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I, Lori A. Kroeger , hereby submit this original work as part of the requirements for the degree of Doctor of Philosophy in Educational Studies.

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Neural Correlates of Error Detection in Math Facts

Student's name: **Lori A. Kroeger**

This work and its defense approved by:

Committee chair: Rhonda Douglas Brown, PhD

Committee member: Vincent Schmithorst, PhD

Committee member: Suzanne Boyce, PhD

Committee member: Chung-Yiu Chiu, PhD

Committee member: Marcus Johnson, PhD

3029

Neural Correlates of Error Detection in Math Facts

A dissertation submitted to the

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by

Lori Kroeger

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M. Ed. Xavier University

May 1999

B. S. Xavier University

August 1995

Committee Chair: Rhonda Douglas Brown, Ph. D.

Co-Chair: Vincent J. Schmithorst, Ph.D.

Abstract

Previous studies have examined the relative contribution of domain-general and domain-specific mechanisms supporting the development of mathematics cognition, yielding mixed results. Two etiological origins have been proposed for children struggling with mathematics, the first resulting from a neurobiological deficit in the parietal region of the brain, leading to a pure mathematical disability, specific to mathematical processing; the second, resulting from a deficit in domain-general cognitive mechanisms related to working memory, visual-spatial processing, and attentional control. The precise etiology has yet to be determined. It is clear, however, that children who experience mathematical difficulties (MD) use less developmentally mature strategies and commit more errors than their typically achieving (TA) peers and are less proficient at recognizing when an error has occurred. This study investigated the neural correlates of error detection capabilities in arithmetic problems using a combined behavioral and functional Magnetic Resonance Imaging (fMRI) design. Error detection abilities were examined in a group of 21 adolescents, 7 of whom were identified as MD. Participants engaged in a novel Error Detection task, which consisted of 40 addition, subtraction, and multiplication problems presented along with a proposed solution. All problems were presented in the center of the visual field (50% vertical). Participants identified if the solution was correct, indicating Yes or No, via button press (e.g., 5 + 9 = 14; 3 x 8 = 32). As this task is novel to neuroimaging studies of mathematics, it is positioned to provide preliminary data regarding behavioral performance and patterns of neural activation and deactivation related to error detection abilities in mathematics. The results indicate that the TA group significantly ($Z = 2.72$, $p = 0.006$) outperformed the MD group on task accuracy. While no differences in activation patterns were found between MD and TA participants, the TA group had significantly more deactivation in the default mode network (DMN) as compared to the MD group, most notably in the amygdala. Failure to suppress DMN activation during cognitively demanding tasks (e.g., mathematical calculations) may leave a child susceptible to interference from extraneous, non-task related activation; thereby, increasing the potential for lower accuracy scores and less efficient neural processing. Although participants in the current study are still undergoing developmental changes, these results suggest that the differences between TA and MD adolescents' ability to detect mathematical errors may be related to differences in the DMN and that at least in the case of error detection, domain-general cognitive processing deficits may contribute to an inability to detect mathematical errors. These results have implications for both educational programming and intervention practices. By understanding the neural networks supporting arithmetic processing, educators, intervention specialists, and administrators will be better equipped to make curricular and programmatic decisions that address the deficits encountered by children who struggle with mathematics learning.

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CHAPTER I

Statement of the Problem

> *If you can both listen to children and accept their answers not as things to just be judged right or wrong but as pieces of information which may reveal what the child is thinking you will have taken a giant step toward becoming a master teacher rather than merely a disseminator of information* (Easley & Zwoyer, 1975, p. 25).

In this chapter I provide an intentionally broad overview of the development of numerical and mathematical cognition and the relative importance of mathematics cognition in the world at large. In addition, the three literature bases serving as the theoretical framework for this dissertation, Mathematical Cognition, Mathematical Disabilities, and Cognitive Neuroscience of Mathematics Learning are briefly introduced.

Quantitative Skills in the Real World

We are born into and live in a world of quantity and number. We use numbers to communicate with each other, to organize information, and to function in 21st century society. The past 50 years or so have been witness to dynamic changes in how we view the development of cognitive skills, including mathematical competencies. Piagetian views held that a child's numerical and mathematical skills and abilities develop slowly as the result of direct experience with numerical and arithmetical observations and interactions. In contrast, the Behaviorists suggested that babies were blank slates, upon which all quantitative skills were to be inscribed. It is now widely recognized that numerical competency begins early in life, developing from and building upon an innate quantity processing system (Geary, 1994, 1995, 2000; Starkey, Spelke, & Gelman, 1990). In recent years, we have come to understand and appreciate that innate quantitative skills exist at, or shortly after, birth, and are evident across species. While there remains speculation and debate as to whether this processing system is dedicated solely to numerical quantity or shared with other quantitative tasks, there is little doubt that the numerical and mathematical competencies that allow us to use meaningfully use quantity and number develop very early in life.

Research has demonstrated that human infants are born with immature, yet measurable knowledge regarding the nature of numeracy, including an implicit understanding of small quantity arrays (Starkey et al., 1990), early counting concepts and immature counting procedures (Gelman & Gallistel, 1978), the effects of addition and subtraction (Wynn, 1992), and quantity relationships (Lipton & Spelke, 2003; see Geary, 2006, for a review) each within what Geary (1994, 1995, 2000) refers to as biologically-primary abilities. In contrast, number names, counting, and arithmetic are culturally dependent activities, requiring specific and focused instruction. These are the skills children spend year after year learning in the classroom. Concepts such as Arabic numeral representation (Spelke, 2000), the base-ten system, (Geary, 2002), and complex arithmetic and the procedures necessary to solve such problems (Fuson & Kwon, 1992) are among those included in Geary's (1994, 1995, 2000) biologically-secondary math abilities.

Mathematical competencies, such as these, have become increasingly important in 21st century society and are related to earnings, productivity, and employability "above and beyond the influence of literacy, years of schooling, and intelligence" (Geary, 2000, p. 11). Fluency and competency in mathematics is necessary across many disciplines, including: health care, teaching, and construction. The majority of the quantitative skills and knowledge required for success in industrialized society require explicit, careful, and repetitive instruction during the school-age years; very different from the innate skills developing over the first months and years of life. As such, ensuring the development of quantitative skills is of critical importance to both the individual's success and for progression of society at large.

Unfortunately, not all children become competent and fluent in mathematics. Difficulty learning mathematical skills and developing mathematical competencies comes with a price. Not only do these children fail to develop the early skills and conceptual understanding that more complex mathematical concepts build upon, they are at risk for life-long reduction in wage earnings and employability (Geary, 2011a; Mitra, 2002; Terrell, 2007). It is estimated that between 5.9% and 13.8% of school age children have a learning disability in mathematics (i.e., Mathematics Disability [MD]) (Badian, 1983; Barbaresi, Katusic, Colligan, Weaver, & Jacobsen, 2005; Fuchs, Deshler, & Reschly, 2004; Geary, 2004; Gross-Tsur, Manor, & Shalev, 1996; Kosc, 1974). While an agreed upon definition of MD has yet to be operationalized, it is generally recognized that children with MD face deficits in general cognitive abilities, as well as domain-specific abilities related directly to mathematics and that a sub-set of these children may have deficits in intelligence.

A number of domain-general cognitive abilities support numerical and mathematical processing, including: working memory (Murphy, Mazzocco, Hanich, & Early, 2007), long-term memory retrieval (Ashcraft, 1985), attention, and inhibition to response (Engle, Tuholski, Laughlin, & Conway, 1999; Passolunghi, Cornoldi, & De Liberto, 1999; Passolunghi & Siegel, 2004). Domain-specific skills known to support the understanding and development of number and quantity (i.e., mathematics) include: number sense, counting knowledge, and arithmetic procedures (Butterworth, 2005; Butterworth & Reigosa, 2007; Geary 1990; 1993, 2010a). In addition, children with MD make more errors, commit certain types of errors, and fail to recognize errors to a lesser extent than their typical achieving peers (Geary, 2011b; Raghubar et al., 2009; Siegler, 1988). Deficits in any one (or more) of these areas may put a child at risk for MD.

This dissertation examines error recognition abilities across a sample of children with a wide range of mathematical abilities. The research questions addressed by this study are: Does the detection of specific types of errors in arithmetic problems have specific neural signatures? Does the detection of specific types of errors in arithmetic problems correlate with performance on a standardized achievement test? What is the deactivation pattern of the DMN in relation MD status on the *Error Detection* task?

The central purpose of this dissertation is to investigate the neural mechanisms supporting mathematical cognition, specifically those supporting error detection abilities in addition, subtraction, and multiplication problems. Through a combined approach utilizing both functional Magnetic Resonance Imaging (fMRI) and behavioral methodologies, this study investigates the neural correlates associated with performance on an *Error Detection* task.

Three bodies of literature are used in support of this study: Mathematics Cognition, Mathematics Learning Disabilities, and Cognitive Neuroscience of Mathematics Learning. Research from the field of Mathematics Cognition has provided an understanding of the various mechanisms supporting typical mathematics learning, including both domain-general and domain-specific cognitive mechanisms. Math cognition experts have also identified common errors made by children who struggle in learning mathematics (Geary, 2011b; Raghubar et al., 2009; Siegler, 1988). The field of mathematical disabilities has seen an upsurge of research dedicated to identifying subtypes of MD based on what is known about how children solve arithmetic problems and the types of errors they make while doing so (Geary, 1993, 2010b). In an attempt to integrate the biological and behavioral components of numerical and mathematical cognition, the fields of neuropsychology and neuroscience have begun to investigate how the brain engages in mathematical processing (Campbell & Clark, 1988; Dehaene & Cohen, 1995, 1997; Dehaene, Piazza, Pinel, & Cohen, 2003; McCloskey, Caramazza, and Basili, 1985; McCloskey, Solko, & Goodman, 1986). The present study draws upon each of these fields to understand the neural mechanisms supporting the ability to detect errors and to examine the types of errors commonly made by children with a wide range of achievement levels. Such an approach permits this study to examine both the behavioral (i.e., task performance) and biological (i.e., neural response) contributions to the commitment of errors during arithmetic problems.

Purpose of the Present Study

The present study assumes a developmental systems approach to understanding numerical processing and mathematical competencies. Viewing "individual development as hierarchically organized into multiple levels (e.g., genes, cytoplasm, cell, organ, organ system, organism, behavior, environment) that can mutually influence each other" (Gottlieb, 1991, p. 5) (see Figure 1) the developmental foundation upon which this study rests assumes that biological and environmental influences cannot be understood separate from one and other. For this reason, I believe conducting empirical research that aims to understand functioning both within and between each level of development (i.e., genetics, neural activity, behavior, and environment) is not just a good practice, but a necessary step toward fully appreciating how any one system affects the others (Brown & Bjorklund, 1998). Examining the effects of these seemingly mutually exclusive levels through the lens of multiple levels of analysis will permit "further understanding [of] the complexity of interactions underlying developmental and individual differences in cognition" (Brown & Chiu, 2006, p. 288).

Figure 1. Influences on Human Development

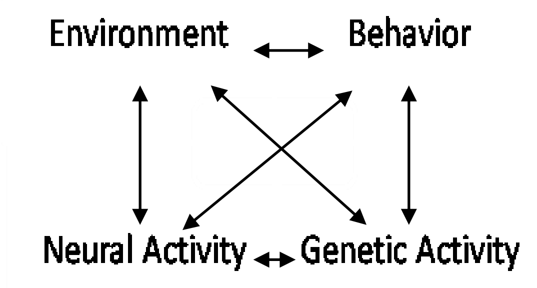

Figure 1. Levels and relationships of influences on human development. Adapted from "Experiential canalization of behavioral development: Theory" by G. Gottlieb, 1991, *Developmental Psychology*, *27*, p. 6. Copyright 1991 by the American Psychological Association.

As such, this study utilizes a combination of behavioral measures and neuroimaging technology, specifically fMRI, to investigate the neural correlates of mathematical processing associated with error detection. The primary purpose of this study is to examine error detection skills as related to performance on the *Error Detection* task. The task is composed of forty simple arithmetic problems (i.e., single- and double-digit addition, subtraction, and multiplication problems) typically encountered by elementary school-age children within academic contexts.

Implications

This study holds important implications for educational curriculum and intervention programming for children with mathematical disabilities. By understanding children's ability to detect errors when they are made and the specific types of errors children commit when calculating arithmetic problems, specific and appropriate interventions can be designed to address these deficits. By observing the neural correlates associated with the failure to detect errors, we will gain an understanding of the cognitive mechanisms supporting this ability. Understanding of the types of errors frequently committed by children who struggle with mathematics may provide better diagnostic tools to identify the specific deficits facing a particular child, thereby resulting in targeted intervention. With such knowledge, educational and intervention programming can be designed to help children choose problem solving strategies aimed at reducing the likelihood of an error occurrence and procedures for validating their answer. This chapter opened with a quotation from Easley and Zwoyer (1975) suggesting that children's errors have the power to yield insight into what the child is thinking, and that by examining those errors we can become better equipped to teach our children.

It should be noted at the outset that this study represents a first attempt to investigate mathematical error detection abilities utilizing a combined behavioral and fMRI paradigm and, as such, contains exploratory hypotheses. It is my sincere hope that this study will fill not just a gap in the literature regarding the neural mechanisms supporting the ability to detect mathematical errors, but furthermore, that the knowledge gained will be utilized by both researchers and educators whose aim is to help children understand the complex world of mathematical learning and thinking.

Chapter I has been a brief presentation of the literature and statement of the purpose of the current study. Chapter II will provide a detailed review of the literature from the fields of Mathematics Cognition, Mathematics Learning Disabilities, and Cognitive Neuroscience of Mathematics Learning. Literature detailing subtypes of mathematical disabilities will be discussed, along with a review of the major cognitive mechanisms supporting mathematical thinking and learning, addressing both domain-specific and domain- general cognitive abilities. Chapter III provides details regarding the hypotheses, predictions and methodological design of the current study, participant characteristics, measures, and procedures. In Chapter IV, the results of the statistical analyses are reported. Chapter V is a discussion of these findings, as they are related to the literature presented and suggestions for future directions of research.

CHAPTER II

Review of the Literature

This chapter will provide a review of the relevant literature that serves as the theoretical framework for this study. Three bodies of literature have been reviewed in support of this study: Mathematics Cognition, Mathematics Learning Disabilities, and Cognitive Neuroscience of Mathematics Learning. Each of these bodies of research has contributed to my understanding of how children with and without learning disabilities learn mathematics and the neural mechanisms that support this learning. The field of Math Cognition has a long standing interest in the study of mathematics learning, investigating how children develop number sense, learn mathematical concepts, apply mathematical procedures, and more recently in understanding the types of errors they make when calculating arithmetic problems. The second field, Mathematics Learning Disabilities, has provided a framework by which I have come to understand the unique characteristics and needs of children who struggle with mathematics learning. Understanding how learning occurs for children to whom mathematics comes naturally tells one side of the story. From these children, researchers have gained an understanding of the cognitive mechanisms that support typical learning and development. Studying children who struggle with mathematics learning tells another part of the story. The types of errors they make and the challenges they face in detecting errors provides insight into their cognition. Finally, by studying research from the field of Cognitive Neuroscience of Mathematics Learning, I have come to understand the neural mechanisms known to support mathematics cognition. Although ‘younger’ than the other fields, Cognitive Neuroscience of Mathematics Learning has much to offer in understanding how the human brain processes number and learns arithmetic, both for those who develop typical mathematical skills and those who struggle to learn mathematics.

This dissertation is situated at the junction of these three fields of study. By combining what is known about the cognitive mechanisms supporting mathematical development with the errors commonly committed by children who struggle with mathematics, and the neural circuitry supporting numerical and mathematical processing, I have created an *Error Detection* task as the central experimental measure for this dissertation.

Mathematics Cognition

The field of Mathematics Cognition arose from research conducted within the fields of Cognitive Psychology and Mathematics Education, and has become a legitimate field in its own right. Research has addressed both the domain-general and domain-specific cognitive mechanisms supporting mathematics learning, and, more recently, has examined the types of errors made by children who struggle with mathematics. Although the etiology of MD is as yet unknown, two predominant views exist. The first suggests that MD is related to a deficit in general cognitive mechanisms, particularly those related to working memory and attentional control resulting in a co-occurring form of MD, (cMD). In contrast, other research suggests a core deficit in number sense lies at the root of MD; termed a Pure MD (pMD), it is believed to be distinct to mathematics and to not share overlap with other disabilities.

Domain-general Cognitive Mechanisms

Research investigating the general cognitive mechanisms that contribute to mathematics cognition, points toward: working memory, visuospatial processing, and attentional control as fundamental to the development of sound mathematical thinking and success. Of these three, working memory has received the most attention by researchers to date.

Working memory. Working memory is most often understood as the process(es) by which one item is held aside for later consideration, while another item(s) is being actively processed. Baddeley and Hitch's working memory model (Baddeley, 2001; Baddeley & Hitch, 1974), by far the most influential model, subdivides working memory into three components, two slave systems that manage and process stimuli, the phonological loop and the visuospatial sketchpad; and the central executive, which monitors and coordinates information from these systems.

With regards to mathematics, fact retrieval is thought to be processed through the phonological loop (PL) with rote, over-learned arithmetic facts stored as part of the semantic memory system (Geary, 1993, 2010a). The visuospatial sketchpad (VSSP) is thought to be primarily responsible for coordinating spatial information, such as conceptual and procedural use of a number line (Geary et al., 2009) and multi-columnar arithmetic (Heathcoat, 1994; Raghubar, Cirino, Barnes, Ewing-Cobbs, Fletcher, & Fuchs, 2009; Russell & Ginsburg, 1984). Serving as a general coordinator, activating attentional control, and prohibiting the interference of unnecessary information, the central executive (CE) serves as a gateway between the PL and VSSP.

The relative contribution of each subcomponent of the working memory system is not yet fully understood. In fact, the relationship between deficits within any one of these subcomponents and resulting mathematical difficulties remains unclear.

> Many LA [low achieving] children do not have working memory deficits on standard measures of the central executive, phonological loop, or visuospatial sketch pad, but a

> subset of them may have specific deficits on the inhibitory control subcomponent of the central executive. (Geary, 2010, p. 131)

It is clear that changes occur within the working memory system over the developmental period of childhood, possibly resulting in differential importance or reliance on any one subsystem (Geary, Hoard, Nugent & Byrd-Craven, 2008). Meyer, Salimpoor, Wu, Geary, and Menon (2010) reported changes in the role of working memory components between second and third grade; where the central executive was the best predictor of math achievement in second grade, and the VSSP for third (see Raghubar, Barnes, & Hecht, 2010, for review of working memory and mathematics).

Visualspatial processing. The role of visualspatial processing is even less defined than WM in terms of mathematics learning. Most research examining the relationship between visualspatial processing and mathematics has linked the VSSP to spatial tasks such as alignment of numerals in multi-digit problems and incorrect transcribing of numerals when writing them (Heathcoat, 1994; Raghubar et al., 2009; Russell & Ginsburg, 1984). Such studies have found that children, at varying developmental levels, commit errors related to the mis-alignment and use of numerals in arithmetic problems with vertical columns. Raghubar et al. (2009) identified the miswriting of numerals as a common error made by children, particularly those with MD, when calculating multi-digit arithmetic problems in a paper-and-pencil format. Heathcoat (1994) described the VSSP as a blackboard, of sorts, where partial problems are visually stored while various arithmetical operations are performed. The exact role of visualspatial processing as related to mathematics remains unclear. In fact Raghubar et al. (2009) note that , visual representations and visual WM are not the same as spatial working memory making it difficult to discern the role of each, considering that relatively few studies that have investigated their contribution to mathematics cognition.

Attentional control. The research investigating attentional control and performance in mathematics has suggested a strong relationship between the two, more so than with RD (Gross-Tsur et al., 1996; Shaywitz, Fletcher, & Shaywitz, 1994). Children who have low performance in mathematics have more difficulty than their typical developing peers on tasks requiring cognitive task switching (e.g., Wisconsin Card Sorting Task) and tasks with the potential for high interference (e.g., Stroop Test) (Bull, Johnston, & Joy, 1999; Bull & Scerif, 2001). The relationship between attentional control and mathematical performance is at the very root of the co-occurring form of MD (cMD), which is thought to result from domain-general cognitive deficits, including working memory, attentional control, and inhibition to response.

Research has suggested that certain mathematical errors may be the result of deficits in attentional control, rather than a deficit in mathematics per se. In particular, children with poor attentional control have difficulty switching between arithmetical operations and inhibiting the interference of irrelevant information. After calculating several problems necessitating addition, children with attentional deficits who struggle with mathematics have difficulty switching to subtraction (Jordan & Hanick, 2000; Rourke, 1993; however, see Raghubar et al., 2009 for alternative findings. Geary and colleagues (Geary, Hoard, & Bailey, 2011) found that fact retrieval deficits in young children may be related to an inability to suppress irrelevant information during the retrieval processes.

Domain-specific Cognitive Mechanisms

In addition to the domain-general cognitive abilities described above, a number of domain-specific abilities support mathematics learning. It is becoming increasingly understood that a well-developed number sense, developmentally mature counting concepts and the use of mature calculation procedures (Butterworth, 2005; Butterworth & Reigosa, 2007; Geary 1990; 1993, 2010a) all support mathematics cognition.

Number sense. The concept of number sense "includes an implicit and potentially inherent understanding of the *exact quantity* of small collections of actions or objects and of symbols (e.g., Arabic numerals) that represent them (e.g., '3' = ■■■), and of the *approximate magnitude* of larger quantities" (Geary, 2010a, p. 130). Errors made by children with a deficit in number sense include the inability to quickly and accurately identify the exact quantity of a small set of objects (i.e., 3 or 4), difficulty adding or subtracting small quantities from a small set of objects (i.e., 3 – 1 = 2), and difficulty estimating the magnitude of a larger set of objects and the results of arithmetic problems (Geary, 2010a).

Counting concepts. The acquisition of increasingly sophisticated counting concepts develops slowly throughout childhood. One of the first tasks of elementary school children, at least in Western cultures, is teaching the basic structure of the base-10 number system. Children learn the relationship between number names and numerals, and learn concepts such as one-to-one correspondence and cardinality. Children who struggle with mathematics have more difficulty learning these early counting concepts than their typically developing peers (Geary, Hoard, Byrd-Craven, Nugent, & Numtee, 2007; Geary, Bow-Thomas, & Yao, 1992), tend to rely on comparatively immature counting procedures and back-up strategies for a longer time than their typically developing peers (Geary et al., 2007), use developmentally less mature counting procedures and commit more errors during counting tasks.

Calculation strategies. The variability in calculation strategies exhibited in young children has been well documented by Siegler (1999). Children's calculation strategies gradually progress from simple to complex with practice, experience, and time. The most immature calculation strategies rely on counting to arrive at the answer. In the case of addition, the *Count From 1*strategy is utilized by the youngest and most developmentally immature child by counting each addend in a given problem beginning with “1”; for 2 + 3, the child begins by counting (perhaps with fingers) “1, 2” followed by “1, 2, 3” and only then combining the counts, “1, 2, 3, 4, 5”). The *Shortcut Sum* strategy is an extension of the *Count from 1*, in that the child counts directly to the sum in one continuous count (e.g., “1, 2, 3, 4, 5”). Using the *Count from First* strategy, the child will count the digits beginning with the first addend (e.g., in this example the first addend is 2, so the count progresses “2, 3, 4, 5”). As the calculation strategies mature and the child discovers or is taught the *Min* strategy, learning to count the summation beginning with the larger digit and adding on the smaller digit (in this example, beginning with 3, so that the count progresses “3, 4, 5”). The most developmentally mature strategy is direct retrieval, where no overt or covert counting is required to arrive at the answer to an arithmetic problem. The development of direct retrieval requires the accurate and consistent pairing of arithmetic problems with their solutions over a period of time and with practice (Siegler, 1996).

As new calculation strategies are learned and practiced, developmentally less mature strategies are slowly replaced. However, children with MD are slower to make the transition to more sophisticated strategies and often fail to make the switch to direct retrieval at all (Geary, 1993; Geary, Widaman, Little, & Cormier, l987; Fleishner, Garnett & Shepherd, 1982). These children tend to rely on less mature strategies, leaving themselves open to the commitment of more frequent errors when calculating arithmetic problems (Geary, Brown & Samaranayake, 1991; Shalev, Auerbach, Manor, & Gross-Tsur, 2000; Ostad, 1997).

Common Error Types During Simple Arithmetic Calculations

While the cognitive mechanisms discussed above provide an overview of the cognitive components supporting numerical and mathematical processing, researchers have also begun to examine the *types* of errors committed by children who struggle with mathematics (Dehaene & Cohen, 1995, 1997; Geary et al., 2011; Jordan & Hanick, 2000; Raghubar et al., 2009; Rourke, 1993; Siegler, 1988). This examination has provided rich detail regarding the areas of mathematics learning that are most problematic for children with MD, and has validated some of the work on MD subtypes (Jordan, Hanich, & Kaplan, 2003a; Raghubar et al., 2009). Four error types have been discussed in the by literature as frequently committed by children with MD: *string intrusion* (Geary et al., 2011; Siegler, 1988), *wrong operation* (Jordan & Hanick, 2000; Raghubar et al., 2009; Rourke, 1993), *associated fact* (Siegler, 1988), and *global errors* (Dehaene & Cohen, 1995, 1997) (see Table 1).

String intrusion errors. Rather than representing true calculation, an error committed by string intrusion occurs when the answer provided is simply the next number in the string of digits (4 x 7 = 8), belonging to either the first or second addend. String intrusion errors are common during calculation and fact retrieval by young children (Geary et al., 2011; Siegler, 1988) and represent counting more so than calculation.

Wrong operation errors. Children who incorrectly calculate the answer to an arithmetic problem by switching operations, while maintaining the original digits, are said to commit wrong operation errors (i.e., 4 + 8 = 32) (Jordan & Hanick, 2000; Raghubar et al., 2009; Rourke, 1993). These problems often occur when a new operation is introduced after two or more consecutive same operation problems (Jordan & Hanick, 2000; Rourke, 1993).

Associated fact errors. The third error type occurs when children recall the answer to a nearby or associated fact (i.e., 3 x 9 = 24; rather than 27, where 3 x 8 = 24). This error type may be related to an inability to inhibit or suppress extraneous information (Geary, 2011; Siegler, 1988).

Global errors. The fourth error type is discussed in Dehaene's triple-code model (Dehaene & Cohen, 1995, 1997; Dehaene et al., 2003) which predicts simultaneous processing of numerical stimuli through both the direct and indirect processing pathways, allowing the indirect pathway to detect any gross errors committed by the direct pathway (i.e., 2 x 3 = 23) (see Cognitive Neuroscience of Mathematics Learning section for details on this model). Global errors represent no real use of mathematical calculation, but instead simply combine the digits in the arithmetic problem.

The wrong operation and associated fact errors may be related to a sub-component of working memory that serves as an executive control function supporting inhibition of irrelevant information (see Geary, 2011 for brief discussion). An alternative view is that deficits of this type are result from relative weakness in accessing or manipulating nonverbal representations of number, such as the mental number line (Cohen et al., 2000).

Table 1.

Common Errors Committed in Simple Arithmetic

Error Type	Example
String Intrusion Errors	4 x 5 = 6
Associated Fact Errors	5 + 7 = 13
Wrong Operation Errors	9 x 3 = 12
Global Errors	2 + 8 = 28

Common Error Types During Multi-digit Arithmetic Calculations

The errors described above are related to simple arithmetic calculations. Raghubar et al. (2009) identified procedural errors commonly committed during multi-digit calculation, among them: *problems borrowing across zero, problems carrying, and no decrement with borrowing*. In addition, they identified *problems with alignment of the digits* as an additional error type committed during multi-digit calculations (see Table 2).

Problems borrowing across zero. Children who have difficulty borrowing across zero fail to carry out the necessary procedures for re-grouping when the numeral zero appears in the minuend (i.e., the number to be subtracted from in a math problem). Geary (2000) explained, "when there is a 0 in the tens column many children will directly borrow from the hundreds column, a reflection of their failure to understand the base-10 system; most Asian children do not make this type of error" (p. 14). Such findings support the necessity of a well-developed understanding of the base-10 system to the development of mathematics cognition.

No decrement with borrowing. When committing this error type, children fail to perform the necessary re-grouping procedures during subtraction. The following example for solving the problem 814-329 illustrates this error.

> 10 ones must be 'borrowed' from the tens column and moved to the units column so that the operation 14 - 9 can be completed. Many children fail to understand that the 1 added to the 4 to make 14 represents 1 set of 10 units; they conceptually treat this as 1. (Geary, 2000)

Problems carrying. Problems carrying are those reflecting a procedural error when re-grouping during addition. Such error types are evident when the child fails to understand the conceptual or procedural steps necessary in carrying over excess quantity (i.e., quantities greater than nine) from one column to another when using the operation of addition.

Misalignment of the digits. Errors of this type are most often associated with the incorrect alignment of columns during multi-digit arithmetic problems and incorrectly reading and transcribing numerals. When children are required to transcribe horizontal problems into a vertical format or to write arithmetic problems presented verbally are particularly prone to this committing this type of error.

Table 2.

Common Errors Committed in Multi-digit Arithmetic

Problem Type	Example
Problems borrowing across zero	1005 - 98
Problems with carrys	2589 + 423 = _____
No decrement with borrowing	753 - 89
Misalignment of numerals	76 + 321 = _____

Error Detection

Math Cognition researchers have begun to examine not only the types of errors that children make, but their ability to detect errors when they do occur. Siegler (1988) described the ability to detect errors in terms of the confidence criterion, something akin to an internal monitoring system. When performing arithmetic calculations, a child can choose between direct retrieval and strategy use. If the child chooses direct retrieval, an internal confidence criterion is set against which the child checks the plausibility of the answer based on what she believes to be the correct answer for the given problem. If an incorrect answer is retrieved and the child is successful in recognizing the error, she is said to have a high confidence criterion; a child who does not recognize the implausibility of an incorrect answer is deemed to have a low confidence criterion. This relates to the interaction of the direct and indirect transcoding paths in Dehaene's triple-code model (Dehaene, 1995, 1997; Dehaene et al., 2003), which suggest that the two paths operate in unison to serve as an internal error checking system. Overall, children who struggle with mathematics learning commit more errors than their typical developing peers, are less able to detect errors that have occurred (Geary, 2011; Raghubar et al., 2009; Siegler, 1988), and fail to recognize errors in their own work (Sigler, 1988).

Mathematics Learning Disabilities

Since the 1968 recognition of individuals with learning disabilities (LD) as a federally designated group, research committed to understanding the nature, development and prognosis of learning disabilities has increased. In fact, students identified with specific learning disabilities are the largest group of students with disabilities receiving services under the Individuals with Disabilities Education Act (IDEA) (U.S. Department of Education, 2009). Even so, much work lies ahead and many challenges remain. Three decades after the designation of people with learning disabilities as a federally protected group, the field remains riddled with controversy. Although specifics are debated still today, it is generally agreed that children with learning disabilities are a heterogeneous group exhibiting difficulties in learning, despite having adequate intelligence, vision, hearing, and emotional skills, and appropriate instructional opportunities (Lyon, Fletcher, Fuchs, & Chhabra, 2006). A considerable literature base has established the development of language and reading disabilities (RD) (Shaywitz, B., Lyon, & Shaywitz, S., 2006; Temple, et al., 2003; Weismer, Plante, Jones, & Tomblin, 2005); however, comparatively little has emerged regarding the nature and progression of MD (Dehaene & Cohen, 1995; Fazio, 1999; Geary & Hoard, 2001; cf. Rasanen & Ahonen, 1995). While much can be said about the field of learning disabilities as a whole, for the purpose of the present study the focus is restricted to mathematics learning disabilities.

Prevalence of MD

Of the research conducted, large-scale studies indicate that children with MD comprise between 6% and 7% of the school-age population, a level comparable to RD (Badian, 1983; Geary & Hoard, 2001; Gross-Tsur et al., 1996; Kosc, 1974; Shalev et al., 2000). Furthermore, there is a high rate of co-occurrence between these disabilities, with a reported 40% of children with MD also having a RD (Lewis, Hitch, & Walker, 1994). In addition, MD and attention deficits often co-occur as well, making diagnosis, intervention, and remediation an increased challenge (Fletcher, 2005; Marshall, Hynd, Handwerk, & Hall, 1997; Zentall, 1990; Zentall, Smith, Lee, & Wieczorek, 1994).

Definition of MD

The DSM-IV-TR defines MD as a deficit in mathematical ability that is one standard deviation or more below what would be expected given a child's chronological age, measured intelligence, and educational experiences (American Psychological Association, DMS-IV-TR, 2000). If the definition alone were not vague enough, another challenge lies with the multiple and seemingly interchangeable terms used to define challenges to mathematics learning, among them: dyscalculia, acalculia, math dyslexia, and math learning difficulties. These terms, while seemingly interchangeable are often used to describe very different groups of children struggling with mathematics, with no standardization within the field. To complicate matters further, if a child meets the general definition of a learning disability and is identified has having one or more of the characteristics of a child struggling with mathematics, he still must be formally identified; a process that varies dramatically from school-to-school, district-to-district and state-to-state.

Characteristics of children identified with MD

While, by and large, it is agreed upon that children with MD are a heterogeneous group displaying a wide range of abilities and deficits, certain core characteristics have emerged as indicators of MD. These factors include: poor or underdeveloped number sense, the reliance on immature strategies during procedural execution, low reliance on direct retrieval of math facts, a high error rate when direct retrieval is utilized (Geary et al., 2011) and persistent, ongoing difficulties acquiring mathematical competencies and fluency. That is, poor performance, in spite of normal intelligence, vision, hearing, and emotional skills, and appropriate instructional opportunities, for more than one academic year (Geary et al., 2007; Murphy, Mazzocco, Hanich, & Early, 2007). It appears these core deficits are shared by the many of children who struggle with mathematics learning.

Mazzocco (Mazzocco & Thompson, 2005) and Geary (Geary et al., 2009) have reported characteristics associated with early poor math achievement that are predictive of a subsequent MD diagnosis. Mazzocco and Thompson (2003) identified four mathematical skills that are linked with, and in fact, predictive of MD: magnitude judgments, mental addition of one-digit numbers, reading numerals, and number constancy. From an original sample of 226 kindergarten children, Mazzocco and Thompson (2005) isolated 23 children who experienced persistently low math achievement, defined as low standardized math test scores in both second and third grades. Seeking to examine the specific cognitive and neuropsychological measures most effective at predicting poor performance in math, the authors examined logistic regression models that best predicted an identification of MD three years later (i.e., in third grade), using kindergarten predictors of: standardize math test scores, measures of visual perception, rapid naming tasks, IQ measures, and selected demographic variables. A core subset of four kindergarten characteristics was found to be highly predictive of MD: "reading numerals, number constancy, magnitude judgments of one-digit numbers, and mental addition of one-digit numbers" (p.150). Lower scores (or a fail on a pass-fail scale) on these measures resulted in an increased likelihood of MD classification in both second and third grades. These findings suggest that these four skills may represent core, early developing, quantitative abilities necessary for optimal performance in mathematics within the context of formal schooling, at least during second and third grades.

Similar research reported by Geary et al (2009) identified four stable groups of first graders: math learning disabled, low achieving, typical achieving, and high achieving. Cognitive profiles of these groups included several notable findings. In general, children in the different groups demonstrated not only different levels of mathematical competence at the outset, but also progress at different growth rates. "The best constellation of variables for predicting membership in the MLD [math learning disabled] class included IQ and the phonological loop and visuospatial sketchpad scores" (p. 425); the next most accurate predictors (after IQ and Working memory measures) included scores from a Number Line task (Siegler & Booth, 2004), the Number Sets test (Geary et al., 2007), and the count error task (Geary et al., 2009). Interestingly, while the MLD group had difficulty with correct retrieval of addition facts, this did not emerge as their most serious deficit, suggesting "an earlier emerging and potentially more fundamental deficit may exist in their number sense" (p. 426). In comparison to their MLD peers, the low achieving group exhibited moderate difficulties with fact retrieval and number sense, but no deficits in working memory. The high achieving group was primarily characterized by strong visuospatial skills, well-developed number sense, and strong and accurate use of retrieval-based procedures for recalling addition facts.

Taken together, these findings suggest the possibility of two very different etiologies of MD, those who have deficits in core number sense and those with a deficit related to variances in working memory components.

Identification of Mathematical Disabilities

To complicate matters further, if a child meets the general definition of a learning disability and is identified has having one or more of the characteristics of a child struggling with mathematics he still must be formally identified as having a mathematics disability. Historically, students were identified as having a learning disability based on a discrepancy between their measured level of intellectual ability (i.e., IQ score) and their actual level of achievement. Recent arguments suggest this method is not reliable (Francis et al., 2005). An alternative approach, often utilized in research, makes use of cutoff criterion scores from standardized tests, most commonly the Woodcock Johnson Achievement Test (WJIII; Riverside Publishing, 2008) and the Wechsler Individual Achievement Test (WIAT; Psychological Corporation, 1999). This too, presents a challenge; scores ranging from the 5th to 30th percentile have been reported in the literature to identify children as learning disabled (Geary et al., 2007). What's more, Murphy et al. (2007) found that the characteristics associated with MD are dependent on the cutoff criterion that is chosen, with cognitive profiles varying as a direct result of the criterion utilized for group classification. Geary (2004) notes that "a score lower than the 20th or 25th percentile on a mathematics achievement test combined with a low-average or higher IQ score are typical criteria for diagnosing MLD [mathematics learning disabilities]" (p. 5). The Response to Intervention (RtI) method, although not widely used within research at the present time, is a third model that attempts to answer the challenges created by the discrepancy based approach. Under RtI, a student is identified as learning disabled only after she has demonstrated delays in achievement *and* has not responded to intervention efforts within the classroom (Fuchs, Mock, Morgan, & Young, 2003). Such a method may, yet again, result in very different cognitive profiles of children classified as MD. Geary (2004) explains that in addition to the individual differences contributing to learning disability identification, variations within instructional approaches may also play a role in the identification of MD.

> Instruction that focuses on mathematics as an applied domain tends to de-emphasize the learning of procedures and mathematical facts and to emphasize conceptual understanding (National Council of Teachers of Mathematics, 2000), whereas procedures and facts are more heavily emphasized in instruction that approaches mathematics as a scientific field to be mastered. (California Department of Education, 1999, p.4)

As such, the instructional environment the child is in may dictate whether he or she is deemed as having difficulty with a particular aspect of mathematics learning. In spite of the challenges, research has continued to investigate aspects of MD with particular attention to the examination of MD subtypes.

MD Subtypes

In 1993, Geary provided a review of the domain-specific abilities known to support mathematics cognition and identified the characteristics of specific deficits and categorized them into three MD subtypes: Semantic, Procedural, and Visuospatial. Fact retrieval deficits, including low reliance on direct retrieval, high error rate with direct retrieval, and variable response times were identified as the earmarks of the *Semantic subtype*. The *Procedural subtype* is manifested by immature calculation procedures, high error rates executing procedures, and delays in understanding arithmetic procedures. Children said to experience the *Visuospatial subtype* display deficits spatially manipulating numbers in tasks such as multi-digit arithmetic and place value determination. Since that time, research has validated the Semantic and Procedural subtypes (Jordan, et al., 2003a; Raghubar et al., 2009, respectively).

Nearly two decades later Geary (2010) revisited the proposed subtypes of MD, both recognizing number sense as a previously unforeseen MD subtype (Geary, 2010; Hanich, Jordan, Kaplan, & Dick 2001; Jordan, et al., 2003; Raghubar, et al., 2009) and acknowledging the mixed support in the literature for the visuospatial subtype. While research continues to examine potential subtypes of MD, no clear cut determination has been reached.

Taken together, the research on MD, paints a picture of a child who may or may not face deficits in number sense yielding difficulties with approximate math tasks, number estimation and comparison activities; may or may not exhibit fact retrieval deficits or be characterized by high error rates and inconsistent response times when recalling basic arithmetic facts; may or may not be challenged by procedural deficits, resulting in misapplication of arithmetic procedures and strategies; and may or may not have deficits in working memory and attentional control, which lead to an increased likelihood of error commitment. At the same time, this child may or may not recognize errors when they do occur and may or may not have an adequate monitoring system to break the error cycle, thereby opening themselves to the chance of repeating the same error patterns over and over again.

Regardless of the exact source of the deficit, the overall result remains the same; children who struggle with mathematics tend to avoid situations that call upon these skills and are at increased risk of failing to develop the complex and multi-dimensional mathematical skills necessary for success in society (Rivera-Batiz, 1992). Thus, it is critical that appropriate, effective interventions, designed in alignment with what we know to be the best practices associated with mathematics learning, be developed for use in remediation of deficit skills (Kroeger, Brown, & O'Brien, 2012).

Math Anxiety

Although not yet established in the literature as correalationally related to any of the MD subtypes, it is known that anxiety related to mathematics has a direct effect on one's performance (Faust, 1996; Hembree, 1990). Hembree's (1990) meta-analysis of 151 studies indicated that higher levels of math anxiety are related to poorer performance on arithmetic tasks and avoidance of mathematical experiences. Faust (1996) confirmed this, reporting anxiety effects on performance of an addition task. Participants identified as either having low or high anxiety regarding mathematics were presented with a verification task requiring them to identify if the stated answer to the problem was true or false. High anxious participants were slower to decide that the answer was false when the answer differed by only one from the correct answer (e.g., 4 + 7 = 12), and were less accurate as the stated answers increased in deviation from the correct answer (e.g., 6 + 9 = 58), the opposite pattern of what would be expected. The poor performance that many with math anxiety experience may be related to an individual's inability to regulate feelings of anxiety as "treatment can restore the performance of formerly high-anxious students to the performance level associated with low mathematics anxiety" (Hembree, 1990, p. 44). The cause of this increased anxiety is as yet unclear; however, research from the neuroscience field suggests that the amygdala may play a role in anxiety regulation (Roozendall, McEwen, & Chattarji, 2009). In fact, research has indicated that increased levels of stress hormones lead to impaired memory retrieval and working memory (Roozendall, Barsegyan, & Lee, 2007).

Cognitive Neuroscience of Mathematics Learning

The third body of literature contributing the theoretical framework of the present study, Cognitive Neuroscience of Mathematics Learning, has yielded a number of neuropsychological models addressing the development of mathematical cognition. McCloskey and colleagues (McCloskey, Caramazza, & Basili, 1985; McCloskey, Solko, & Goodman, 1986) proposed a neuropsychological model consisting of three, independent systems supporting numerical processing: number-comprehension, number-production, and calculation, each supported by an underlying format-independent quantity code. The number-comprehension system transforms both Arabic and lexical number stimuli into semantic representations for use by the calculation system, which interprets arithmetical operation signs (e.g., +, -), carries out calculation procedures, and stores basic arithmetic facts. The output from the calculation system (i.e., the answer to the problem) serves as the input for the number-production system; this system is responsible for generating verbal and Arabic responses.

Campbell and Clark (1988) argue that the McCloskey model (1985, 1986) is not complex enough to fully explain the dynamic nature of numerical and mathematical processing, and that "the complexities inherent in number processing cannot readily be accounted for by distinct, modular systems of comprehension, calculation, and production, but can be accommodated by assuming specific, multifunction codes" (Campbell & Clark, 1988, p. 205). Their model proposes a format-specific representation of number and quantity that are related through interconnectivity between the codes, with each having the potential to activate within comprehension, production, and calculation functions.

At the present time, the most influential model of numerical processing and the one enjoying the most examination within research, is Dehaene's triple-code model (Dehaene &

Cohen, 1995, 1997; Dehaene, Piazza, Pinel, & Cohen, 2003). Under this model, numerical information is processed through one of three format-dependent systems: verbal, visual, or quantity. The interconnectivity between each system is regulated through two major paths. The direct pathway processes numerical information without regard to its quantitative meaning, transforming numerals from Arabic format into an auditory-verbal representation, utilized in the retrieval of rote math facts; the indirect pathway processes the quantitative value associated with numbers, allowing for comparative and estimation tasks. Many tasks involve both pathways and are supported by the central executive function of working memory that relies on the frontal lobe, and an error detection system that may be part of the Anterior Cingulate Cortex.

The Triple-Code Model of Numerical Processing

The triple-code model, (Dehaene & Cohen, 1995, 1997; Dehaene et al., 2003) describes three parietal circuits believed to support various components of numerical processing, hypothesizing that these circuits, or systems, are supported by distinct neuroarchitectures and relate to performance on specific tasks (see Figure 2). These

> three circuits coexist in the parietal lobe and capture most of the observed differences between arithmetic tasks: a bilateral intraparietal system associated with a core quantity system, a region of the left angular gyrus associated with verbal processing of numbers, and a posterior superior parietal system of spatial and nonspatial attention. (Dehaene et al., 2003, p. 488)

Figure 2. Parietal Circuits of the Triple-Code Model of Numerical Processing

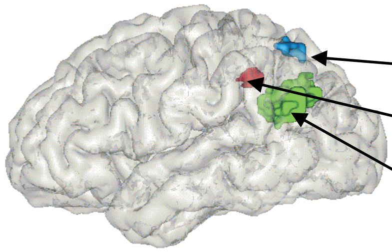

Figure 2. Parietal Circuits of the Triple-Code Model of Numerical Processing. PSPL = posterior superior parietal lobule. AG = angular gyrus. hIPS = horizontal segment of the intraparietal sulcus. Adapted from "Three Parietal Circuits for Number Processing" by S. Dehaene, M., Piazza, P. Pinel., & L. Cohen, 2003, *Cognitive Neuropsychology, 20,* p. 494. Copyright 2003 Psychology Press Ltd.

The triple-code model is a clear indication that quantitative processing replies on multiple brain regions, many of which are not specific to number or quantity. Although still speculative in nature, this model (Dehaene et al., 2003) has been validated to some extent through empirical research using both behavioral and neuroimaging designs (Ansari., 2008; Ansari & Dhital, 2006; Grabner et al., 2007; Holloway, Price, & Ansari, 2010; Jordan, Hanich, & Kaplan, 2003; Molko et al., 2003; Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004; Piazza, Pinel, Le Bihan, & Dehaene, 2007; Pinel, Piazza, Le Bihan, & Dehaene, 2004; Price, et al., 2007; Raghubar et al., 2009; Stanescu-Cosson et al., 2000). In the sections that follow, I provide a description of each system, the localization of each within the brain, and a review of the relevant research pertaining to each system.

The quantity system. The horizontal segment of the intraparietal sulcus (hIPS) processes quantity and number nonverbally, only in reference to the quantitative meaning of a given number (i.e., What is four?; How much is four?). This *quantity system* supports arithmetical operations and mathematical tasks requiring quantitative representation, such as those related to exact calculation, in particular subtraction (Chochon, F., Chochon, L., van de Moortele, & Dehaene, 1999; Lee & Kang, 2000); symbolic (i.e., number words and Arabic digits) and nonsymbolic (i.e., dot or block arrays) magnitude comparison (Ansari & Dhital, 2006; Holloway et al., 2010; Molko et al., 2003; Piazza et al., 2007; Price, et al., 2007); numerosity detection (Piazza et al., 2004); and number comparison (Pinel et al., 2004) tasks. The *quantity system* has received extensive research attention as deficits within its functioning are thought to possibly represent a pMD that is unique to numerical and quantitative processing tasks that are supported by neural activation in the parietal lobe (Rubinsten & Henik, 2009). Despite its relative prominence in research, it is not yet clear if this system is specific to numerical and mathematical processing or is shared with other processing systems and tasks.

Ansari and Dhital (2006) reported activation in the intraparietal sulcus (IPS) in both children and adults during a nonsymbolic magnitude processing task, with greater IPS activation in adults, suggestive of developmental changes in activation patterns. The same study reported additional regions of activation in the dorsolateral prefrontal cortex (DLPRC) and the left inferior frontal gyrus (LIFG) in children, indicative of greater reliance on working memory and attentional resources utilized during developmental periods.

Piazza et al., (2007) extended this research by examining IPS activation during a magnitude processing task of both symbolic and nonsymbolic stimuli. Participants were permitted to adapt to a set of quantities presented as either Arabic numerals or dot arrays. After a period of adaptation, participants were presented with a change in either quantity (i.e., absolute size of quantity represented), notation (i.e., Arabic numerals or arrays), or both. Increased IPS activation was evident whenever a change in number quantity occurred, invariant of a change in the presentation condition. These results provide “a first piece of evidence for an abstract coding of approximate number in the parietal cortex” (Piazza et al., 2007, p. 296) and demonstrate “that the magnitude code of the parietal cortices is common to numerosities and numerical symbols" (Piazza et al., 2007, p. 298).

Using fMRI with adult participants, Holloway et al., (2010) investigated brain regions supporting both symbolic and nonsymbolic magnitude processing hypothesizing that nonsymbolic processing would be supported by regions in the superior parietal lobe, while symbolic processing would activate regions found in the left tempropariental junction. Their results provide support for these hypotheses suggesting "that while there is evidence of a common abstract representation of numerical magnitude, there are also important differences in the pathways mediating the mapping from external representations to internal ones" (p. 1016).

Further evidence suggests that the hIPS may show impaired functionality in participants identified with dyscalculia of both genetic and developmental origin as compared to their typical developing peers (genetic origin: Molko et al., 2003; developmental origin: Price et al., 2007). Molko et al. (2003) report behavioral results consistent with previous studies, (e.g., lower accuracy on arithmetic task; longer reaction time on word and non-word reading tasks), as well as, functional differences in activation patterns association with both exact and approximate calculation tasks with adults identified with dyscalculia of genetic origin (i.e., Turner Syndrome). Additionally, anatomical abnormalities were identified indicating structural differences in the brain regions supporting these tasks.

> fMRI revealed a functional correlate of the arithmetic impairment: there was insufficient recruitment of the right intraparietal sulcus as a function of number size. The morphological analysis showed an abnormal length, depth, and sulcal geometry of the right intraparietal sulcus, reflecting an important anatomical disorganization of this region in TS [Turner Syndrome]. (Molko et al., 2003, p. 853)

In similar work, Price et al. (2007) provide evidence suggesting that developmental dyscalculia may stem from impaired functioning of the hIPS, reporting that the right hIPS is not recruited to the same extent as in their typical developing peers, resulting from "either a weakened parietal representation of numerical magnitude in DD [developmental dyscalculia] and/or a reduced ability to access and manipulate numerical quantities" (p.R1042). On a magnitude comparison task, children with DD performed more poorly than their typical developing peers, with a significant group by distance (i.e., small v. larger distances between magnitudes) interaction. Activation patterns in the hIPS, fusiform gyrus, medial prefrontal cortex are suggesting of "abnormalities in the functional neuroanatomy underlying numerical magnitude processing in DD" (Price et al., p. R1042).

In addition to magnitude comparison tasks, the hIPS has also been shown to support processing of number comparison tasks. Pinel et al., (2004) have demonstrated activation in the hIPS during comparison tasks across differing modalities (e.g., number, size and luminance), and that each of these comparisons are mediated by a respective distance effect (i.e., number processing is mediated by the numerical distance effect (Moyer & Landauer, 1967); physical size is mediated by a size distance effect that is similar to the numerical distance effect). Furthermore, each dimension (i.e., number, size, and luminance) is accompanied by activation peaks which although "are neither processed by a parcellation of highly specialized cortical subregions nor by a single generic comparison system" (p. 990) nevertheless are suggestive of a "distributed coding along the length of the intraparietal sulcus, with partially different local peaks for each dimension, … but considerable interdimensional overlap and with convergence toward precentral cortex" (p. 990-991).

On a more basic level, the hIPS is also activated during numerical recognition tasks. Piazza et al. (2004) have reported results suggestive of some level of shared neural mechanisms supporting numerosity recognition in both adult humans and the macaque monkey and "provides important support for the notion that all humans start life with a nonverbal representation of approximate number inherited from our evolutionary history" (p. 553).

Taken together, these results support the predication of the triple-code model (Dehaene, 2003) regarding the role of the hIPS in semantic, quantitative processing of numerical representations. The evidence does not, however, resolve the question of domain specificity, that is, whether a dedicated neural network exists specifically for processing number (versus nonsymbolic stimuli). In fact, Piazza et al. (2007) argue that "the question of domain specificity might be an ill-posed question, or at the very least, one very difficult to answer with fMRI alone" (, p. 302).

The verbal system. Comprised primarily of the left angular gyrus (AG), the *verbal system* supports exact calculation tasks, in particular those requiring the retrieval of rote, well-learned arithmetic facts (e.g., multiplication facts and addition facts that sum to less than ten). Because the *verbal system* processes numerical stimuli as strings of words, rather than as Arabic digits or magnitude estimations, it provides no information whatsoever regarding quantity. Proposed to be part of the language system supporting verbal, short-term memory and reading tasks, (for reviews, see Fiez & Petersen, 1998; Paulesu, Firth, & Frackowiak, 1993; Price, 1998) the AG "contributes to number processing only inasmuch as some arithmetic operations, such as multiplication, make particularly strong demands on a verbal coding of numbers" (Dehaene et al., 2003, p. 494) and is therefore is not dedicated solely to numerical processing.

Research demonstrated increased AG activation in exact calculation tasks requiring multiplication or addition fact retrieval (Chochon et al., 1999; Gruber, Indefrey, Steinmetz, & Kleinschmidt, 2001; Lee, 2000) as opposed to subtraction and division tasks. Stanescu-Cosson et al. (2000) examined activation differences between exact and approximate calculation problems, with both small (1-5) and large (5-9) addends and found increased AG activation for exact calculation addition tasks, particularly when the addends sum to less than 10, and an increase in parietal activation during approximation tasks. Additionally, an increase in parietal activation was found when calculating (under both exact and approximate conditions) with large numbers, as opposed to small.

Grabner et al. (2007) examined the effect of individual differences in mathematical competence in mental calculation. Controlling for IQ, they found that mathematically competent adults displayed greater activation in the left angular gyrus during a task requiring them to determine if the solution to a presented multiplication problem was correct or incorrect, when compared to their less mathematically competent peers. Their work "provided first evidence that the activation of parietal cortices during mental calculation is modulated by individual differences in mathematical competence independent of other intellectual abilities" (p. 354).

Left AG activation was further confirmed by Grabner et al. (2009) whose results underscore the role of the AG in retrieval of arithmetic facts. Results from post-scanner self-reported strategy use for arithmetic problems indicated greater left AG activation associated with self-reported retrieval strategies when compared with procedural based strategies. Furthermore, their "analyses demonstrated that arithmetic problem solving strategy predicts unique variance in lAG [left angular gyrus] activation over and above task difficulty and individual differences in mathematical competence" (p. 607).

As the verbal system is not dedicated to quantitative processing, but shares a certain degree of overlap between mathematics and reading this may account for the fact that many children demonstrate co-morbid MD/RD (Ackerman & Dykman, 1995, Fazio, 1999; Geary, 2000, 2001; Lewis, Hitch & Walker, 1993); and that as much as 43% of the 6.4% of children classified as MD demonstrated poor reading achievement and 56% of the 4.9% of children who were RD demonstrated poor math achievement Badian (1983).

The visual system. The third circuit, the *visual system*, comprised of the posterior superior parietal lobule (PSPL) is active during tasks that place a demand on "a variety of visuospatial tasks including hand reaching, grasping, eye and/or attention orienting, mental rotation, and spatial working memory" (Dehaene et al., 2003, p. 498), thereby supporting tasks that require number comparison, multi-digit subtraction, multiple operations, and number counting. As such, this system is not specific to number processing. This system has, by far, been privy to the least amount of research activity and

> any reconciliation of those sparse and disparate data set must remain tentative. The hypothesis that we would like to propose is that this region, in addition to being involved in attention orienting in space, can also contribute to attention selection on other mental dimensions that are analogous to space, such as time. (Dehaene et al., 2003, p. 498)

Triple-code Model Transcoding Pathways

In addition to the three systems for numerical processing, the triple-code model proposes two distinct transcoding pathways linking them. The Direct pathway acts in such a way to allow communication between the between the verbal and visual systems. This pathway is primarily utilized during the retrieval of rote, well-learned arithmetic facts (e.g., 2 + 3 = 5) and processes numerals with no regard to the quantitative value of the numerals. In contrast, the Indirect pathway permits the systems to interact in such a way as to generate quantitative meaning from the numerals, allowing for meaningful comparisons of magnitude and approximation tasks. (e.g., Which is More? 2 or 3).

In addition to facilitating communication between the systems, the triple-code model proposes that the pathways may serve as an internal error detection system. If the *direct route* produces an unrealistic answer to an arithmetic problem (i.e., 2 + 3 = 23) the *indirect route* may be available to detect this error. Prefrontal areas and the anterior cingulate may coordinate processing of the stimuli, hold intermediate results in working memory, and be available to detect errors.

Default Mode Network

Like most research using functional neuroimaging, the research described above generally examined the increase in MRI signals during cognitive tasks. An increase in MRI signal correlating with cognitive task performance has been well established in the literature (Ogawa, Lee, Kay, & Tank, 1990), and serves as the framework for using the BOLD method within neuroimaging. While the majority of functional imaging research investigates brain regions exhibiting this pattern of increased activation, Raichle and colleagues (Raichle et al., 2001) have reported a network within the brain that follows the opposite pattern, showing a negative MRI signal change during cognitive tasks. The brain regions involved in this negative signal change have come to be known as the Default Mode Network (DMN) and include: the posterior cingulate, precuneus, anterior cingulate, medial frontal region, and the lateral parietal region. They propose that the DMN represents the baseline level of neuronal functioning that exists during an awake, resting state (i.e., resting quietly, with open eyes) (Raichle et al., 2001). The authors noted that an increase in signal change within this network is associated with increased blood flow to the regions in the absence of cognitive goal-related demands.

Davis et al. (2009) examined activation patters during approximate and exact arithmetic tasks with children experiencing math difficulties. They reported task-related activation differences in areas primarily "found in anatomical regions associated with domain-general cognitive resources that support higher level arithmetic skill but are not specific to mathematical processing" (Davis et al., 2009, p. 2474). In addition, they reported the novel finding of an increase in deactivation within the anterior and posterior cingulate, part of the DMN and recommended that future studies examine the DMN in children with and without mathematical difficulties. In addition to the task-related effect of the DMN, there appears to be a developmental effect. Developmental changes within the DMN occur during childhood with children showing less deactivation in the DMN than adults during exact and approximate calculation and magnitude tasks (Davis et al., 2009; Kucian et al., 2008).

Summary

Each of the bodies of literature introduced above Mathematics Cognition, Mathematical Learning Disabilities, and Cognitive Neuroscience of Mathematics Learning, have traditionally operated from independent frameworks, and addressed independent questions regarding mathematics learning. With recent calls for interdisciplinary research methodologies and collaboration across disciplines, (Twardosz, 2007; see also Varma, McCandliss, & Schwartz, 2008, for a review) cognitive psychologists, neuroscientists, and educators have begun partnering to investigating how the brain processes number and quantity, what this means for mathematics learning, and how educators can use that information to help children struggling with mathematics. While this dissertation literature review has provided a discussion of these fields as separate disciplines, it should be noted that the goals of the present study lie at the intersection of the fields of Mathematical Cognition, Mathematical Learning Disabilities, and Cognitive

Neuroscience of Mathematics Learning, assuming that each field has much to learn from and much to offer the others.

CHAPTER III

Methods

The present study utilizes a combination of behavioral and neuroimaging data to examine neural correlates of error detection for specific arithmetic problems. In this chapter, a detailed description of the research questions, hypotheses and predictions, study design, participants, measures, and procedures employed in the present study are provided. The research protocol for this study has been approved by the Institutional Review Board (IRB) at Cincinnati Children's Hospital Medical Center (CCHMC) and assigned study number 2011-1498.

The Current Study

The current study addressed three research questions. First, Does the detection of specific types of errors in arithmetic problems have specific neural signatures? It is hypothesized that the detection of specific types of errors on arithmetic problems (i.e., *Error Detection* task) does have specific neural signatures. Neural signatures are predicted in the left prefrontal region and anterior cingulate cortex. Furthermore, activation levels are hypothesized to be moderated by participants' mathematics achievement level as measured by a standardized achievement test. It is predicted that differential activation patterns will be associated with lower accuracy for participants experiencing Math Difficulties (MD) in comparison to participants with Typical Achievement (TA).

Second, Does the detection of specific types of errors in arithmetic problems correlate with performance on a standardized achievement test? It is hypothesized that the detection of specific types of errors on arithmetic problems does correlate with performance on a standardized achievement test. Participants with differential patterns of activation are predicted to have lower accuracy on the achievement test.

Third, What is the deactivation pattern of the DMN in relation MD status on the *Error Detection* task? Performance on the *Error Detection* task is hypothesized to be related to differential activation of the DMN. Specifically, it is predicted that the cognitive demands of the task will correlate with the degree of DMN deactivation, such that lower performance on the *Error Detection* task will correlate with a lesser degree of DMN deactivation as compared to those participants with higher task performance.

Participants

The sample for the present study consisted of 21 participants enrolled in or having recently completed grades seven and eight across several school districts near a large mid-western city. All participants were recruited via email or letters of invitation and recruitment flyers distributed through schools. The invitation letters and recruitment flyers provided a brief description of the study and instructed parents or guardians to contact the researcher for additional information. Communication with the family regarding participation eligibility and scheduling occurred through email or telephone, based on the family's preference.

Inclusion and exclusion criteria. Due to the research design and use of MRI technology, consideration for inclusion in the present study required the following criteria be met: enrollment in grade seven or eight at the time of data collection (or recent completion); normal gross neurological examination; full scale intelligence quotient (IQ) score greater than 85 (or confidence interval within the normal range); and signed child assent and parental consent. Children with any of the following standard MRI safety restrictions were excluded from participation: presence of a medical implant device, such as a pacemaker or neuro-stimulator;

presence of metal orthopedic pins or plates above the waist; presence of orthodontic braces or a permanent retainer; heightened anxiety or the inability to readily communicate with personnel operating the MR equipment; identification of any exclusion criteria listed on the standard checklist of MRI exclusion criteria used by the CCHMC Radiology department in routine clinical scanning (see Radiology Magnetic Resonance Imaging (MRI) Safety and Screening Form, Appendix A, see Measures section for details) ; pregnancy; full scale IQ score lower than 85 on neuropsychological assessment; or a history of head trauma noted by the parent or guardian.

Participant demographics. The final sample (n = 21) for this study included: 12 males; 10 participants in seventh grade; average age = 13 years, 5 months; average IQ score = 100.4. All demographic and neuropsychological data are summarized in Table 3.

Table 3.

Participant Demographics and Neuropsychological Data

	Typical Achieving	Math Difficulties	*p*-Value
N participants	14 (9m; 5F)	7 (3M; 4F)	0.35
Age, in years	13.5 ± 0.7	13.1 ± 0.4	0.20
WASI FSIQ Score	106.2 ± 10.1	94.6 ± 9.2	0.02*
WJ III Letter Word	65.2 ± 2.8	62.4 ± 4.9	0.112
WJ III Word Attack	27.4 ± 3.3	23.7 ± 4.7	0.048*
WJ III Calculation	27.9 ± 3.1	20.1 ± 2.7	< 0.001*
WJ III Math Fluency	103.5 ± 22.0	67.3 ± 21.3	0.002*

Note: Means and standard deviations (±) are reported for all demographic and neuropsychological data. Statistically significant *p*-values are denoted with an asterisk.

No participants had been previously diagnosed with a learning disability in mathematics. One male participant with MD had been previously diagnosed with a learning disability in reading, but was not receiving assistance for the learning disability at the time of data collection. One male participant with MD received individual tutoring for mathematics after school from his teacher twice per week, despite not being identified as MD by the school. One male participant with TA and one female participant with MD had Full Scale Intelligence Quotient (FSIQ) scores below 85; however, their FSIQ was within normal range when examining the 95% confidence interval so their data were included in the analyses, with FSIQ as a covariate. In total, three male participants had been diagnosed with Attention Deficit Disorder (ADD) or Attention Deficit Hyperactivity Disorder (ADHD). Two of these participants were taking medication, one of whom was classified as MD for this study, with the other two classified as TA.

Per standard protocol, all radiological examinations performed at CCHMC are reviewed by a neuroradiologist and findings are reported to the researcher. Two participants were reported to have clinically significant findings. The scan review for one male with TA indicated cerebellar tonsillar ectopia, consistent with Chiari I anomaly. A female participant with TA was found to have findings correlated with left mastoid symptoms. Findings for both participants were reported to the parents or guardians following protocol established by CCHMC. Although these findings were clinically significant, they were not deemed to influence performance in this study. The data for these participants were, therefore, retained in the analyses.

Nine of the participants had completed a prior study conducted by the researcher and faculty advisor (Kroeger et al., 2010); the remaining 11 participants were newly recruited for participation in the present study. For the purposes of the current study, participants were classified into one of two mathematics ability groups: Math Difficulties (MD; n = 7) and Typical Achievement (TA; n = 14). Determination of mathematical performance and group membership was made by the researcher and was based on the Math Calculation Skills cluster percentile rank from the Woodcock-Johnson III Achievement Test (WJ III) (Riverside Publishing Company, 2001). Participants scoring at or below the 35th percentile were identified as having MD; those participants with Math Calculation scores above the 35th percentile were identified as TA. To the degree possible, the sample was matched on gender, age, and grade; however, it should be noted that due to the sample size and MRI restrictions, matched pairs were not obtained for the entire sample.

Site of Study

All neuroimaging and neuropsychological data for the present study were collected at CCHMC. The MRI scans performed as part of this study followed a procedure similar in nature to that routinely used during clinical MRI scanning, with the exception of two notable departures: all scans were performed at the Imaging Research Center (IRC) at CCHMC on a 3.0 Tesla Philips Achieva scanner and imaging methods were based on the Blood Oxygenation Level Dependent (BOLD) method (see fMRI Paradigm Section for details).

Design

The current study utilized a Quasi-Experimental, Between Subjects design to investigate the relationships between pre-existing group membership (i.e., MD and TA) and performance on the *Error Detection* task. This design was chosen to allow for meaningful comparisons to be drawn from between the two, non-randomized groups of participants.

This research study necessitated a quasi-experimental design as the two groups of interest are not able to be randomized. Placement within either group is determined by the participants' score on a standardized achievement test of mathematics performance. This characteristic should be static, in that it is not possible for the researcher to randomization MD status. Rather, MD status serves as a pre-existing characteristic of each participant and binds the researcher to place that participant within a specific group. The independent variable is the Group status (i.e., MD or TA) and the dependent variables are the accuracy performance on the *Error Detection* task and the associated neural activation.

Measures

A number of measures were used in this study, including a CCHMC standard MRI safety protocol form, standardized paper-and-pencil tests, paper-and-pencil tasks created by the researcher and the fMRI math tasks. The Radiology Magnetic Resonance Imaging (MRI) Safety and Screening Form is a standard CCHMC form used when a child participates in research at CCHMC requiring MRI scanning. A measure of intelligence was determined through administration of the WASI. Participant demographic data and pertinent history were collected via the Demographic Questionnaire that was created by the researcher. The researcher-designed *Complex Multi-digit* task was administered to examine the types of errors made when calculating multi-digit arithmetic problems. To obtain a measure of achievement in mathematics and reading, subtests of the Woodcock Johnson III (WJ III) were administered. Four experimental math tasks, *Exact Calculation*, *Approximate Calculation*, *Magnitude Comparison*, and *Error Detection* made up the neuroimaging tasks of his study and were administered on a Philips Achieva 3T MRI scanner.

Radiology Magnetic Resonance Imaging (MRI) safety and screening form. As part of the standard protocol at the CCHMC IRC, parents or guardians of all research participants must complete the Radiology Magnetic Resonance Imaging (MRI) Safety and Screening Form (see Appendix A) prior to the scan. This form instructs parents or guardians to answer five questions regarding their child's medical history. The first four questions ask parents to answer "Yes/not sure" or "No" to questions regarding: their child's prior surgical history; any medical devices that have been implanted or inserted into their child; any injury their child has sustained as a result of a metal fragment (i.e., bullet, BB, or shrapnel); and work that has been performed by their child using metal grinding equipment. The form provides space to write an explanation for any question answered "Yes/not sure". The final question instructs parents or guardians to answer "Yes" or "No" indicating if they have any questions or concerns regarding the MRI scanning of their child. Parents are instructed to sign and date the form; it is then reviewed and initialed by both the researcher and the certified MRI technician. One copy of this form was retained by the researcher in the participant's file and one copy remained on file at the IRC at CCHMC.

Wechsler Abbreviated Scale of Intelligence. A full scale IQ score was obtained through administration of the Vocabulary and Matrix Reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (WASI; PsychCorp, 1999). This intelligence measure is appropriate for use with individuals ages 6-89. Due to the lengthy testing process, and consideration of the effects that testing fatigue would pose for the experimental math tasks, administration of only two subtests was selected. This is an appropriate choice when testing time is a constraint (WASI Manual, 1999).

The Vocabulary subtest provides a measure of the verbal knowledge of the test taker and is highly correlated with general intelligence; the Matrix Reasoning subtest provides a good measure of the individual's nonverbal reasoning and general intelligence (WASI Manual, 1999). All protocol set forth by the test publishers and detailed in the WASI Manual were followed for administration of both subtests. The Vocabulary subtest asks individuals to provide the definition of a stated word, read by the researcher and viewed by the test taker on a page in the WASI Stimuli Book. Based on the response, individual test items are scored 0, 1, or 2 points; the subtest raw score is the sum of these points. The Matrix Reasoning subtest asks test takers to identify the missing piece in a picture. The WASI Stimuli Book provides pictures, each with one missing piece and five answer selections per test item. Items are scored 0 or 1 point based on the correct answer as indicated by the WASI Manual. The raw score for the Matrix Reasoning subtest is the summation of the individual test item scores for that subtest. T-Scores and IQ equivalents were obtained using the conversion tables provided in the WASI Manual.

Because of the high reliability and stability associated with IQ scores, these data were not collected for those nine participants for whom IQ data was established by Kroeger et al., 2010.

The WASI Manual reports a stability coefficient of .85 when the Vocabulary and Matrix Reasoning subtests are used to obtain a full scale IQ score.

Demographic questionnaire. Demographic data was collected for each participant through a questionnaire completed by their parent or guardian (see Appendix B). Items included questions regarding the participants' age, grade, prior diagnosis of a learning disability and factors associated with such a diagnosis, including: participation in a remedial assistance program for the disability; the age at which assistance was initiated; the location of where the assistance takes place (e.g., school, private therapist, private learning center); the frequency of the assistance; previous diagnosis of neurological impairments (e.g., Autism); previously diagnosed psychological disorders (e.g., Attention Deficit Disorder or Attention Deficit/Hyperactivity Disorder); and the participant's handedness.

Complex multi-digit calculation task. All participants were asked to complete a 24 item, paper-and-pencil *Complex Multi-digit Calculation* task (see Appendix C). This task, designed by the author of this dissertation, was created to examine the types of problems commonly committed by children when calculating multi-digit arithmetic problems; specifically, when calculating two- to four-digit addition and subtraction problems.

The problems were created based on research conducted by Raghubar et al. (2009). While that research identified a number of error types, the *Complex Multi-digit Calculation* task created for the present study examined only a subset of the error types. This was necessary due to the fact that the researcher of the present study was interested in determining if children commit particular errors when calculating multi-digit arithmetic problems; whereas the goal of Raghubar et al. (2009) was to determine which types of errors are committed by children. The *Complex Multi-digit Calculation* task replicated problems that would allow for these errors to be committed. The three error types were: problems borrowing across zero, problems with carrys, and no decrement with borrowing (see Table 4). For this task, 8 problems of each type were designed. As 50% of the problems in this task were presented in a horizontal format, the opportunity to examine misalignment of digits was also permitted by the data.

Table 4.

Sample Complex Multi-digit Calculation Task Problems

Problem Type	Example
Problems borrowing across zero	1005 - 98
Problems with carrys	2589 + 423 = _____
No decrement with borrowing	753 - 89
Misalignment of numerals	76 + 321 = _____

Woodcock Johnson III achievement test. The Letter-Word Identification, Word Attack, Calculation, and Math Fluency subtests of the WJ III, Form A (Riverside Publishing Company, 2001) were administered to each participant by the researcher or a trained research assistant. This measure is appropriate for use with individuals ages 2 – 90+. All protocol established by the test publisher and provided in the administration manual were followed during administration of this test. The order of administration remained the same for each participant: Letter-Word Identification, Word Attack, Calculation, and Math Fluency. This order was established in consideration of the fact that the testing measure was administered immediately following the completion of the *Complex Multi-digit Calculation* task. In order to provide a brief measure of relief from competing math problems, the language-based subtests of the WJ III were administered prior to the math subtests.

Letter-Word Identification subtest. The Letter-Word Identification subtest instructs the individual to read a list of English words. One point is earned for each word that is pronounced correctly; zero points are earned for incorrectly pronounced words. This is an untimed subtest; the individual completes the test when he or she has reached the ceiling, which is the end of the test or when the individual has mispronounced six consecutive words.

Word Attack subtest. The Word Attack subtest requires test takers to read from a list of pseudo-words. These stimuli, while composed of many characteristics of English language words, are novel, in that they are not real words. One point is earned for each correct pronunciation; zero points are scored for incorrect pronunciation. This subtest is untimed, with individuals completing the subtest when the ceiling has been reached, either at the completion of the list of words or when six consecutive mispronunciations have occurred. The raw score for both the Letter-Word Identification and the Word Attack subtests are the summation of the individual test item scores for each subtest.

Calculation subtest. The Calculation subtest of the WJ III requires individuals to complete a paper-and-pencil worksheet of arithmetic problems. The problems become progressively harder with each consecutive problem. This is an untimed subtest that is completed when the individual completes the subtest or reaches the ceiling. The ceiling occurs at the completion of all subtest items or when the participant incorrectly solves six consecutive problems.

Math Fluency subtest. The Math Fluency subtest, a paper-and-pencil worksheet of simple arithmetic problems (single-digit addition, subtraction, and multiplication) requires test takers to write the solution to each problem. This is a three minute timed test. The individual works for the entire three minutes or until he or she has completed all the subtest items. Raw scores for the Math Fluency and Calculation subtests are determined by summation of the scores from the individual test items for each subtest. For both math subtests, participants score one point for each correct answer (incorrect answers are assigned zero points).

Participant classification. For the purposes of this study, the Percentile Rank from the Math Calculation Skills Cluster of the WJ III was used as a determination of participants' overall math performance and group placement with regard to mathematical disability status. The WJ III testing package provides test administrators with scoring software. The scoring software package utilized in the present study was the WJ III Normative Update (NU) Compuscore and Profiles Program, Version 3.1 (Riverside Publishing Company, 2008), which includes updated normative data based on the 2005 United States census statistics.

This software program permits the entry of demographic information and raw score data for each test taker. Upon report selection, the program generates the following data for each subtest: Raw score, Age or Grade Equivalency (based on selected preference), Percentile Rank, within the 95% band and a Standard Score. An additional feature of the software program is the generation of Cluster Test scores, derived from groups of subtests that, when administered together, provide a more comprehensive snapshot of a particular skill. Based on the subtests administered in the present study, the software program generated Cluster scores for: Basic Reading Skills, based on performance on the Letter-Word Identification and Word Attack subtests; and Math Calculation Skills, based on performance on the Calculation and Math Fluency subtests.

The choice to use percentile rank markers for group placement was based on current literature suggesting that children who struggle with mathematics have differing cognitive profiles based on the severity of their learning difficulties (Geary, Hoard, & Bailey, 2011; Geary et al., 2007; Jordan, Hanich, & Kaplan, 2003; Murphy, Mazzocco, & Early, 2007). The consensus from the current literature indicates that children with more severe cognitive deficits

> tend to score at or below the 10th national percentile on mathematics achievement tests grade after grade, perform poorly on many mathematical cognition tasks, and tend to have below average scores in reading, working memory, and general intelligence (IQ). The children with less severe difficulties tend to have average reading ability, IQ, and working memory competencies but score between the 10th and 25th percentiles on mathematics achievement tests across grades. (Geary, Hoard, & Bailey, 2011, p. 1)

The classifications system described above was utilized in the present study, with one notable departure: classifications of MD were based on a percentile ranking at or below the 35th percentile on the Math Calculation cluster score. This departure was necessary due to the relatively small sample size of the present MRI study, in comparison to studies that rely on behavioral methodologies and, therefore, often have larger sample sizes.

A similar score is generated through the WJ III Normative Update (NU) Compuscore and Profiles Program for administered reading subtests. The Basic Reading Skill composite score for the present study was generated as a function of the Letter-Word Identification and Word Attack subtests. It should be noted that this composite score was not used to determine MD status, group membership, or during data analysis for the current study.

fMRI scanner system. All neuroimaging data were collected on a Philips Achieva 3T MRI scanner equipped with an audiovisual system for task presentation (see Procedures section for scan details).

fMRI math tasks. A block-design was utilized to administer the four math tasks: *Exact Calculation* task, *Approximation Calculation* task, *Magnitude Comparison* task, and *Error Detection* task. The first three were created by the author and her advisors; the final task was created by the author of this dissertation. While the *Error Detection* task is the sole focus of this dissertation, a brief overview of the other tasks is provided.

Exact calculation task. The *Exact Calculation* task consisted of 80 math problems, each limited to addition or subtraction of two or three-operand, single-digit problems. All two-operand problems (n=48) were restricted to single-digit addition and multiplication problems. All three-operand problems (n=32) required both addition and subtraction of 3 single digits (addition first in 50% of trials) (see Table 5). The math problem was displayed in the center of the visual field (50% vertical), with the answer choices presented in the left and right visual fields adjacent to the math problem. The *Exact* task required participants to choose the exact, correct answer to the displayed math problem. Participants were instructed to choose from two answers, one that was the exact, correct answer and one that was near the exact answer, but not correct. The near, but incorrect answer was off by 1 or 2 units from the correct answer. Answer choices were made via button press. This task is based on the work of Stanescu-Cosson et al. (2000).

Approximation task. The Approximation task consisted of 48 multi-digit arithmetic problems presented in the center of the visual field. This task consisted of three digit addition and subtraction problems, and one-, two-, or three-digit multiplication problems. All math problems were displayed in the center of the visual field (50% vertical), with the answer choices presented adjacent to the math problem, in the left and right visual fields. The answer choices for the *Approximate Calculation* task were both incorrect, however, one was near the correct answer; the other choice being approximately one order of magnitude removed from the correct answer (see Table 5). This task is based on the work of Stanescu-Cosson et al. (2000).

Exact and approximate comparison trials. Comparison trials for the *Exact* and *Approximate* tasks consisted of three identical numbers, one near the center-top of the visual field and two just below this number, but located in the left and right visual fields. For each trial, one of the numbers located in the left or right visual field was a different color than the number in the center. Via button press, participants indicated which number from the left or right visual field was the same color as the number presented in the center of the visual field. This task was designed to control for motor activation associated with response generation and visual activation. As the *Exact* task was designed with only single-digit numerals, the comparison trial problems were limited to single-digit numerals (see Table 5). The number of comparison trials for both the *Exact Calculation* and *Approximate Calculation* tasks matched the number of problems of experimental trials.

Magnitude comparison task and comparison trials. The *Magnitude Comparison* task consisted of block arrays and required participants to determine Which is More? or Which is Less? Each decision condition (More or Less) was presented as a separate block. Prior to each block, a brief display indicated which quantity decision was required. During each block, two quantity arrays of squares, with values ranging from one to nine, were presented on the left and right sides of the visual field. All quantity differences between the two arrays were at least 2, except for those arrays whose largest quantity was 2 or 3. Participants indicated their answer choice via button press (see Table 5). Comparison trials for this task required participants to indicate, via button press, on which side of the visual field (i.e., right or left) a large block appeared. This comparison was chosen to control for visual processing. (see Table 5).

Error Detection task. The *Error Detection* task consisted of 40 addition, subtraction, and multiplication problems presented along with a proposed solution. All problems were presented in the center of the visual field (50% vertical) (see Table 5 for examples; see Appendix D for complete task list). Participants were instructed to identify if the presented solution was correct by indicating Yes or No, via button press. The Yes and No answer choices were presented on the left and right sides of the visual field, respectively. Comparison trials for the *Error Detection* task required participants to view two numbers and determine if the color of the two numbers was the same by indicating Yes or No via a button press (see Table 5 for examples; see Appendix E for complete task list). The comparison trials for this task were designed to control for activation associated with visual and motor activity. As this task represents the core of this dissertation, a detailed discussion is provided below.

Table 5.

Math Task Experimental and Control Trials

Task	Experimental Trials			Comparison Trials			
Exact	9	7 + 2	11			5	
	3	6 - 4	2	5			5
Approximate	21	9 + 4	11			1	
	8	15 - 6	18	1			1
Magnitude Comparison							
Error Detection	YES	5 – 4 = 9	NO	YES	5	5	NO
	YES	6 x 3 = 18	NO	YES	8	8	NO

The *Error Detection* task utilized in the present study was designed to test the patterns of neural activation associated with the identification of errors in solved arithmetic problems. The problems, created by the researcher, are based on the available literature detailing types of mathematical errors (Dehaene & Cohen, 1995, 1997; Geary et al., 2011; Raghubar et al., 2009; Siegler, 1988).

In total, 40 problems were presented with the correct answer displayed on 50% of trials. The remaining problems (n = 20) presented incorrect solutions that represented typical errors made by children who struggle with mathematics, including: *String Intrusion* errors, *Associated Fact* errors, *Wrong Operation* errors, and *Global* errors (see Chapter 2, Mathematics Cognition Section for a summary of the research respective to each error condition). The number of incorrectly solved problems was balanced across each of the four error conditions, resulting in five problems associated with each error condition.

String intrusion errors. Trials presenting problems based on String Intrusion errors consisted of addition, subtraction, and multiplication problems whose incorrect answer was the next highest or lowest number in a string of digits following either the first or second operand in the problem (see Table 6).

Associated fact errors. Associated Fact errors are presented in trials whose errors reflected the answer to a near, or associated, arithmetic fact (see Table 6). Each of these errors represented answers to problems plus or minus one or two units for either numeral in the math problem.

Wrong operation errors. Wrong Operation errors are those problems whose incorrect solutions represented the use of an incorrect mathematical operation, with the same numerals maintained (see Table 6).

Global errors. The final problem type is directly associated with the triple-code model (Dehaene & Cohen, 1995, 1997; Dehaene at al., 2003). For problems classified as Global Errors, the incorrect answer represented an answer in which no actual arithmetic is performed; rather the numerals in the problem are simply combined (see Table 6).

Table 6.

Sample Error Conditions for Error Detection Task Problems

Error Type	Example
String Intrusion Errors	4 x 5 = 6
Associated Fact Errors	5 + 7 = 13
Wrong Operation Errors	9 x 3 = 12
Global Errors	2 + 8 = 28

Procedures

Consent and assent. Upon arrival at CCHMC, the child participant and their parent or guardian were met by a member of the research team and escorted to the IRC. The researcher explained the consent and assent process to both the child and their parent or guardian. All parties were instructed to read the Consent and Assent documents (see Appendices F and G) and inform the researcher of any questions or concerns regarding participation in the study. After all questions and concerns were addressed to the satisfaction of the child and their parent or guardian, assent and consent were obtained; the family was provided one signed copy of each document; the other signed copy of each document was retained by the researcher.

After obtaining consent and assent, the researcher reviewed the Radiology Magnetic Resonance Imaging (MRI) Safety and Screening form with the parent or guardian and provided instructions for completing the form. Upon completion, the researcher and a registered radiological technologist reviewed the form with the participant and their parent or guardian and reviewed the procedures used in MRI scanning. If the parent or child participant had any questions, they were addressed at this time.

The participant was instructed to remove all jewelry, pens, pencils, cellular phones, belt buckles and any other metallic objects from clothing as these objects are incompatible to the strong magnetic field of the MRI scanner. These items were either stored in a locker or left with the participant's parent or guardian, based on their preference.

Intelligence testing. At this time, the 11 participants who had not completed the Kroeger et al. (2010) study were asked to complete the Vocabulary and Matrix Reasoning subtests of the WASI (see Measures section for details). For each participant, administration of the Vocabulary subtest occurred first. All standard administration protocol provided by publisher (WASI Manual, 1999) was followed. After completing the Radiology Magnetic Resonance Imaging (MRI) Safety and Screening form, and the intelligence testing, if necessary, participants were provided with a brief training session on the math tasks utilized in the scanner.

Experimental task training. Following the consent and assent process, and IQ testing if necessary, each participant was provided training on the math tasks utilized during the scan. Because this study was conducted in conjunction with another study whose findings will be reported elsewhere, a total of four math tasks were presented within the fMRI paradigm; therefore training occurred for each of the four math tasks. During training on the experimental tasks, participants viewed a series of four training problems and four comparison problems per task (n = 32 training problems) on a desktop computer. These problems, while similar in nature to the tasks used in the fMRI task paradigm, were different from the experimental trials presented as part of the functional MRI paradigm.

The training protocol consisted of four separate runs, one for each task so as to model the fMRI paradigm that was to be utilized in the scanner to the highest degree possible. The participant first saw the task name and directions on the computer monitor, which were read aloud by the researcher. Upon ensuring that the participant understood the directions, the four experimental trials were presented first, with fixed inter-stimulus intervals, matching that of the actual trials used in the in-scanner tasks (see below for exact details pertaining to each task). The researcher ensured that the participant understood the task requirements and how to locate the answer choices. As part of the same run, immediately following the experimental trials, the four comparison trials were viewed.

Due to MRI restrictions on movement, an MRI compatible button box is regularly utilized in research studies to enable participants to select answers to cognitive tasks presented in the scanner. As part of the training session, instructions were provided on use of the button box in selecting the answer choices. Participants were reminded of the importance to remain still in the scanner and avoid any unnecessary and abrupt movements. Any questions regarding the tasks or expectations were addressed by the researcher at this time.

The participant was then escorted into the outer scanner room where final verification by both the researcher and the certified MR technician ensured that the participant had no metal on his or her person.

fMRI preparation. After a final verification by the researcher and MR technician that no metal was present on the participant's person, he or she was escorted into the scanner room and asked to recline in a supine position on the bed of the Philips Achieva 3T Scanner. A registered MR technician was responsible for ensuring the safety of the participant and their comfort within the scanner.

An MRI-compatible audiovisual system was used to project the math tasks during the functional scanning and to allow prerecorded video programs (e.g., VHS or DVD) to be presented to the participant during the locator and anatomical scans. This procedure allows the participant to relax and reduces anxiety during the initial locator and survey scans and during the anatomical scan at the end of the functional scanning. During functional scanning, the video system was used to visually present the math task paradigms. This system is equipped with headphones to provide additional sound isolation from the scanner and to allow for audio communication between the participant, the MR technician, and the researcher while the scan is in progress. The MR technician ensured that the participant was comfortable and that the headphones were secure prior to initiating the scan.

In order to obtain MR signals, a radiofrequency (RF) coil, serving as a receiving antenna, was placed over the participant's head. The RF coil, a cylindrical device open at both ends, at no time came into contact with the participant's body. The MR technician was responsible for ensuring the placement and comfort of the participant as the RF coil was put in place. The participant was provided with the MRI-compatible button box. The button box has two raised buttons on the front panel of the box. Participants were instructed to press the left button to select the answer choice on the left side of the visual field, and to press the right button to select the answer choice on the right side of the visual field. In addition, the participant was provided with an emergency button clipped to their shirt or pants and instructed on how to use it to alert the control room of any problems or concerns during the scanning process. Use of the emergency button activates an alarm in the control room and stops the scan. For participants' safety, closed circuit video monitoring was also used during the entire scan.

fMRI paradigm. As noted above, the present study was conducted simultaneously with another research study utilizing the same theoretical framework and research design. This resulted in the administration of four experimental math tasks to each participant: *Exact Calculation, Approximate Calculation, Magnitude Comparison, and Error Detection.* All four math tasks were designed to test skills pertaining to the three codes of representation proposed by Dehaene's triple-code model (1995, 1997) and relationships between them. To control for the neural activation associated with the motor movements, visual processing, and cognitive functions associated with generating responses during the experimental trials, comparison trials were embedded as separate blocks within each functional run.

For each math task, the experimental trials and their associated comparison trials were presented as separate blocks, with the experimental trials first. The specific number of experimental and comparison trials varied between tasks (see below for specific information regarding each task). Participants' responses to each problem and response time data were stored along with the neuroimaging data for each of the experimental and comparison trials.

The functional image data collected in this study are based on the BOLD method (Ogawa, Lee, Kay, & Tank, 1990). This method produces brain images that reflect cerebral activity associated with sensory, motor, or cognitive activity by measuring changes in the magnetic properties of hemoglobin correlated with the oxygenation of blood in the cerebral vessels. As deoxygenated hemoglobin is paramagnetic and oxygenated hemoglobin is diamagnetic, these changes in magnetic susceptibility result in changes to the overall magnetization of the hemoglobin in cerebral regions experiencing increased blood flow due to activation. Use of MRI technology allows for images to be generated that reflect this change in magnetization due to localized cerebral activation.

fMRI signal acquisition. Upon commencement of the scanning procedure, an initial pre-scan was conducted during which adjustments were made to the scanner for optimized signal detection, including adjustments to: the RF transmit power; the uniformity of the main magnetic field, Bo; and the current in several electromagnets (shim coils) located within the main magnet. During this time, the participant viewed a pre-recorded program via the audio-visual system. Upon completion of the pre-scan adjustments, the functional scanning began. Prior to each scan, the researcher informed the participant, via the intercom system, that the scan was beginning, provided directions for the functional tasks and checked on the participant's comfort.

Participants were reminded that they would hear several loud noises during scanning and to remain as still as possible.

fMRI scan attributes and procedures. fMRI scans were performed in the transverse plane on a Philips 3T Achieva MRI system. A T2*-weighted, gradient-echo, EPI method was used for fMRI scans with the following parameters: TR = 2000 ms, TE = 32 ms, matrix 64 x 64 pixels, FOV = 25.6 x 25.6 cm, slice thickness = 5 mm, SENSE factor = 2, 35 slices acquired covering the entire brain. A 3D, high resolution, T1-weighted, MP-RAGE whole brain scan was acquired.

Immediately preceding the scan for each math task, the participant was able to view the directions specific to each task on the screen and the researcher verbally read the directions to the participant via the intercom system. The directions for each task instructed participants to choose the answer to the problem by pressing the left or right button on the button box. These buttons corresponded to the left and right answer choices as viewed on the screen.

All paradigms were presented in a block-design, using Presentation software (Neurobehavioral Systems, Albany, CA). The tasks were administered in four separate runs. To the degree possible based on the sample size and characteristics, every effort was made to balance the order across participants. All tasks were presented using a self-paced design allowing the participant a pre-determined amount of time in which to select an answer. The ordering of all trials was randomized at runtime.

For the *Exact Calculation* task, participants were presented with a new visual stimulus every 3.5 seconds for the two-operand problems, every 5 seconds for the three-operand problems, and every 2.5 seconds for the comparison trials. These parameters resulted in the following block-design: 12 two-operand problems, with a run time of 42 seconds per block; 8

three-operand problems with a run time of 40 seconds per block; and 12 comparison trials with a run time of 30 seconds per block. In total, four blocks of each type were presented, yielding a total scan time of 7 minutes and 28 seconds.

The *Approximate Calculation* block presented a new experimental trial every 5 seconds and a new comparison trial was presented every 2.5 seconds. These parameters yielded the following design: 12 experimental trials with a run time of 60 seconds per block; and 12 comparison trials with a run time of 30 seconds per block. Four blocks of each type were presented, resulting in a total task scan time of 6 minutes.

Stimuli for the *Magnitude Comparison* task were presented every 3 seconds for both the experimental and control trials, preceded by a 2 second instruction screen, directing the participant to choose either the "Which is More" or "Which is Less" condition. These parameters yielded the following block design: 10 experimental trials, along with the 2 second instruction (directing participants to the correct decision condition for that run, Which is More? or Which is Less?) screen for a runtime of 32 seconds; 10 comparison trials, with a 2 second instruction screen (directing participants to choose the side of the screen where the single square appeared) resulting in a runtime of 32 seconds. Six blocks of each type were presented, yielding a total task scan time of 6 minutes and 24 seconds.

The *Error Detection* task was run under the following paradigm: experimental trials were presented every 3.5 seconds; comparison trials every 2.5 seconds. The block-design that resulted yielded 12 experimental trials, with a runtime of 42 seconds and 12 comparison trials, with a runtime of 30 seconds per block. In total, 4 blocks of each type were presented resulting in a total scan time of 4 minutes and 48 seconds. Over the four blocks, participants were presented with 48 experimental error detection trials and 48 comparison trials.

The total time required for obtaining informed consent and assent, training the participant (see section on experimental task training for details), completion of the functional and anatomical imaging scans, and all post-scanner neuropsychological testing was approximately two and one half hours. The time in the scanner did not exceed ninety minutes. At any time during the study, the child participant or their parent or guardian was permitted to discontinue participation by notifying the researcher. During the scans, the child was able to inform the researcher and MR technologist of their desire to cease participation through the intercom, video camera, or alarm system. All participants and parents or guardians were informed of this right and instructed on use of the intercom alarm system prior to the scanning session.

Participants were scanned as they were recruited. In order to facilitate scheduling at the convenience of the participants and their families, randomization of participants was not employed in this study.

At the conclusion of the scanning session, the participant was escorted by the researcher to a nearby testing room to complete two behavioral tasks: the *Complex Multi-digit Calculation* task and selected subtests of the WJ III. After all behavioral testing was completed, the participant was escorted back to their parent or guardian. Compensation for participation in the form of a $100.00 gift card was given to the participant at this time. A member of the research team then escorted the participant and their family to the main concourse of the hospital.

CHAPTER IV

Statistical Analyses and Results

While this dissertation was part of a larger study that will be presented elsewhere (Schmithorst, Brown, & Kroeger, under review), Chapter IV will present the data analysis and results pertaining to the *Error Detection* task, as that is the sole focus of this dissertation. However, some details regarding statistical analyses related to the other tasks are, at times, necessarily addressed in order to establish a context by which the *Error Detection* data can best be understood.

Statistical Analyses

The neuroimaging data from the current study were analyzed using protocols written in IDL (ENVI, Boulder, CO) and SPM8 (Wellcome Dept. of Cognitive Neurology, London, UK). As is standard protocol in fMRI data analysis, motion correction parameters were established and motion correction procedures were performed prior to statistical analysis of the functional data. In selecting the optimal volume for motion correction reference, this study utilized an intensity-based cost function where the selected volume was the one with the minimum cost function as compared to all other frames (Szaflarski et al., 2006; see Schmithorst, Brown, & Kroeger, under review, for specific details regarding the statistical parameters of this procedure). A pyramid iterative algorithm was used to perform the motion correction (Thevenaz et al., 1998). Following the motion correction, the cost function was recalculated to ensure that the selected volumes met the standard threshold of minimum intensity. For each participant, activation T-maps were computed using the General Linear Model (GLM) assuming the hemodynamic response function (HDF). Scanner drift was accounted for by incorporating a cosine basis set into the design matrix. Using SPM8 routines, T-maps were converted into Montreal Neurologic Institute (MNI) stereotactic space to allow for comparisons across and between participants.

Group activation and deactivation maps were created using one-sample T-tests, where the t-scores were converted to Z-scores and filtered with a Gaussian filter width $\sigma = 4$ mm. To ensure a minimum intensity threshold of $Z \geq 8.0$ and clusters meeting a minimum of 65 voxels, a Monte Carlo simulation was performed (Ledberg et al., 1998). This analysis was run for three separate groups: all participants, MD participants, and TA participants.

To examine group differences in activation, a second level analysis was run using the GLM, with MD status identified as the variable of interest; age, gender, IQ and the square root of the number of frames retained were used as covariates of no interest. Only those voxels that showed activation or deactivation from the MD or TA groups were included in this analysis. The Monte Carlo simulation was re-run, yielding an intensity threshold of $Z > 5.5$ and a 50 voxels minimum cluster threshold (family-wise error corrected $p < .01$ for all tasks).

Additionally, regions of interest (ROI) were established from the group activation map over all experimental tasks and were subsequently used to examine activation and deactivation differences between the MD and TA groups. Post-hoc analyses for establishing ROIs were designed to avoid "double dipping," a situation that results when the statistical comparison used to select the ROI is the same as the one used on the data drawn from the established ROI. In other words, the ROI were not taken from the MD/TA difference maps, but from the group activation map (Kriegeskorte et al., 2009; Vul & Pashler, 2012). Group means and standard errors (see Table 7) were calculated for each ROI (posterior cingulate/precuneus, medial prefrontal/anterior cingulate, medial orbitofrontal/anterior cingulate, left superior temporal/angular gyrus, right superior temporal/angular gyrus) (see Figure 3).

Table 7

Group Means and Standard Deviations for Defined Regions of Interest

	PosteriorCingulate	MedialPrefrontal	MedialOrbitofrontal	LeftAngularGyrus	RightAngularGyrus
Math Difficulties	-0.22 +/- 0.87	-0.24 +/- 0.40	-0.29 +/- 0.69	-0.30 +/- 0.68	-0.16 +/- 0.77
Typically Achieving	-1.16 +/- 0.69	-0.92 +/- 0.52	-0.95 +/- 0.84	-0.87 +/- 0.67	-1.23 +/- 0.53

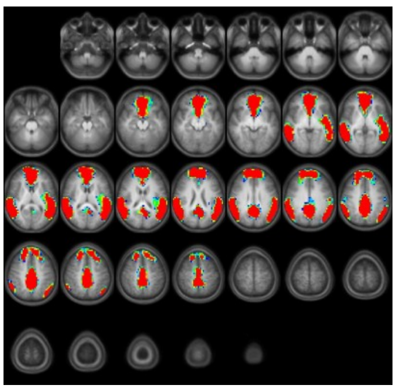

Figure 3. Default-mode network regions (including medial orbitofrontal, medial prefrontal, posterior cingulate/precuneus, and superior temporal/angular gyri) with significant deactivation (*p* < 0.01 family-wise error (FWE) corrected) during math task performance. These regions were used for all subsequent ROI analyses. Images are presented in radiologic orientation.

Results

Neuropsychological testing. Overall, participants experiencing TA outperformed participants experiencing MD on all neuropsychological subtests of the WASI and WJ III. For a number of these subtests, statistically significant differences were found between the MD and TA groups.

Wechsler Abbreviated Scale of Intelligence performance. FSIQ mean scores were within normal range for both the MD and TA groups, despite two participants with MD having calculated FSIQ scores below 85. When examining confidence intervals, these participants'

FSIQ scores fell within normal range; therefore, the decision was made to retain their data (see Table 3). Means and standard deviations for each group were $M = 94.6$, $SD = 9.2$ and $M = 106.2$, $SD = 10.1$, for participants with MD and TA, respectively. While the FSIQ score was within normal range for both groups, a statistically significant difference was found between the MD and TA groups ($t = 2.55$, $p = 0.02$); therefore FSIQ was used as a covariate in the fMRI analyses.

Woodcock-Johnson III performance. Performance on each subtest of the WJ III was examined for both groups. For each subtest, the TA group outperformed the MD group, with three of the subtests reaching statistical significance (see Table 3).

Letter-Word Identification. Both groups performed within normal range on the Letter-Word Identification WJ III subtest. Means and standard deviations for the MD and TA group were $M = 62.4$, $SD = 4.9$ and $M = 65.2$, $SD = 2.8$, respectively. No statistically significant differences were found between the groups ($t= 1.67$, $p = 0.112$).

Word Attack. Performance on the WJ III Word Attack was within normal range for both the MD and TA groups. A statistically significant difference was found between the MD and TA groups ($t = 2.11$, $p = 0.048$), with the TA group ($M = 27.4$, $SD = 3.3$) outperforming the MD group ($M = 23.7$, $SD = 4.7$).

Math Fluency. Performance on the WJ III Math Fluency subtest was within normal range for the TA group, but below normal range for the MD group. Statistically significantly differences were found for the MD and TA groups ($t = 3.6$, $p = 0.002$), with the TA group ($M = 103.5$, $SD = 22.0$) outperforming the MD group ($M = 67.3$, $SD = 21.3$).

Math Calculation. Performance on the WJ III Calculation subtest was significantly different for the MD and TA groups ($t = 5.63$, $p < 0.00$), with the TA group ($M = 27.9$, $SD = 3.1$)

performing significantly higher than the MD group ($M = 20.1$, $SD = 2.7$). Scores for the TA group were within normal range, while the MD groups scored below normal range.

Error detection task performance. Participants with MD demonstrated significantly lower accuracy than the TA group on the *Error Detection* math task. MD and TA group mean scores and standard deviations are: $M = 29.3$, $SD = 5.4$ and $M = 39.9$, SD = 7.1, respectively (Wilcoxon Rank-Sum Test, $Z = 2.72$, $p = 0.006$). This task was particularly difficult for the participants with MD. As a function of the block design and stimuli timing parameters, participants were presented with 4 blocks of 12 experimental trials, for a total of 48 *Error Detection* problems. Of these 48 problems, the MD group performed with an average of only 61.04% accuracy, while the TA group showed good performance with an average of 83.13% correct. It should be noted that 40 problems were developed for the task; therefore, some problems were repeated.

fMRI group analysis results. The GLM was utilized during a second level analysis to examine group differences in activation and deactivation on the *Error Detection* task, identifying MD status as a variable of interest. This analysis examined neural activation and deactivation patterns for all participants.

Neural activation. Neural activation for the *Error Detection* task (see Figure 4) was seen in the cerebellum, bilateral middle occipital region, the left dorsolateral prefrontal cortex, and bilaterally in the posterior regions of the intraparietal sulcus.

Neural deactivation. Deactivation for the *Error Detection* task (see Figure 4) was evident in the angular and middle temporal gyri, the posterior cingulate, medial orbitofrontal region, prefrontal region, and bilaterally in both the inferior temporal region and the amygdala.

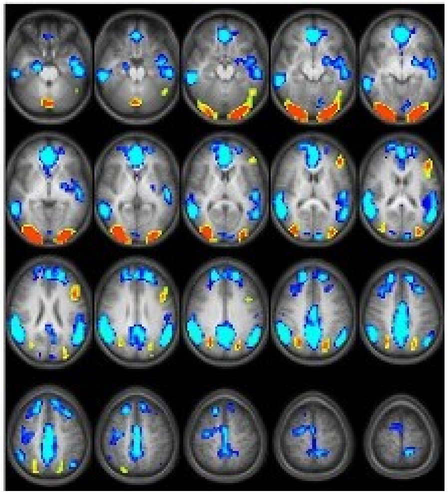

Figure 4. Group activation (hot colors) and deactivation (cold colors) maps ($p < 0.01$ FWE corrected) for Error Detection task. Images are presented in radiologic orientation. Slice locations: Z = -25 mm to Z = +70 mm.

fMRI comparisons between MD and TA participants. A subsequent analysis examined the differences in neural activation and deactivation patterns between participants with MD and those who are TA.

Differences in activation. No regions of activation reached statistical significance when examining the differences in neural responses between participants with MD and TA (see Figure 5).

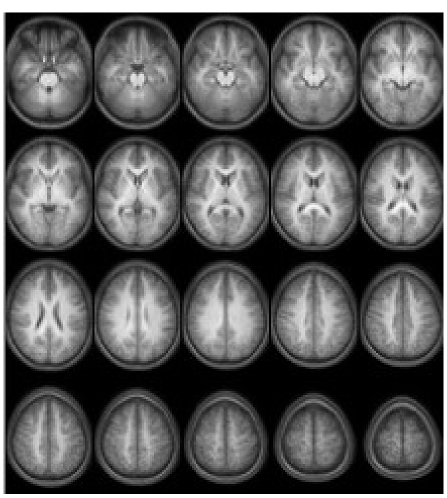

Figure 5. Regions with significant ($p < 0.01$ FWE corrected) activation differences between participants with math difficulties (MD) and typical achievement (TA). Images are presented in radiologic orientation. Slice locations: Z = -25 mm to Z = +70 mm.

Differences in deactivation. Regions with significantly greater deactivation for participants with TA included: bilaterally in the superior temporal/angular gyrus; medial orbitofrontal/anterior cingulate; medial prefrontal region; posterior cingulate/precuneus; bilaterally in the amygdala; the putamen, bilaterally; and bilaterally in the precentral gyrus (see Figure 6).

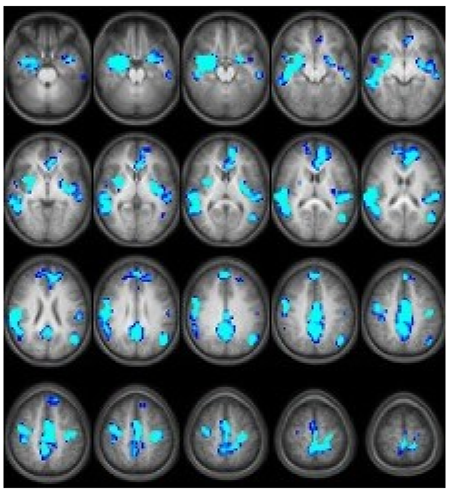

Figure 6. Regions with significant ($p < 0.01$ FWE corrected) deactivation differences between participants experiencing math difficulties (MD) and typical achievement (TA), (TA > MD). Images are presented in radiologic orientation. Slice locations: Z = -25 mm to Z = +70 mm.

Results for participants without ADHD

Each of the analyses described above were re-run excluding the three participants diagnosed with ADHD, two identified as TA and one identified as MD. The results reported below are from the remaining participants ($n = 18$). Specifically, the differences between the results from the sub-set of 18 participants without ADHD and the results reported above, with all participants, are reported.

fMRI group analysis results. The GLM was utilized for a second level analysis to examine group differences in activation and deactivation on the *Error Detection* task, keeping MD status as a variable of interest, this time excluding the three participants with ADHD.

Neural activation. No significant differences in neural activation were evident for the *Error Detection* task.

Neural deactivation. Significant neural deactivation was evident in the amygdala (see Figure 7).

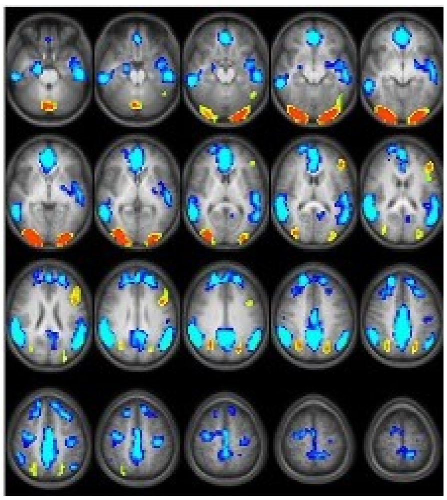

Figure 7. Group activation (hot colors) and deactivation (cold colors) maps ($p < 0.01$ FWE corrected), excluding participants with diagnosed ADHD) performing math tasks: Images are presented in radiologic orientation. Slice locations: Z = -25 mm to Z = +70 mm.

fMRI comparisons between TA and MD participants. A subsequent analysis examined the differences in neural activation and deactivation patterns between participants with MD and those who are TA, excluding those three participants with diagnosed ADHD. The exclusion of these participants did not yield any statistical differences in levels of activation (see Figure 8) or deactivation (see Figure 9) on the *Error Detection* task.

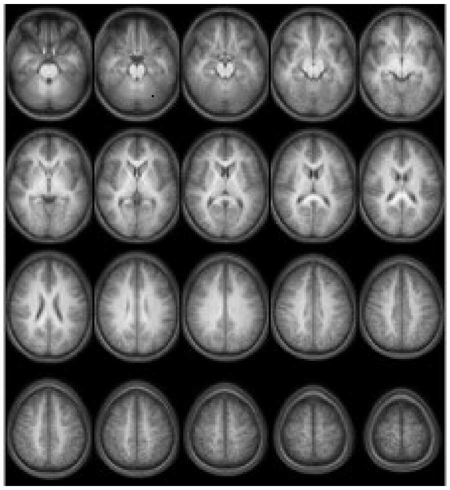

Figure 8. Regions with significant ($p < 0.01$ FWE corrected) activation differences between participants with math difficulties (MD) and typical achievement (TA), (TA > MD), excluding participants with diagnosed ADHD. Images are presented in radiologic orientation. Slice locations: Z = -25 mm to Z = +70 mm.

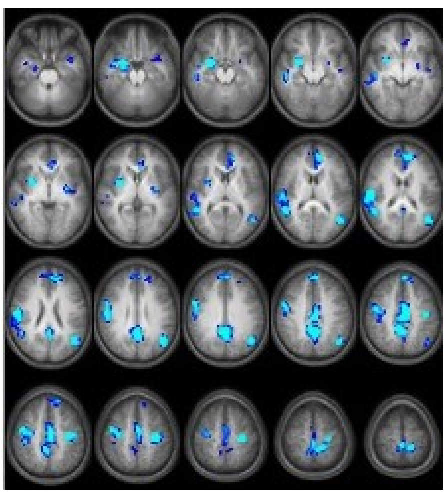

Figure 9. Regions with deactivation differences, that did not reach statistical significance, between participants experiencing math difficulties (MD) and typical achievement (TA), excluding participants with diagnosed ADHD. Images are presented in radiologic orientation. Slice locations: Z = -25 mm to Z = +70 mm.

CHAPTER V

Discussion

Although research has indicated that the prevalence of MD is similar to that of RD (Badian, 1983; Geary & Hoard, 2001; Gross-Tsur et al., 1996; Kosc, 1974; Shalev et al., 2000), historically, the field of MD has received less attention by the research community, despite the fact that an increasing number of jobs require the use of quantitative skills and knowledge (Geary, 2000; Geary, 2011a; Mitra, 2002; Terrell, 2007). The need for additional research on MD is becoming increasingly recognized.

Broadly, this study has sought to examine the behavioral and neural correlates of error detection capabilities in children with and without MD through the lens of three literature bases: Mathematics Cognition, Mathematical Learning Disabilities, and Cognitive Neuroscience of Mathematics Learning. Taking a Developmental Systems approach (Gottlieb, 1991), the author believes that by investigating MD through multiple levels of analysis (i.e., neural and behavioral), a more complete picture of MD can be understood. To that end, a combined fMRI and behavioral paradigm was employed to investigate the neural mechanisms supporting error detection capabilities in adolescent children with and without MD.

The triple-code model(Dehaene & Cohen, 1995, 1997; Dehaene et al., 2003), which served as the neuroscientific model of numerical processing upon which the central experimental measure of this dissertation was based, proposes that pathways may serve as an internal error detection system. If the *direct route* produces an unrealistic answer (i.e., 2 + 3 = 23) the *indirect route* is available to detect this error. Prefrontal areas and the anterior cingulate may coordinate processing of the stimuli, hold intermediate results in working memory, and be available to detect errors. Results from the current study suggest that in addition to the parietal lobe regions supporting numerical processing hypothesized by the triple-code model, brain regions supporting domain-general cognitive mechanisms such as attentional control and anxiety regulation may support mathematical task performance.

Research from the fields of Mathematics Cognition has identified both domain-specific and domain-general cognitive mechanisms supporting mathematics learning and their contribution to MD. Although the precise etiological foundation of MD has not yet been determined, recent studies have suggested two possible substrates. The first is proposed to exist as a result of a neurobiological deficit within the parietal region and to be related to a pure Mathematical Disability (pMD) (Rubinsten & Henik, 2009), one that is not shared with other disorders or difficulties. The second, and likely the more prominent etiology, appears to be related to deficits in domain-general cognitive mechanisms that support learning across a variety of tasks and activities, a so-called co-morbid mathematical disability (cMD) (Fletcher, 2005; Marshall, Hynd, Handwerk, & Hall, 1997; Zentall, 1990; Zentall et al., 1994).

The distinction between a pMD and cMD suggests that the prior arises from a neurobiological deficit in the parietal region of the brain, leading to impairments in domain-specific numerical and arithmetical abilities. A pMD deficit would result in a severe form of MD where basic mathematical skills such as subitizing, estimating, and approximation are impaired. This deficit would be phylogenetically expressed as a deficit in mathematics processing alone. Alternatively, a cMD would yield mathematical processing deficits arising from domain-general processing impairments. As such, a cMD would be expected to share a high co-occurrence rate with other disorders and disabilities, including attentional disorders and reading disabilities, including dyslexia. In fact, research suggests a high degree of overlap between children with mathematical and reading disabilities and those who experience both mathematical difficulties and attentional disorders (Fletcher, 2005; Marshall et al., 1997; Zentall, 1990; Zentall et al., 1994). Such a disability is proposed to be related to deficits that may include working memory, long-term memory retrieval, attentional control, and inhibition to response, and may have a potential relationship with a diagnosis of ADHD. Research from the field of Mathematics Learning Disabilities has indicated that the prevalence of mathematics difficulties which co-occur with attentional and working memory difficulties is even higher than those co-occurring with RD (Berch & Mazzocco, 2007). Deficits in any one of these domains may yield learning difficulties in a number of academic disciplines, mathematics included.

This dissertation addressed three research questions. First, Does the detection of specific types of errors in arithmetic problems have specific neural signatures? It was hypothesized that the detection of specific types of errors on arithmetic problems would have specific neural signatures in the left prefrontal region and anterior cingulate cortex. Data from the current study suggest that mathematical error detection abilities do have a specific neural signature with group activation maps showing neural activation in the cerebellum, bilateral middle occipital region, left dorsolateral prefrontal cortex, and posterior regions of the intraparietal sulcus, bilaterally. The hypothesized regions of activation were not entirely supported, activation was seen within the left prefrontal region; no activation was seen in the anterior cingulate. This may be due to the small sample size or the age of the participants, who while still within the developmental period are not young children, but adolescents. Support for the prediction that activation levels would be moderated by participants' MD status was not found, as no differences in activation levels were found between MD and TA participants. This, too, may be due to the small sample size or the fact that the present study employed a relatively liberal cutoff criterion for determining MD status, likely resulting in a cMD sample.

The second research question addressed by this dissertation asked, Does the detection of specific types of errors in arithmetic problems correlate with performance on a standardized achievement test? It was hypothesized that the detection of errors would correlate with performance on a standardized achievement test. The data indicate that participants identified as having MD, based on low performance on a standardized achievement test, had a particularly difficult time detecting errors on the *Error Detection* task. In fact, their proportion of correct answers did not exceed the chance level. It is clear, from these data, that children who are experiencing MD do, in fact, experience more difficulty than their TA peers recognizing errors when they have occurred. In addition to these children committing more errors than their TA peers, they are also less adept at recognizing errors when they do occur.

The third research question asked, What is the deactivation pattern of the DMN during the *Error Detection* task? It was hypothesized that performance on the *Error Detection* task would be related to differential deactivation of the DMN, specifically that lower performance on the *Error Detection* task would correlate with a lesser degree of DMN deactivation as compared to those participants with higher task performance. The data from the present study support this hypothesis with the novel finding of deactivation in the amygdala during the *Error Detection* task. Furthermore, MD participants showed statistically significant less reduction in deactivation than their TA peers, that is to say greater activation levels in the DMN than the TA cohort. Neuroimaging research has found anxiety regulation to be related to amygdala function and that increased stress may result in less efficient working memory and a reduction in memory retrieval (Roozendall, Barsegyan, et al., 2007; Roozendall, McEwen, et al., 2009). The differentiation in amygdala deactivation found in the current study may be suggestive of an internal mechanism used to suppress feelings of “math anxiety” (Hembree, 1990) through superior downregulation of emotional circuitry within participants experiencing TA. A well established inverse relationship between mathematics performance and mathematics anxiety has been established (Faust et al., 1996; Krinzinger et al., 2010; Ma, 1999; Newstead, 1998).

While there is relatively little research conducted on mathematics using neuroimaging technology, even less has examined the role of the DMN in terms of mathematics performance. Results from Davis et al. (2006) support the relationship between the mathematical performance and domain-general mechanisms, citing “the majority of group differences [in neural activation patterns] were located in the domain-general regions” (p. 2478). The results from the present study agree with those from Davis et al. (2006) with deactivation present within the DMN, and differential deactivation differences related to MD status.

The present study found no differences in neural activation patterns between the MD and TA groups on the *Error Detection* task. This finding may be a function of utilizing a relatively high cutoff criterion score on the mathematics achievement test as the criterion for group placement, which in turn likely yielded a study sample comprised of cMD children. Given this, the lack of activation differences in the parietal region between the MD and TA groups is not unexpected. If the sample had been comprised of primarily pMD children, different activation patterns may have been found.

The most notable results are the deactivation differences between the MD and TA groups. As would be expected with a cMD sample, significant differences were found in the relative deactivation of the DMN, with the MD group displaying less DMN activation than the TA group. When participants with ADHD were excluded from the analysis, DMN deactivation differences were seen in the amygdala, suggestive of a possible relationship between anxiety suppression and cMD. In fact, this finding is in agreement with other research that has established a correlation between ADHD and DMN deactivation on cognitively demanding tasks (Christakou et al., 2012). If cMD children share many of the neurobiological traits as children with ADHD, possible treatment options for cMD children may include those used in the treatment of ADHD.

Understanding the neurobiological substrates of pMD and cMD are necessary for design, implementation, and delivery of optimal intervention programming for children experiencing MD. Taking a pure behavioral approach to investigating these distinctions may provide an incomplete picture of MD as they often result in similar behavioral manifestations, despite very different neurological foundations.

Future Research and Limitations

If, as suggested by the data from the present study, cMD children share a neurobiological etiology with ADHD, although they themselves may be subclinical for an ADHD diagnosis, future research should examine the use of remediations and interventions commonly used in educational and clinical settings for the treatment of ADHD with children with cMD. Future research should also examine the use of alternative analysis procedures to examine the relationship between neural activity and error detection performance. Since the majority of imaging studies have relatively small sample sizes (as compared to studies employing only behavioral methods) it may be difficult to obtain a sample with adequate representation of MD participants. As the delineation of these groups is somewhat arbitrary, it may be that using mathematical achievement in a regression model would serve as a better statistical analysis approach.

Future research should examine DMN activation utilizing resting-state fMRI with a larger sample size. In addition, as a developmental effect is known to exist for the regulation of the DMN (Kucian et al., 2008) and for the neurobiological mechanisms utilized for mathematical processing, and that these changes occur in as little as one year (Rosenberg-Lee et al., 2011) future studies should examine differential activation and deactivation patterns longitudinally or using a cross-sectional design. This would allow for developmental comparisons of the DMN. As deficiencies in structural connectivity in MD children have been previously seen (Rykhlevskaia et al., 2009), future studies may make use of Diffusion Tensor Imaging (DTI) or High-Angular Resolution Diffusion Imaging (HARDI) studies to investigate DMN impairment.

A potential limitation of the present study is the somewhat small sample size. To address this limitation a conservative significance threshold of $p < 0.01$ FWE corrected was used, in place of the typical $p < 0.05$ threshold, false discovery rate (FDR) corrected. Despite this change in significance threshold, statistically significant results were still obtained. This is taken as an indication of a robust effect size. That said, future research examining error detection capabilities should employ an increased sample size to allow for an adequate range of mathematics achievement levels.

Analysis of data from the present study regarding the accuracy and neural correlates associated with specific error types has yet to be performed. That data, which may be reported elsewhere, may yield further insight into the neural mechanisms supporting error detection abilities.

Implications for Education

While neuroimaging results do not, at least at the present time, directly impact classroom teaching, important implications for education do exist. If MD does result from two very different etiological foundations, it is critical to understand the cognitive mechanisms underlying each type of deficit. To date, no standardized measure exists to diagnose MD, as such educators need to be aware of these different substrates and be prepared to closely examine the errors that children who struggle with mathematics commit. This dissertation opened with a quotation from Easley and Zwoyer (1975) suggesting that there is great value in examining errors, and that doing so may “reveal what the child is thinking” (p. 25). I believe that a wealth of information lies in these errors and if researchers and educators alike carefully examine them we will be positioned to better understand children’s’ errors in thinking and to make appropriate programmatic decisions regarding intervention.

While both pMD and cMD may result in similar behavioral manifestations (i.e., poor performance on mathematical measures) the origination of the deficits may be very different, thus requiring different intervention and remediation approaches. A pMD, resulting from a deficit in the parietal lobe, would necessitate programming designed to remediate impaired numerical processing abilities, including: deficits in number sense, counting, and simple calculation. Alternatively, a cMD, resulting from co-occurring deficits in general cognitive mechanisms, would suggest that intervention designed to increase working memory, executive function, attentional control, and inhibition to response are necessary. These intervention components may be similar to those in place for remediation of ADD/ADHD. Educators, including classroom teachers, intervention specialists, and administrators need to work together in examining the etiological foundation of MD deficits and in the design and implementation of intervention programs that meet the specific learning needs of each group.

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Appendices

Appendix A

Radiology Magnetic Resonance Imaging
(MRI) Safety and Screening Form

Name:____ Date_____________

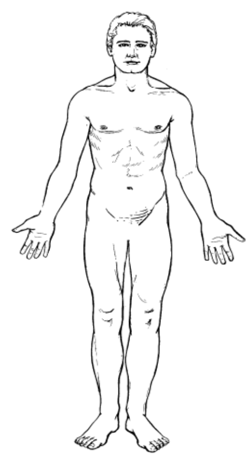
An MR safety screening sheet must be filled out for each person prior to entering the MR scan room. Parent or legal guardian should fill out the sheet for their child (under 18 years old). Please answer all questions and review the sheet with the technologist and nurse before entering.

1) Have you or your child had any prior surgeries, operations, or medical procedures? Yes/not sure No

2) Do you or your child have any medical devices, like a pacemaker, nerve stimulator, defibrillator, cochlear implant, baclofen or insulin pump, artifical heart valve, or programmable shunt? (please refer to the poster) Yes/not sure No

3) Have you or your child had any injury caused by a metal fragment or object, such as a BB, bullet, or shrapnel wound, including any eye injury? Yes/not sure No

If you answered yes/not sure to any of the above 3 questions, please list the type of surgery, injury, or device and mark the location on the drawing.



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4) Have you or your child ever worked with metal grinding tools, such as a lathe? Yes/not sure No

5) Do you have any other questions or concerns about MR scanning for you or your child? Yes No

____

Signature of Parent or Guardian (Patient if she/he is 18 years or older)

I have reviewed this screening form with the patient/parent/guardian.

Initial__________ Initial__________

Appendix B

Demographic Questionnaire

Please check the correct box and fill in the necessary blank space.

Start Here

1. Child's age: □ 9 □ 10 □ 11 □ 12 □ 13 □ 14

2. Child's highest grade completed: □ 5th □ 6th □ 7th □ 8th

3. Has your child ever been diagnosed with a learning disability?
□ Yes □ No

4. If your child has been diagnosed with a learning disability, what subject is their disability in?
□ Reading □ Math □ Both reading and math

5. If your child has a disability are they getting help from their school, a tutor, or other person for their disability?
□ Yes □ No

6. If your child is getting help with their disability, what age were they when they first got the help?

____

7. If your child is getting help for a disability, how often does your child get this help?

____

8. If your child gets help for a disability where do they get this help (school, counselor, psychologist, tutor, etc.)?

____

9. Has your child ever been diagnosed with a neurological impairment, such as Autism?
□ Yes □ No

10. If your child has been diagnosed with impairment, please tell me about your child's diagnosis. If additional space is required, please use the back of this form.

11. Has your child ever been diagnosed with a psychological disorder, such as ADD/ADHD?
□ Yes □ No

12. If your child has been diagnosed with a psychological disorder, please use the space below to tell me about your child's diagnosis. If additional space is required, please use the back of this form.

13. Which hand does your child usually write with?
□ Left □ Right □Both

Appendix C

Complex Multi-digit Task

Date of evaluation: ____
Name of person administering test: ______________________________

Do as many of these addition and subtraction problems as you can. Do them one after the other without skipping any. Please use a pencil and show all your work.

717 - 39	481 – 98 = _____	804 - 27
305 - 60 = _____	975 - 78	511 – 35 = _____
705 - 93	358 + 55 = _____	754 +69
307 – 58 = _____	124 +76	199 + 22 = _____
1,748 - 889	1,278 – 719 = _____	3,826 + 282
1,008 – 679 = _____	4,500 - 904	5,287 + 118 = _____

2, 931
+672

6,129 – 417 = _____

4,671
-382

3,002 – 466 = _____

9,004
-589

3,182 + 578 = _____

Appendix D

Error Detection Task

5 x 8 = 9

12 x 6 = 13

8 – 5 = 7

21 – 8 = 9

11 + 4 = 5

6 + 9 = 10

3 x 9 = 24

12 x 4 = 60

1 + 8 = 10

14 + 6 = 19

12 – 7 = 4

9 – 4 = 6

6 x 3 = 6

11 x 7 = 18

15 – 2 = 17

7 – 4 = 11

8 + 3 = 5

16 + 2 = 14

6 x 2 = 62

16 x 5 = 165

21 + 5 = 215

4 + 3 = 43

7 – 6 = 76

18 – 4 = 184

7 + 1 = 8

9 + 5 = 14

3 + 6 = 9

2 + 8 = 10

12 + 3 = 15

17 + 2 = 19

13 + 9 = 22

22 + 7 = 29

$2 - 1 = 1$

$7 - 2 = 5$

$9 - 6 = 3$

$6 - 4 = 2$

$16 - 5 = 11$

$11 - 3 = 8$

$14 - 9 = 5$

$23 - 13 = 10$

$9 \times 6 = 54$

$7 \times 4 = 28$

$5 \times 3 = 15$

$2 \times 8 = 16$

$13 \times 3 = 39$

$25 \times 4 = 100$

$11 \times 8 = 88$

$12 \times 7 = 84$

Appendix E

Error Detection Control Task

5	5
7	7
6	6
3	3
4	4
7	7
9	9
1	1
5	5
8	8
2	2
4	4
2	2
7	7
6	6
1	1

3	3
4	4
9	9
8	8
2	2
8	8
5	5
0	0
0	0
3	3
6	6
1	1
0	0
9	9
0	0
0	0
5	5

6	6
7	7
1	1
3	3
4	4
9	9
8	8
2	2
5	5
7	7
6	6
4	4
8	8
2	2

Appendix F

CINCINNATI CHILDREN's HOSPITAL MEDICAL CENTER
PARENTAL PERMISSION
FOR Participation in a Research Study

STUDY TITLE: NEURAL CORRELATES OF MATHEMATICS COGNITION AND SPECIFIC LEARNING DIFFICULTIES

SPONSOR NAME: Dept. of Radiology; University of Cincinnati

INVESTIGATOR INFORMATION:

Vincent Schmithorst, Ph.D.	(513) 600-0584
Principal Investigator Name	Telephone Number 24 hr Emergency Contact

INTRODUCTION:

You are being asked to give permission for your child to participate in a research study. Before agreeing to give permission for your child to participate in this study, it is important that you read and understand the following explanation. It describes, in words that can be understood by a lay person, the purpose, procedures, benefits, risks and discomforts of the study and the precautions that will be taken. It also describes the alternatives available and your right to withdraw your child from the study at any time. No guarantee or assurance can be made as to the results of the study. Participation in this research study is completely voluntary. Refusal to participate will involve no penalty or loss of benefits to which you or your child are otherwise entitled. You may withdraw your child from the study at any time without penalty.

WHO IS CONDUCTING THE RESEARCH STUDY?

The study is directed by Vincent Schmithorst, Ph.D., the researcher at Cincinnati Children's Hospital and Lori Kroeger, M.Ed., a researcher at the University of Cincinnati. Dr. James Leach is responsible for the medical supervision of this research.

Funds to conduct this study are being provided by the University of Cincinnati and Cincinnati Children's Hospital Medical Center (CCHMC).

WHY IS THIS RESEARCH BEING DONE?

The purpose of this research study is to establish what areas of the brain are normally used during math problem solving. The knowledge and experience gained from imaging mathematical functions in your child's brain may be helpful in the future in better understanding how math difficulties and their intervention affect the brain and its function. This is a continuation of the study of math and reading abilities that your child participated in during the 2008-2009 school year with Dr. Rhonda Brown, Ph. D. and Lori Kroeger, M.E. that was conducted through the University of Cincinnati.

WHY HAS YOUR CHILD BEEN ASKED TO TAKE PART IN THIS RESEARCH STUDY?

Your child is being asked to participate in this research study because he/she is currently in 7th or 8th grade and meets the criteria for inclusion in the research study and may have been a part of a group of children who have participated in the study “The Role of Long-term Memory in Math and Reading Abilities”. We now wish to find out which areas of your child’s brain are involved in math problem solving.

WHO SHOULD NOT BE IN THE RESEARCH STUDY?

Your child should not continue participation in this study if his/her medical history has changed so that he/she now has any electronic implants such as pacemakers or neuro-stimulators. Additionally, your child should not participate if your child is a female of childbearing age and there is any possibility of pregnancy. Your child may be asked to complete a pregnancy test by urine. It is also important that you inform the MRI technologist if your child has any metallic implants such as orthopedic pins or plates.

HOW LONG WILL YOUR CHILD BE IN THE RESEARCH STUDY?

Your child will be in the research study for approximately 3 hours. Participation in this research study will involve 1 study visit. The researcher may decide to end your child’s participation in this research study at any time, without your or your child’s permission, for any of the following reasons: the study doctor determines that it is in your child’s medical best interest, the study is ended early for any reason, or new information becomes available.

HOW MANY PEOPLE WILL TAKE PART IN THE RESEARCH STUDY?

Approximately 25 people will take part in this study at Cincinnati Children’s Hospital Medical Center.

WHAT IS INVOLVED IN THE RESEARCH STUDY?

If you agree to allow your child to participate and your child qualifies for this study, the following tests and procedures will be performed:

1. After all metal objects and jewelry are removed from your child’s body and clothing, he/she will be taken into the magnet room, and will lie down on a movable table that slides into the 3 Tesla MRI scanner.

2. Your child's head will be surrounded by a special antenna (RF coil), which picks up the radio signals used to make the images of his/her brain. While your child is in the magnet, he/she will be in constant contact with the technologist performing the examination outside the magnet room through a closed circuit television camera and an intercom system.

3. While in the magnet your child will be asked to perform several simple tasks at specific times while pictures of the brain are made. These tasks will involve solving math problems. Your child will be given instructions over the intercom telling him/her when to perform each task and when to rest.

4. Brain activity in response to these math problems will be recorded in the pictures of your child's brain. The total time spent in the scanner will not exceed 90 minutes.

5. The doctors will look at the scans of your child's brain immediately. If the scans are of poor quality due to motion of your child's head or technical problems, your child may be asked to repeat one or more scans, thus prolonging the examination past the 1.5 hour limit. If your child is not comfortable in the scanner at any time he/she can contact the technologist using the intercom or alarm button and ask to be removed from the scanner.

6. The pictures of your child's brain activity, as well as the pictures of your child's brain's structure will be used for the study.

7. In addition to the MRI scan, we may also administer a demographic questionnaire and ask your child to complete a math worksheet as part of this research study. We may also administer 2 math sections and 2 reading sections of a standardized achievement test. For the math tests, your child will be asked to solve math problems using a paper and pencil. For the language tests, your child will be asked to read two lists of words or non-words aloud. This will be done by a research team member outside of the MRI scanner in a testing room. In addition, we may administer an intelligence test to ensure that your child meets criteria for inclusion in this research study.

WHAT ARE THE RISKS AND DISCOMFORTS OF THE RESEARCH STUDY?

There are no known biological risks to MRI imaging. The main discomforts involved in MRI include anxiety and potential claustrophobia. The children enrolled in this study are carefully instructed as to what to expect. If your child becomes uncomfortable and does not wish to proceed, the examination will be immediately terminated. Your child will be screened for any metal objects that might become dislodged by the magnet and produce harm as a projectile. These will all be removed prior to entering the scanner room. Your child will not be given any sedation in order to perform this study.

There may be unknown or unforeseen risks associated with study participation.

The math problems your child will be asked to solve and the lists of words and non-words they will be asked to read are very similar to the types of math problems and word lists they are exposed to in typical school work. Children who have difficulty with these types of math problems and word lists may experience embarrassment or frustration while completing these tasks. These tasks are not expected to cause more than minimal discomfort. You and/or your child may contact the researchers about any discomfort experienced during the study.

WHAT ARE THE REPRODUCTION RISKS?

Because the strong magnetic fields may affect an unborn baby, if your child is a female of childbearing potential, she will not participate in this research study if there is a possibility that she could be pregnant. Your child agrees to inform the investigators if she has any reason to suspect a pregnancy at the time of the MRI scan.

ARE THERE DIRECT BENEFITS TO TAKING PART IN THE RESEARCH STUDY?

If you agree to allow your child to take part in this research study, your child will not receive a direct medical benefit.

The MRI scan being done is designed to answer research questions, not examine your child's brain medically. This MRI scan is not a substitute for one a doctor would order. It may not show problems that would be picked up by a clinical MRI scan.

However, the images are capable of revealing gross abnormalities. If we believe that we have found a medical problem in your child's MRI scan, we will ask a doctor who is trained in the reading of MRI scans, a neuroradiologist, to help us review the scan. If the neuroradiologist thinks that there may be an abnormality in your child's MRI scan, we will contact you and will help you get medical follow-up for the problem. If you have a primary care doctor for your child, we can also contact him or her, with your permission. If the study detects an abnormality in your child's MRI scan, then this information may become part of the hospital record.

The information learned from this research study may benefit other children with difficulties in mathematics in the future. This research is part of a study that will help us to see how and where the brain functions when mathematics is used. The results of this study may improve our understanding of mathematical development and representation in the brain, and thus affect educational and intervention practices.

WHAT OTHER CHOICES ARE THERE?

Instead of being in this research study your child may choose not to participate.

HOW WILL INFORMATION ABOUT YOUR CHILD BE KEPT PRIVATE AND CONFIDENTIAL?

Cincinnati Children's Hospital Medical Center and/or the Investigator will take the following precautionary measures to protect your child's privacy and confidentiality of your child's research and/or medical records:

1. All pictures obtained from the MRI scan and used for research purposes will be coded, and will not contain your child's name, medical record number, or any other protected health information belonging to you.
2. Electronic and hard-copy records containing your child's PHI will be password protected or locked at all times, with only authorized, study-related personnel having access to them.
3. Reports or publications generated as a result of this research will not contain any of your child's personal identifiers.

A copy of this consent form will be included in your child's medical research record.

Your child will be registered in the Cincinnati Children's Hospital Medical Center's computer system as a research participant.

By signing this consent form you are giving permission for representatives of the Cincinnati Children's Hospital Medical Center ("CCHMC"), the Investigator and CCHMC employees involved with the research study including the Institutional Review Board and the Office for Research Compliance and Regulatory Affairs, and any sponsoring company or their appointed agent to be allowed to inspect sections of your child's medical and research records related to this study.

WILL THE RESULTS OF MY CHILD'S RESEARCH-RELATED TESTS BE AVAILABLE?

All data gathered as a result of your child's participation in this study, including results of MRI scans, and mathematical and neuropsychological testing, will be made available upon request.

WHAT IF NEW INFORMATION BECOMES AVAILABLE DURING THE RESEARCH?

The investigator will tell you and your child about new information from this or other studies that may affect your child's health, welfare, or willingness to stay in this study.

The information from the research study may be published; however, your child will not be identified in such publication. The publication will not contain information about your child that would enable someone to determine your child's identity as a research participant without your authorization.

WHAT ARE YOUR COSTS TO BE IN THIS STUDY?

The child's parent or legal guardian will be responsible for the usual costs of medical care. However, there will be no extra cost involved with participation in the research study.

WILL YOU/YOUR CHILD BE PAID TO PARTICIPATE IN THIS RESEARCH STUDY?

You will receive the following reimbursement for the costs/inconvenience/time associated with your child's participation in the research study.

You will be compensated with a $100 Visa or Master Card gift card for reimbursement for travel and other out-of-pocket expenses associated with your child's participation in this research study upon your child's completion of the study procedures.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT?

Your child's participation in this study is completely **voluntary**. You or your child may choose either to take part or not to take part in this research study. Your decision whether or not to participate will not result in any penalty or loss of benefits to you or your child and the standard medical care for your child's condition will remain available to him/her.

If you decide to allow your child to take part in the research study, you are **free to withdraw** your permission and discontinue your child's participation in this research study at any time. Leaving the study will not result in any penalty or loss of benefits to your child.

If you are a CCHMC employee, your opportunities, rights, and benefits will not be jeopardized by your child's withdrawal from or by your child's refusal to take part in this study.

If you or your child has questions about the study, you will have a chance to talk to one of the study staff or your child's regular doctor. Do not sign this form unless you have had the chance to ask questions and have received satisfactory answers.

Nothing in this parental permission form waives any legal rights you or your child may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

ABILITY TO CONDITION TREATMENT ON PARTICIPATION IN THIS STUDY

You have a right to refuse to sign this parental permission form and Authorization to use/disclose your child's Protected Health Information for research purposes.

If you refuse to sign this consent, you and your child's rights concerning treatment, payment for services, enrollment in a health plan or eligibility for benefits will not be affected.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

For questions, concerns, or complaints about this research study or to report a research-related injury, you can contact the researchers Dr. Vincent Schmithorst at (412) 692-3212 or **Lori Kroeger** at **(513) 600-0584.** Researchers are available to answer any questions you may have about the research at any time.

If you have general questions about your child's rights as a research participant in this research study, or questions, concerns, or complaints about the research, you can call the Cincinnati Children's Hospital Medical Center Institutional Review Board at 513-636-8039. You can also call this number if the research staff could not be reached, or if you wish to talk to someone other than the research staff.

HIPAA AUTHORIZATION FOR USE/DISCLOSURE OF PROTECTED HEALTH INFORMATION FOR A RESEARCH STUDY

We understand that information about you and your health is personal and we are committed to protecting the privacy of that information. Because of our commitment to protect your privacy, we must obtain your written authorization (permission) before we may use or disclose (release) your "protected health information" (sometimes referred to as "PHI") related to the study described to you. This form provides that authorization and helps us make sure that you are properly informed of how this information will be used or disclosed. Please read the information below carefully before signing this form either for you, as the participant, or as the personal representative (parent, legal guardian, etc.) for the participant. Note that when we refer to "you" or "your" throughout this document, we are referring to the participant, even when this form is signed by the participant's personal representative.

USE AND DISCLOSURE COVERED BY THIS AUTHORIZATION

If you sign this document, you give permission to Cincinnati Children's Hospital Medical Center ("Cincinnati Children's") to use or disclose your medical and research information for the purpose of this study. Your PHI that will be used and disclosed in connection with this study consists of:

- Your Cincinnati Children's medical records
- Your research record for this study
- Results of your laboratory tests
- Clinical and research observations made during your participation in the study
- In the event that your medical record contains such information, information concerning HIV testing or the treatment of AIDS or AIDS-related conditions, drug or alcohol abuse, drug-related conditions, alcoholism, and/or psychiatric/psychological conditions (but not psychotherapy notes).

WHO WILL DISCLOSE, RECEIVE AND/OR USE THE INFORMATION?

This form authorizes the following to disclose, use and receive your PHI:

- Every research site of the study (including Cincinnati Children's and each site's research staff and medical staff)
- Every health care provider who provides services to you in connection with the study
- Any laboratories and other individuals and organizations that analyze your PHI in connection with the study
- The Sponsor and the people and companies they use to oversee, administer and/or conduct the study
- Federal regulatory agencies, other foreign regulatory agencies, and others as required by law
- The members of the Cincinnati Children's Institutional Review Board and staff of the Office of Research Compliance and Regulatory Affairs
- The Principal Investigator and members of the study's research team
- Data Safety Monitoring Board (if applicable)

By signing this document, you are authorizing Cincinnati Children's to use and/or disclose your PHI for this study. The purpose for the uses and disclosures is to conduct the study explained to you during the informed consent process and to ensure that information relating to the study is available to all parties who may need it for research purposes.

Those persons who receive your information may not be required by Federal privacy laws (such as the Health Insurance Portability and Accountability Act, also known as "HIPAA") to protect it and may share the information with others without your permission, if permitted by laws governing them.

You may revoke (choose to withdraw) this authorization at any time after you have signed it by providing the Principal Investigator (listed on the first page of the informed consent document) with a written statement that you wish to revoke it. Your revocation will be effective immediately and your PHI can no longer be used or disclosed for this study by Cincinnati Children's and the other persons or organizations that are identified above, except to the extent that Cincinnati Children's and/or the other persons or organizations identified above have already acted in reliance on the Authorization. In addition, the information may continue to be used and/or disclosed to preserve the integrity of the study.

Unless you notify us in writing of your decision to withdraw this authorization to use and disclose your PHI, it will expire at the end of the study. If the study involves the creation or maintenance of a research database repository, this authorization will not expire.

If you refuse to sign this authorization, you may not be able to receive research-related procedures and may not be able to continue in this study. However, your rights concerning treatment not related to this study, payment for services, enrollment in a health plan or eligibility of benefits will not be affected.

For further information about your rights, please see the Cincinnati Children's Notice of Privacy Practices on our website at http://www.cincinnatichildrens.org/about/corporate/hipaa.

SIGNATURES:

I have read the information given above. The investigator or his/her designee has personally discussed with me the research study and have answered my questions. I am aware that, like in any research, the investigators cannot always predict what may happen or possibly go wrong. I have been given sufficient time to consider if my child should participate in this study. I hereby give my permission for my child to take part in this study as a research study subject. I will receive a copy of this signed form for my records.

_______________________________________ ____________________

Signature of Participant's Parent or Legally Authorized Representative* Date

____

*Complete below if signed by a Personal Representative (parent, legal guardian, etc.)

____

Description of Personal Representative's Authority to Sign for Participant

____

Printed Name of Personal Representative

_______________________________________ ______________________

Signature of individual obtaining permission Date

Appendix G

Assent Form

<u>STUDY TITLE:</u> NEURAL CORRELATES OF MATHEMATICS COGNITION AND SPECIFIC LEARNING DIFFICULTIES

<u>SPONSOR NAME:</u> Dept. of Radiology; University of Cincinnati

INVESTIGATOR INFORMATION:

<u>Vincent Schmithorst, Ph.D.</u>	<u>(513) 600-0584</u>
Principal Investigator Name	Telephone Number 24 hr Emergency Contact

WHAT IS RESEARCH?

We are asking you to be in a research study. Research is a way to test new ideas. Research helps us learn new things.

Being in research is your choice. You can say Yes or No. Whatever you decide is OK. We will still take good care of you.

WHY ARE WE DOING THIS RESEARCH?

In this research study we want to learn more about how your brain works when you solve math problems.

We are asking you and other children to be in the research, because we would like to take pictures of your brain while you solve math problems.

WHAT WILL HAPPEN IN THE RESEARCH?

Before the scan, you will be asked to solve some math and language problems. You will be given one short math test and one short language test. For the math questions, you will use blocks to make the same design as you will see in a picture; for the language problems, you will be asked to give the definition of words the researcher reads to you.

To take pictures of your brain, you will need to lie still inside a machine called an MRI. You will need to stay there for about 1 ½ hours.

You will hear some loud noises. You will wear headphones so it will not sound so loud.

During part of the time, you will be able to watch a movie inside the MRI. You may tell us which movie you would like to watch. At other times, you will be asked to solve math problems while the scanner is running.

After the scan is over and you are outside the scan room, you will be given 3 short math tests and two language tests. For the math tasks, you will solve some math problems using a paper and pencil. For the language tasks, you will be asked to read two lists of words out loud. .

The entire visit will last about 3 hours.

If you are pregnant you cannot have the MRI. If you think that you may be pregnant, you will be asked to complete a urine pregnancy test. The results of that test may have to be shared with your parent(s) or guardian(s).

WHAT ARE THE GOOD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

Being in this research may not help you right now. When we finish the research, we hope that we will know more about what your brain does when you solve math problems. This may help other children with math difficulties later on.

WHAT ARE THE BAD THINGS THAT CAN HAPPEN FROM THIS RESEARCH?

The sound of the MRI will be loud. You will wear earphones to make the sound less loud.

Your head will be inside a small tube. You may find this uncomfortable or it may make you nervous.

If you get too uncomfortable or too scared, you may press a button to let one of us know you would like to come out of the scanner. We will take you out of the scanner right away.

WHAT ELSE SHOULD YOU KNOW ABOUT THE RESEARCH?

Being in the research is your choice. You can say Yes or No. It is OK to say No. No matter what you decide, we will still take good care of you.

If you say Yes now and change your mind later that is also OK. You can stop being in the research at any time.

If you want to stop being in the research, all you have to do is tell one of the doctors or nurses here at the hospital.

Take all the time you need to make your choice. Ask us any questions you have.

It is also okay to ask more questions after you decide to be in the research. You can ask questions at any time.

CHILD'S ASSENT

After you have read this form and talked about this research with your parents and the doctors or nurses you need to decide if you want to be in this research.

If you want to be in this research you should sign or write your name below.

________________________________ ____________________

Child's Assent Date

________________________________ ____________________

Signature of Person Obtaining Assent Date