schwent, & Picton, 1973; Kappenman & Luck, 2012). The P2 is also implicated in aspects of early attention as well as sensory registration processes (Adams et al., 2017; Davies et al., 2010; Davies & Gavin, 2007). Researchers examining the N2 component have fairly consistently related its amplitude to executive discrimination processes, especially during tasks requiring participants to inhibit behaviors to specific stimuli (Heil et al., 2000; Patel & Azzam, 2005). The P3 component has stirred more debate, though researchers generally agree that it is related to higher-order cognitive processes including decision evaluation, working memory, and general executive function (Polich, 1993, 2007; Verleger et al., 2005). Finally, the E-wave has been associated with anticipation and sustained attention processes (Hämmerer et al., 2010; Walter et al., 1964).

Based on the functional associations established in the literature, the stream of neural processing may be labeled with more cognitively-specific constructs in place of the simple ERP component labels. For instance, rather than N1 → P2 → N2 → P3 → E-wave → RT, one might suggest that the model could be conceptualized as Sensory → Registration → Discrimination → Evaluation → Anticipation → Task Behavior. We can assess the extent to which this suggested labeling scheme representing phases of neural processing is appropriate by employing more complex models. Specifically, future research could examine whether each phase of neural processing maps onto different cognitive constructs, like attention and executive function, assessed using additional measures. Such a model could also indicate whether the effect of "age" is better conceptualized as maturation within specific cognitive abilities rather than as a simple unitary construct representing general development over time. However, more complex models require additional participants beyond that used in the present study.

Future Directions

The present study only investigated the stream of processing of cognitive ERP components starting with the N1. However, there are a number of more sensory-based components that occur chronologically earlier than the N1, such as the N20 and P50 (for a review, see Kappenman & Luck, 2012). As stated before, increasingly complex models would require additional participants, thus adding in components like the N20 and P50 may require additional data collection. Future research may choose to further examine the extent to which these and other sensory-based ERP components influence the full stream of decision-making processes in the brain with larger samples.

Conclusions

The present study demonstrated the utility of combining principles of connectionist theory with sophisticated statistical approaches for understanding brain-behavior relationships in typically-developing children. By modeling the full time course of an ERP as a phase sequence of neural processing, and by utilizing a latent variable path analysis approach, we were able to detect strong, stable predictive relationships between chronologically-ordered ERP components. Using the full stream of neural processing, we were able to significantly predict simple task behaviors to a greater extent than any single ERP component on its own. In addition, we were able to detect unique effects of age, and of the P2 component that were not detected by more traditional analysis techniques like bivariate correlations. The established latent variable model holds promise for future work in exploring the functional associations of each phase of neural processing, which could be useful for developmental and clinical investigations.

CHAPTER IV – STUDY 3

For several decades, many researchers have been focused on better understanding the development of measures of neural processing. To do so, many studies examine how a single psychophysiological measure, like the amplitude of an event-related potential (ERP) component, correlates with a single measure representing development, typically “age” measured in months or years, or how that ERP component differs between different age groups (e.g., Cragg, Fox, Nation, Reid, & Anderson, 2009; Hämmerer et al., 2010; Jonkman et al., 2003; Taylor et al., 2016). Although such investigations have been informative and lead to additional inquiry into the inner workings of the brain across development, there are two primary weaknesses with this statistically- and conceptually-simplistic approach: 1) the potential for interference from compounded measurement error, and 2) the failure to effectively represent the complexities of brain processing and maturation.

Simple bivariate correlations, as well as other traditional statistical approaches like *t* tests and ANOVAs, are easily confounded by measurement error. In populations that are inherently more variable in their brain processing and performance, including children, it is possible that a simple statistical analyses may lead to spurious or even suppressed results due to the inflated measurement error in the data. Gavin and Davies (2008) suggested that any psychophysiological measure (PM), including an ERP component, is comprised of multiple sources of variance that can be simply written as:

$$PM = Effect_{STIMULUS} + Effect_{STATE} + Effect_{TRAIT} + Effect_{PM\_PROCESSING} + ME \qquad (1)$$

In equation 1, Gavin and Davies (2008, p. 428) indicate that the combined effects of the *stimulus processing* involved in eliciting the component, the *state* of the individual participant during measurement (e.g., mood, sleepiness), the *trait* characteristics of the individual (e.g., general attention abilities, maturation level), the *signal processing techniques* employed to calculate the ERP component (e.g., filtering and averaging of EEG signals), and *measurement error* (ME) all contribute to the overall variance of the ERP component measure. By employing a simplistic bivariate correlation technique (or other basic analysis), most of these sources of variance remain uncontrolled, forcing all of the unaccounted-for variance to be compounded into the ME term (see equation 2 below reprinted from Gavin & Davies, 2008, p. 428). By inflating the error term, researchers are effectively inflating their risk for type I and type II errors. Thus, it is possible that researchers are missing, or even misinterpreting important developmental effects in their ERP measures.

$$PM = \text{Effect}_{\text{STIMULUS}} + \text{ME}_{\text{TOTAL}} \tag{2}$$

The second major weakness of utilizing simplistic statistical methods to study the development of neural processing is that the analyses can handle relatively few variables in a single query. The result is often small effects that over-simplify the issues of both neural processing *and* development. Considering neural processing, examination of a single ERP component in isolation effectively disregards the complex, systematic nature of neural processing represented in the full time-course of an ERP. With respect to development, Johnson and de Haan (2011) describe the simple measure of "age" as a compound construct, which could potentially represent numerous aspects of cognitive and physical maturation within the individual. In essence, simplistic statistical approaches are unable to capture the complexities of brain processing and development, leading to potentially inaccurate conclusions about the nature of neural processing across maturation within functional domains of cognition.

Study 2 investigated the importance of the full time-course of an ERP in understanding task-specific behaviors in typically-developing children. Specifically, we suggested that the full sequence of ERP components represented in an averaged ERP can be viewed as phases of systematic neural processing in accordance with principles of connectionist theory (Hebb, 1949; McNaughton & Nadel, 1990; Raftopoulos, 1997). Applying this perspective to ERPs, the succession of components can be interpreted as a phase sequence of stimulus-to-response decision-making. The process begins with early *Sensory* processing (N1), followed by *Registration* of sensory information (P2), then the executive *Discrimination* of the stimulus (N2), followed by decision *Evaluation* (P3), and finally culminating in *Anticipation* processes (E-wave) before executing a *Task Behavior* (see *Study 2*).

The study findings indicated that when modeling the full ERP as systematic phases of neural processing, the fully-mediated model yielded a significant, moderate prediction to reaction times (*Sensory* → *Registration* →*Discrimination* → *Evaluation* → *Anticipation* → *Task Behavior*). The effect was strengthened and stabilized by utilizing a *latent* variable approach, which removed measurement error and state-specific effects (i.e., $\text{Effect}_{\text{STATE}}$) from the data. Interestingly, the resulting model also indicated significant age effects on the N2 (*Discrimination*) and P3 (*Evaluation*) latent variables. Although not statistically significant, there were also small age effects on the N1 (*Sensory*) and P2 (*Registration*) latent variables. Because unique age effects were found for each of the latent variables in the full path analysis, the results suggested that "age" may not account for the same aspects of development within each of the ERP component measures (see *Study 2*). The findings were in accordance with Johnson and de Haan's (2011) suggestion that "age" is merely a substitute variable representing the development of multiple cognitive abilities.

Research suggests that each phase of neural processing described in *Study 2* seems to be influenced by attention and executive function abilities within the individual, which are commonly measured using behavioral assessments. Attention can be simply defined as a set of abilities important for regulating capacity-limited systems in the brain (Manly et al., 2001; NIMH, 2011; Petersen & Posner, 2012; Posner & Petersen, 1990). Attention can be further broken down into the domains of *Control Attention* (i.e., selectively targeting stimuli while ignoring distractors, switching attentional focus between tasks) and *Sustained Attention* (i.e., maintaining focus to a relatively unrewarding task; for reviews, see *Study 1.2*; Manly et al., 2001; Petersen & Posner, 2012; Posner & Petersen, 1990). Executive function can be conceptualized as a set of abilities important in moderating ongoing cognitive activity in order to support goal-directed behaviors (Barkley, 2012; NIMH, 2011; Zelazo, Carlson, & Kesek, 2008).

Researchers have suggested a more prominent relationship between *Control Attention* and the N1 (Kappenman & Luck, 2012), and P2 components (Adams et al., 2017), a relationship between *Executive Function* and the N2 (Lamm et al., 2014), and P3 components (Polich, 2007), and a relationship between *Sustained Attention* and the E-wave component (Petersen & Posner, 2012) of the ERP. It is possible that development within each of these cognitive domains may account for at least a portion of the developmental effects present along different phases of the complete ERP.

The purpose of the present study is to examine to what extent each of these three cognitive abilities (i.e., *Control Attention*, *Sustained Attention*, and *Executive Function*) can be used to represent development within each of the phases of neural processing represented in the full time-course of an ERP modeled as a latent variable phase sequence. We begin by confirming the presence of different cognitive constructs as measured by behavioral assessments in *Study*

3.1. We hypothesize that we will find a three-factor model of cognitive constructs, such that we can define *Control Attention*, *Sustained Attention*, and *Executive Function* abilities within children. Then, in *Study 3.2* we explore how each of the obtained cognitive constructs differentially predicts each of the five latent phases of brain processing using the model structure established in *Study 2*. We begin this effort by examining a fully-specified model in which each cognitive construct predicts each phase of processing (see Figure 4.1A). We then explore a reduced model depicting only the relationships that we hypothesize to be strongest based on prior literature (see Figure 4.1B).

Study 3.1

Rational and Purpose

Many researchers argue that both attention and executive function are critical for successfully engaging in everyday activities (e.g., Barkley, 2012; Carlson, Zelazo, & Faja, 2013; Petersen & Posner, 2012; Posner & Petersen, 1990). Researchers and clinicians commonly assess an individual's abilities within each of these cognitive domains using batteries of behavioral assessments that have been clinically validated. For example, the Test of Everyday Attention for Children (TEA-Ch) consists of nine game-like subtests that have been standardized for children ages 6- to 16-years-old and purports to measure three subtypes of attention: Selective, Shifting, and Sustained Attention (Manly et al., 2001; Manly et al., 1999). However, more recent work examining the factor structure of the TEA-Ch in 8- to 12-year-old children indicated only two subtypes of attention: Control and Sustained Attention (*Study 1.2*). Researchers and clinicians also utilize a number of measures claiming to measure aspects of executive function, such as inhibition, task or performance monitoring, and task switching. Such measures include the classic Color-Word Stroop Task (Golden, 1978) and the Wisconsin Card Sorting Task (Heaton, 2003).

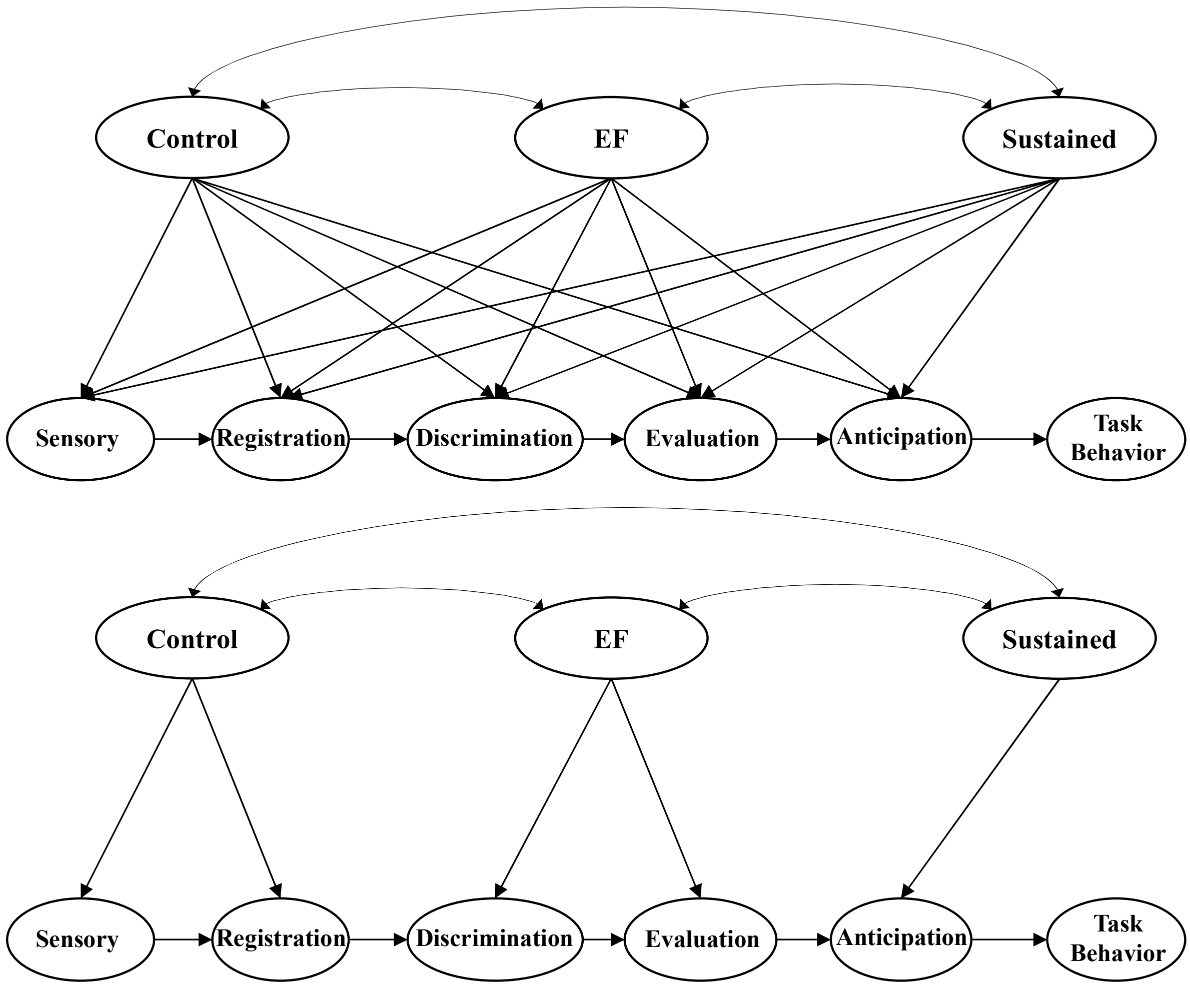

Figure 4.1. The hypothesized models being tested in the current study: A) the full model with all three cognitive constructs predicting all five latent variables of neural processing; B) the reduced model with only the hypothesized predictive relationships between cognitive constructs and latent variables of neural processing.

As neuroimaging technologies have become more accessible, researchers have explored the neural underpinnings of attention and executive function processes. Interestingly, both cognitive constructs seem to occupy multiple diffuse, but overlapping brain networks spanning mainly prefrontal, frontal, and parietal areas of the brain (Cicerone & Maestas, 2014; Gratton et al., 2016; Petersen & Posner, 2012). These areas and their interconnections to other parts of the brain are known to develop over prolonged periods of time, with maturation correlating strongly to better performance in the cognitive domains of attention and executive function (Casey, Giedd, & Thomas, 2000; Casey, Tottenham, Liston, & Durston, 2005).

The purpose of the present study is to explore how common behavioral assessment measures, which purport to measure different aspects of attention and executive function, separate into different cognitive constructs in a sample of typically-developing children. Based on prior literature, we hypothesize that we will find a three-factor solution comprising *Control Attention*, *Sustained Attention*, and *Executive Function*. We also aim to show developmental effects within each of the cognitive constructs. Specifically, we hypothesize that increasing age will be associated with better performance within the cognitive domains. The factor structure obtained in this study will serve as the foundation for *Study 3.2*, which will further explore how developmentally-sensitive cognitive constructs differentially relate to neural processing measures.

Methods

Participants. Data were collected from a total of 113 neurotypical children between the ages of 7 and 13 years (49 males; M = 10.23 years, SD = 1.54) during two sessions scheduled one-to-two weeks apart (note: this is an extension of the sample in *Study 2*; Wave 1 = 57, Wave 2 = 56). Like in *Study 2*, no participants were excluded based on performance due to the use of estimation procedures in our statistical software. Details are described below. Participants had no reported neurological or developmental diagnoses, nor were they currently taking any psychopharmaceutical medications, as reported by parents. Parents of children signed informed consent forms, and child participants signed assent forms. Children received their choice of a t-shirt or cocoa mug after completing their first visit, and their choice of a t-shirt, cocoa mug, or $10 after their second visit. All procedures were approved by the local university institutional review board.

Procedure. During each session, electroencephalographic (EEG) data were collected while children performed a simple, visual Go/No-Go task on a computer. The same task was performed during both sessions. Details of the EEG data collection will be described further in *Study 3.2*. Following EEG data collection, children completed a battery of behavioral assessments.

Tests completed following EEG during the first session focused on general intelligence, attention, and executive function abilities. Assessments included: the Wechsler Abbreviated Scales of Intelligence (WASI), the d2 Test of Attention, Selective A's, Crossing Off A's, the Color-Word Stroop Task, and a computerized version of the Wisconsin Card Sorting Task (WCST-CV4). The WASI was used as a control measure and will not be discussed further in this study. For each child, the WASI was always completed first, the WCST-CV4 was always completed last, and the other assessments were administered in a counterbalanced order. Following EEG during the second visit, participants completed the TEA-Ch, an assessment of Control Attention and Sustained Attention abilities (*Study 1.2;* Manly et al., 2001).

Behavioral Assessments.

d2 Test of Attention. Despite its name, the d2 Test of Attention has been validated in the literature as an assessment of scanning accuracy and speed, learning, and strategy development (Bates & Lemay, 2004; Brickenkamp & Zillmer, 1998). In the test, children were given a sheet of paper with 14 lines of letters ("d" or "p"). Each letter had between one and four dash marks, which appeared above and/or below the letter. Children were instructed to cross out each letter “d” with two dashes while ignoring all other letters. The child had 20 seconds for each line and was instructed to work as quickly as possible. The d2 Test of Attention has good test-retest reliability, $r = .89 - .92$ (Spreen, 1998). From this test, we utilized the total number of correctly processed items score (i.e., TN-E).

Selective A’s. Selective A’s is a cancellation task developed at Brock University. In the task, children were presented a full sheet of randomly-scattered letters (A-through-Z) and instructed to cross out as many letter “A’s” as they can in one minute. Children were instructed to ignore all other letters. There were 80 total target letters on the sheet. Children received a score based on the number of “A’s” that they were able to cross out in the allotted time.

Crossing Off A’s. Crossing Off A’s, which was also developed at Brock University, is a simple motor control task for Selective A’s. Children were presented with a sheet of 22 rows, each of which had 19 letter “A’s” and instructed to cross out as many A’s as possible within one minute. Participants were specifically instructed to begin at the top left corner of the sheet and cross of each individual “A” moving across the rows from left-to-right, and from the top of the page to the bottom. Children received a score based on the total number of “A’s” that they were able to cross out in the allotted time.

Color-Word Stroop Task. The classic color-word Stroop Task is a well-established measure of inhibitory control, concentration, and mental flexibility (Golden, 1978; Strauss, Sherman, & Spreen, 2006). The Stroop Task was administered in a three-step sequence. Each step consisted of a single page of test items. Items were arranged in 5 columns with 20 test items. First, the child was presented with a sheet of color words printed in black ink (e.g., GREEN). The child was instructed to read the words out loud starting at the top left corner of the page, and then reading down each column as quickly as possible for 45 seconds. The second sheet consisted of colored X's (e.g., XXXX). The child was supposed to say the color of the ink out loud, again starting at the top left corner and working down each column as quickly as possible for 45 seconds. The last page consisted of color words printed in incongruent-colored ink (e.g., GREEN). The child was instructed to state the color of the ink out loud and ignore reading the word. Again, the child starts at the top left corner and works down each column as quickly as possible for 45 seconds. The color-word Stroop Task is normed for ages 5-to-80 years and has good test-retest reliability (r = .73-.89; Strauss et al., 2006). From this assessment, we examined two scores: the color-word score, and the interference score.

WCST-CV4. The WCST-CV4 is a computerized version of the classic Wisconsin Card Sorting Task, designed to assess aspects of cognitive control including perseveration and task switching (Heaton, 2003). The task was administered on a Windows Surface Pro tablet with touch-screen capability. Children were presented with the tablet, which displayed four key cards at the top of the screen in accordance with the traditional, physical card administration. At the bottom of the screen was a test card. The administrator provided the child with instructions from the assessment manual and told to touch the key card that they thought the test card matched. Cards could be matched on three dimensions: color, shape, or number of items of a card. Children were not told how to match the cards. After each selection, the tablet provided feedback about whether the selection was "right" or "wrong" and then provided a new test card at the bottom of the screen. The computerized administration followed the same rules as the classic physical administration: children had to match ten consecutive cards correctly on a given rule, and then the rule changed. The task finished once the child either completed six categories (i.e., 10 consecutive correctly-matched cards based on 1) color, 2) shape, 3) number, 4) color, 5) shape, 6) number), or once the child ran out of test cards (128 total test cards available in a single administration). The WCST has not been officially validated in its computerized form, however the classic administration shows high convergent validity with other measures of cognitive control and has been normed for ages 7-to-89 years (Heaton, 2003). The test has low test-retest reliability (r = .12 - .72), however this is expected due to the learning and changes in task strategy that are required to be successful in the task (Strauss et al., 2006). From this test, we examined the learning to learn score, the number of perseverative error, and the failure to maintain set score.

TEA-Ch. The TEA-Ch purports to measure three subtypes of attention via nine game-like subtests (Manly, Robertson, Anderson, & Nimmo-Smith, 1999). Specifically, Manly et al. (2001) indicated that the TEA-Ch subtests measure aspects of Selective Attention (*Sky Search* and *Map Mission* subtests), Sustained Attention (*Score!*, *Sky Search DT*, *Score! DT*, *Walk Don't Walk*, and *Code Transmission* subtests), and Shifting/Control Attention (*Creature Count* and *Opposite Worlds* subtests). However, *Study 1.2* showed that in a younger sample of neurotypical American children, the subtests actually comprised only a two-factor model: Control Attention and Sustained Attention. During the assessment, children were asked to complete different auditory and visual tasks like counting the number of sounds on an audio recording, or circling specific symbols on a map. Raw scores were obtained for each subtest based on aspects of the child's time and accuracy on each task. The TEA-Ch is standardized for ages 6-to-16 years, and the subtests have moderate-to-high test-retest reliability ranging from r = .57 - .87 (Manly et al., 2001; Manly et al., 1999).

Data analysis.

Missing values. Five children did not complete the second session and thus received null values for all TEA-Ch measures. One child did not receive a score for *Sky Search* DT due to a recording error during the test administration. Not all children completed the WCST-CV4. The data in the present study were collected in two waves, and the WCST-CV4 was only incorporated into the data collection procedures for Wave 2. Thus, the previously-published sample of 57 children (see Taylor et al., 2016) had no data for this assessment. An additional 2 children's data on the WCST-CV4 were lost due to computer malfunctions, and the *WCST Learning to Learn* score could not be calculated for one child. Several children refused to complete one or more tasks during the first session. Within modeling procedures, missing values were estimated in Mplus version 7.3 using full-information maximum likelihood (FIML) procedures.

Scoring behavioral assessments. Each of the behavioral assessments was scored according to its respective manual. Each of the selected measures produces scores on different scales, which can become problematic in modeling efforts. Thus, we transformed the raw scores from each assessment into Z-scores based on the distribution of scores obtained from the study sample. The process ensured that each of the measures was comparable in scale while retaining the integrity of individual differences in development and general abilities that are captured in the raw scores. The Z-score transformation was performed using SPSS version 24.

Descriptive statistics. Analyses began with basic descriptive statistics for each of the behavioral assessment raw scores for basic inspection. We also performed Pearson product-moment correlations to examine the interrelationships among the measures in order to serve as a foundation for further modeling efforts. All initial descriptive analyses were completed using SPSS version 24.

Modeling the cognitive constructs. In order to determine the factor structure of the cognitive constructs, we conducted an exploratory factor analysis. Specifically, we included the

Z-scores for each of the 17 selected measures from the behavioral assessments, as indicated above. We examined the resulting factor structure for indicators of model fit to determine the most appropriate factor structure. To evaluate overall model fit, we used the model fit criteria suggested by Hu and Bentler (1999), including comparative fit index (CFI) > .95, root mean square error of approximation (RMSEA) < .06, and standardized root mean square residual (SRMR) < .08. We also examined the chi-square test of model fit, where a non-statistically significant test indicates perfect fit of the model to the data.

Results and Discussion

Descriptive statistics. Means, standard deviations, and number of children with complete data on each dependent measure from the behavioral assessments are reported in Table 4.1. Correlations among the behavioral assessment measures indicated a number of weak-to-moderate relationships, suggesting that the selected variables should be appropriate for exploratory factor analysis (see Table 4.2). Additionally, there were differential relationships across the measures, implying the possibility of multiple factors.

Modeling the cognitive constructs. We utilized an exploratory factor analysis to define cognitive constructs based on the behavioral assessment measures. The original solution, which included all listed measures, resulted in a single-factor solution wherein model fit did not meet the criteria established by Hu and Bentler (1999): $\chi^2(119) = 254.13$, $p < .001$; RMSEA = .10, 90% CI [.84, .12], $p < .001$; CFI = .80; SRMR = .11. Additional solutions including two, three, and four factors did not converge. Further examination of the single-factor solution showed that the *WCST Failure to Maintain* Set and the *TEA-Ch Code Transmission* scores loaded poorly onto the factor (.031 and -.051, respectively). Thus, we removed these two measures and re-ran the exploratory factor analysis.

Table 4.1.
Means, standard deviations, and number of children with complete data on each dependent measure obtained from the behavioral assessments.

Measure	*N*	*M*	*SD*
d2 TN-E	112	284.64	80.35
Selective A's Total	113	38.76	9.58
Crossing Off A's	113	100.14	21.87
Stroop Color-Word Score	112	29.97	9.42
Stroop Interference Score	112	-.53	6.08
WCST Learning to Learn	54	-.80	3.13
WCST Perseverative Errors	55	10.56	8.06
WCST Failure to Maintain Set	55	.71	1.12
TEA-Ch Sky Search	105	3.96	1.26
TEA-Ch Score!	105	8.12	1.89
TEA-Ch Creature Counting	105	4.32	1.16
TEA-Ch Sky Search DT	104	1.63	4.53
TEA-Ch Map Mission	105	42.93	11.53
TEA-Ch Score! DT	105	16.09	2.36
TEA-Ch Walk Don't Walk	105	11.24	4.35
TEA-Ch Opposite Worlds	105	31.49	7.01
TEA-Ch Code Transmission	105	33.07	5.74

Note: All means and standard deviations are based on the raw scores obtained from each behavioral assessment (i.e., before Z-score transformations).

The second analysis yielded multiple solutions, though the three-factor solution was the most parsimonious solution with the best model fit: $\chi^2(63) = 68.76$, $p = .29$; RMSEA = .03, 90% CI [.00, .07], $p = .80$; CFI = .99; SRMR = .05. Results of the analysis, including factor loadings, eigenvalues, and correlations among factors are shown in Table 4.3. As indicated in the results, the third factor was comprised of only the two measures from the *Stroop Task*, and the *Color-Word* score was over-estimated on the factor (i.e., the factor loading exceeded 1.0). In favor of simplicity, we chose to remove the third factor from further analyses, thus retaining only the first two factors and their structures shown in Table 4.3.

Factor 1 was comprised of the *Selective Attention* measures from the TEA-Ch, as well as measures from the d2 Test of Attention, Selective A's, and Crossing Off A's, all of which have scores that are highly dependent on processing speed and selective attention to a target. In turn, *Factor 2* consisted of the *Sustained Attention* measures from the TEA-Ch, and measures from the WCST, and are measures which are arguably more complex in nature than those comprising *Factor 1*. Namely, the TEA-Ch *Sustained Attention* measures are primarily dual-task assessments, requiring a higher level of processing in order to be successful on the task. Additionally, the WCST is thought to measure higher-order aspects of processing, particularly with respect to task strategies. Interestingly, the *Shifting Attention* measures from the TEA-Ch loaded relatively equally onto both factors. Based on their respective structures, one might interpret *Factor 1* as more representative of selective attention and processing speed (Bates & Lemay, 2004; Brickenkamp & Zillmer, 1998; Manly et al., 2001; Manly et al., 1999), and *Factor 2* as more representative of sustained attention and task strategy (Heaton, 2003; Manly et al., 2001; Manly et al., 1999).

Using the final two-factor model, we conducted a simple SEM analysis to determine whether the established cognitive constructs did in fact include developmental effects, which is critical for *Study 3.2*. The two cognitive factors were modeled in accordance with the structure established in the exploratory factor analysis, with all parameters being freely estimated. *Factor 1* and *Factor 2* were correlated with one another. Age served as a control variable on each of the factors. The resulting model indicated good fit: $\chi^2(73) = 93.45$, $p = .05$; RMSEA = .05, 90% CI [.00, .08], $p = .48$; CFI = .96; SRMR = .06. All variables significantly loaded onto their respective latent factors (see Figure 4.2). For *Factor 1*, a higher latent factor score indicated *poorer* overall abilities within the construct. In contrast, a higher latent factor score for *Factor 2* indicated *better* abilities within the cognitive construct. The correlation among factors suggested that better abilities within one cognitive construct was related to better abilities within the other

Table 4.2

Intercorrelations among each of the behavioral assessment Z-scores.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. d2 TN-E	—																
2. Selective A's Total	.58***	—															
3. Crossing Off A's	.52***	.51***	—														
4. Stroop Color-Word	.58**	.57***	.56***	—													
5. Stroop Interference	.30**	.31**	.24*	.77***	—												
6. WCST Learning to Learn	.33*	.14	.22	.23	.022	—											
7. WCST Perseverative Errors	-.14	-.20	-.20	-.13	.003	-.31*	—										
8. WCST Failure to Maintain Set	-.064	-.052	.039	.008	-.13	.085	.11	—									
9. TEA-Ch Sky Search	-.52***	-.62***	-.55***	-.51***	-.26**	-.31*	.17	-.021	—								
10. TEA-Ch Score!	.27**	.28**	.30**	.24*	.02	.19	-.19	-.38***	-.18	—							
11. TEA-Ch Creature Counting	-.44***	-.51***	-.50***	-.58***	-.26**	-.35*	.34*	.12	.50***	-.19	—						
12. TEA-Ch Sky Search DT	-.16	-.29**	-.17	-.28**	-.19	-.27	.23	-.13	.22*	-.16	.26**	—					
13. TEA-Ch Map Mission	.45***	.64***	.67***	.47***	.19*	.18	-.20	-.045	-.56***	.35***	-.44***	-.23*	—				
14. TEA-Ch Score! DT	.38***	.45***	.37***	.49***	.23*	.30*	-.24	-.11	-.44***	.41***	-.47***	-.41***	.38***	—			
15. TEA-Ch Walk Don't Walk	.22*	.32**	.36***	.39***	.21*	.28	-.18	-.083	-.38***	.22*	-.47***	-.16	.40***	.44***	—		
16. TEA-Ch Opposite Worlds	-.51***	-.54***	-.57***	-.66***	.38***	-.21	.32*	.023	.57***	-.20*	.58***	.34**	-.52***	-.54***	-.40***	—	
17. TEA-Ch Code Transmission	.30**	.44**	.44***	.51***	.29**	.34*	-.31*	-.068	-.45***	.27**	-.65***	-.31**	.38***	.57***	.65***	-.58***	—

$^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$

Table 4.3
Results of the exploratory factor analysis exploring the behavioral assessment measures.

Measures	**Factor 1**	**Factor 2**	**Factor 3**
d2 TN-E	**.54**	.079	.12
Selective A's Total	**.68**	.13	.001
Crossing Off A's	**.76**	-.016	.040
Stroop Color-Word Score	.17	.006	**1.02**
Stroop Interference Score	-.003	-.054	**.73**
WCST Learning to Learn	-.072	**.46**	.002
WCST Perseverative Errors	-.019	**-.44**	.17
TEA-Ch Sky Search	**-.68**	-.17	.094
TEA-Ch Score!	.16	**.29**	-.003
TEA-Ch Creature Counting	**-.33**	**-.37**	-.11
TEA-Ch Sky Search DT	.089	**-.55**	.020
TEA-Ch Map Mission	**.87**	-.022	-.11
TEA-Ch Score! DT	.003	**.80**	-.001
TEA-Ch Walk Don't Walk	.21	**.39**	.001
TEA-Ch Opposite Worlds	**-.39**	**-.38**	-.11
Eigenvalues	6.08	1.43	1.22
Correlations:			
Factor 1 with Factor 2	.63		
Factor 1 with Factor 3	.53		
Factor 2 with Factor 3	.50		

Note: Reported factor loadings are the Geomin rotated loadings produced by Mplus version 7.3. Bolded factor loadings indicate the strongest factor loading for a given measure, thereby indicating with which factor a given measure fits best. The results listed are based on the second exploratory factor analysis conducted, after removing *WCST Failure to Maintain Set* and *TEA-Ch Code Transmission* scores from the analysis.

cognitive construct, $\varphi = -.60$, $p = .005$. Importantly, the model indicated significant age effects on both factors (*Factor 1*: $\beta = -.81$, $p < .001$; *Factor 2*: $\beta = .50$, $p = .001$). The data suggested that older children tended to have better abilities within both cognitive domains compared to their younger peers. The findings were in accordance with prior literature indicating that general attention and executive function abilities should improve with age (Casey et al., 2000; Casey et al., 2005). We conducted one final analysis in which we simply left out the age control variable.

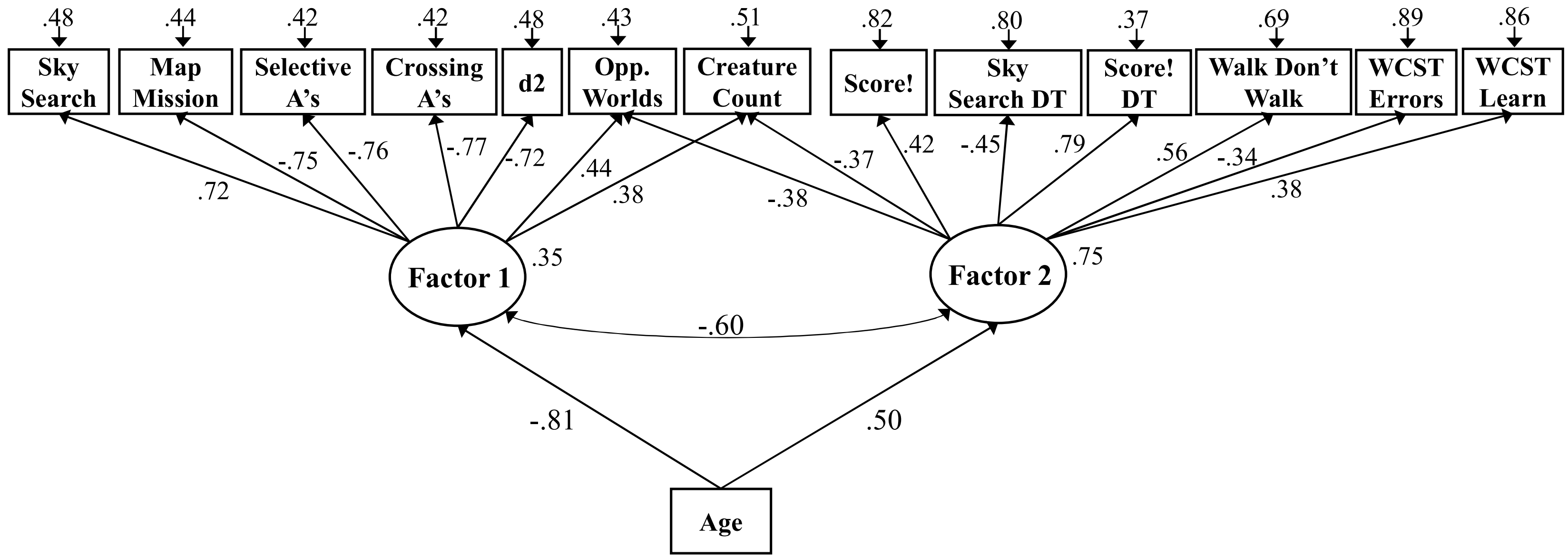

Figure 4.2. The obtained model of cognitive constructs defined by behavioral assessment measures. Age is used as a control variable in order to explore developmental effects present within each construct. All reported coefficients are standardized. Disturbances are reported at the upper right of each latent variable in the model. All coefficients in the model were statistically significant.

All conclusions regarding factor structure and the correlation between factors remained the same. Factors loadings from this model were retained for *Study 3.2*.

Conclusions for Study 3.1

In this study, we were able to show that behavioral assessments, which purport to measure aspects of attention and executive function, do indeed factor out into separate, but related cognitive constructs in a sample of typically-developing children. Although the factor structure did not match our hypothesis that we would differentiate three constructs, *Control Attention, Sustained Attention,* and *Executive Function*, we did establish a two-factor model of cognitive abilities. Based on the obtained factor structures, *Factor 1* seemed to be more representative of selective attention and processing speed. Each of the measures that loaded highest onto *Factor 1* had a significant speed component wherein the child was instructed to perform a task as quickly as possible, or to find as many target items as possible within a specified time limit (Brickenkamp & Zillmer, 1998; Manly et al., 2001; Manly et al., 1999).

Factor 2 was comprised of what Manly et al. (2001) deemed the *Sustained Attention* tasks, as well as some executive function measures (i.e., the WCST), which at first glance seemed counter-intuitive. However, *Factor 2* is arguably comprised of measures requiring higher-order levels of cognitive processing. For example, there were two dual-task measures from the TEA-Ch, which require the child to simultaneously attend to two different tasks, *Walk Don't Walk* from the TEA-Ch, which requires the child to carefully inhibit prepotent responses (Manly et al., 2001; Manly et al., 1999), and the two measures from the WCST, which purport to measure aspects of strategy and task switching (Heaton, 2003). Interestingly, recent work suggests that *Sustained Attention* should actually be categorized as an executive function because it is a form of goal maintenance, a critical aspect of executive function (Barkley, 2012; NIMH, 2011; Zelazo et al., 2008). *Creature Counting* and *Opposite Worlds*, the two *Shifting Attention* tasks from the TEA-Ch, loaded relatively equally onto both cognitive factors. It is possible that the time sensitivity of each of the tasks (similar to *Factor 1* measures) in combination with the complex task-switching required to be successful (similar to *Factor 2* measures) caused the tasks to load onto both cognitive factors. Further work is needed to validate the cognitive constructs comprised in the two factors obtained in this study.

Importantly, we were able to show that both of the obtained factors had significant developmental effects such that with increasing age, children tended to have better abilities within both cognitive domains. The finding was in accordance with prior work indicating that in cases of neurotypical development, attention and executive function abilities should improve over the course of maturation in children (Casey et al., 2000; Casey et al., 2005). The effect of age was stronger for *Factor 1* than it was for *Factor 2*, suggesting that one cognitive domain may reflect more individual differences in maturation compared to the other. Based on the findings, we can conclude that the obtained factors do in fact represent different aspects of cognitive development, which can be utilized for further work examining the development of measures of neural processing.

Study 3.2

Rationale and Purpose

Prior work showed that viewing the succession of ERP components in an averaged ERP as a systematic phases of stimulus-to-response processing offers a new, more holistic view of neural processing in children performing decision-making behaviors (see *Study 2*). Importantly, throughout the stream of neural processing, results revealed small-to-moderate age effects on the different phases of neural processing. The findings indicated that there were unique developmental effects to be explored throughout the decision-making process. It is possible that development of several different cognitive abilities may account for the unique age effects noted at different phases of neural processing (Johnson & de Haan, 2011).

Literature suggests that phases of brain processing, represented by each of the ERP components of interest from the N1 through the E-wave, may be differentially related to aspects of attention and executive function abilities (Adams et al., 2017; Kappenman & Luck, 2012; Lamm et al., 2014; Petersen & Posner, 2012; Polich, 2007). Different cognitive abilities, which are housed in diffuse neural networks that develop at different rates (Casey et al., 2000; Casey et al., 2005), may be more informative in understanding the development of neural processing when compared to simple "age" measures.

This study expands on prior work by substituting "age" with distinct cognitive constructs that represent development within specific domains of cognition. Thus, the purpose of the present investigation is to offer a more refined view of the developmental effects that are present within each of the phases of neural processing represented in an averaged ERP by testing an elaborated biobehavioral model of decision-making in children. We specifically examine how the two cognitive constructs obtained in *Study 3.1*, which capture aspects of attention and executive function abilities, differentially relate to phases of neural processing predicting task behavior, modeled in accordance with *Study 2*: *Sensory* (N1) → *Registration* (P2) → *Discrimination* (N2) → *Evaluation* (P3) → *Anticipation* (E-wave) → *Task Behavior* (reaction time). Based on previous literature, we hypothesize that each phase of neural processing will relate more strongly to one of the two cognitive factors, which may suggest a greater influence of development within one neural network over the other at any given point in the decision-making process.

Methods

Participants and procedure. Participants were the same as those included in *Study 3.1*. The complete procedure for EEG recordings is described in *Study 1.1*. For clarity of this study, we include some information on the procedure below. During each session, electroencephalographic (EEG) data were collected while children performed a simple, visual Go/No-Go task on a computer. During each trial of the task, children saw a sequence of two stimuli. First, a circle, either red or green, was displayed in the center of the screen for 250 ms. Then the screen went blank for 1750ms before a picture of a car appeared in the center of the screen with a duration of 250ms. If the circle at the beginning of the trial was green, children were instructed to press a button in front of them as quickly as possible after the car appeared on the screen (i.e., a Go trial). However, if the circle was red, the children were instructed not to press the button (i.e., a NoGo trial). The task consisted of 40 Go and 40 NoGo trials presented in a pseudorandom order. The same task was performed during both sessions. Following EEG data collection on each day, children completed a battery of behavioral assessments, described in detail in *Study 3.1*.

Electrophysiological recording. Details of the EEG recording equipment and procedures for the 57 children in Wave 1 are reported in Taylor et al. (2016, pp. 165-166), and in *Study 1.1*. EEG data recorded from the additional 56 children in Wave 2 were collected using a 64-channel BioSemi ActiveTwo system with Ag/AgCl sintered electrodes. Scalp electrodes were positioned according to a modified 10-20 system (American Electroencephalographic Society nomenclature guidelines, 1994) with additional common mode sense (CMS) and driven right leg (DRL) sensors, which served as reference and ground, respectively. An additional six sensors were placed on the face (on the left supra- and infra-orbital regions, and on the left and right outer canthi) and both the left and right earlobes to record eye movements and provide sites for offline re-referencing.

Electrophysiological data reduction. EEG data were reduced using previously established methods (see *Study 1.1*, Taylor et al., 2016). Following data reduction, only averaged ERPs depicting brain processing during correct Go trials were analyzed further. Correct Go trials were defined as any trial in which a green circle appeared before the car, and the participant pressed the button after the car appeared on the screen. Separate averaged ERPs were derived for each session.

The averaged ERPs were processed using a Matlab routine which allows for automatic scoring and visual inspection of ERP components, and, when necessary, allows for manual marking of components. All ERP component measurements were reviewed by one trained research assistant. Baseline-to-peak amplitudes for the N1, P2, N2, and P3, and the averaged amplitude in the time window of the E-wave were measured via the Matlab routine. All components were measured at site Cz. The N1 was defined as the most negative amplitude in the 70-170ms window, P2 as the most positive peak in the 150-300ms window N2 window as the most negative amplitude in the 250-400ms window, and P3 as the post positive peak in the 400-650ms window. The E-wave was measured as the averaged amplitude in the 1800-2000ms window. All ERP component time windows were selected based on prior research (e.g., Hämmerer et al., 2010; Kappenman & Luck, 2012; Kropp et al., 2000; Taylor et al., 2016).

In addition to ERP component measures, averaged reaction times were derived for correct Go trials for each participant. Reaction times were calculated by the amount of time between the onset of the imperative stimulus (i.e., the car) and the participant's button press for each trial. Then, an average reaction time was computed for each session separately, for each individual participant.

Data analysis.

Missing values. If a child had fewer than 12 correct Go segments (i.e., fewer than 30% of possible Go trials) remaining following EEG data reduction procedures, ERP component amplitudes were not measured for that session. Measuring ERPs comprised of relatively few trials could potentially introduce additional confounds into the data, including a poor signal-to-noise ratio in the data. It is noteworthy that all children did perform the task well enough to be included in the study (i.e., all children correctly performed more than 12 Go trials each session). Loss of data was simply due to movement artifacts (e.g., eye blinks). A total of 14 children in session 1, and 23 children in session 2 had insufficient data for adequately measuring ERP component amplitudes. In addition, 5 children did not complete the second session and thus had no data for any session 2 ERP components or task reaction times. Within modeling procedures, all missing values were estimated in Mplus version 7.3 using full-information maximum likelihood (FIML) procedures.

Descriptive statistics. Analyses began with basic descriptive statistics for ERP component amplitudes and average reaction times during the ERP task. We also performed Pearson product-moment correlations to examine the interrelationships among the measures of interest (ERP component amplitudes, reaction times, and behavioral assessments) to set the foundation for building models of brain processing, task behavior, and cognitive abilities. All initial descriptive analyses were completed using SPSS version 24.

Previously established models. The latent variable path model of neural processing predicting task behaviors was defined in accordance with prior work (see *Study 2*). Specifically, one latent phase of neural processing, defined by two sessions of an averaged ERP component amplitude, predicted the next phase in chronological order from the N1 through the E-wave. The full stream of processing then predicted reaction times during the ERP task as follows: *Sensory* (N1) → *Registration* (P2) → *Discrimination* (N2) → *Evaluation* (P3) → *Anticipation* (E-wave) → *Task Behavior* (reaction time). In the present study, the same path *structure* was retained (i.e., the latent variable compositions, the interrelationships between each latent variable), however all parameters were allowed to freely vary. In prior work, age served as a control variable on all latent variables. However, we did not include age as a control variable in the present investigation as the purpose of this study was to determine whether cognitive constructs could be used to account for development in the full biobehavioral model. In order to examine cognitive abilities, we retained the two-factor model of cognitive abilities established in *Study 3.1*. In the present investigation, we fixed the factor loading coefficients to those obtained in *Study 3.1*, but all other parameters (i.e., means, variances, correlations) were freely estimated.

Establishing a biobehavioral model. The biobehavioral model was established by combining the model of brain processing predicting task behavior with that of the cognitive abilities. Specifically, the two factors representing cognitive constructs were used as predictors of each of the five latent phases of neural processing. After examining how each of the cognitive constructs related to the phases of brain processing, we established a second model in which we removed the weaker of the two predictive coefficients (i.e., either the prediction from cognitive *Factor 1* or cognitive *Factor 2*) to each of the latent brain measures. The goal of this step was to reduce the number of parameters being estimated, thereby increasing our statistical power to detect significant effects.

All models were examined for model fit. To evaluate overall model fit, we used the model fit criteria suggested by Hu and Bentler (1999), including CFI > .95, RMSEA < .06, and SRMR < .08. We also examined the chi-square test of model fit, where a non-statistically significant test indicates perfect fit of the model to the data. We performed a simple chi-square difference test to determine whether reducing the number of predictive relationships between cognitive factors and phases of brain processing significantly impacted model fit.

Results and Discussion

Descriptive statistics. Means, standard deviations, and number of children with complete data on each dependent measure from the Go/No-Go task (i.e., ERP component amplitudes and task reaction times) are reported in Table 4.4. Additionally, the grand averaged ERPs from session 1 and session 2 Go trials are shown in Figure 4.3. Correlations between ERP component measures and behavioral assessment measures indicated few significant relationships (see Table 4.5). All correlations, including those that reached statistical significance, were relatively small effects. Interestingly, the pattern of effects varied across sessions, with some correlations reaching significance for session 1 but not for session 2 and visa versa. Additionally, some relationships between a given behavioral measure and an ERP component changed in direction across sessions. For instance, the correlation between the *WCST Number of Perseverative Errors* and the P3 ERP component amplitude shifted from negative in session 1 (r = -.13), to positive in session 2 (r = .24). Overall, the correlations supported the notion that among developing children, traditional methods of establishing brain-behavior relationships yield weak and variable results.

Establishing a biobehavioral model. We first tested a model in which both cognitive construct factors were modeled as predictors of each of the five latent phases of neural

Table 4.4.
Means, standard deviations, and number of children with complete data on each dependent measure obtained during the Go trials of the Go/No-Go ERP task, including ERP component average amplitudes (µV) and ERP task average reaction times (ms).

Measure		*N*	*M*	*SD*
Session 1	N1	98	-6.59	4.47
	P2	99	9.44	5.11
	N2	99	-6.09	6.77
	P3	99	10.37	5.88
	E-wave	99	-2.43	5.11
	Reaction time	113	290.59	97.27
Session 2	N1	85	-6.24	4.36
	P2	85	8.38	5.63
	N2	85	-7.08	6.44
	P3	85	8.66	5.23
	E-wave	84	-3.70	5.21
	Reaction time	108	297.84	127.76

processing. Model fit indices were mixed, with some meeting the criteria established by Hu and Bentler (1999), and some approaching the criterion levels: $\chi^2(261) = 346.92$, $p < .001$; RMSEA = .05, 90% CI [.04, .07], $p = .32$; CFI = .91; SRMR = .10. Although not all fit indices were within the expected range, it is highly possible that the model in the present study is still viable. Iacobucci (2010) and Marsh, Hau, and Wen (2004) criticize strict adherence to "golden rules" like those set by Hu and Bentler (1999), particularly in the case of complex models with small-to-moderate sample sizes (i.e., $N < 250$), like the present model. Data simulations show that in such situations, model fit criteria are likely to cause over-rejection of viable models.

Rather, researchers and statisticians suggest alternative model fit criteria that can more readily accommodate complex models in smaller samples without over-rejecting viable, well-specified models. Specifically, Iacobucci (2010) suggests examining the ratio of chi-square to its degrees of freedom, with a ratio less than or equal to 3.0 indicating good fit ($\chi^2/\mathrm{df} \leq 3$), in addition to a CFI near .90 and SRMR near .09. In the present investigation, the adjusted chi-

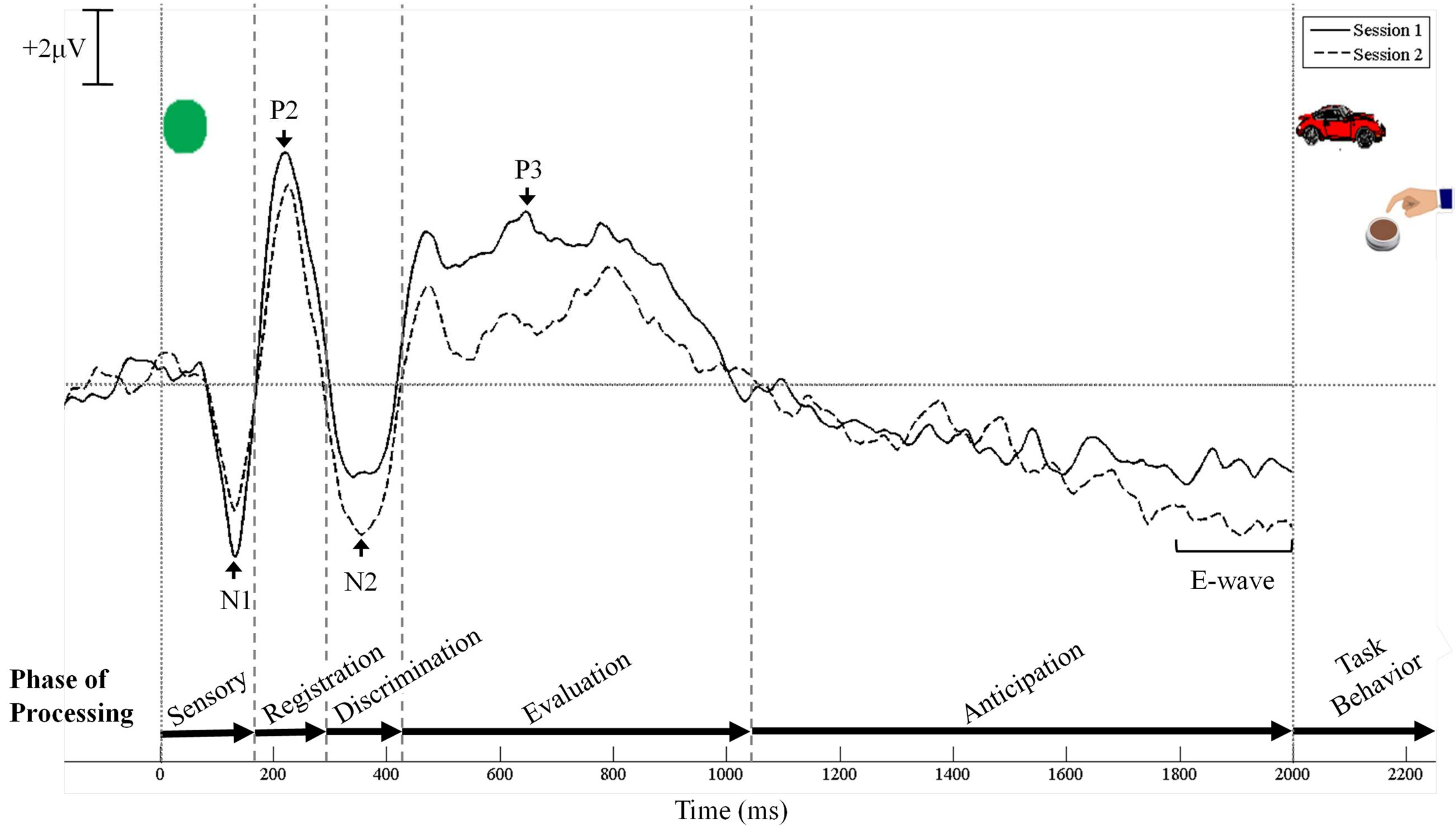

Figure 4.3. The grand averaged event-related potentials for session 1 and session 2 Go trials measured at site Cz. ERP components are labeled on the figure. Example stimuli (i.e., a green circle and a car) as well as an indicator of participant responses (i.e., a button press) are shown at the top of the figure to demonstrate the nature of the Go/No-Go task. Vertical gray dashed lines separate the different phases of stimulus-to-response decision-making during the Go/No-Go Task. Conceptual labels corresponding to the phases of processing are presented at the bottom of the figure.

Table 4.5
Intercorrelations between brain measures and behavioral assessment Z-scores.

	ERP Component Measures									
	Session 1					Session 2				
Behavioral Assessments	**N1**	**P2**	**N2**	**P3**	**E-wave**	**N1**	**P2**	**N2**	**P3**	**E-wave**
Factor 1										
TEA-Ch Sky Search	-.17	.034	-.13	.17	.073	-.19	.070	> .001	.13	.11
TEA-Ch Map Mission	.022	-.084	.16	-.082	-.13	.14	-.044	.044	-.092	**-.22*****
TEA-Ch Opposite Worlds[a]	-.066	-.036	-.16	.13	.18	-.048	.009	-.18	-.038	.20
TEA-Ch Creature Counting[a]	-.14	.067	-.074	.059	.18	-.089	-.092	-.021	.11	.18
d2 TN-E	.023	-.032	.060	-.18	-.11	.16	.034	.058	-.18	-.11
Selective A's Total	.17	.015	.18	-.13	-.13	.14	-.044	.072	-.14	-.009
Crossing Off A's Total	.080	-.13	.066	-.18	**-.36*****	.16	-.014	.032	-.16	**-.35****
Factor 2										
TEA-Ch Score!	.005	-.17	-.045	-.072	.026	.039	.002	.027	-.055	-.079
TEA-Ch Sky Search DT	.068	-.14	-.057	-.006	.074	.084	-.19	-.090	.001	.024
TEA-Ch Score! DT	.080	-.019	.14	-.13	-.16	-.092	-.073	.080	-.014	-.11
TEA-Ch Walk Don't Walk	**.29****	-.19	**.24***	-.040	-.17	.16	-.15	.15	-.018	-.11
WCST Learning to Learn	-.097	-.21	.091	.030	-.16	-.011	-.21	.14	-.083	.020
WCST Perseverative Errors	-.12	.033	-.088	-.13	.25	-.039	.14	.18	.24	.11

* $p < .05$, ** $p < .01$, *** $p < .001$

[a]The TEA-Ch subtests *Opposite Worlds* and *Creature Counting* loaded onto both factors, however the correlations are only listed under a single factor in this table to avoid redundancy.

square ratio is well within acceptable limits (χ^2/df = 1.33), as are the CFI and SRMR values. Given the exploratory nature of the model, and the relatively small N for a complex model, the model can be deemed as being adequate indicating that this is in fact a viable model. However, future work should replicate this study with larger samples to confirm the viability of the model.

Cognitive constructs. Overall, the findings from *Study 3.1* held true even when the cognitive factors were introduced into the larger biobehavioral model. A greater score for *Factor 1* was indicative of *poorer* overall abilities within the cognitive domain. In turn, a greater score for *Factor 2* was indicative of *better* overall abilities within the cognitive domain. The two factors were significantly correlated such that better abilities within one cognitive domain was related to better abilities within the other cognitive domain, $\varphi = -.72$, $p < .001$. The correlation between factors was slightly stronger than was found previously.

Brain processing predicting task behavior. The model indicated that, in accordance with prior findings (see *Study 2*), one phase of neural processing significantly and strongly predicted the next in chronological order from *Sensory* (N1) through *Anticipation* (E-wave). Additionally, the full stream of processing significantly predicted *Task Behavior* (reaction time). Almost all coefficients, including factor loadings, correlations, and predictive coefficients, were similar to those established in prior work in which "age" was used as a control variable on each latent variable. However, there were notable differences in the relationships extending to *Task Behavior*. Both the correlation between *Registration* and *Task Behavior* ($\varphi = -.73$, $p = .002$), and the predictive relationship from *Anticipation* to *Task Behavior* ($\beta = .95$, $p < .001$) increased in comparison to findings from prior work ($\varphi = -.50$, $p = .03$, $\beta = .45$, $p = .02$, respectively, see *Study 2*).

Cognitive constructs predicting phases of brain processing. Although there was only one statistically significant prediction, the model indicated differential predictive relationships from each of the cognitive constructs to each of the latent phases of brain processing (see Table 4.6). Specifically, *Factor 1* seemed to have stronger predictive relationships to *Sensory*, *Registration*, and *Evaluation*, whereas *Factor 2* related more strongly to *Discrimination* and *Anticipation*. Based on these findings, we explored a reduced model in which the cognitive construct prediction that was the weakest (based on standardized predictive coefficients and *p*-values) was removed from the model. Thus, each phase of neural processing was being predicted by only one of the cognitive constructs.

Table 4.6
The unstandardized and standardized predictions and standard errors (SE) of predictions from cognitive constructs to latent phases of neural processing obtained in the reduced model.

	Unstandardized		**Standardized**		
Factor 1 Predicting:	**b**	**SE**	**β**	**SE**	***p***
Sensory	**-1.69**	**.83**	**-.44**	**.21**	**.04**
Registration	1.33	1.24	.26	.24	.29
Discrimination	-.28	1.62	-.045	.27	.87
Evaluation	2.23	1.52	.39	.26	.14
Anticipation	-.36	1.14	-.067	.21	.75
Factor 2 Predicting:					
Sensory	-2.16	1.67	-.32	.26	.19
Registration	-.40	2.40	-.044	.26	.87
Discrimination	3.86	3.35	.36	.30	.25
Evaluation	-1.26	3.16	-.12	.31	.69
Anticipation	-3.32	2.22	-.35	.23	.14

Reduced model results. The reduced model included only the predictive relationships from *Factor 1* to *Sensory*, *Registration,* and *Evaluation*, and from *Factor 2* to *Discrimination* and *Anticipation* (see Figure 4.4). Model fit was similar to that of the previous (full) model:

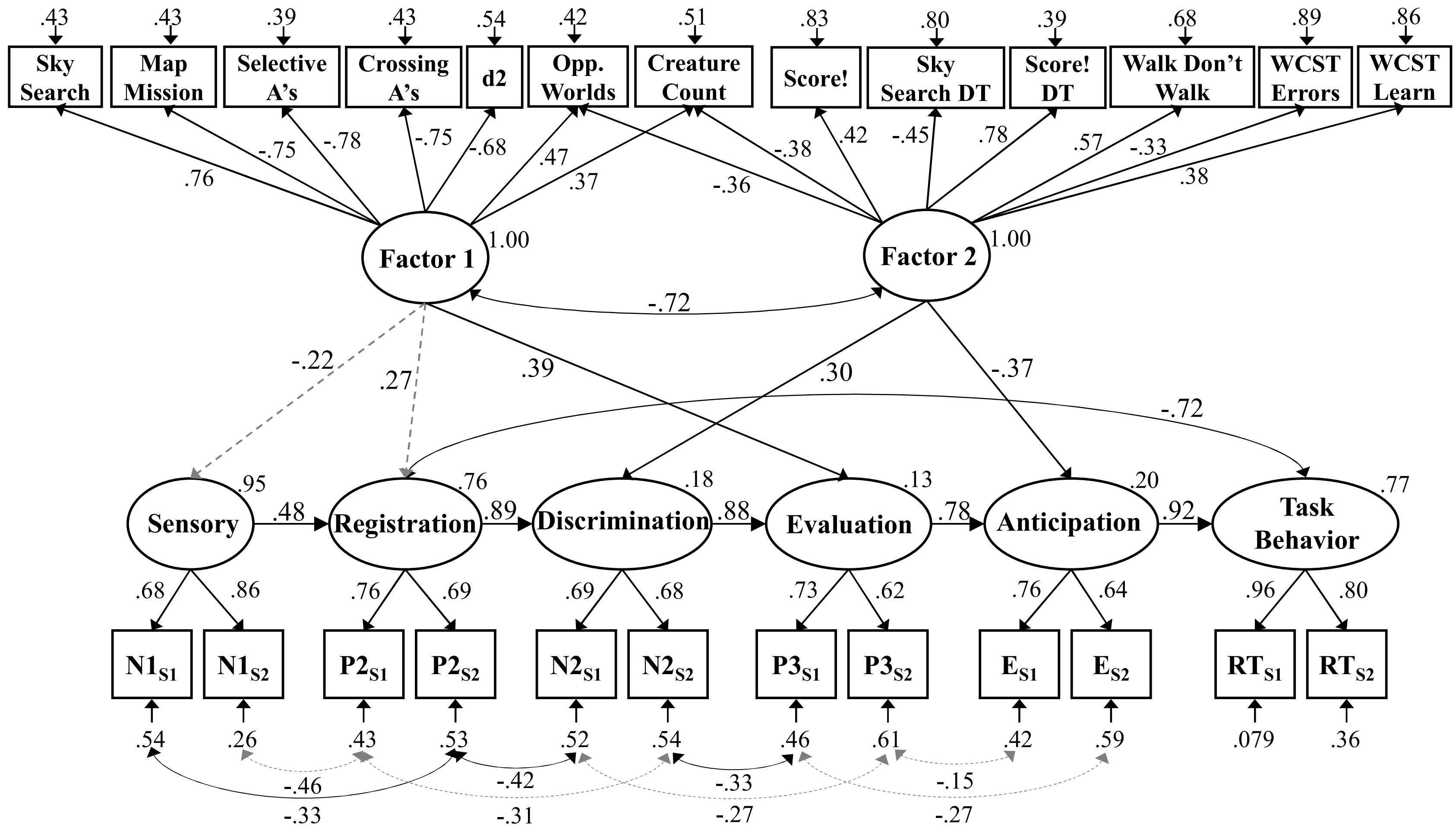

Figure 4.4. *The reduced biobehavioral model where cognitive constructs defined by behavioral assessment measures predict latent variables defined by ERP component measures. All reported coefficients are standardized. Disturbances are reported at the upper right of each latent variable in the model. Gray dotted lines indicate non-statistically significant relationships. Note: S1 = session 1 measure; S2 = session 2 measure; E = E-wave; RT = reaction time.*

$\chi^2(266) = 350.22$, $p < .001$; RMSEA = .05, 90% CI [.04, .07], $p = .36$; CFI = .91; SRMR = .10. Again, using a combination of Hu and Bentler's (1999) strict recommendations, and Iacobucci's (2010) more flexible recommendations that better accommodate complex models with small sample sizes, model fit indices suggested that the reduced model is plausible. A chi-square comparison of model fit between the full model and the reduced model indicated that there was no significant difference in model fit, $\Delta\chi^2(4) = 3.30$, $p = .51$. Thus, the reduced, more parsimonious model can be considered the more appropriate analysis.

Although there were some minor shifts in coefficients, all conclusions from the prior model held true with respect to stream of brain processing predicting task behavior, and the structure and correlation between the cognitive construct factors (see Figure 4.4). Removing the weaker predictive relationships between cognitive factors and latent phases of brain processing did improve statistical power to detect significant effects in the data. Whereas the full model only indicated one statistically significant prediction, the reduced model revealed three significant predictions from cognitive constructs to latent phases of brain processing, with a fourth prediction approaching statistical significance (*Factor 1* → *Registration*: $\beta = .27$, $p = .05$). Interestingly, the predictive relationship from *Factor 1* to *Sensory* was no longer statistically significant in the reduced model, though the relationship would likely reach significance with additional subjects ($\beta = -.22$, $p = .11$).

The predictive relationships between the cognitive constructs and the latent phases of neural processing indicated different patterns with respect to the directionality of the relationship. For instance, better abilities within the cognitive domain represented by *Factor 1* predicted *smaller* N1 amplitudes (*Sensory*), and *larger* P2 (*Registration*) and P3 (*Evaluation*) amplitudes. In turn, better abilities within the cognitive domain represented by *Factor 2* predicted *smaller* N2 amplitudes (*Discrimination*) and *larger* E-wave amplitudes (*Anticipation*).

Conclusions for Study 3.2

The present study demonstrated that developmentally-sensitive cognitive constructs, which likely represent aspects of attention and executive function, may differentially relate to phases of neural processing that occur during decision-making behaviors (see Figure 4.4). *Factor 1*, which seemed to represent aspects of selective attention and processing speed, related strongest to the *Sensory*, *Registration*, and *Evaluation* phases of neural processing. The findings were reasonable given previous literature suggesting that the N1 and P2 ERP components are sensitive to aspects of selective attention to a task (Adams et al., 2017; Kappenman & Luck, 2012). Literature regarding the functional associations of the P3 component are more mixed, with some researchers suggesting that the P3 is more related to attention and others arguing that the P3 is more heavily influenced by higher-order processes characterized as executive functions (for a review, see Polich, 2007). It is possible that some ERP tasks may require more higher-order processing than the Go/No-Go task utilized in the present study. Thus, the P3 elicited during more complex tasks may relate more strongly to cognitive constructs that better capture aspects of executive function. *Factor 2*, which seemed to represent aspects of sustained attention and task strategy, related strongest to *Discrimination* and *Anticipation*. Again, the findings were reasonable given prior literature relating the N2 component to executive discrimination processes (Patel & Azzam, 2005), and the E-wave component to sustained attention processes (Petersen & Posner, 2012).

Interestingly, better cognitive abilities within each of the cognitive domains implied different directionality of effects on the phases of neural processing (i.e., smaller or larger amplitude ERP components). ERP component amplitudes have been interpreted as indications of 1) the intensity of neural processing required, and 2) the amount of neural resources devoted to processing information (Stern et al., 2001; Walhovd et al., 2008). Given these interpretations of ERP component amplitudes, we can infer how abilities within the two different cognitive domains may be affecting neural processing.

Through the first four phases of neural processing (*Sensory*, *Registration*, *Discrimination,* and *Evaluation)*, better abilities within the cognitive domain represented in either *Factor 1* or *Factor 2* were related to smaller ERP component amplitudes relative to baseline. The findings may suggest that children who generally have better, more matured attention and executive function abilities generally require fewer neural resources, or less intensive neural processing to successfully process the cue stimulus (i.e., the green circle) and make a decision about the appropriate response (i.e., respond to the upcoming imperative stimulus). Interestingly, the pattern was reversed for the final phase of neural processing; better, more matured abilities within the cognitive domain represented by *Factor 2* were related to *larger* E-wave amplitudes. The data suggest that children with better cognitive abilities related to sustained attention and task strategy may engage in more intensive anticipation processing leading up to the presentation of the imperative stimulus.

Interestingly, prior work exploring the full time-course of an averaged ERP indicated little-to-no effect of "age" on *Anticipation* ($\beta = -.050$, $p = .71$; see *Study 2*). However, the present study showed that a developmentally-sensitive cognitive construct (*Factor 2*) was significantly related to *Anticipation* in the full stream of processing ($\beta = -.37$, $p = .002$). Further work is required to disentangle the unique effects of trait cognitive abilities and development in order to determine which individual differences are most influential at this phase of neural processing.

Discussion

The present study demonstrated the potential of utilizing SEM analyses to simultaneously model multiple complex brain-behavior relationships through the full time-course of an ERP. The findings offer a new lens for understanding the complexities of neural processing and development in children while performing decision-making behaviors. In the first study, we established a simple model of developmentally-sensitive cognitive constructs using measures from validated behavioral assessments. By using Z-score transformations in place of simple raw scores, or assessment-specific standardized scores, we were able to capture unique developmental effects within the collection of measures. The two obtained cognitive factors likely represent aspects of attention and executive function abilities based on assertions in the literature (Bates & Lemay, 2004; Brickenkamp & Zillmer, 1998; Golden, 1978; Heaton, 2003; Manly et al., 2001; Manly et al., 1999; Strauss et al., 2006). Although further work is required to determine exactly what constructs are represented by the factors, the two-factor structure was reasonable based on current discussion of attention and executive function in the literature (NIMH, 2011).

The second study tested a biobehavioral model of decision-making behaviors in children. Specifically, the model simultaneously examined how two developmentally-sensitive cognitive constructs, defined by behavioral assessments, differentially related to latent phases of neural processing across the full time-course of an averaged ERP. By first approaching the ERP as a phase sequence in accordance with connectionist theory (McNaughton & Nadel, 1990; Raftopoulos, 1997), we were able to better represent the systematic nature of neural processing during decision-making behaviors. Using a latent variable path analysis ultimately reduced the amount of measurement error in the data (*Study 2*; Gavin & Davies, 2008; Kline, 2011), thereby allowing us to better detect and examine even small effects in the data.

The results indicated differential relationships between the cognitive constructs and phases of neural processing, suggesting unique influences of developmentally-sensitive cognitive abilities at different points in the decision-making process during the ERP task. These data supported other researchers' claims that "age" is likely a multifaceted variable that represents maturation within a number of cognitive and biological domains; however, the simple variable of "age" may not have the resolution to provide insights into the slight changes occurring in the brain as a decision is being made (Johnson & de Haan, 2011). Future work may consider exploring the influences of additional constructs on phases of neural processing as it is likely that more than just attention and executive function are important during any given phase of the decision-making process. For instance, it is possible that aspects of motor development (Cameron et al., 2012), memory functioning (Sprondel et al., 2011), or more refined domains of executive function such as inhibition and organization (Zelazo et al., 2008) may each have unique effects on neural processing patterns. However, such an investigation would require larger samples in order to accommodate the increased complexity of the model.

Future Directions

Future research should examine the generalizability of the models established in the present study. The models should be tested using a new sample of children in order to confirm that the models are viable outside of the specific sample obtained in this study. Additionally, researchers should consider exploring how the models may change when the brain processing is elicited during other tasks. The present investigation offered a view of decision-making behaviors in children performing a simple visual Go/No-Go task. However, researchers utilize a multitude of tasks varying in complexity and stimulus modality in order to elicit an ERP. Different tasks may indicate slightly different patterns of stimulus-to-response processing. Likewise, each phase of neural processing may vary in its relationship to developmentally-sensitive constructs, like attention and executive function, as the task demands change.

CHAPTER V

Summary of Findings

The overall goal of this series of studies was to demonstrate the advantages of utilizing advanced statistical analysis techniques to better understand complex brain-behavior relationships in typically-developing children. *Study 1* examined a simple model in which a single ERP component measure (the E-wave) and measures of attention defined by behavioral assessments were related to behaviors during the ERP task (reaction times). The investigation began with more traditional statistical approaches, including Pearson Product Moment correlations between E-wave amplitudes and averaged reaction times measured during two separate sessions. The resulting correlations were small, indicating that the E-wave amplitude and averaged reaction times only shared 7.9 – 9.6% of their variance on a given session (see *Study 1.1*). The finding was in accordance with prior literature showing weak and variable relationships between brain and behavior measures (e.g., Brydges et al., 2014; Foti et al., 2016; Kaltwasser, Hildebrandt, Recio, Wilhelm, & Sommer, 2014). However, after moving to a latent variable model and adding in trait behavioral measures of attention, we were able to account for 47.7% of the variance in a latent variable of reaction time (see *Study 1.2*). Specifically, by simultaneously examining the influence of multiple, measurement error-free variables on the RT latent variable, we explained an overall greater proportion of the variance in children's task behavior than was possible with simpler analyses. This is likely because simpler analysis techniques such as correlations are easily burdened by measurement error and are unable to cohesively model complex multivariate relationships.

The study was a powerful move toward better understanding the interrelationships between brain measures, trait abilities, and behaviors in typically-developing children. However, there was notable room for improvement; namely, even after utilizing a latent variable approach, the relationship between the E-wave and reaction time to the ERP task was small and failed to reach statistical significance. *Study 2* attempted to remedy this weakness by considering additional aspects of neural processing that chronologically precede the E-wave component.

Study 2 assessed the utility of path analysis approaches at varying levels of complexity in order to better detect brain-behavior relationships. Using principles of connectionist theory (Hebb, 1949; McNaughton & Nadel, 1990; Raftopoulos, 1997), we viewed the full time-course of the cognitive ERP from the N1 component through the E-wave and task behavior as a phase sequence in which one component successively predicted the next in chronological order leading to a behavioral response (N1 → P2 → N2 → P3 → E-wave → reaction time). We first tested two separate models: one path analysis for each session of data using simple manifest-level variables. In both models, one component significantly predicted the next through the full stream of processing from the N1 through the E-wave (see *Study 2*). However, the prediction from the E-wave to reaction time was only significant in the session 1 model. Overall, the effects were small, and each manifest variable reflected a large residual variance (see Figure 3.2). Thus, we tested a latent variable path analysis with the intent of better managing variance in the data, thereby increasing our power to detect strong, stable relationships among the variables.

The latent variable path yielded moderate-to-strong, statistically significant predictions from one ERP component to the next from the N1 through the E-wave (see Figures 3.3 and 3.4). Additionally, the full stream significantly predicted behavior during the ERP task to a greater degree than either of the manifest-level path analyses, giving credence to the *latent variable* path analysis approach for understanding brain-behavior relationships. Interestingly, the findings suggested differential effects of age at each phase of neural processing, with coefficients reaching statistical significant for the N2, P3, and reaction time latent variables (see *Study 2*).

The nature of path analysis suggests that the identified age effects were likely comprised of different sources of variance. Specifically, each step of a path analysis takes into account the variance that was previously accounted for by other variables. Thus, the significant age effect on the P3 exists *above and beyond* the age effects present prior to the P3 in the full path analysis, including the N2. The same is true of the significant age effect on reaction times. Given these data, it is likely that the effect of "age" is not a solitary construct, but rather represents multiple developmental constructs that uniquely influence each phase of the decision-making process. The data were in accordance with previous researchers' assertions that "age" is not a solitary construct, but rather serves as a representation of multiple aspects of cognitive and biological maturation (Johnson & de Haan, 2011). Thus, the final study in this series of investigations explored possible cognitive constructs that may account for at least a portion of the developmental effects within each of the phases of neural processing.

In *Study 3*, we examined the interrelationships between each of the phases of neural processing, and two developmentally-sensitive cognitive constructs representing aspects of attention and executive function. Given the more cognitively-conceptual nature of the study, we attached new labels to each of the phases of processing based on their hypothesized functional associations in the literature: *Sensory* (N1) → *Registration* (P2) → *Discrimination* (N2) → *Evaluation* (P3) → *Anticipation* (E-wave) → *Task Behavior* (reaction time). The findings indicated that the *Sensory*, *Registration*, and *Evaluation* phases of processing were more strongly related to cognitive *Factor 1*, which encompassed aspects of selective attention and processing speed abilities (see Figure 4.4). In turn, the *Discrimination* and *Anticipation* phases of processing were more strongly related to cognitive *Factor 2*, which captured aspects of sustained attention and task strategy abilities. With this elaborated biobehavioral model of systematic phases of processing, we were able to achieve a strong, statistically significant prediction from brain to behavior. The prediction coefficient was notably larger than previously achieved in a simpler model that just used "age" to account for maturation effects.

Import to the Field

Effectively Managing Variance

In this series of investigations, we demonstrated that latent variable approaches are viable methods for managing sources of variance in data collected from children, who are inherently more variable in their brain processing and performance. In Gavin and Davies' (2008) original series of equations, the researchers suggested that any psychophysiological measure (PM) is comprised of multiple sources of variance, including measurement error (ME; see equation 1 reprinted from Gavin & Davies, 2008, p. 428).

$$PM = Effect_{STIMULUS} + Effect_{STATE} + Effect_{TRAIT} + Effect_{PM\_PROCESSING} + ME \qquad (1)$$

Latent variables are comprised of only the *common variance* among the manifest variables that define the construct, thus latent variables are free of measurement error (Kline, 2011). Additionally, because our latent variables of neural processing were defined by the combination of ERP component measures across two sessions, any state-specific effects that may have varied during each recording session (e.g., hunger, mood, fatigue) were also removed from the final latent variable. Thus, the variance comprising our latent variables representing psychophysiological measures (PM_{LATENT}) can be simply described as follows (see *Study 3*):

$$PM_{LATENT} = Effect_{STIMULUS} + Effect_{TRAIT} + Effect_{PM\_PROCESSING} \tag{2}$$

We were also able to account for at least a portion of the trait-specific variance in the ERP measures, namely maturation, by incorporating developmentally-sensitive cognitive constructs into our structural models. Thus, we further diminished the $Effect_{TRAIT}$ in our data in the final model presented in *Study 3*. By reducing the amount of "nuisance" variance in the neural measures, we had greater power to detect brain-behavior relationships than is possible when sources of ME and other trait- and state-specific effects confound the data. Importantly, our established latent variables of neural processing were much more stable than the simple manifest-level measures of ERP component amplitudes, which consistently show weak-to-moderate test-retest reliability in children (e.g., *Study 2;* Meyer et al., 2014; Segalowitz & Barnes, 1993; Taylor et al., 2016).

Collectively, the data in this series of investigations make a case for the use of latent variables when working with psychophysiological measurements obtained from children. It is possible that latent variable approaches may also be useful in investigations of other groups of individuals who tend to be variable in neural processing and performance, such as individuals with clinical diagnoses. Further investigation is required to determine the usefulness of latent variables above and beyond latent variables in different populations.

Modeling Systems of Processing

In addition to the benefits defining latent variables of brain processing and performance, this series of investigations demonstrated the utility of structural equation modeling (SEM) for depicting *systems* of processing leading to task behaviors. In *Study 2*, we showed that no single latent variable representing a phase of brain processing could successfully predict behaviors during the ERP task. Rather, the full time-course of the ERP from the N1 through the E-wave component was necessary in order to significantly predict task behavior. Thus, one might conclude that each ERP component is a small, but critical piece of a larger story when trying to understand brain and behavior. By further refining our structural model with developmentally-sensitive cognitive constructs in place of our simple "age" variable in *Study 3*, we significantly enhanced our ability to predict task behavior, more than doubling our standardized predictive coefficient from *Anticipation* (E-wave) to *Task Behavior* (reaction time).

In sum, SEM techniques allowed us to 1) model systematic neural processing leading to a task behavior *and* 2) simultaneously examine the unique influences of different cognitive abilities on each phase of processing. The findings from this series of studies underscore the importance of examining the full system of neural processing that occurs during decision-making behaviors. Interestingly, several recent investigations by other research groups have attempted to examine brain-behavior relationships using latent variable approaches with SEM, though their results have been relatively weak, as described below (Brydges et al., 2014; Kaltwasser et al., 2014).

Brydges et al. (2014) attempted to use the N2 and P3 component amplitudes and latencies as predictors of executive function abilities in a sample of 215 typically-developing children age 7- to 9-years-old. The researchers defined three latent variables based on their ERP measures, each defined by a single manifest variable: N2 amplitude, P3 amplitude, and P3 latency. The researchers' intent was to define a latent variable for each ERP component measure based on the combination of multiple manifest-level variables measured during different task conditions. However, the authors noted problems with multicollinearity among their ERP measures and thus relied on simple difference scores or composite scores to represent the variance in their data. In their final model, all three latent variables representing ERP component measures were simultaneously modeled as predictors of executive function abilities. Only two of the three predictions reached statistical significance, though all coefficients were weak (β's = -.27 - .17). Interestingly, the established model included no linkages between the ERP component latent variables, either in the form of correlations or predictions from one component measure to another (Brydges et al., 2014).

Another study by Kaltwasser et al. (2014) examined whether measures of P100, N170, and N250r (i.e., early repetition effect; ERE) amplitudes and latencies could be used to predict aspects of facial processing and general cognitive abilities. Data were collected from a sample of 110 neurotypical adults ages 18- to 38-years. Latent variables of ERP components were defined using multiple measures of the same component. Specifically, each component amplitude and latency was measured separately for each of four blocks of trials presented during the ERP task. The researchers then examined 10 separate models wherein a single latent variable representing an ERP component measure predicted multiple aspects of either facial processing (four separate constructs) or cognitive abilities (three separate constructs). Of the 35 total predictions from measures of brain processing to functional constructs, 28 predictive coefficients (β's) were ±.30, with the largest coefficient being -.47 (Kaltwasser et al., 2014). Thus, the majority of predictions from brain to behavior were relatively small even within data collected from neurotypical adults, who tend to be much less variable in neural processing and performance compared to children.

In each of these recent studies (Brydges et al., 2014; Kaltwasser et al., 2014), the established models of brain-behavior relationships failed to acknowledge the systematic nature of neural processing. Namely, Kaltwasser et al. (2014) only examined a single latent ERP measure in any given model. In contrast, Brydges et al. (2014) examined three latent ERP measures in a single model, but neglected to relate the ERP measures to one another in any manner. The model structures and findings mirror those of *Study 1* in the present series of investigations, wherein a single latent variable representing the E-wave amplitude was related to task behavior and trait measures of attention, again only yielding weak relationships.

The compilation of evidence from these three studies (*Study 1*; Brydges et al., 2014; Kaltwasser et al., 2014) implies that simply using a latent variable approach is not enough to detect strong, stable brain-behavior relationships. It is critical to recognize that ERP components elicited during decision-making tasks do not occur in isolation of each other. Each component that presents during the full time-course of an ERP plays a unique and crucial role in the full process of decision-making leading to task behaviors. Thus, moving forward, the field should strongly consider incorporating multiple measures of neural processing into their analyses, *and* consider appropriate ways to model the interrelated nature of those measures. In doing so, researchers may be better able to detect brain-behavior relationships in a variety of populations, both across development and across clinical spectra.

Contrast to current recommendations. Despite compounding evidence that a single neural measure is insufficient for understanding the complexities of human behavior and cognition, some notorious researchers still recommend pursuing more simplified views of brain processing. Unfortunately, such recommendations are centered around the notion that researchers should also continue to rely on more simplistic statistical approaches to understanding their data. For example, a recent review by Luck and Gaspelin (2017) examined the use of multifactorial ANOVA designs in ERP research. The authors specifically focused on the exponentially-inflation of type I errors (i.e., false positives) with added factors and levels of analysis in exploratory ANOVA designs, which are commonly utilized in ERP studies (Cramer et al., 2016; Luck & Gaspelin, 2017). Interestingly, rather than steering researchers toward more sophisticated statistical designs that are robust to such effects, Luck and Gaspelin (2017) recommend that researchers narrow their exploration of their data.

For example, rather than including two ERP component measures in their ANOVA, Luck and Gaspelin (2017) suggest focusing on just one component of interest and disregarding the other in order to limit the number of factors, or the number of statistical tests conducted in a single investigation. Likewise, the authors suggest that instead of including an ANOVA factor that comprises measurements of an ERP component from multiple electrode sites, researchers should collapse their measurement and simply take an average across all sites of interest, or take a simple difference score between sites of interest.

These recommendations are made in spite of knowledge that averages and difference scores can actually increase the amount of measurement error in an ERP measure (Gavin & Davies, 2008), thus making the detection of significant effects even more challenging. Additionally, the recommendations ignore the possibility that more sophisticated statistical techniques may be beneficial for the field as more and more researchers recognize that the brain is comprised of multiple dynamic networks and systems of processing (Bear & Cooper, 1990; Friston et al., 2003; Laufs et al., 2003; Liljenström, 2010; Lowe et al., 2016; Park & Friston, 2013). It is possible that many researchers in the field of neuroscience do not yet understand that statistical techniques like SEM are appropriate for use in their studies.

The nuance of "golden rules" in SEM. Researchers and statisticians tend to rely on "golden rules" to determine under what circumstances a statistical method is appropriate to use, and how to decipher the results. With respect to SEM, a number of rules have been widely (and in some cases strictly) taught, including the notion that sample sizes must always exceed 200, and every structural model must meet specific criterion cutoff levels across all possible fit indices (Hu & Bentler, 1999; Kline, 2011). Unfortunately, many of the simple mores specific to SEM are derived from a history of studies conducted in the applied social sciences, which often rely on data collection methods that yield notoriously small effect sizes, such as survey data of personal opinions (Iacobucci, 2010; Marsh et al., 2004; Wolf et al., 2013). Statisticians have now recognized that these "golden rules" may be overgeneralized and may inappropriately inhibit researchers in other fields of study from utilizing statistical methods such as SEM.

Sample size, effect size, and model identification. A number of researchers in biologically-based fields, such as neuroscience, are quickly deterred from using SEM techniques due to the recommendation that sample sizes must always exceed 200. Data in these fields can be difficult and time-consuming to collect (Gavin & Davies, 2008), making this standard unattainable in some cases. However, recent work suggests that this "golden rule" of sample size is over-generalized and may be inaccurate under different circumstances.

All statistical methods, regardless of their simplicity or complexity, are subject to the import of statistical power: the probability of correctly detecting statistically significant effects within a set of data. Statistical power is based not only on *sample size*, but also on *effect sizes* within the data. Simply stated, smaller samples are required for detecting increasingly large effects, even in the context of SEM analyses (Kim, 2005; MacCallum, Browne, & Sugawara, 1996; Marsh et al., 2004). As demonstrated in *Studies 2 and 3*, neuroscience techniques are capable of producing large effects when sources of variance are appropriately managed, with standardized predictive coefficients reaching the $\beta = .80 - .95$ range. Thus, we were able to test several viable models of brain-behavior relationships in children with data obtained from fewer than 200 participants. It is possible that other researchers in fields such as neuroscience and biological science may also be able to successfully implement SEM analyses with relatively small samples given the potential for large effects in biologically-based data.

Of course, statistical power is not the only issue that determines required sample sizes in SEM analyses. The required number of observations increases with increasing model complexity and more parameters being freely estimated (Iacobucci, 2010; Kline, 2011). This issue is not one of statistical power, but rather model identification; one must have more observations of data than there are freely estimated parameters in a given model. Thus, researchers in *any* field who wish to pursue increasingly complex models must determine how many observations are required to achieve model identification. Simpler models involving only a few variables will require fewer participants' data to achieve model identification than a more complex model, like the final biobehavioral model presented in *Study 3*.

In sum, researchers must be careful not to overgeneralize the required sample size for SEM analyses. There are a several determining factors, including statistical power and model identification, which may vary from one study to another, and from one field of research to another. Moving forward, researchers should identify the number of parameters they expect to include in a model, and identify expected effect sizes in their data sets a priori. In doing so, researchers can conduct power analyses to determine appropriate sample sizes for their investigations rather than simply denying the use of SEM techniques based on mores that may be inappropriate to their field of study.

Model fit indices. A number of researchers have made suggestions regarding appropriate fit indices for determining whether a given model is viable, with one of the most notable recommendations coming from Hu and Bentler (1999). In their study, Hu and Bentler (1999) conducted a series of data simulations in order to determine a set of "acceptable" fit cutoffs for different indices of model fit. For example, the researchers suggest a comparative fit index (CFI) > .95, a standardized root mean squared residual (SRMR) < .08, and a root mean squared error of approximation (RMSEA) < .06. These recommendations are in addition to the commonly-interpreted chi square, which researchers recommend be non-statistically significant, indicating perfect model fit (Kline, 2011).

Interestingly, although these cutoff criteria are deemed recommendations even in their respective publications, many researchers misguidedly interpret them as firm rules. In fact, Hu and Bentler (1999) and other researchers specifically note that not all cases of modeling should be treated the same. The level of scrutiny suggested by Hu and Bentler (1999) is more specific to investigations exploring data from large sample sizes. Researchers have noted that different model fit indices, including chi-square, RMSEA, CFI, and SRMR, are all subject to bias based on sample size (Hu & Bentler, 1999; Iacobucci, 2010; Marsh et al., 2004). Many of the recommended cutoff levels for fit indices are prone to over-reject models that only include a small sample size, with the issue compounding for increasingly complex models (Hu & Bentler, 1999; Iacobucci, 2010). That is to say, researchers attempting to use SEM techniques with data collected from smaller study samples ($N < 250$) are more susceptible to incorrectly deeming a model "not viable" or "misspecified" if they rely on strict rules for model fit cutoffs.

Researchers must be careful when interpreting their model fit statistics from small-sample studies, which may be more common in biologically-based fields of study like neuroscience. It is important to recognize that the established cutoffs reported by Hu and Bentler (1999) and other researchers are mere *recommendations*, not strict rules, and that these recommendations are subject to bias depending on the nature of the data. Establishing a new set of recommendations for model fit cutoffs with small samples may be helpful for fostering the use of SEM in small-sample studies in future research.

Limitations and Future Directions

The series of studies presented in this dissertation had a number of strengths, which allowed us to effectively test a biobehavioral model decision-making processes in typically-developing children. However, there were several limitations that could be addressed in future research to improve the models and further refine the field's understanding of brain-behavior relationships in children. Specifically, 1) the latent variables defining aspects of neural processing could be elaborated to more robustly capture the nature of brain processing, and 2) additional cognitive constructs representing aspects of development could be included in the model to better dissociate unique effects of maturation.

Creating Robust Latent Variables

Determining scalp sites. In this series of studies, latent variables representing phases of neural processing were derived from the combination of two ERP component amplitudes measured during two separate recording sessions. Each ERP component amplitude was measured from a single scalp site, Cz. It is widely known that the electrical signals that are recorded via EEG spread from their original sources in the brain through the brain, blood, skull, and scalp via volume conduction (for reviews, see Kappenman & Luck, 2012; van den Broek, Reinders, Donderwinkel, & Peters, 1998). Signals distribute broadly throughout the assorted conductive media at varying speeds, contributing different amounts of electrical activity to electrode sites placed across the scalp. Thus, the electrical activity that is recorded at any given scalp site is likely comprised of signals from dispersed areas of the brain, not just from brain regions residing directly below the recording site. Given the nature of volume conduction of electrical signals, it is likely that we effectively monitored ongoing activity across dispersed networks in the brain by utilizing measurements from a single, central location in our latent variables.

It is possible, however, that scalp sites other than Cz may have better resolution of the activity produce by specific networks. For instance, certain ERP components indicative of specific aspects of visual perception are not readily visible or measureable at Cz. Rather, visually-evoked potentials such as the P23, P30, and P35, which are believed to originate from the primary visual area of the occipital cortex, are best measured at site Oz (Kappenman & Luck, 2012). By simply measuring ERP components from Cz in the present studies, we were unable to observe these and other ERP components that may be important in understanding early visual perception during the task.

In contrast, certain ERP components, such as the P3, have a wide scalp distribution and are readily measured from multiple scalp sites. In fact, the P3 measured from more frontal sites, like Fz (i.e., P3a), is believed to represent different functional abilities compared to the P3 measured from more posterior sites, like Pz (i.e., P3b; Polich, 2007). Future research may explore how ERP components measured from additional scalp sites can contribute to the model of decision-making behaviors established in *Studies 2 and 3*. It is possible that by incorporating additional phases of processing into the model, or by incorporating measurements of a single

ERP component from multiple scalp sites, researchers may be able to further elucidate the systematic nature of neural processing leading to task behaviors during the task.

Alternative neural measures. The present series of investigations included only ERP measures of neural processing. However, there are a number of alternative neural measures that can be examined within EEG data. Each alternative view of the collected data can potentially provide a unique perspective on the neural processing occurring during decision-making behaviors in children.

For example, an EEG is the compilation of electrical oscillations at multiple frequencies which researchers have divided into different "bands" including delta (.5 – 3.5Hz), theta (4 – 7.5Hz), alpha (8 – 13.5Hz), beta (14 – 29Hz), and gamma band oscillations (30 – 70Hz). A number of studies utilize time frequency analysis, a data reduction technique that allows researchers to decompose an EEG signal into its assorted frequencies and better examine the dynamics of different oscillations, such as power (i.e., how strong the oscillation is) and phase-locking (i.e., how "in-rhythm" oscillations of different frequencies are with one another or with a specific event). Using these techniques, researchers have noted functional cognitive, sensory, and motor correlates within each of these bands (Harmony, Alba, Marroquín, & González-Frankenberger, 2009; Heinrich, Kolev, Rothenberger, & Yordanova, 2009; Christoph S. Herrmann, Strüber, Helfrich, & Engel, 2016; Karakaş & Barry, 2017; Paul Sauseng & Klimesch, 2008; P. Sauseng et al., 2006).

When calculating an averaged ERP, researchers may exclude some frequency bands from the EEG signal via bandpass filtering in order to increase the visibility of specific ERP components (Chang et al., 2012). However, it is possible that some of the oscillations that are reduced or removed from the signal could elucidate aspects of sensory, cognitive, or motor processing during the task that are not captured by the resulting ERP. Researchers continue to show evidence that event-related oscillations, like ERPs, can contribute to our understanding of brain processing during a task (e.g., Christoph S Herrmann & Knight, 2001; Paul Sauseng & Klimesch, 2008).

Future research should consider elaborating the latent variable structure defined in the present series of investigations with time-frequency approaches. For instance, a researcher may choose to measure power within specific event-related oscillation bands coinciding with an ERP component (e.g., theta power during the time window of the N2 component), and include those measures in the latent variable composition. Thus, the resulting latent variable would be comprised of neural processing measures obtained from different analysis strategies, which each provide a unique lens for examining brain function. Using such an approach may allow researchers to better capture the nature of ongoing neural processing during the task. By better representing the complexities of brain processing, we may be able to better understand the complex interrelationships between trait abilities, neural processing, and behaviors.

Elaborating on Cognitive Constructs and Trait Abilities

Study 3.2 tested a biobehavioral model of decision-making behaviors in children. The study included an exploration of how two cognitive constructs representing aspects of attention and executive function abilities differentially related to phases of neural processing. Although the model yielded promising results that agreed with current literature, it is possible (and likely) that the model does not yet capture the multitude of developing cognitive and motor abilities that contribute to decision-making behaviors in children.

For example, researchers have suggested links between the E-wave component and motor abilities, including motor preparation and motor control (Banaschewski et al., 2008; Flores, Digiacomo, Meneres, Trigo, & Gómez, 2009; Jonkman, 2006). Other more commonly studied ERP components, like the P3, have been associated with a multitude of cognitive abilities including attentional orienting, reward evaluation, inhibition, and working memory processes (Gaspar et al., 2011; Polich, 2007; Wu & Zhou, 2009). The body of literature suggests a plethora of functional associations for any given ERP component. Thus, it is likely that the model presented in *Study 3.2* falls short of capturing the breadth of cognitive and motor abilities that contribute to neural processing.

Future studies should work to incorporate additional measures of trait abilities into their models in order to more completely represent the dynamic, complex relationships between brain and behavior. Of course, as noted earlier, as the models researchers develop become increasingly complex, the required sample size for the study also increases. Achieving large samples in developmental neuroscience-based studies can be particularly challenging due to both time- and financial-burdens associated with data collection (Gavin & Davies, 2008). With respect to time commitments, collecting the amount of data utilized in the present series of investigations required approximately 565 hours of contact time with participants (2.5 hours per session, 2 sessions each for 113 participants). That does not include the time required for recruitment, training research assistants to collect data, preparing for and cleaning up after data collection, and then scoring and processing all of the collected data. Adding behavioral assessments of motor and cognitive abilities to testing protocols would increase the time burden as well as the financial burden for a given study. Researchers must be prepared to commit significant time to a study protocol in order to collect sufficient data to elaborate on the models established in *Study 3.2*.

Considering financial burdens, every session of data collection has an associated cost. Researchers must consider the cost per session to collect their neuroscience-based data (e.g., EEG recordings, MRI scans), plus the cost for materials for their battery of selected cognitive and motor assessments (e.g., the TEA-Ch, the WCST-CV4), and the cost for their labor (e.g., research assistant or technician wages). Costs incurred include the initial purchase of all equipment and testing kits as well as disposable materials, such as gel for EEG recordings, and participant-specific materials, like recording forms for behavioral assessments. The tools that researchers choose to use in their studies can widely vary, thereby impacting the overall cost of the study. However, costs continue to compound as researchers continue to add more and more measures to their study protocols. Thus, moving forward researchers will need to carefully consider the best approach to collecting data and establish a battery of assessments that can both address the research questions of the investigation, *and* fit within the budget of the research lab.

Potential for Clinical Applications

The current series of studies examined brain-behavior relationships in a sample of neurotypically-developing children. However, a growing body of evidence suggests that children with neurodevelopmental disorders, such as autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD) exhibit differences in both neural processing and general cognitive and motor abilities compared to their typically-developing peers (Banaschewski et al., 2008; Buchmann, Gierow, Reis, & Haessler, 2011; Davies et al., 2010; Gavin et al., 2011; Tye et al., 2014). Given that individual ERPs may differ between clinical diagnostic categories, it is also possible that the full stream of processing (i.e., N1 → P2 → N2 → P3 → E-wave → Task Behavior) may also vary between groups. It is also possible that the relationships between cognitive constructs and each phase of neural processing may differ from one group to another.

Future work should consider expanding the model established in *Study 3.2* to clinical populations in order to better understand how *systematic processing* varies between clinical groups. In doing so, researchers may be able to better understand *how* and *why* children with different diagnoses struggle with specific aspects of everyday functioning, like properly integrating sensory information, or adequately attending to a task. In other words, rather than examining simple differences on a small array of behavioral or neural measures, researchers could establish *profiles* of systematic processing that are specific to diagnostic groups. Researchers and clinicians could use this information to develop more sensitive diagnostics, and more targeted intervention techniques. Such a line of inquiry would be in accordance with the goals of the Research Domain Criteria (RDoC), which strives to understand a spectrum of individual differences at multiple levels of measurement (Cuthbert, 2014; Cuthbert & Insel, 2010; Insel et al., 2010; Miller, Rockstroh, Hamilton, & Yee, 2016).

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