Attention to Number:
A neurocognitive foundation for mathematical competence

By

Eric D. Wilkey

Dissertation

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

NEUROSCIENCE

May 11, 2018

Nashville, Tennessee

Approved:

Gavin R. Price, PhD

Laurie E. Cutting, PhD

Frank Tong, PhD

Blythe A. Corbett, PhD

ACKNOWLEDGMENTS

I would first and foremost like to thank my advisor Gavin Price for taking on my mentorship as a scientist in the fullest sense of the term. From guidance in scientific rigor, methodology, and integrity to the habits that sustain a long-term career in investigation, he was and is stalwart advocate. He urged me to cultivate a sense of excitement about our work and a healthy respect for the non-scientific aspects of my life that feed me, both of which will make overcoming future obstacles more manageable.

Thank you to all of my committee members for their feedback and encouragement throughout the research process: Laurie Cutting, Frank Tong, and Blythe Corbett. It is not often that doctoral work actually goes as planned and I owe that trajectory to the team of concerned scientists who prodded me along the way with knowledgeable questions about all of the things that could go wrong.

I would also like to thank my fellow lab members: Darren Yeo, who always has a fix for that thing that has held you back for two days and is the best person in the world to travel to conferences with; Courtney Pollack, who will make sure you test your assumptions and whose feedback is unparalleled; and Ben Conrad, who inspires me to take my analytic techniques further.

None of this would have been possible without the support of my family and I am immensely grateful for them. My father exemplifies a tireless work ethic that extends to all activities and circumstances, no matter who, if anyone, is watching. He also manages to build community wherever he goes. My mother, who has dedicated her life to educating children, demonstrates a tenacity that people should watch out for if they stand in the way of a developing child. My sister, whose generosity of spirit knows no bounds, has provided a lifetime of support.

Finally, I cannot properly communicate the gratitude I have for my wife, Megan. She is the most supportive and loving person a partner could ever ask for in this journey. Her unique ability to savor the bits of life that most of us rush past makes every day more enjoyable. Further, her dedication to advocacy for women and minorities of all kinds has served as a sobering reminder of the larger forces at play affecting my research. It reminds me to continually shift my perspective from the fine-grained approach of neuroimaging and psychometrics to a broader look at social factors and then back again. I thank her for making my work better and more fun at the same time.

TABLE OF CONTENTS

TABLE OF CONTENTS

LIST OF TABLES

Table Page

LIST OF FIGURES

INTRODUCTION

Mathematical thinking pervades nearly all aspects of modern life, from personal accounting to understanding important information about one's health. Accordingly, individuals with poor mathematical skills are less likely to graduate high school, go to college, have steady employment (Bynner, Parsons, Bynner, & Parsons, 2006; Geary, Hoard, Nugent, & Bailey, 2013; Goodman, Sands, & Coley, 2015; Ritchie & Bates, 2013; Rivera-Batiz, 1992), and are at a higher physical and mental health risk (Duncan et al., 2007; Hibbard et al., 2007; Parsons & Bynner, 2005). And yet, an estimated 1 in 4 economically active adults in the United States is functionally innumerate, lacking the ability to engage in and manage mathematical demands of a range of situations required in adult life (Gross, Hudson, & Price, 2009). For many, even with adequate support and educational resources, becoming fluent in basic mathematics is extremely difficult for a range of reasons (Butterworth & Laurillard, 2010). The development of mathematical skills requires the training and cooperation of a host of neurocognitive mechanisms with functions ranging from perceiving and maintaining numerical information to executing attentional demands of multi-step mathematical procedures. Any one of these requisite mechanisms is a potential source of difficulty on the path to mathematical competence. By understanding how these mechanisms function biologically, we may come to understand their developmental origin in the brain, atypical trajectories in that development, and potentially gain insight into paths for improved pedagogical techniques, diagnosis of learning disabilities, and remediation of specific deficits.

In addition to the normal range of difficulties that most students encounter while learning mathematics, an estimated 3-6% of the population is affected by the specific mathematics learning disability developmental dyscalculia (DD) (Shalev, Auerbach, Manor, & Gross-Tsur, 2000; Szűcs & Goswami, 2013). These individuals display difficulties with fundamental aspects of numerical processing from very early ages and continue to struggle with math, even when given the same schooling opportunities as their peers. The Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases-10 (ICD-10) categorize DD as a neurodevelopmental disorder with a biological origin (i.e. an interaction of genetic, epigenetic, and environmental factors) characterized by difficulties with processing numerical information, learning arithmetic facts, and performing accurate or fluent calculations (American Psychiatric Association, 2013). Despite the significant negative consequences, a detailed consensus characterization of the neurocognitive deficits associated with DD and their causes remains lacking. The current collection of studies investigates the neurocognitive mechanisms that serve as a foundation for the development of mathematical competence in typically developing individuals and may be atypical in those with DD.

One such mechanism, proposed to be foundational for math development, is often referred to as the approximate number system (ANS)(Halberda, Mazzocco, & Feigenson, 2008) or number sense (Stanislas Dehaene, 2011). This is the system used to order, compare, add, or subtract numerical magnitudes without reference to symbols. A significant body of research has provided evidence of a relation between individual differences in the processing of numerical magnitudes and the development of mathematical skills associated with atypical developmental trajectories (Mazzocco, Feigenson, & Halberda, 2011; Piazza et al., 2010). Further, neuroimaging evidence of structural and functional differences in the neural substrates of the ANS have been related to mathematical competence in a number of studies (Iuculano, Tang, Hall, & Butterworth, 2008; Mejias, Mussolin, Rousselle, Grégoire, & Noël, 2012; Mussolin, Mejias, Noël, & Noel, 2010; Price, Holloway, Räsänen, Vesterinen, & Ansari, 2007; Szkudlarek & Brannon, 2017). However, despite widespread correlational findings, a detailed *mechanistic* understanding of the link between processing of numerical magnitudes, individual differences in the neural substrates of the ANS, and mathematical competency remains lacking.

In recent years, several studies have indicated that measures of individual differences in numerical magnitude processing may not be measuring ANS acuity alone (Gebuis & Reynvoet, 2012; Dénes Szűcs, Nobes, Devine, Gabriel, & Gebuis, 2013). For example, behavioral measures of ANS acuity relate to mathematics achievement across development and levels of math achievement (Chen & Li, 2014; Schneider et al., 2017), but recent findings indicate that those same measures of ANS acuity, and their subsequent relation to mathematics, are heavily influenced by the presence of non-numerical visual cues of the task stimuli that increase executive function demands (Fuhs & McNeil, 2013; Gilmore et al., 2013; Szűcs et al., 2013). Therefore, the relation between task performance and math may depend on executive function demands rather than ANS acuity. This interpretation would support a long history of research relating deficits in domain-general mechanisms such as inhibitory control (Blair & Razza, 2007; Espy et al., 2004; Szűcs et al., 2013), verbal and visuospatial working memory (Bull & Scerif, 2001; Geary, 2004), and attention (Ashkenazi, Rubinsten, & Henik, 2009; Hannula, Lepola, & Lehtinen, 2010) to the development of mathematical skills and deficits in mathematics.

In light of findings showing the involvement of executive function in tasks designed to measure ANS acuity, the potential confound in stimulus design may also be viewed as the opportunity to explore the relation between magnitude processing and executive function. Rather than an investigation of the modular account of magnitude processing, whereby typical and atypical development are thought of in terms of the acuity of the ANS, the problem of congruency in the nonsymbolic number comparison task can be used to explore magnitude processing as a more dynamic system that is recruited under a variety of conditions, including heightened attentional load and cognitive control. Therefore, to investigate this issue, the current collection of three studies examines the neurobiological mechanisms underlying numerical magnitude processing and executive function that are critical for the development of competence in mathematics. In the course of a large-scale behavioral study of middle school children that includes a DD sample, a neuroimaging study of typically developing high school adolescents, and a neuroimaging study of typically developing 3^{rd} and 4^{th} graders, three studies provide evidence that the biological interplay of magnitude processing mechanisms and attention mechanisms, which can be described as domain-specific attention, or *attention to number*, represents a neurocognitive construct related to the development of mathematical competence.

1.1 Numerical Magnitude Processing Efficiency and Mathematical Competence

The perception of numerical magnitudes is ubiquitous across humans and appears to function similarly across a wide range of animal species (for a review, see Nieder, 2016), and infants as young as 6 months old are able to discriminate sets of objects on the basis of numerosity (Starkey, Spelke, & Gelman, 1990; Xu & Spelke, 2000). Early evidence for specific impairment of numerical magnitude processing mechanisms comes originally from neurological case studies of math deficits originating from individuals with parietal lesions who exhibited specific calculation deficits for approximation, addition, and subtraction (Delazer & Benke, 1997; Warrington, 1982). Often, these deficits were dissociable from memorized arithmetic factual knowledge such as access to multiplication tables (Dehaene & Cohen, 1997; Lemer, Dehaene, Spelke, & Cohen, 2003). Since then, electrophysiological recordings in nonhuman primates have identified populations of neurons in the lateral prefrontal cortex and ventral intraparietal sulcus (IPS) that code for numerosity irrespective of the sensory modality of stimuli (i.e. auditory or visual) (Nieder, 2012; Nieder & Miller, 2004; Viswanathan & Nieder, 2013), indicating that the ability to perceive and process numerical magnitude has identifiable neural substrates.

Most neural models of numerical magnitude perception begin with object identification that then feeds into a summation code, which abstracts number of objects over object position (see Nieder, 2016, for a review). The summation code then feeds into a number-selective code where populations of neurons in the superior parietal lobe have Gaussian response functions with peaks tuned to specific magnitudes (Nieder & Dehaene, 2009; Verguts & Fias, 2004). This number-selective code forms the basis of the so-called approximate number system or number sense (Dehaene, 1997). Accordingly, numbers that are closer together in magnitude have more overlapping neural representation compared to numbers that are further apart, which are thought to be more distinct in neural representation. As a result, people are slower and less accurate when discriminating between numbers that are closer together in numerical magnitude versus those that are further apart. This so-called ‘ratio effect’ can be modeled as a function of the numerical ratio between number pairs (Moyer & Landauer, 1967). Therefore, in principle, to measure individual differences in ANS acuity, one need only measure the degree of overlap in the distribution of neighboring magnitude response functions. The nonsymbolic number comparison task attempts to do this by measuring accuracy rates and response times as participants judge which of two groups of objects (e.g. dots or squares) is more numerous. In general, a smaller effect of ratio on accuracy and reaction time, or even simply higher accuracy rates and lower response times, are thought to indicate increased precision of numerical representation in the brain (Halberda et al., 2008)

As mentioned, there is considerable support for a relation between numerical representation efficiency and mathematics achievement, both across the full range of mathematics achievement (for meta-analyses, see Chen & Li, 2014; Schneider et al., 2017) and as a marker for DD (for reviews, see Iuculano, 2016; Szkudlarek & Brannon, 2017). Beginning with a retrospective study by Halberda, Mazzocco, & Feigenson (s2008) that linked performance on the nonsymbolic number comparison task in 9th grade to math achievement in Kindergarten through 6th grade, a number of studies have supported the claim that ANS acuity is related to math abilities ranging from counting to arithmetic to algebra (Chen & Li, 2014; Schneider et al., 2016) and that reduced ANS acuity may represent a core deficit in DD (Mazzocco, Feigenson, & Halberda, 2011; Piazza et al., 2010).

Further, just as behavioral performance on the number comparison task has become a widely used metric of ANS acuity, neural activity during nonsymbolic number comparison has frequently been employed to measure individual and group differences in the neural substrates of the ANS. Ansari & Dhital (2006) showed that adults exhibited a greater effect of numerical distance (akin to the ratio effect, but calculated as a linear distance between two numerical stimuli rather than a ratio) in the left intraparietal sulcus (IPS) than children. Though behavioral performance on the task was similar between children and adults, this pattern of greater modulation in response to numerical difficulty was interpreted as indicating ontogenetic development of magnitude processing mechanisms. With a similar logic, Price et al. (2007) demonstrated that, in DD children, the right IPS was not modulated by numerical distance, while their typically developing peers demonstrated patterns more similar to the children of Ansari & Dhital's study, with greater response to more difficult number comparison trials. Further, this pattern of results has even been demonstrated with symbolic number during a number comparison task with Arabic digits, where arithmetic competence correlated with a greater neural ratio effect in the left IPS (Bugden, Price, McLean, & Ansari, 2012). These studies together would indicate that greater modulation of the IPS in response to numerical magnitude should correlate with enhanced mathematical abilities. In line with these functional findings, structural analyses have also demonstrated that development of the IPS is related to mathematical competence. For example, analyses of cortical volume have linked greater grey matter volume in the left IPS to enhanced mathematical competence in typically developing 1st and 2nd grade children (Price, Wilkey, Yeo, & Cutting, 2016), reduced grey matter volume in the right IPS to the presence of DD (Rotzer et al., 2008), and both reduced cortical thickness and white matter volume in fronto-parietal structures to DD (Ranpura et al., 2013). Given this evidence, many researchers suggest that deficits in symbolic number processing, arithmetic fluency, and higher order mathematical thinking stem from a core deficit in the ANS, subserved by neural correlates in the IPS (Butterworth et al., 2011; Iuculano, Tang, Hall, & Butterworth, 2008; Wilson & Dehaene, 2007).

However, heterogeneity of findings that correlate functional activation during number processing to mathematical competency is more common than convergence. For example, in the only study relating neural correlates of nonsymbolic number comparison processing to mathematics achievement in typically developing adults, Gullick et al. (2011) found that the neural ratio effect in a nonsymbolic number comparison task is negatively correlated with mathematics achievement (i.e. greater response for more difficult trials correlated with low math performance) in bilateral perisylvian structures. And, atypical activation patterns in other brain regions during nonsymbolic number comparison have also been associated with DD including parieto-occipital regions (Dinkel, Willmes, Krinzinger, Konrad, & Koten, 2013), supplementary motor area and fusiform gyrus (Kucian, Loenneker, Martin, & von Aster, 2011), and inferior parietal regions (Kaufmann et al., 2009). In short, though there is some consensus that numerical magnitude processing relates to the development of mathematical competence, there is much disagreement as to the true mechanistic nature of this relation (Dénes Szűcs & Goswami, 2013), its causal role in DD (Mazzocco & Räsänen, 2013), and whether associated deficits are isolated to numerical magnitude processing or may be concomitant with deficits in symbolic representation of number or issues related to executive functions (Fias, Menon, & Szűcs, 2013; Rousselle & Noël, 2007; Szűcs, Devine, Soltesz, Nobes, & Gabriel, 2013). Therefore, despite some convergence of findings relating the function and structure of the IPS to ANS function and mathematical abilities, the biological nature of what produces the neural ratio effect is poorly understood, as is the logic of why a more efficient or accurate ANS would demonstrate a greater ratio-dependent response. Without a solid mechanistic account of these effects grounded in the biology of magnitude processing mechanisms, heterogeneity of findings may continue to be more common than convergence.

In the current literature, most researchers draw a link between the ANS model and the neural distance effect observed during number comparison tasks, attributing this observed effect to either (1) increased overlap in underlying magnitude representations for numbers that are closer together (Ansari, 2008; Pinel, Dehaene, Rivière, & LeBihan, 2001) or (2) attention/response selection demands (Göbel, Johansen-Berg, Behrens, & Rushworth, 2004). However, under careful scrutiny of their physiological underpinnings, neither of these accounts is sufficient on their own. In the case of the first explanation, representational overlap, the link between increased neural response and smaller distances between stimuli is unclear. The traditional argument has been that the recruitment of overlapping neural populations recruits more neural activity, and thus, a greater BOLD response in a set of voxels (Ansari, 2008). However, the only plausible explanation for increased BOLD response due strictly to underlying magnitude representation would be an increase in activity in the neurons shared by each numerical representation that is greater than the sum of their involvement in either representation independently. Otherwise, there would be no increase in neural activity with near distances. This is physiologically possible, but this scenario would result in increased neural activity in the populations of neurons shared between the two numerical magnitudes. If this were true, the neural system would be more likely to confuse the two numbers as a function of distance, which is physiologically unviable and out of step with findings that suggest a greater neural response to close numbers is indicative of greater maturation (Ansari & Dhital, 2006). In fact, the reverse could present a more parsimonious argument. That is, one might expect that if stimuli are close together in numerical value, if they are represented by neural populations that overlap, one would expect *less* BOLD activity in the IPS, if only because fewer neurons are active due to the magnitude-selective neurons having tighter tuning curves. In the case of the second explanation for the neural distance effect, that of attention/response selection, the account does not explain the large quantity of studies that tie activity in the IPS directly to magnitude encoding. Though models of ANS acuity likely explain certain properties of frontal and parietal neurons that code for magnitude, the link between their function and mathematical competence is still unclear.

1.2 Measurement of Magnitude Perception and Control of Visual Stimuli

One problem undermining our understanding of the link between magnitude processing and mathematics development is the reliance on nonsymbolic number comparison as a measure of numerical acuity. Conventionally, nonsymbolic number comparison performance has been interpreted as a measure of numerical magnitude processing efficiency (De Smedt, Noël, Gilmore, & Ansari, 2013). However, recent research suggests that the task may be measuring more than number processing alone. Specifically, several studies have shown that nonsymbolic number comparison performance is highly influenced by the visual parameters of task stimuli (Gebuis & Reynvoet, 2011, 2012; Leibovich & Henik, 2013; Dénes Szűcs et al., 2013). In general, visual properties such as surface area and object size covary with numerosity. If these properties are not controlled when creating stimuli, participants can rely on non-numerical cues to select the more numerous array. Thus, to ensure participants employ a strategy focused on numerosity, stimuli are designed such that, in some trials, the more numerous dot set has a greater surface area or dot size (congruent trials), and in other trials a lesser surface area or dot size (incongruent trials) (e.g. Dehaene, Izard, & Piazza, 2005).

Recent studies suggest that performance on incongruent trials may drive the relation between nonsymbolic number comparison and mathematics performance (Bugden & Ansari, 2015; Clayton, Gilmore, & Inglis, 2015; Cragg, Keeble, Richardson, Roome, & Gilmore, 2017; Fuhs & McNeil, 2013; Gilmore et al., 2013; Keller & Libertus, 2015). For example, Gilmore et al. (2013) and Fuhs and McNeil (2013) found that only performance on incongruent trials of the nonsymbolic number comparison task was related to mathematics performance across a wide range of mathematics achievement in primary school and preschoolers respectively. To explain this specific relation, the authors of those studies suggest that incongruent, non-numerical visual cues in the comparison task require participants to inhibit their visually-based response before making a quantity-based judgment, thus engaging inhibitory control mechanisms. Accordingly, both Gilmore et al. and Fuchs and McNeil posit that inhibitory control and selective attention demands of incongruent trials, rather than numerical acuity, drive the relation between nonsymbolic comparison performance and mathematics. Indeed, after controlling for inhibitory control, the relation between mathematics performance and nonsymbolic comparison was no longer statistically significant in both studies. Similarly, in a study comparing performance of children with DD versus their typically developing (TD) peers, Bugden and Ansari (2015) found that children with DD only differed on incongruent trials. A follow-up analysis showed that children's visuo-spatial working memory predicted numerical acuity on incongruent trials, indicating that visuo-spatial working memory may be an important cognitive process utilized for extraction of numerosity in the presence of other visually salient information. The results of these studies indicate that the link between performance on nonsymbolic comparison tasks and math achievement may be explained by cognitive processes used to extract numerical magnitude from stimuli in the face of conflicting visual information rather than simply an individual's acuity of the representation of numerical magnitudes. However, it should be noted that at least two studies continue to find a relation between number comparison performance and mathematics achievement, even after controlling for executive function abilities (Gilmore, Keeble, Richardson, & Cragg, 2015; Keller & Libertus, 2015)

Neuroimaging research using the nonsymbolic comparison task indicates that recruitment of neural resources also differs as a function of congruency condition. In a study of typically developing adults, Leibovich, Vogel, Henik, and Ansari (2015) showed that incongruent trials are associated with greater activity in the superior frontal gyrus and left inferior/middle frontal gyri, but less activity in the right middle temporal and posterior cingulate gyri, than congruent trials. However, Leibovich et al (2015) examined activation during numerical versus non-numerical processing as a function of congruency, as opposed to examining the effect of congruency on ratio-dependent task activity. In order to investigate how differences in congruency specifically relate to processing of numerical information, the effect of congruency on numerical magnitude-specific activation must be evaluated. Just as a behavioral ratio effect has become a hallmark measure of ANS acuity, ratio-dependent blood-oxygen-level dependent (BOLD) response has become a neural proxy (i.e. the neural ratio effect)(Bugden et al., 2012). However, prior to the current work, no study has investigated whether the neural ratio effect during nonsymbolic numerical magnitude processing is affected by the congruency of visual cues, and consequently, whether these potential differences in neural activity relate to math achievement. Understanding how differences in congruency require the recruitment of unique neural resources or how they differentially recruit known magnitude processing mechanisms may shed light on why numerical magnitude encoding appears to be related to math competency only in the face of conflicting visual cues, as well as elucidating the precise role of neural mechanisms that support processing of numerical information.

1.3 Attention as a Factor for the Development of Mathematical Competence

When selecting a participant pool for "pure dyscalculia", participants with ADHD, dyslexia, or other neurological condition are often excluded in order avoid confounds. However, it should be noted that nearly 40% of individuals with DD also have dyslexia (Lewis, Hitch, & Walker, 1994). Comorbidity between the two is likely an important facet of DD itself and this exclusion criteria leaves an important issue under-explored. Several researchers have argued that domain-general cognitive deficits are the underlying cause of poor arithmetic performance in DD individuals and the disorder has been linked to deficits in phonological ability (Swanson & Sachse-Lee, 2001), inhibitory control (Blair & Razza, 2007; Espy et al., 2004; Szűcs et al., 2013), spatial processing (Rourke & Conway, 1997), verbal and visuospatial working memory (Bull & Scerif, 2001; Geary et al. 2004), and attention (Ashkenazi et al., 2009; Hannula et al., 2010). Furthermore, working memory and spatial processing are two cognitive domains that frequently correlate with math ability and DD diagnosis. In a study of 12 students in 3rd and 4th grade who performed poorly on a test of arithmetic and age-matched peers, researchers administered a battery of 10 working memory tasks (McLean & Hitch, 1999). Executive and spatial aspects of working memory were determined to be important indicators of poor arithmetic attainment. Further, neuroimaging experiments have also linked working memory deficits and DD. For example, Dumontheil and Klingberg

(2012) demonstrated that activity in the left IPS correlated with working memory capacity and predicted poor arithmetic achievement two years later. Therefore, based on both behavioral and neuroimaging evidence, individual differences in attention mechanisms relate directly to measures of mathematics achievement.

In addition to the presence of a direct relation between attention mechanisms and math, attention mechanisms may influencing the relation between ANS measures and math. Evidence that congruency factors drive the correlation between nonsymbolic number comparison task performance and mathematical competency raises the possibility that the link to mathematics achievement is actually related to individual differences in attention rather than ANS acuity (Fuhs & McNeil, 2013; Gilmore et al., 2013). For example, during the number comparison process, attentional mechanisms are called upon to resolve competing visual cues, inhibiting irrelevant stimulus dimensions, thereby prioritizing numerosity as the salient visual feature for response selection. With this explanation, a cohort of individuals could possess the exact same numerical acuity but vary widely in their ability to inhibit competing stimulus features, resulting in a wide array of accuracy rates and response times in the number comparison task. And, because it has been well established that various components of executive function correlate with mathematics (Blair & Razza, 2007; Bull & Scerif, 2001; Espy et al., 2004), it would not be surprising that these metrics correlate with achievement. This account would explain why several studies have found that only performance on incongruent trials of the number comparison task relates to math achievement (Gilmore et al., 2013, 2015) or the presence of a math learning disability (Bugden & Ansari, 2015). In this explanation, no actual relation to numerical acuity is necessary. Further, an explanation based on individual differences in attention may provide an alternate interpretation of neuroimaging findings in humans. Attention mechanisms and magnitude processing mechanisms largely converge in both frontal and parietal regions (Petersen & Posner, 2012; Sokolowski et al., 2016), including the bilateral intraparietal sulcus (IPS) and inferior frontal gyrus (IFG), making it difficult to disentangle their respective contributions to task-related activity without strict controls and additional analyses. Differences in neural activation in the IPS or frontal regions in response to numerical stimuli may equally be driven by attentional demands that depend on task difficulty, response selection (Göbel et al., 2004), or resolution of conflicting visual cues.

1.4 Attention to Number

To summarize, evidence from behavioral studies that index acuity of the ANS indicate that task performance correlates with mathematics achievement, both in typically developing populations, and as a marker of DD. However, it has now come to light that attention and executive function demands heavily influence measures of ANS acuity. Furthermore, a large body of research demonstrates a link between individual differences in domain-general general mechanisms of attention and the development of mathematical competence. From this research, the question follows, how, then, are attentional mechanisms of executive function related to the processing of numerical magnitudes? And second, what are the neurocognitive mechanisms underlying the relation between nonsymbolic number comparison and math? Is it ANS acuity, attention, or a biological interplay of the two?

Executive function components of attention, such as inhibitory control or working memory, are often cited as domain-general mechanisms. However, if we apply this concept to a specific scenario, such as an arithmetic word problem, it becomes apparent that the content of attentional focus and inhibitory control is inextricably linked with the given domain-specific mechanism. In practice, the distinguishable components of cognitive theory give way to the physical reality that maintaining information in one's consciousness for the duration of an arithmetic problem, and shifting attention among numerical values, is likely to involve the interaction of a host of neural mechanisms within the frontal-parietal network. Magnitude encoding neurons in the IPS or lPFC (Nieder, 2016) will likely receive input signals to sustain activity, or will become synchronized in rhythm with other parts of the network, to accomplish this task. To solve the arithmetic problem, one must maintain this magnitude information while simultaneously encoding new information so that they may be integrated in the process of doing arithmetic. This integration of domain-specific processing with so-called domain-general mechanisms may be another potential source of impairments that manifest as deficits specific to mathematical content.

Therefore, while both magnitude processing and attentional mechanisms provide plausible paths for individual differences in math competency, and potential sources of difficulty associated with DD, one further possibility is a form of domain-specific attention, or *attention to number*. Rather than a generalized attentional component across domains, it may be that the way executive function mechanisms interact with magnitude processing mechanisms is a critical factor for acquiring mathematical competency. In regards to number comparison tasks, it may explain why performance on number comparison tasks relates to math achievement beyond non-numeric measures of executive function (Keller & Libertus, 2015) and also why congruent trials are less related to achievement than incongruent trials. However, within the construct of attention to number, there are multiple neural mechanisms that may be at work. On the one hand, increased attention can be achieved by increasing the saliency of a particular percept, or in other words, turning up the gain for neural activity related to a particular stimulus dimension, such as number. This type of response has been demonstrated in multiple modalities, from hearing (Kerlin, Shahin, & Miller, 2010) to vision (Bisley, 2011; Hillyard, Vogel, & Luck, 1998). For example, covert attention to the left side of a fixation cross (i.e. no movement of the eyes) will increase neural response in the right extrastriate visual cortex, which corresponds to the left visual field (Mangun, Hopfinger, Kussmaul, Fletcher, & Heinze, 1997). On the other hand, increased attention to number could be achieved by suppressing competing perceptual information. For example, cell recordings in the lateral intraparietal area in monkeys show that ignoring a pop-out distractor cue suppresses neural response in areas of the brain that control visual salience (Ipata, Gee, Gottlieb, Bisley, & Goldberg, 2006). These two mechanisms, that of increased gain and suppression of competing information, are likely to work in concert to enable attention to number in the context of a number comparison task. Less efficacy of their action may result in a deficit of attention to number.

One point of clarification is warranted regarding the current study's intentionally broad use of the construct of attention. The principal form of attention investigated in the current study, whereby a child was directed to respond to a choice in stimuli by isolating the correct visual dimension (i.e. number of dots or arrow orientation), is known by several names. A long history in cognitive neuroscience, espoused by Posner and Peterson (Petersen & Posner, 2012; Posner & Petersen, 1990), has delineated attention systems of the human brain based on anatomical organization, associated neurotransmitters, and their dissociable cognitive functions. In their model, the focus of the current tasks fall principally under the control of fronto-parietal "executive attention" and "orienting" networks. Psychologists, on the other hand, tend to use the term "executive function" to refer broadly to an array of top-down, effortful mental processes needed for concentration and paying attention that are a subset of attention more broadly (Diamond, 2014), which is further broken down into inhibition, working memory, and cognitive flexibility (Miyake et al., 2000). Thus far, research on the effect of congruency in number comparison tasks has mainly focused on inhibitory control components of executive function without much discussion of their underlying neural mechanisms (Clayton & Gilmore, 2014; Fuhs, Kelley, O'Rear, & Villano, 2016). However, we hypothesize that attention to number is likely to involve both increased focus of cognitive resources to numerical information and the inhibition of irrelevant information. Therefore, attention to number is a term we use to begin to investigate domain-specific attention while leaving open the possibility that multiple neural mechanisms are captured by the paradigm utilized in the current study.

1.5 Outstanding Questions

Already, diagnostic tools for math learning disability (Brian Butterworth & Laurillard, 2010; Nosworthy, Bugden, Archibald, Evans, & Ansari, 2013) and early learning interventions (Park & Brannon, 2014, 2016; Räsänen, Salminen, Wilson, Aunio, & Dehaene, 2009; Szűcs & Myers, 2016) are being developed which target measurement of and training of the nonsymbolic number system. However, in light of the research described above, these efforts may be premature. In order to understand the link between the influence of attentional factors in the nonsymbolic comparison task, the basic systems that encode numerical magnitude in the brain, and their link to math achievement, a detailed understanding of the neural mechanisms underlying the influence of visual cues on the perception of numerical magnitudes is essential. With this understanding, diagnostic tools and interventions may target specific neurocognitive mechanisms underlying math skills. Without it, they are at risk of targeting behaviors that merely correlate with math achievement but do not reflect cognitive mechanisms fundamental to its development.

Therefore, the current collection of three studies aims to better understand the attentional factors that interact with numerical magnitude processing mechanisms by asking three basic questions. First, is attention to number a factor related to math achievement beyond either acuity of the ANS or domain-general executive function? Second, how are numerical magnitude processing mechanisms affected by issues of interfering stimulus dimensions such as congruency of visual cues? And third, do individual differences in *attention to number* relate to the development of mathematical competence?

1.6 Overview of Experiments

To address the above questions, three independent studies were completed investigating the influence of congruency/incongruency of visual parameters in the nonsymbolic number comparison task and their relation to measures of attention and mathematical competence. The first study (Chapter 2) is a longitudinal, behavioral study exploring the relation among congruent and incongruent trials on the nonsymbolic number comparison task as it relates to group differences in middle school math achievement (i.e. DD, low math achievement, and typical achievement) while controlling for other non-numerical components of executive function. The large-scale and longitudinal nature of this data, composed of math achievement measures dating from Pre-K to 7^{th} grade, allowed for the creation of achievement group based on sustained achievement levels. Further, the designation of a DD group was not formed on the basis of a discrepancy criteria (i.e. discrepancy between IQ or expected achievement and mathematics achievement), but rather very low math achievement from beginning of formal schooling through middle school. This DD designation criteria allowed for the investigation of *attention to number* as a factor related to math achievement while controlling for other non-numerical measures of executive function, without excluding individuals with comorbid deficits, which may be critical to understanding the development of math skills and of DD itself. Therefore, the focus of this study was to investigate the relation between number specific executive function, as indexed by incongruent trials on the nonsymbolic number comparison task, and mathematics achievement, both as a factor related to DD and also across the full range of achievement.

The second study (Chapter 3) is an fMRI study of high-school aged students who participated in a larger study of arithmetic, symbolic, and nonsymbolic number processing. This analysis investigated the issue of congruency and its influence on the neural mechanisms supporting numerical magnitude perceptions and subsequent relation to mathematics achievement as measured by the preliminary scholastic aptitude test (PSAT). It first investigates whether the frequently-used metric, the neural ratio effect, differs as a function of congruency in order to compares neural substrates of the ANS in differing attentional states. Further, it is the first study to separate neural response by congruency condition in the nonsymbolic number comparison task to investigate their relation to mathematics achievement independently. In light of the suspected difference in attentional demands of each condition, neural correlates of the task are likely to differ as well.

The third study (Chapter 4) again utilizes fMRI measures of neural activity during the nonsymbolic number comparison task split by congruency. However, Study 3 differs in two principal ways from Study 2. First, participants are children in 3rd and 4th grade rather than high school students. Second, the children also completed an Erickson flanker task while scanning, designed to closely mirror the attentional demands of congruency issues in the nonsymbolic number comparison task, but in a non-numeric domain. This allows for the cognitive subtraction of increased attentional demand in a numerical task minus increased attentional demand in a non-numerical task, resulting in a more stringently controlled evaluation of neural activity related to *attention to number*, and a principled approach to our third question regarding the biological interplay of the neurocognitive systems dedicated to magnitude processing and attentional allocation?

Together, these three studies investigate the biological interplay of magnitude processing mechanisms and attention mechanisms that represented a form of domain-specific attention, or *attention to number*, that may provide further insight into current theories about the relation between ANS acuity and math development, as well as an additional mechanism that may be the source of difficulties in learning mathematical skills.

CHAPTER 2

DYSCALCULIA AND TYPICAL MATH ACHIEVEMENT ARE ASSOCIATED WITH INDIVIDUAL DIFFERENCES IN NUMBER-SPECIFIC EXECUTIVE FUNCTION

2.1 Introduction

Mathematical thinking pervades nearly all aspects of modern life, from personal accounting to understanding important information about one's health. Accordingly, individuals with poor mathematical skills are less likely to graduate high school, go to college, have steady employment (Bynner et al., 2006; Rivera-Batiz, 1992), and are at a higher physical and mental health risk (Duncan et al., 2007; Hibbard et al., 2007; Parsons & Bynner, 2005). The development of mathematical skills can be affected by a range of factors including education, home environment, and reading ability. However, a substantial body of research indicates that individual differences in the cognitive system used to perceive and manipulate numerical magnitudes, often labeled the Approximate Number System (ANS) (Feigenson, Dehaene, & Spelke, 2004), play a foundational role in mathematics development (Chen & Li, 2014; Schneider et al., 2017; Schwenk et al., 2017). Further, an estimated 3-6% of the population is affected by the specific mathematics learning disability developmental dyscalculia (DD) (Shalev, Auerbach, Manor, & Gross-Tsur, 2000; Szűcs & Goswami, 2013). Individuals with DD display difficulties with fundamental aspects of numerical processing from very early ages and continue to struggle with math, even when given the same schooling opportunities as their peers. However, the nature of these numerical deficits and their relation to the abilities of typically developing populations remains poorly understood.

The ANS, Mathematics Achievement, and Dyscalculia

The most commonly used behavioral measure of ANS function is the nonsymbolic number comparison task. In this task, participants judge which of two groups of objects, such as dots or squares, is more numerous. Higher accuracy rates and faster response times are thought to indicate higher acuity and enhanced efficiency of the ANS (Inglis & Gilmore, 2014). There is considerable support for a relation between efficiency of the ANS and mathematics achievement, both as a marker for DD (for reviews, see

Iuculano, 2016; Szkudlarek & Brannon, 2017), and across the full range of mathematics achievement (for meta-analyses, see Chen & Li, 2014; Schneider et al., 2017).

Accordingly, the dominant theory regarding a core deficit in DD proposes an impairment of the ANS, in part because individuals with DD have been shown to perform more poorly in tasks designed to measure the ANS, such as the nonsymbolic number comparison task (Mazzocco, Feigenson, & Halberda, 2011; Mejias, Mussolin, Rousselle, Grégoire, & Noël, 2012). Further, neuroimaging research suggests that individuals with DD have atypical structure and function of proposed neural substrates of the ANS, such as the intraparietal sulcus (Ashkenazi, Black, Abrams, Hoeft, & Menon, 2013; Dinkel et al., 2013; Kaufmann et al., 2009; Christophe Mussolin et al., 2010; Gavin R. Price et al., 2007; Rosenberg-Lee et al., 2015; Rotzer et al., 2008; Rykhlevskaia, Uddin, Kondos, & Menon, 2009). Given this evidence, many researchers suggest that deficits in symbolic number processing, arithmetic fluency, and higher order mathematical thinking stem from a core deficit in the ANS (Butterworth et al., 2011; Iuculano, Tang, Hall, & Butterworth, 2008; Wilson & Dehaene, 2007). Though there is some consensus that the ANS is atypical in individuals with DD, there is much disagreement as to the true mechanistic nature of this deficit (Dénes Szűcs & Goswami, 2013), its causal role in DD (Mazzocco & Räsänen, 2013), and whether the deficit is isolated to the ANS or may be concomitant with deficits in symbolic representation of number or issues related to executive functions (Fias, Menon, & Szűcs, 2013; Rousselle & Noël, 2007; Szűcs, Devine, Soltesz, Nobes, & Gabriel, 2013). Adding to this complication, individual differences in ANS acuity consistently correlate with mathematics across the full range of achievement (Justin Halberda et al., 2008; Keller & Libertus, 2015; Schneider et al., 2017), suggesting the relation is not isolated to group differences that identify severe mathematics deficits, but rather extends broadly across achievement levels. As a result, it remains unclear as to whether DD represents a qualitatively distinct subgroup with distinct cognitive deficits or is the lowest extreme of a continuous distribution. This distinction is important for developing appropriate intervention strategies to remediate low mathematics skills (Butterworth & Kovas, 2013; Henik, Rubinsten, & Ashkenazi, 2011).

Nonsymbolic number comparison as a measure of the ANS?

One problem undermining the link between ANS function and mathematics development is the reliance on nonsymbolic number comparison as a measure of ANS acuity. Conventionally, nonsymbolic number comparison performance has been interpreted as a measure of ANS function (De Smedt et al., 2013). However, recent research suggests that the task may be measuring more than ANS acuity alone. Specifically, several studies have shown that nonsymbolic number comparison is highly influenced by the visual parameters of task stimuli (Gebuis & Reynvoet, 2011, 2012; Leibovich & Henik, 2013; Dénes Szűcs et al., 2013). In general, visual properties such as surface area and object size covary with numerosity. If these properties are not controlled when creating stimuli, participants can rely on non-numerical cues to select the more numerous array. Thus, to ensure participants employ a strategy focused on numerosity, stimuli are designed such that, in some trials, the more numerous dot set has a greater surface area or dot size (congruent trials), and in other trials a lesser surface area or dot size (incongruent trials) (e.g. Dehaene, Izard, & Piazza, 2005).

Recent studies suggest that performance on incongruent trials may drive the relation between nonsymbolic number comparison and mathematics performance (Bugden & Ansari, 2015; Clayton, Gilmore, & Inglis, 2015; Cragg, Keeble, Richardson, Roome, & Gilmore, 2017; Fuhs & McNeil, 2013; Gilmore et al., 2013; Keller & Libertus, 2015). For example, in a study comparing nonsymbolic number comparison performance in children with DD versus typically developing (TD) peers, Bugden and Ansari (2015) found that children with DD only differed on incongruent trials. A follow-up analysis showed that children's visuo-spatial working memory predicted ANS acuity on incongruent trials, indicating that visuo-spatial working memory may be an important cognitive process utilized for extraction of numerosity in the presence of other visually salient information. Similarly, studies by Gilmore et al. (2013) and Fuhs and McNeil (2013) found that only performance on incongruent trials of the nonsymbolic number comparison task was related to mathematics performance across a wide range of mathematics achievement in primary school and preschoolers respectively. To explain this specific relation, the authors of those studies suggest that incongruent, non-numerical visual cues in the comparison task require participants to inhibit their visually-based response before making a quantity-based judgment, thus engaging inhibitory control mechanisms. Accordingly, both Gilmore et al. and Fuchs and McNeil posit that inhibitory control and selective attention demands of incongruent trials, rather than ANS acuity, drive the relation between nonsymbolic comparison performance and mathematics. Indeed, after controlling for inhibitory control, the relation between mathematics performance and nonsymbolic comparison was no longer statistically significant in both studies.

Still, the contribution of executive function to the relation between nonsymbolic number comparison and mathematics performance remains unclear. In contrast to Gilmore et al. (2013) and Fuhs and McNeil (2013), both Keller and Libertus (2015) and Gilmore et al. (2015) found that the relation between accuracy in the number comparison task and mathematics persisted when controlling for inhibitory control. Further, all four of these studies focused on inhibitory control in a TD sample, while Bugden et al.'s (2015) findings related performance on incongruent trials of the nonsymbolic comparison task to group differences between DD and TD children. In addition to the group differences versus individual differences distinction between studies, Bugden et al. investigated the role of visuo-spatial working memory as opposed to inhibitory control. While dominant models indicate that executive function can be divided into the broad categories of working memory/updating, inhibitory control, and attention shifting (Rebecca Bull & Scerif, 2001; Miyake et al., 2000), most prior studies on nonsymbolic comparison and mathematics achievement have controlled for only one aspect of executive function, either working memory or inhibitory control. As a result, the more fine-grained mechanistic relations between executive function deficits and ANS deficits have been difficult to determine. To address these issues, the current study focuses on two outstanding questions regarding the relation among the ANS, executive function, and mathematics achievement in typically and atypically developing individuals.

First, what are the mechanisms underlying the relation between performance on incongruent trials of the nonsymbolic comparison task and mathematics achievement as compared to congruent trials? Previous studies have framed the correlation between nonsymbolic comparison performance and mathematics achievement as attributable to *either* individual differences in the ANS or executive function. However, an additional possibility is that incongruent trials on the nonsymbolic number comparison task represent an *interaction* of executive function and the ANS, or in other words, a *number-specific executive function*. Consistent with this suggestion, experimental studies have demonstrated a distinction between executive function related to numerical and non-numerical content. In a study of DD adults, individuals with DD had difficulty recruiting attention to numerical information but not non-numerical information under heightened cognitive load (Ashkenazi et al., 2009). In children, Bull & Scerif (2001) demonstrated that inhibitory control and working memory of numerical information accounts for significant variance in individual differences of mathematics ability beyond similar non-numerical measures of executive function. Therefore, to appropriately account for the possibility of an interaction between executive function and the ANS, executive function must be measured in both non-numerical and numerical contexts.

Second, is the relation among executive function, nonsymbolic number comparison, and mathematics achievement a specific facet of atypical development, comprising a specific characteristic of DD that sets the disorder qualitatively apart from typical developmental trajectories, or is the relation a characteristic of a broad range of typical mathematics skill development? Previous research appears to suggest that measurements of the ANS correlate with mathematics across the full range of mathematics achievement (Schneider et al., 2017). At the same time, studies suggest that the ANS of individuals with DD is neurobiologically atypical and functions differently than that of their TD peers (Mazzocco et al. 2011; Price et al. 2007). Distinguishing between these alternatives may provide meaningful implications for intervention strategies.

The Current Study

To address the questions above, the current study investigates the relations among ANS function, executive function, and DD by examining performance on the nonsymbolic comparison task, separately for congruent and incongruent trials, while controlling for multiple aspects of executive function. Importantly, executive function here is measured in a non-numerical context. To build directly on previous work, we take a similar approach as Mazzocco et al. (2011). We first compare performance in the nonsymbolic comparison task across multiple mathematics achievement groups (DD, low achieving, and typically achieving) defined through multiple years of consistent achievement, including the first three years of school entry. Second, we consider the relation between performance on the nonsymbolic comparison task and mathematics achievement more broadly through a regression analysis with a large sample that includes the full range of mathematics achievement. In the first analysis, if DD is characterized by a distinct core deficit of the ANS, performance on both congruent and incongruent trials of the task should distinguish among achievement groups. If, on the other hand, DD is characterized by deficits specific to inhibitory control, performance on only the incongruent trials of the nonsymbolic comparison task should account for achievement group differences, but not after controlling for measures of non-numerical executive function. However, if impaired number-specific executive function underlies DD, we would expect group differences between the DD group and the other achievement groups on incongruent trials, but not congruent trials, after controlling for non-numerical, domain-general executive functioning. Similarly, in the second analysis, if number-specific executive function is related to individual differences in mathematics achievement across a wide range of achievement, not only a distinction between DD and the other achievement groups, performance on incongruent trials should predict mathematics achievement beyond what can be accounted for by congruent trials and multiple components of non-numerical executive function.

2.2 Method

Participants

The current sample was drawn from a study of students who participated in an earlier longitudinal study of early mathematical skills (Pre-K to 1st grade) (Hofer, Lipsey, Dong, & Farran, 2013). The analytic sample for the original study included 771 children. In the follow-up study, we were able to locate 628 students attending public school in the 2013-14 year in the same district as they attended in Pre-K (16 had withdrawn from the study in 1st grade and were not contacted for further participation, 29 had moved out of the state, 53 had moved out of the district, and 45 were not located despite all efforts). Of those 628, we obtained parental consent and assessed 506 children in the 2014-2015 school year. English language learners (*n* = 43) were excluded because non-native language of mathematics instruction could lead to low mathematics achievement for reasons other than the cognitive factors investigated in the current study.

Our final sample comprised 448 students for whom we had measures of mathematics achievement from 2 of the 3 early time points (spring of Preschool, Kindergarten, and 1st grade) and from 2 of the 3 later time points (5th, 6th, and 7th grades), reading achievement measured at the end of Kindergarten, executive function measured at 6th or 7th grade, and working memory measured at 5th or 6th grade. The final sample was 56.5 % female, 9.6% white, 87.1% black, 0.7% Hispanic, 1.1% Middle Eastern, 0.2% Asian or Pacific Islander, and 1.3% other races (no further distinction of race was available). Of the 448 students who should have been in 6th grade in the 2014-15 school year if they had not been retained or promoted early at any point, 78 (17.4%) were still in 5th grade and 1 (0.2%) had been promoted to 7th grade. Students were located in 76 schools in the first year of the follow-up study (5th grade), including 31 elementary schools, 27 middle schools, 11 charter schools, and 7 Innovation Cluster schools (i.e., schools that had been targeted for additional resources to boost low student achievement). Family income level was inferred on the basis of whether participants qualified for free or reduced lunches (i.e., family income less than 1.85 times the U.S. Federal income poverty guideline). In the current sample, 88.6% of participants qualified for free and reduced lunch, 10.3% did not, and 1.1% individuals were missing economic status data. Pre-K through 1st grade and 5th through 7th grade waves of data collection were used for defining mathematics achievement groups, and nonsymbolic comparison performance was utilized from 6th grade because concurrent measures of working memory and executive function were available for children in that year. Mean age at the end of pre-K, the first data point in the current analysis, was 5.1 years (*SD* = 0.3, range = 4.5-6.4). See Supplementary Table 2.3 for full table of descriptive statistics.

Achievement Groups

Our first set of analyses asked whether performance on congruent or incongruent trials of nonsymbolic number comparison distinguished children with DD from their low achieving and typically achieving peers. Previous research investigating deficits of the ANS in both behavioral and neuroimaging studies has largely used mathematics achievement scores below a certain threshold as a diagnostic criterion for DD. One commonly used threshold for defining DD is performance in the lowest 10^{th} percentile of standardized mathematics achievement tests (Dinkel et al., 2013; Mazzocco et al., 2011). In addition, previous research has distinguished between individuals with mathematics learning disability (dyscalculia) from individuals with mathematics learning difficulties (i.e. less severe mathematics impairments). Whereas individuals with DD are hypothesized to have neurobiologically mediated cognitive deficits specific to magnitude processing, the etiological basis for individuals with mathematics learning difficulties may be broader in scope. Several studies comparing groups of student achieving in the lowest 10^{th} percentile to those in the 11^{th} – 25^{th} percentiles reveal important qualitative differences in cognitive profiles (Geary, Hoard, Byrd-Craven, & Nugent, 2007; Mazzocco & Myers, 2003), notably indicating that the lowest achievement group had an impairment in nonsymbolic magnitude processing compared to all other achievement groups (Mazzocco et al., 2011). Therefore, in the current study, we assigned participants to three different mathematics achievement groups, dyscalculic individuals (DD: $\leq 10^{th}$ percentile), low achieving individuals (LA: 10^{th} - 25^{th} percentile), and typically achieving individuals (TA: 25^{th} - 95^{th} percentile). With these grouping criteria, 22 children met the criteria for DD, 12 for LA, and 188 for TA. Only one individual consistently scored > 95^{th} percentile, a commonly used criterion for school placement in gifted and talented programs, and a common threshold for designating high achieving groups in research (e.g. Hoard, Geary, Byrd-Craven, & Nugent, 2008; Mazzocco et al., 2011). This individual was removed from further analysis. Analyses were replicated with another commonly used threshold for determining DD (achievement < 1.5 *SD* below population mean) and included in Appendix A. Using this alternative threshold did not alter any results.

Individuals were placed in achievement groups if their mathematics achievement scores were consistently in the designated achievement range at two of the three early assessments (PreK-1st grade) AND two of the three later assessments (5th-7th grades). Given these criteria, 222 children fit into consistent achievement groups across early and later assessment periods, thus excluding 226 children respectively from the full sample of 448 whose achievement level varied beyond the defined threshold across time points. Descriptive statistics for the achievement group sample (n = 222) are broken down by achievement group in Table 2.1.

Many previous studies have attempted to isolate the neurocognitive mechanisms of DD by studying a group of individuals with pure developmental dyscalculia compared to a control group (Landerl, Bevan, & Butterworth, 2004; Mussolin et al., 2009; Rotzer et al., 2008), meaning that both DD and control groups are matched on IQ and other cognitive abilities. The current study does not take this approach for two reasons. First, research suggests that defining learning disability groups through discrepancy criteria excludes many individuals with dyscalculia who suffer from comorbid learning disabilities or other developmental issues. Most estimates suggest that 20-40% of individuals with DD also have dyslexia (Shalev, 2004; Willcutt et al., 2013; Wilson et al., 2015) and around 25% also have attention deficits (Landerl, Göbel, & Moll, 2013; Shalev et al., 1995; Shalev, 2004). This suggests that DD is inherently heterogeneous and would better be characterized by a framework whereby individuals are designated as DD through proof of consistent, low mathematics achievement over time with the presence of adequate educational opportunity (Fuchs, Morgan, Young, & Rise, 2003). Therefore, rather than exclude non-discrepant individuals, the current study follows previous literature (Mazzocco et al., 2011) and investigates differences in the ANS while controlling for reading achievement and domain-general executive function. Second, the current study examines the intersection of attention mechanisms and magnitude processing mechanisms. Any attempt to define groups as a function of broader measures of achievement would impede investigation of individual differences in executive function, which is known to correlate with academic achievement.

Table 2.1. Descriptive statistics for achievement subgroups.

Achievement Group Sample	DD (n = 22, 7 females)			LA (n = 12, 6 females)			TA (n = 188, 106 females)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Age (years), Pre-K	5.1	0.5	4.5-6.4	5.0	0.3	4.7-5.5	5.1	0.3	4.5-5.6
Age (years), 6th grade	12.2	0.5	11.4-13.4	12.0	0.3	11.6-12.5	12.0	0.3	11.4-12.6
Nonsymbolic Comparison (accuracy, %)	71.5	5.3	62.9-81.4	78.2	6.4	70.0-87.1	75.8	5.0	58.6-91.4
Backward Corsi* (z-score of max span)	-1.21	1.22	-2.4-0.95	0.03	0.57	-0.75-0.95	0.37	0.85	-2.44-2.65
Hearts and Flowers* (z-score of accuracy, %)	-1.29	0.79	-2.33-0.82	-0.16	0.83	-1.90-1.83	0.40	0.83	-1.90-1.83
Letter-Word Identification (WCJ-III, standard score)	91.4	9.90	75-113	97.4	11.9	73-113	115.1	11.9	85-144

* z-scores presented based on full sample of 448 individuals.
WCJ-III = Woodcock Johnson III. KM-3 = KeyMath-3.

Procedure

All students assented and students' families consented to participate, and the study was approved by the IRB. Assessments were conducted by trained members of the research staff. The nonsymbolic number comparison task and executive function tasks were administered during the Spring semester of the students' 6th grade year via tablet computer. Testing for mathematics achievement was completed in a quiet location at the students' school with one-to-one assistance from trained staff during the student's Pre-K, Kindergarten, 1st grade, 5th grade, 6th grade, and 7th grade years. Reading achievement was assessed at the end of Kindergarten.

Cognitive Tasks

Nonsymbolic number comparison. Participants were presented with two sets of dots simultaneously and asked to indicate via button press which set was more numerous (i.e., which set contained more dots). The set on the left side of the screen contained yellow dots and the set on the right side contained blue dots, which corresponded to color-coded left and right buttons. Response sides were fully counterbalanced. Trials consisted of 1200 ms stimulus presentation followed by 1800 ms of fixation.

Seven ratios were presented, ranging from .33 (5 vs. 15) to .9 (9 vs. 10). See Figure 2.1 for a task diagram and Supplementary Table 2.4 for a list of all ratios. The number of dots in each stimulus ranged from 5 to 15. Each ratio was presented 10 times for a total of 70 trials, which were preceded by 6 practice trials of the easiest two ratios. If individuals did not correctly respond to at least 4 of the 6 practice trials, practice trials were repeated up to two times. If participants did not answer 4 out 6 correctly on any practice run, they did not proceed to the experimental trials. Ratios, stimulus presentation times, and order of presentation were modeled after Odic, Hock and Halberda (2014). To control for the possibility that participants might utilize a strategy based on visual cues rather than number of dots, the following visual properties of dot sets were varied using a modified version of the MATLAB code recommended by Gebuis & Reynvoet (2011): convex hull (area extended by a stimulus), total surface area (aggregate value of dot surfaces), average dot diameter, total circumference, and density (convex hull divided by total surface area). In approximately one quarter of the trials (22 of 70) all four visual properties were congruent with greater numerosity (i.e. the greater number of dots had a greater convex hull, surface area, etc.). In another approximate quarter of the trials (18 of 70), all four visual properties were incongruent with greater numerosity. In the remaining trials, visual properties were mixed congruent and incongruent.

Analyses of task effects include all trials. Analyses directly addressing the research questions include trials that were either fully congruent (22 trials) or incongruent (18 trials) on all five visual parameters. Mixed congruency trials were excluded. Performance was calculated as mean number of items correct and as a weber fraction. Weber fractions were calculated

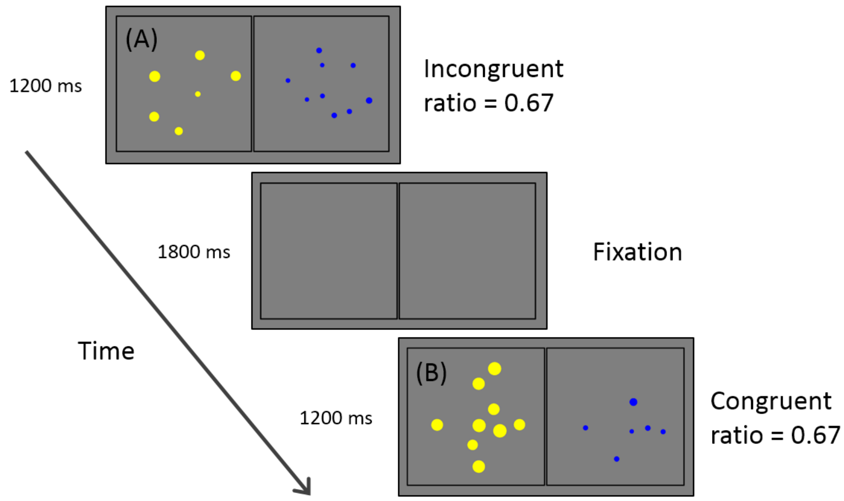


Figure 2.1. Nonsymbolic number comparison stimuli and paradigm timing. (A) Incongruent trial example of ratio 0.67 (smaller number dot set/larger number dot set, 6/9 = 0.67). (B) Congruent trial example, also of ratio 0.67.

according to the method utilized by Halberda et al. (2008). Of the sample of 448 individuals, 446 had weber fraction models that fit when modeling all trials at the 6^{th} grade year. Correlations with weber fractions are reported in the analyses of tasks effects to facilitate comparison with previously published research. However, the model implementing Levenberg–Marquardt least squares fit used to calculate weber fractions did not provide a sufficient fit with the few number of trials available within congruency conditions (as indicated by whether the model predicted a significant amount of variance, $p < .05$). Further, a growing body of literature suggests that mean accuracy is strongly correlated with and possibly more reliable than ratio dependent metrics such as the weber fraction (Gilmore, Attridge, & Inglis, 2011; Inglis & Gilmore, 2014). Therefore, in the current study, mean accuracy percentages were used instead of weber fractions to index performance on each of our number comparison tasks.

Working memory. The backward Corsi block-tapping test (Corsi, 1972) provided a measure of visuo-spatial working memory. In this computerized task, children first viewed squares that lit up in a sequence on the screen, and then the students were asked to tap the squares in the reverse order in which they lit up. The task consisted of 16 total possible trials, including two practice trials. The student was given 2 attempts to correctly repeat the reverse sequence per sequence length. The sequence length of squares increased from 2 to 8 across the task. If the student correctly answered at least 1 of the 2 attempts correctly, the student then proceeded on to the longer (more difficult) sequence. The score of interest was the highest span with a correctly repeated sequence. At the 6th grade assessment, 22 children (of n = 448) did not proceed from instruction in the backward Corsi to successful completion of a trial, indicating noncompliance with the task or a failure to understand instructions. Scores on outcome measures and covariates of interest for these children were different, on average, from those children who successfully completed the task (nonsymbolic accuracy $t(446) = 3.728$, $p < .001$, Cohen's $d = 0.794$; Hearts and Flowers mean accuracy $t(446) = 3.508$, $p < .001$, Cohen's $d = 0.716$; 6th grade mathematics achievement $t(446) = 2.587$, $p = .010$, Cohen's $d = 0.613$). Therefore, to avoid nonrandom missing data and include these children in our analyses, backward Corsi max span from the 5th grade was used, where available. To maintain the relative position of children's scores in the 5th grade among other children's 6th grade scores (5th grade mean max span = 4.52, 6th grade mean span = 4.88), both years of backward Corsi max spans were z-scored and 5th grade z-scores of the 22 children were used instead of 6th grade z-scores, which were used for the other 426 children.

Inhibitory control and task switching. The Hearts and Flowers task (Wright & Diamond, 2014) was used as measure of students' task switching and inhibitory control. In this task, the child was first presented with a heart on either side of the screen and instructed to press the button that corresponds to the side of the screen with the heart. This first block comprised 12 trials. In the second block of trials (also 12 trials), the child was presented with flowers and asked to press the button that is opposite the side of the flower. In the third set of trials, the child was randomly presented with either a heart or a flower and asked to follow the rule that corresponds to hearts and flowers respectively. The third block comprised 48 trials. To index executive function we used mean accuracy from the third, mixed-condition block of trials, and as such, our measure captures both task switching and inhibitory control (Diamond, 2014). One child was not assessed at 6th grade for Hearts and Flowers, but a score from 7th grade was available. The same z-score method described above was utilized to create a score for this child and z-scores were utilized for all subsequent analyses.

Academic Achievement

Reading achievement: Woodcock Johnson III (WCJ-III) – Letter-Word Identification. The WCJ-III (Woodcock, McGrew, & Mather, 2001) is a standard assessment of a range of skills, designed to be used with people ages 2 to 90+. The letter-word identification subtest assesses children's letter and sight word identification ability with the correct pronunciation. Items include identifying and pronouncing letters and words presented to the child (e.g. "A" or "dog"). Age-normed standard scores were calculated as an early measure of reading achievement measured at the end of Kindergarten and then converted to percentile ranks.

Mathematics achievement.

WCJ-III – Quantitative Concepts and Applied Problems. Quantitative Concepts and Applied problems subtests were administered at the end of each school year during Pre-K, Kindergarten, and 1st grade. Individually-administered, Quantitative Concepts has two parts and assesses students' knowledge of mathematical concepts, symbols, and vocabulary, including numbers, shapes, and sequences; it measures aspects of quantitative mathematics knowledge and recognition of patterns in a series of numbers. The Applied Problems subtest is an untimed verbal and picture-based measure of a student's ability to analyze and solve mathematics problems, beginning with the application of basic number concepts. At each early time point, age-normed standard scores were calculated for each subtest and averaged together to create a composite measure of mathematics competence representing a broad range of mathematics skills. These scores were subsequently converted to percentile ranks.

KeyMath 3. The KeyMath 3 Diagnostic Assessment (Connolly, 2007) is a comprehensive, norm-referenced measure of essential mathematical concepts and skills. It was administered at the end of each school year during 5th, 6th, and 7th grades. We used three subscales out of the five subscales in the Basic Concepts area. (1) Numeration: The Numeration subtest measures an individual's understanding of whole and rational numbers. It covers topics such as identifying, representing, comparing, and rounding one-, two-, and three-digit numbers as well as fractions, decimal values, and percentages. It also covers advanced numeration concepts such as exponents, scientific notation, and square roots. (2) Algebra: The Algebra subtest measures an individual's understanding of pre-algebraic and algebraic concepts. It covers topics such as sorting, classifying, and ordering by a variety of attributes; recognizing and describing patterns and functions; working with number sentences, operational properties, variables, expressions, equations, proportions, and functions; and representing mathematical relations. (3) Geometry: The Geometry subtest measures an individual's ability to analyze, describe, compare, and classify two-and three-dimensional shapes. It also covers topics such as spatial relations and reasoning, coordinates, symmetry, and geometric modeling. In order to index a broad range of mathematics achievement, we averaged scale scores from the three subscales into a composite measure (KM Composite). Scale scores in the KeyMath 3 are age-normed to reflect population means of 10 and a standard deviation of 3 for each subtest. Mathematics competence was indexed using a composite score calculated as the mean of the age-scaled scores of the three KeyMath 3 subtests administered to capture performance in a wide range of mathematical skills. This score was then converted to a percentile rank to compose mathematics achievement groups across measures of mathematics achievement in the early grades (PreK-1st grade) and late measures of mathematics achievement (5th grade to 7th grade). The relation between KeyMath 3 scores and other measures was not linear, so when conducting analysis that assumed a linear relation (e.g. bivariate correlation, partial correlation, or regression), we instead used the cube root of KeyMath 3 percentile rank.

2.3 Results

Task Effects

Nonsymbolic comparison task performance profiles were consistent with previously published findings (e.g., Lyons, Nuerk, & Ansari, 2015), showing a significant effect of ratio on mean accuracy for all trials [$F(6, 447) = 1255.22$, $p < .001$, partial $\eta^2 = 0.737$], and within congruency conditions [$F(6, 447) = 339.01$, $p < .001$, partial $\eta^2 = 0.431$ for congruent trials; $F(6, 447) = 401.17$, $p < .001$, partial $\eta^2 = 0.473$ for incongruent trials]. Further, both mean accuracy and weber fraction were correlated with mathematics achievement at 6th grade (mean accuracy Pearson $r(446) = .191$, $p < .001$; weber fraction Pearson $r(446) =$

-.244, $p < .001$), which is in line with a recent meta-analysis reporting an average correlation of $r = .241$ ($k = 195$) between nonsymbolic comparison and a broad range of mathematics achievement measures across multiple age groups (Schneider et al., 2017). Mean accuracy and weber fractions were highly correlated (Pearson $r(446) = -.919$, $p < .001$).

Achievement Group Comparison Results

To investigate group differences among DD, LA, and TA groups on nonsymbolic comparison on both congruent and incongruent trials, we conducted a two-way (3 x 2), mixed effects ANOVA with achievement group as a between-subject factor, congruency condition of nonsymbolic comparison as a within-subjects factor, and accuracy rate on the nonsymbolic comparison task at 6^{th} grade as the dependent variable. One-way post-hoc *t*-tests were conducted to examine simple main effects and pairwise differences where appropriate. Bonferroni-corrected *p*-values are reported to correct for multiple comparisons for all subsequent analyses and to ensure tests were robust against violations of homogeneity of variances between groups. Because clustering of students within schools did not account for a significant proportion of variation in 6^{th} grade nonsymbolic number comparison accuracy ($\hat{\rho} = .009$, $p = .74$), a multi-level modeling approach to account for the clustering of students within schools was not needed.

Results of the two-way ANOVA indicated a main effect of achievement group [$F(2, 219) = 6.694$, $p = .002$, partial $\eta^2 = 0.058$], a main effect of congruency [$F(1, 219) = 27.570$, $p < .001$, partial $\eta^2 = 0.112$] whereby individuals were more accurate on congruent trials, and an interaction [$F(2, 219) = 4.816$, $p = .009$, partial $\eta^2 = 0.042$]. To characterize the main effect of achievement group, we conducted between-subjects *t*-tests comparing accuracy on the combined congruent and incongruent trials. There was an effect of achievement group between the DD and LA groups [$t(32) = -3.119$, $p = .006$, Cohen's $d = 1.62$] and between the DD and TA groups [$t(208) = -3.287$, $p = .002$, Cohen's $d = 0.769$], with the DD group performing worse than both LA and TA. There was no significant difference between the LA and TA groups [$t(198) = 1.429$, $p = .233$, Cohen's $d = 0.379$]. Further post-hoc tests were conducted to characterize the interaction.

The effect of congruency. Pairwise comparisons were conducted to characterize the simple effect of congruency within achievement groups. There was an effect of congruency in the DD and TA groups [$t(21) = 6.076$, $p < .001$, Cohen's $d = 10.362$ for DD; $t(187) = 6.795$, $p < .001$, Cohen's $d = 0.844$ for TA], but not in the LA group [$t(11) = 0.716$, $p = .489$, Cohen's $d = 0.359$ for LA] (see Figure 2.2 for means).

The effect of achievement group. To characterize the simple effects of achievement group, one-way ANOVAs were conducted within congruency conditions, followed by pairwise comparisons of achievement groups. Results from the ANOVA on accuracy for congruent trials showed no effect of achievement group [$F(2, 219) = .476$, $p = .622$, $\eta^2 = 0.004$] (Figure 2.2). Levene's test of equality of variances showed no significant differences in variance across groups for mean accuracy of congruent trials (Levene's statistic = .383, $p = .682$). To further investigate achievement group differences after controlling for domain-general factors, analyses were repeated as a one-way ANCOVA with the covariates of max span achieved on the backward Corsi, mean accuracy during mixed trials of the Hearts and Flowers task, age at time of testing, and percentile rank on the WCJ-III letter-word identification at the end of Kindergarten. Results from the ANCOVA again indicated there was no effect of achievement group on number comparison performance for congruent trials [$F(2, 215) = .068$, $p = .935$, partial $\eta^2 = 0.001$].

In contrast, results from the ANOVA on incongruent trials showed a significant effect of achievement group on accuracy [Welch's $F(2, 219) = 8.345$, $p = .002$, $\eta^2 = 0.070$]. Levene's test indicated that there were significant differences in variance across groups for mean accuracy of incongruent trials (Levene's statistic = 4.317, $p = .014$), however variance only differed between groups by a factor of 2.56 at most, so Welch's adjusted F was used for the ANOVA. After adjusting for multiple comparisons, post-hoc tests of incongruent trials indicated lower accuracy rates for the DD group than the TA group ($p < .001$, Hedge's $g = 0.870$), lower accuracy rates for DD than LA ($p = .002$, Hedge's $g = 1.046$), and no difference between LA and TA groups ($p = .344$, Hedge's $g = .356$). When controlling for the same non-numerical, domain-general factors as above in an ANCOVA, there was still a significant effect for accuracy on incongruent trials [$F(2, 215) = 4.658$, $p = .010$, partial $\eta^2 = 0.042$]. Post-hoc tests indicated lower accuracy rates for the DD group than the TA group ($p = .045$, Hedge's $g = 0.823$ for adjusted means), lower accuracy rates for the DD group than the LA group ($p = .005$, Hedge's $g = 0.912$ for adjusted means), and no difference between LA and TA groups ($p = .231$, Hedge's $g = 0.585$ for adjusted means). These results replicate the pattern observed in the ANOVA.

In sum, all ANOVAs and ANCOVAs conducted show the same pattern of results whereby: (1) no group differences are observed for congruent trials of the nonsymbolic comparison task, (2) the DD group performs significantly below LA and TA groups on incongruent trials even when controlling for other cognitive factors and early reading achievement, and (3) no group differences are present between LA and TA groups on incongruent trials.

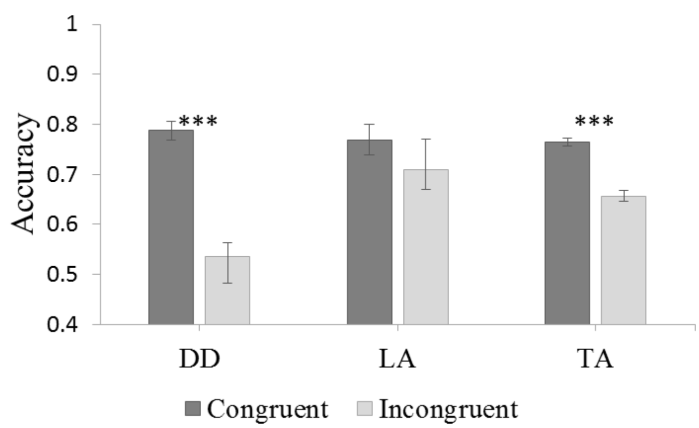


Figure 2.2. Nonsymbolic number comparison accuracy rates by achievement group. LA = low achieving. TA = typically achieving. Error bars represent standard errors. P-values are indicated for differences in accuracy between congruent and incongruent trials (*** $p < .001$).

Full Range of Achievement Results

The last set of analyses examined whether individual differences in nonsymbolic number comparison performance related to standardized mathematics achievement across a wide range of achievement. Specifically, we examined whether 6^{th} graders' accuracy on nonsymbolic number comparison for incongruent and congruent trials predicted concurrent mathematics achievement for the full sample of students (n = 448), and whether the relation changed when controlling for early reading achievement and domain-general executive functioning. For bivariate correlations among measures, see Supplementary Table 2.5. Of note is a moderate, negative bivariate correlation between accuracy rates for congruent and incongruent trials ($r(446) = -.447$, $p < .001$).

Multi-level regression model predicting mathematics achievement. In addition to group comparisons, we used random-effects multi-level models to predict 6th grade mathematics achievement from concurrent experimental measures. Multi-level modeling accounts for the clustering of students within schools, as approximately 23% of the variation in 6th grade mathematics achievement was due to school membership ($\hat{\rho} = .225$, $p < .0001$). Equation (1) illustrates the modeling approach, in which $MATH_{ij}$ represents 6th grade mathematics achievement for each student i in school j. The predictors $INCON_{ij}$ and CON_{ij} represent student-level accuracy on nonsymbolic number comparison for incongruent and congruent trials, respectively; HAF_{ij} represents student-level standardized scores on the Hearts and Flowers task; $CORSI_{ij}$ represents student-level standardized backward Corsi max span scores; $READ_{ij}$ represents student-level age-normed standard scores on the letter-word ID test; and $\boldsymbol{X}_{ij}$ represents a vector of potential student-level covariates, such as gender or age at testing. Due to non-linearity in the relation between mathematics scores and the predictors, models were fit using a transformed outcome (i.e., cubed root).

$$\sqrt[3]{MATH_{ij}} = \beta_0 + \beta_1 INCON_{ij} + \beta_2 CON_{ij} + \beta_3 HAF_{ij} + \beta_4 CORSI_{ij} + \beta_5 READ_{ij} + \beta_6 \boldsymbol{X}_{ij} + (e_{ij} + u_j) \quad (1)$$

Table 2.2 presents parameter estimates, standard errors, significance levels, random effects, and goodness-of-fit statistics for a taxonomy of fitted models describing the relation between mathematics achievement and nonsymbolic number comparison, domain-general executive functioning, early reading achievement, and age at testing in 6th grade. The first model (i.e., M1) displays the grand mean of 6th grade mathematics achievement, across all students and schools, and the intra-class correlation ($\hat{\rho}$ = .225, $p < .0001$) that motivates the multi-level modeling approach. Model M2 shows the relations between accuracy on congruent and incongruent conditions of the nonsymbolic number comparison task and transformed 6th grade mathematics achievement. There is a statistically significant relation between accuracy on incongruent nonsymbolic number comparison and transformed 6th grade mathematics achievement ($z = 4.88$, $p < .0001$), but accuracy on congruent trials is not a statistically significant predictor of mathematics achievement ($z = 1.16$, $p = .25$). Accordingly, accuracy on congruent trials was excluded from subsequent models.

Subsequent models (M3-M5) show that the relation between accuracy on incongruent trials of the nonsymbolic number comparison task and transformed 6th grade mathematics achievement persists after controlling for additional predictors of mathematics achievement. Model M3 shows the relation between accuracy on incongruent nonsymbolic number comparison trials and transformed mathematics achievement, controlling for domain-general executive functioning. Hearts and Flowers and backward Corsi performance have a statistically significant relation with mathematics achievement ($z = 7.71$, $p < .0001$ and $z = 7.12$, $p < .0001$, respectively), controlling for nonsymbolic number comparison. Parameter estimates and statistical significance of relations remain stable when controlling for reading performance in Kindergarten (see Table 2.2, M4) and age of mathematics testing in 6th grade (see Table 2.2, M5), though the magnitudes decrease slightly. Additional models were fit testing demographic variables (e.g., gender) and interaction terms among the nonsymbolic comparison and executive function predictors, however, none were statistically significant (*p'*s ranged from .06 to .98). Further, we conducted a sensitivity analysis to examine whether students with DD may be driving the relationship between performance on incongruent trials and mathematics achievement. To do so, we refit model M5 without the DD subgroup (n = 22). Results were unchanged. Taken together, the analysis suggests that student performance on incongruent trials of nonsymbolic number comparison is predictive of concurrent mathematics achievement, above and beyond non-numerical, domain-general executive functioning, early reading achievement, and age at testing in 6th grade. For detailed explanation of the model fit, see Appendix B.

Table 2.2. Taxonomy of fitted multi-level models describing the relation between the cubed root of 6th grade mathematics achievement and accuracy on nonsymbolic number comparison, separately for incongruent and congruent trials, controlling for working memory, inhibitory control, reading achievement, and age of testing in 6th grade ($n_{schools}$ = 75; $n_{students}$ = 448).

	6th grade mathematics achievement (cubed root)				
	M1	M2	M3	M4	M5
Intercept	0.562*** (0.015)	0.286** (0.091)	0.480*** (0.036)	0.011 (0.072)	-1.084** (0.337)
Nonsymbolic Comparison, incongruent trials, acc.		0.321*** (0.066)	0.144** (0.053)	0.141** (0.051)	0.126* (0.050)
Nonsymbolic Comparison, congruent trials, acc.		0.097 (0.083)			
Backward Corsi, max span			0.054*** (0.008)	0.051*** (0.007)	0.050*** (0.007)
Hearts and Flowers, mixed trials, acc.			0.060*** (0.008)	0.053*** (0.007)	0.051*** (0.007)
Reading achievement, LWID, end of Kindergarten				0.004*** (0.001)	0.005*** (0.001)
Age of KeyMath testing, 6th grade					0.007*** (0.002)
$\hat{\sigma}_u$	0.094*** (0.014)	0.091*** (0.014)	0.073*** (0.011)	0.057*** (0.010)	0.051*** (0.010)
$\hat{\sigma}_e$	0.174*** (0.006)	0.170*** (0.006)	0.150*** (0.005)	0.144*** (0.005)	0.143*** (0.005)
$\hat{\rho}$	0.225*** (0.057)	0.223*** (0.057)	0.190*** (0.050)	0.134*** (0.043)	0.112** (.040)
Log-likelihood	114.559	126.743	185.816	211.721	217.176

$^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$. Acc. = accuracy, LWID = letter-word identification, $\hat{\sigma}_u$ = School-level residual standard deviation, $\hat{\sigma}_e$= Student-level residual standard deviation, $\hat{\rho}$ = Intra-class correlation. Standard errors are in parentheses.

2.4 Discussion

The current study investigated the relation among ANS function, executive function, and mathematics achievement by examining performance on the nonsymbolic comparison task, separately for congruent and incongruent trials, while controlling for multiple components of executive function measured in non-numerical contexts. We investigated this relation first as it relates to group differences among DD, LA, and TA students and then as a factor related to mathematics achievement across a full range of achievement. Results indicated that an interaction of the ANS and executive function mechanisms, beyond either mechanism alone, represents a deficit specific to DD and is also factor related to mathematics achievement across a full range of mathematics achievement levels.

In the first analysis, we compared accuracy rates in the nonsymbolic comparison task across three mathematics achievement levels (i.e. DD, LA, and TA) defined through six years of consistent achievement, including the first three years of school entry (Pre-K-1st grade) and three later years of entry to middle school (5th-7th grade). Our results showed that accuracy on incongruent trials, and not congruent trials, was significantly lower for DD (defined at two different thresholds) compared to LA and TA groups, even after controlling for early reading achievement, visuo-spatial working, inhibitory control, and task shifting. LA and TA groups, on the other hand, did not differ from one another, thus supporting the hypothesis that an impairment in the interaction between executive function and the ANS is characteristic of individuals with DD.

Explanations of the link between ANS and mathematics achievement that involve a dynamic interaction between the ANS and executive function have considerable support from a large body of research linking low mathematics performance with various executive function impairments. These include associations between low mathematics achievement and inhibitory control (Blair & Razza, 2007; Espy et al., 2004; Dénes Szűcs et al., 2013), spatial processing (Rourke & Conway, 1997), verbal and visuospatial working memory (Rebecca Bull & Scerif, 2001; David C Geary, 2004), set shifting (Willcutt et al., 2013), sustained visual attention (Anobile, Stievano, & Burr, 2013), and inattentive behaviors (Fias et al., 2013; Shalev et al., 1995). Further, DD has a high rate of comorbidity with attention-deficit/hyperactivity disorder (Czamara et al., 2013). Though the link is often made between general measures of executive function and mathematics achievement, there is evidence that the relation is specific to measures of executive function involving numerically relevant information. For example, Siegel and Ryan (1989) found that individuals with DD have impairments of working memory related to processing numerical information and not language. Experimental studies have also demonstrated a distinction between executive function to numerical and non-numerical content. Ashkenazi et al. (2009) found that individuals with DD had more difficulty recruiting attention to numerical information but not non-numerical information under heightened cognitive load compared to TD peers. This array of findings has led some to suggest that DD may involve a domain-specific executive function problem (e.g. Bull & Scerif, 2001). In other words, individuals with DD may not have a generally impaired ANS system, but rather have difficulty working with numerical magnitudes under additional executive function demands. Results from the current study showing mathematics achievement group differences in nonsymbolic comparison performance only during incongruent trials, after controlling for non-numerical executive function, lend further support to this hypothesis. Whether this deficit is driven by a failure to upregulate numerical information above competing information, or perhaps a failure to disengage attention from non-numerical information remains an open empirical question.

The current study results contrast with some previous studies using an alternative method for controlling visual parameters of dot stimuli which have not found an effect of congruency on response behaviors (Odic et al., 2014; Odic, Libertus, Feigenson, & Halberda, 2013). However, in those studies, the effect of congruency may be confounded by the fact that degree of visual congruency (and incongruency) is linearly related to trial ratio. This means that in difficult ratio trials, which capture the most variance related to individual differences in ANS acuity, each dot set is very similar in terms of surface area, thus decreasing the likelihood of finding a congruency effect. Although this method may be appropriate for measurement of general ANS acuity, the effects of congruency are difficult to separate from the effects of numerical ratio, since the two are linked so tightly. The current study uses a method of controlling congruency that is more balanced across ratios and controls for a greater number of stimulus properties beyond dot size and surface area (for a detailed discussion, see Clayton et al., 2015). Therefore, the effects of congruency and ANS function are more clearly disentangled in the current study.

One unexpected result from the first, group-wise analysis is that DD and TA groups showed congruency effects, as expected, but LA children did not. Despite this lack of a congruency effect in the current findings for this achievement group, we caution against any strong interpretation of this result. There is a trend in the expected direction for each of the LA children groupings (10^{th} percentile and 6.7^{th} percentiles cutoffs), in which children are more accurate on congruent trials than incongruent trials. Despite the lack of a significant effect, the effect sizes are relatively large (Cohen's d = 0.36 and d = 0.71) and mean differences are 6 accuracy points and 10 accuracy points for each sample respectively. It is likely that the absence of a statistically significant congruency effect for LA children is due to high variance in accuracy on incongruent trials and a lack of adequate power for this comparison, since the group is relatively small.

In the second analysis, we examined whether 6^{th} graders' accuracy on nonsymbolic number comparison for incongruent and congruent trials predicted concurrent mathematics achievement for the full sample of students, and whether the relation changed when controlling for early reading achievement and non-numerical, domain-general executive functioning. The sample for this analysis included a wide range of mathematics achievement levels that included all participants from the first analysis and participants in the broader study that did not consistently achieve in the same level year-to-year. Similar to the logic of the first analysis, if number-specific executive function is related to individual differences in mathematics achievement across a wide range of achievement, performance on incongruent trials should predict mathematics achievement beyond what can be accounted for by congruent trials and early reading achievement, visuo-spatial working, inhibitory control, and task shifting. Indeed, results showed that accuracy on incongruent trials predicted concurrent mathematics achievement even after controlling for early reading achievement, visuo-spatial working, inhibitory control, and task shifting, thus supporting the hypothesis that number-specific executive function relates to individual differences in mathematics achievement across a wide range of achievement levels. Further, the relation remained unchanged when we excluded individuals with DD from the regression. These findings build on previous research that has shown other number-specific measures of executive function relate to mathematics achievement in typically developing and high achieving groups. For example, Dark and Benbow (1994) found that working memory tasks with numerical stimuli were more closely related to mathematical precocity than non-numerical stimuli across a range of tasks in adults. Similarly, studies of children have demonstrated that inhibitory control and working memory of numerical information accounts for significant variance in individual differences of mathematics ability and early numeracy beyond similar non-numerical measures of executive function (Rebecca Bull & Scerif, 2001; Merkley, Thompson, & Scerif, 2016).

Interestingly, bivariate correlations indicated that children with high accuracy on incongruent trials tended to have low accuracy on congruent trials (and vice versa), even though congruent trials were not related to mathematics achievement. This may be important for two reasons. First, if only incongruent trials are related to mathematics achievement, researchers may be tempted to design measures consisting exclusively of incongruent trials. However, this inverse relation may indicate that incongruent trials are inherently related to congruent trials such that removing congruent trials would change the nature of the task demands for incongruent trials. Second, speculation about inhibitory control has dominated the conversation about the cognitive mechanisms underlying the difference between incongruent trials and congruent trials of the nonsymbolic comparison task (Cragg et al., 2017; Gilmore et al., 2015). While inhibitory control may be a factor, the inverse correlation between congruency conditions may indicate that some individuals are unable to switch between strategies that capitalize on visual cues during congruent trials and ignore these cues otherwise. In addition to working memory and inhibitory control, task shifting may contribute to differences in performance between incongruent and congruent trials.

Further, in the current study, accuracy on congruent trials was unrelated to mathematics achievement, either as a factor distinguishing between achievement groups or as a predictor of mathematics achievement. This was true even before controlling for other academic or cognitive factors. Since current theory suggests engagement of the ANS for successful completion of congruent and incongruent trials, we expected a relation, albeit weaker, between mathematics achievement and accuracy rate on congruent trials. However, neither analysis showed a statistically significant relationship between performance on congruent trials and mathematics achievement. Further, the magnitude of this relationship in both analyses was close to zero, showing no trend in the expected direction. This calls into question whether ANS function alone, not measured under high executive function demands, is an important factor related to DD and mathematics achievement more generally. Previous neuroimaging research has shown that congruent and incongruent trials of the nonsymbolic number comparison task recruit different neural mechanisms, with incongruent trials recruiting large portions of the fronto-parietal attention network (Leibovich et al., 2015). Recruitment of additional neurocognitive mechanisms during incongruent trials may be an integral component of the previously assumed direct relation between ANS and mathematics achievement.

Several factors should be taken into account when interpreting the results of the current study. First, participants were recruited from an urban public school system and were mostly from low-income households. Low household income often impedes access to high-quality early mathematics experiences (Ramani & Siegler, 2008), so factors driving mathematics achievement or the relation between nonsymbolic comparison and mathematics achievement may differ across students with differing household incomes. Further, the relation between nonsymbolic number comparison and mathematics achievement in low-income samples has been reportedly lower than middle- and high-income samples (Fuhs et al., 2016; Fuhs & McNeil, 2013). However, effect sizes of the relation between nonsymbolic comparison and mathematics achievement from the current study are in line with previous meta-analyses (Chen & Li, 2014; Schneider et al., 2017). Additionally, the lack of relation between mathematics achievement and congruent trials, and significant relation between mathematics achievement and incongruent trials has been previously reported in low-income (Fuhs & McNeil, 2013) and middle-to-high income individuals (Keller & Libertus, 2015). Further, Price and Wilkey (2017) showed that the mediating relation among nonsymbolic comparison accuracy rates and mathematics achievement in the same group of children as the current study follows the same patterns as previously reported literature from wider SES samples (Lyons & Beilock, 2011), further suggesting the current sample does not diverge from trends found at other income levels.

Second, alternative explanations of the current results are possible. For example, rather than our hypothesis about domain-specific executive function, the current results could indicate that individuals who utilize an appropriate strategy for incongruent trials, whether consciously or not, are better at mathematics. If framed as a task strategy, then strategy selection does not necessarily equate to number-specific executive function. Another alternative is that individual differences in task performance are based not on cognitive efficiencies, but rather a predisposition to focus on one aspect of the visual stimuli. A deficit of number-specific executive function is different than the failure to utilize it. Prior research has documented that individuals with a tendency to spontaneously focus on exact quantities have higher arithmetic abilities (Batchelor, Inglis, & Gilmore, 2015; Hannula et al., 2010). Recently, this line of research has been expanded to incorporate spontaneous orientation to conflicting or irrelevant dimensions of non-numerical magnitude similar to those of the current study (Viarouge et al., 2017). Some evidence indicates that intentional processing of numerical magnitudes is more related to mathematics achievement than automatic processing (Bugden & Ansari, 2011), but further research is needed that directly manipulates numerical information in both nonsymbolic and symbolic formats under differing executive function loads. Research on the underlying neurocognitive mechanisms can also help to distill the root of the differences observed in the current results.

In sum, the two sets of analyses presented here suggest that performance on incongruent trials alone relates to the presence of severe mathematics learning deficits as well as individual differences in mathematics across a wider range of achievement. Results suggest that number-specific executive function is a unique predictor of mathematics achievement beyond measures that target the ANS or executive function independently. In order to understand how the intersection of these multiple cognitive mechanisms relates to the acquisition of mathematics skills, future studies should move from a domain-specific vs. domain-general approach to experiments that deconstruct this framework. In so doing, future hypotheses can more closely address the integration of cognitive mechanisms required to complete a complex task such as mathematical thought.

2.5 Acknowledgments

Eric D. Wilkey designed the research, analyzed the data, and wrote the paper. Courtney Pollack aided in the multi-level modeling utilized for regression analysis and wrote portions of the corresponding results section. Gavin R. Price assisted in the conception of this project, read multiple iterations of the paper, and provided feedback. This work has been submitted for publication with the order of author listed as: **Wilkey, E. D.**, Polack, C., Price, G. R.

This research was supported by the Heising-Simons Foundation (#2013-26) and by the Institute of Education Sciences, U.S. Department of Education, through Grant R305A140126 and R305K050157 to Dale Farran. The opinions expressed are those of the authors and do not represent views of the funders. The authors thank Dale Farran, Kelley Durkin, Kerry Hofer, Jessica Ziegler, Kayla Polk, and Dana True for their assistance with data collection and coding as well as the staff, teachers, and children involved in this research.

2.6 Supplementary Materials

Appendix A. Detailed Results from 6.7th Percentile cutoff sample achievement group analysis.

Supplementary Table 2.3. Supplementary descriptive statistics for experimental and standardized measures.

Supplementary Table 2.4. Task details for number comparison tasks of all formats.

Supplementary Table 2.5. Bivariate correlations between measures included in regression model

Appendix B. Exploration of the model fit.

Appendix A. Detailed Results from 6.7th Percentile cutoff sample achievement group analysis.

To make current results more easily comparable to previous literature that used differing cutoff thresholds for determining DD groups, the current study also examined whether there were differences between two commonly used thresholds for determining a dyscalculic sample. This threshold has varied widely across studies, and has likely contributed to disagreement among findings (Mazzocco & Myers, 2003). Another commonly used threshold is mathematics achievement scores 1.5 standard deviations below the nationally normed means, which is equivalent to performance below the 6.7th percentile (Kaufmann et al., 2013; Gavin R. Price et al., 2007; Rotzer et al., 2009). This threshold resulted in the following achievement groupings: DD, $\leq$ 6.7th percentile; LA, 6.7th – 25th percentile; TA, 25th – 95th percentile. Again, individuals were placed in achievement groups if their mathematics achievement scores were consistently in the designated achievement range at two of the three early assessments (PreK-1st grade) AND two of the three later assessments (5th-7th grades). Given these criteria, 221 children fit into consistent achievement groups across early and later assessment periods, 11 children met the criteria for DD, 22 for LA, and the same 188 children were TA. Descriptive statistics in Table 2.3.

Results

As in the first achievement group sample, there were no differences according to gender distribution percentages of mathematics achievement groups with the 6.7th percentile cutoff grouping (Pearson $\chi^2(2) = 4.045$, $p = .132$, Cramer's V = .132), nor in mathematics achievement ($t(446) = 1.182$, $p = .238$, Cohen's $d = 0.112$) or in nonsymbolic comparison accuracy ($t(446) = 0.780$, $p = .436$, Cohen's $d = 0.074$) at 6th grade, the outcome year of interest for the second set of primary analyses.

Supplementary Table 2.3. Descriptive statistics for experimental and standardized measures.

	10^{th} Percentile Cutoff Sample (n = 222, 116 females)			**6.7^{th} Percentile Cutoff Sample** (n = 221, 115 females)			**Entire Sample** (n = 448, 250 females)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Age (years), Pre-K	5.1	0.3	4.5-6.4	5.1	0.3	4.5-6.4			
Age (years), 6^{th} grade	12.0	0.3	11.4-13.4	12.0	0.3	11.4-13.4	12.0	.32	11.4-13.4
Nonsymbolic Comparison (accuracy, %)	75.5	5.29	58.6-91.4	75.6	5.3	58.6-91.4	74.8	5.48	48.6-91.4
Backward Corsi * (max span)	5.1	1.2	2-8	5.2	1.1	2-8	4.81	1.22	2-8
Hearts and Flowers* (accuracy, %)	76.4	14.4	40-100	76.8	13.9	44-100	73.4	14.5	35-100
Letter-word ID – WCJ-III (K, percentile rank)	111.8	14.1	73-144	111.8	14.2	73-144	109.7	12.7	73-144
Math Achievement- WCJ-III (Pre-K, percentile rank)	51.3	24.9	1.0-95.0	52.4	23.8	1.0-95.0			
Math Achievement- WCJ-III (K, percentile rank)	52.1	24.7	0.0-93.0	52.7	23.8	0.0-93.0			
Math Achievement- WCJ-III (1^{st} grade, percentile rank)	48.1	24.6	0.4-95.5	48.6	24.1	0.4-95.5			
Math Achievement – KM-3 (5^{th} grade, percentile rank)	39.2	23.5	0.5-96.2	39.6	23.1	0.7-96.2			
Math Achievement – KM-3 (6^{th} grade, percentile rank)	42.1	22.7	0.5-92.5	42.4	22.3	1.0-92.5	27.0	23.1	0.5-92.5
Math Achievement – KM-3 (7^{th} grade, percentile rank)	42.6	22.9	0.5-94.1	42.9	22.5	0.5-94.1			

* Raw scores reported here for year available. See sections 2.4.2 and 2.4.3 for a detailed description of scores used for analyses. WCJ-III = Woodcock Johnson III. KM-3 = KeyMath-3.

Detailed Results from 6.7^{th} Percentile cutoff sample achievement group analysis. For the 6.7^{th} percentile cutoff sample, there was an effect of congruency in the DD and TA groups [$t(10) = 3.855$, $p = .003$, Cohen's $d = 1.968$ for DD; $t\ (187) = 6.795$, $p < .001$, Cohen's $d = 0.844$ for TA], but not in the LA group [$t\ (21) = .705$, $p = .068$, Cohen's $d = 0.705$]. The right panel of Figure 2.3 shows the congruency effect for DD and TA groups in the 6.7 percentile cutoff sample. Levene's test of equality of variances showed no significant differences in variance across groups for mean accuracy of congruent trials or incongruent trials. Results from the ANOVA showed that there was no effect of achievement group on number comparison performance for congruent trials [$F(2, 218) = .389$, $p = .679.$, $\eta^2 = 0.003$], but there was a significant effect of achievement group on number comparison performance for incongruent trials [$F(2, 218) = 4.947$, $p = .008$, $\eta^2 = 0.043$]. After adjusting for multiple comparisons, one-tailed post-hoc tests indicated lower accuracy rates for DD than TA children (Bonferroni adjusted $p = .003$, Hedge's $g = 0.997$), lower accuracy rates for DD than LA children (Bonferroni adjusted $p = .011$, Hedge's $g = 0.821$), and no difference between LA and TA groups (Bonferroni adjusted $p = .500$, Hedge's $g = 0.028$).

Results from the ANCOVAs with the covariates of mean accuracy on the Hearts and Flowers mixed trials, max span on the backward Corsi block-tapping test, age at grade 6 testing, and letter-word identification at the end of Kindergarten indicated there was no effect of achievement group on number comparison performance for congruent trials [$F(2, 214) = .208$, $p = .812$, partial $\eta^2 = 0.002$], but there was a significant effect for incongruent trials [$F(2, 214) = 3.356$, $p = .037$, partial $\eta^2 = 0.030$]. After adjusting for multiple comparisons, one-tailed post-hoc tests indicated lower accuracy rates for DD than TA children (Bonferroni adjusted $p = .034$, Hedge's $g = 0.895$ lower accuracy rates for DD than LA (Bonferroni adjusted $p = .017$, Hedge's $g = 0.893$), and no difference between LA and TA groups (Bonferroni adjusted $p = .500$, Hedge's $g = 0.112$). These results replicate the pattern observed in the ANOVA.

The same ANOVAs and ANCOVA's were conducted on groups formed with the 6.7th percentile cutoff threshold for both congruent and incongruent trials and results fit the same pattern as those of the 10th percentile cutoff. In sum, all ANOVAs and ANCOVA's conducted on both the 10th and 6.7th percentile cutoff samples show the same pattern of results whereby: (1) no group differences are observed for congruent trials of the nonsymbolic comparison task, (2) the DD group performs significantly below LA and TA groups on incongruent trials even when controlling for other cognitive factors and early reading achievement, and (3) no group differences are present between LA and TA groups on incongruent trials.

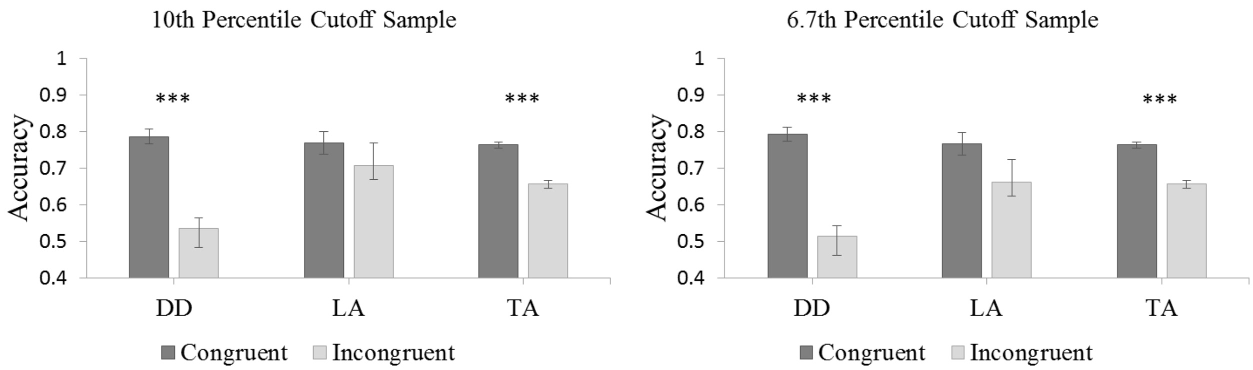


Figure 2.3. Nonsymbolic number comparison accuracy rates for the sample with developmental dyscalculia (DD) defined as achievement below the 10th percentile (left) and 6.7th percentile (right) split by congruency. LA = low achieving. TA = typically achieving. Error bars represent standard errors. P-values are indicated for differences in accuracy between congruent and incongruent trials (*** p < .001).

Supplementary Table 2.4. Task details for number comparison tasks of all formats.

	Nonsymbolic
trials	70 (10 per ratio)
ratio (numerosities)	0.33 (5 v 15)
	0.5 (5 v 10)
	0.67 (6 v 9)
	0.8 (8 v 10)
	0.86 (12 v 14)
	0.88 (7 v 8)
	0.9 (9 v 10)

Supplementary Table 2.5. Pearson *r* values for bivariate correlations between measures included in regression model predicting 6th grade mathematics achievement.

Measure (n = 448)	**1**	**2**	**3**	**4**	**5**
1. Nonsymbolic Comparison, congruent trials, acc.					
2. Nonsymbolic Comparison, incongruent trials, acc.	-.447***				
3. Backward Corsi, max span	-.051	.193***			
4. Hearts and Flowers, mixed trials, acc.	.017	.186***	.242***		
5. Reading achievement, LWID, end of Kindergarten	-.010	.071	.130**	.172***	
6. Mathematics achievement, composite, grade 6	-.067	.226***	.396***	.411***	.412***

* $p < .05$, ** $p<.01$, *** $p < .001$. Acc. = accuracy; LWID = letter-word identification (WCJ-III). The mathematics achievement composite score is cube-root transformed as described below.

Appendix B. Exploration of the model fit.

In order to better interpret the non-linear relation between accuracy on incongruent trials of the nonsymbolic number comparison task and mathematics achievement, we plot this relation in Figure 2.4. This figure shows the fitted relation between untransformed 6th grade mathematics achievement and nonsymbolic number comparison accuracy on incongruent trials for Model M5, holding Hearts and Flowers accuracy, backward Corsi span, early reading achievement, and age at testing in 6th grade at their sample means. As Figure 2.4 shows, the magnitude of the relation between accuracy on incongruent trials and mathematics achievement is greater for students with higher accuracy, on average. For example, the estimated difference between students with 30% and 40% accuracy on nonsymbolic number comparison is associated with a difference of 1.0 percentile rank points in 6th grade mathematics achievement, on average. The difference between students with 75% and 85% accuracy on nonsymbolic number comparison is associated with a difference of 1.3 percentile rank points in 6th grade mathematics achievement, on average.

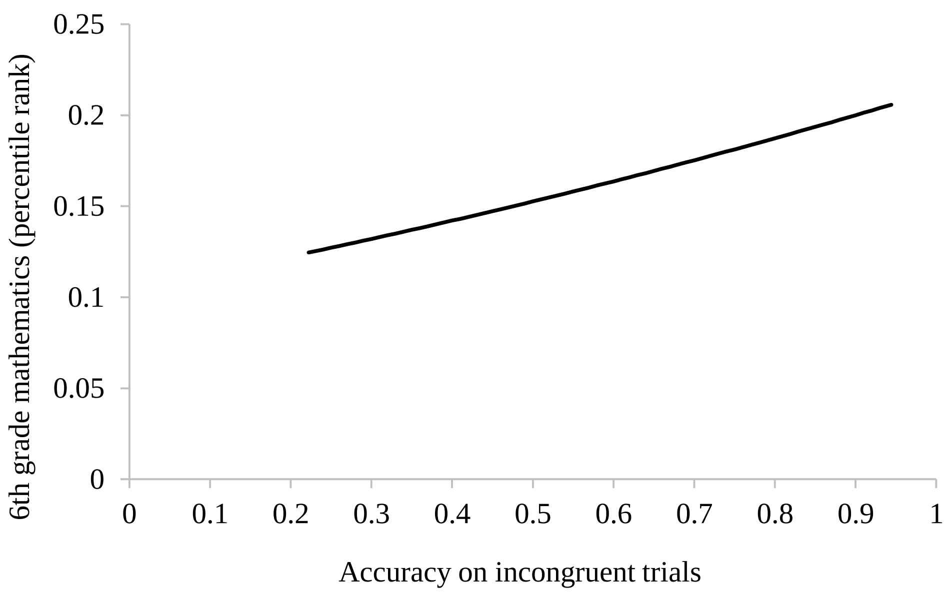


Figure 2.4. Predicted 6th grade mathematics achievement as a function of accuracy on incongruent trials of nonsymbolic number comparison, for students with average domain-general executive functioning and early reading achievement, and of average age at testing in 6th grade.

CHAPTER 3

THE EFFECTS OF VISUAL PARAMETERS ON NEURAL ACTIVATION DURING NONSYMBOLIC NUMBER COMPARISON AND ITS RELATION TO MATH COMPETENCY

3.1 Introduction

Recent neuroimaging evidence of the nonsymbolic comparison task indicates that recruitment of neural resources also differs as a function of congruency condition. In a study of typically developing adults, Leibovich, Vogel, Henik, and Ansari (2015) showed that incongruent trials are associated with greater activity in the superior frontal gyrus and left inferior/middle frontal gyri, but less activity in the right middle temporal and posterior cingulate gyri, than congruent trials. However, Leibovich et al (2015) examined activation during numerical versus non-numerical processing as a function of congruency, as opposed to examining the effect of congruency on ratio-dependent task activity. In order to investigate how differences in congruency specifically relate to processing of numerical information, the effect of congruency on numerical magnitude-specific activation must be evaluated. Just as a behavioral ratio effect has become a hallmark measure of ANS acuity, ratio-dependent activation in the superior parietal lobe has become a neural proxy (i.e. the neural ratio effect)(Bugden et al., 2012). However, no study to date has investigated if the neural ratio effect during nonsymbolic numerical magnitude processing is affected by the congruency of visual cues, and consequently, whether these potential differences in neural activity relate to math achievement. Understanding how differences in congruency require the recruitment of unique neural resources or how they differentially recruit known magnitude processing mechanisms may shed light on why numerical magnitude encoding appears to be related to math competency only in the face of conflicting visual cues, as well as elucidating the precise role of parietal mechanisms in nonsymbolic numerical magnitude processing.

To investigate this issue, we conducted a series of whole-brain analyses using functional magnetic resonance imaging (fMRI) data from a nonsymbolic comparison paradigm run on a typically developing sample (n = 38) of twelfth grade students. First, in order to build on previous research, we investigated the degree to which neural activity is modulated by the ratio of nonsymbolic comparison trials. Second, we investigated differences in neural activity during the task according to visual control condition (i.e. congruent vs. incongruent). Lastly, we correlated the neural ratio effect across the whole brain with math achievement, as measured by the math section of the preliminary scholastic aptitude test (PSAT) and assessed whether correlations between the neural ratio effect and math achievement differed as a function of congruency. In regards to our first analysis, we expected to see increased task-related activity in the intraparietal sulcus and superior parietal regions and the inferior frontal gyrus, likely as a result of greater engagement of numerical magnitude processing, and also increased activity in the anterior cingulate, motor, and motor planning areas as a result of increased task difficulty with more difficult ratios. For our second series of analyses, we hypothesized that there would be greater overall activation and a stronger neural ratio effect during incongruent as compared to congruent trials in the inferior frontal gyrus and superior parietal lobule. For our last set of analyses, which correlated the neural ratio effect with math achievement, we hypothesized that individual differences in the neural ratio effect would correlate with math achievement in the superior parietal lobule and inferior frontal gyrus, but also in regions known to be important for higher-level mathematical processing such as the angular gyrus and the supramarginal gyrus for arithmetic (Grabner, Ansari, Koschutnig, Reishofer, & Ebner, 2013; Gavin R Price, Mazzocco, & Ansari, 2013; Rivera, Reiss, Eckert, & Menon, 2005; Zamarian, Ischebeck, & Delazer, 2009). Further, because recent studies have indicated that the correlation between behavioral performance in the nonsymbolic comparison and math achievement is driven by incongruent trials (Bugden & Ansari, 2015; Fuhs & McNeil, 2013; Gilmore et al., 2013), we hypothesized that the same may be true of the neural ratio effect and math achievement.

3.2 Method

Participants

Participants were 12th grade students who had participated in a large scale longitudinal study (Michèle M M Mazzocco & Myers, 2003). A total of 43 participants took part in the fMRI experiment. Three participants were excluded due to excessive head motion (> 3 mm total displacement per run), one student was removed due to low performance in the scanner (56% accuracy rate, not different from chance), and one participant's data was lost due to an error in data storage. Two additional students with PSAT math scores more than 1.5 standard deviation below the national mean (< 7th percentile) were removed from the sample. This criteria has previously been used to classify individuals as having math learning disability and has been linked to atypical neurobiological development of number processing mechanisms (Kovas et al., 2009; Gavin R. Price et al., 2007). The final imaging sample thus included 36 individuals (14 females; mean age = 17.99 years, range = 17.36-18.79 years). FMRI task analyses include the entire 36-participant sample. For two individuals, Grade 10 PSAT tests scores were not available and standard scores were prorated from 9th grade (n = 1) and 11th grade (n = 1) based on percentile rank. For three additional individuals, PSAT scores were not available at any time and thus were excluded from the PSAT analysis. They were not excluded from the first portion of our analyses because earlier standardized math measures indicated they were in the typically developing range. Thus, the remaining sample for the PSAT analysis (n = 33) represents a wide range of typically developing individuals (PSAT math mean percentile rank = 72st, range = 22-99; PSAT reading mean percentile rank = 62nd, range = 12-99). Little's multivariate test for data missing completely at random (MCAR) indicated that there were not systematic differences according to gender or performance on the nonsymbolic comparison task (RT & accuracy) in groups with or without PSAT scores (Little's MCAR test, chi-square = 2.08, $p = .556$).

Tasks

Multiple tasks were performed during one scanning session including arithmetic verification, digit-matching, and non-symbolic number comparison (results from the arithmetic verification and digit matching paradigms are reported in Price et al., 2013). Only the results of the nonsymbolic number comparison task are analyzed and reported in this study.

Nonsymbolic Number Comparison

The non-symbolic comparison paradigm used in the present study was based on that reported by Halberda, Mazzocco, and Feigenson (2008). Participants were presented with a single array of blue and yellow dots in intermixed locations (Figure 3.1) and required to select, via button press, whether there were more blue or more yellow dots in the array. Trials varied according to the ratio between the dot sets (ratio calculated as the larger number divided by the smaller number, so that in a trial with 17 yellow dots and 13 blue dots, the ratio was 1.308). A total of 160 trials was presented across two runs, with the number of dots per color ranging from 5 to 21, and ratios ranging from 1.182 to 4.2. For behavioral and fMRI analyses, trials were categorized by ratio into 4 ratio bins (mean ratios = 1.21, 1.32, 1.99, 3.21) to ensure each ratio was represented by the same number of trials. Ranges for each bin were 1.18-1.25, 1.3-1.322, 1.67-2.38, and 2.6-4.2 respectively. Each bin had 40 trials and the mean ratio of each bin was used for analyses. In half the trials, the yellow dots were more numerous, and in the other half the blue dots were more numerous. Trial presentation order was randomized with respect to ratio, but fixed across participants. Stimuli were presented for 500ms, with average inter-stimulus interval (ISI) of 6s. ISIs were varied between trials to improve deconvolution of the hemodynamic response function (HRF). Thus, an ISI could be 4, 5, 6, 7 or 8s with a mean ISI across the run of 6s. ISI length and ratio were balanced such that no ISI length was more frequently associated with a given trial type. Following the method described by Halberda et al. (2008) to limit the influence of non-numerical continuous visual parameters, the following controls were utilized. For each ratio, half the trials were dot-size controlled, meaning that the size of the average blue dot was equal to the size of the average yellow dot. On these trials, the set with more dots necessarily also had a larger total area on the screen, thus surface area was visually congruent with the more numerous dot set (Figure 3.1, top). The other half of the trials were area controlled, meaning that the total number of pixels for blue and yellow dots was equal, resulting in an equivalent total surface area for both sets of dots, and thus the surface area was not visually congruent with the more numerous dot set and the more numerous dot set had a smaller average dot size. These trials are referred to as incongruent (Figure 3.1, bottom).

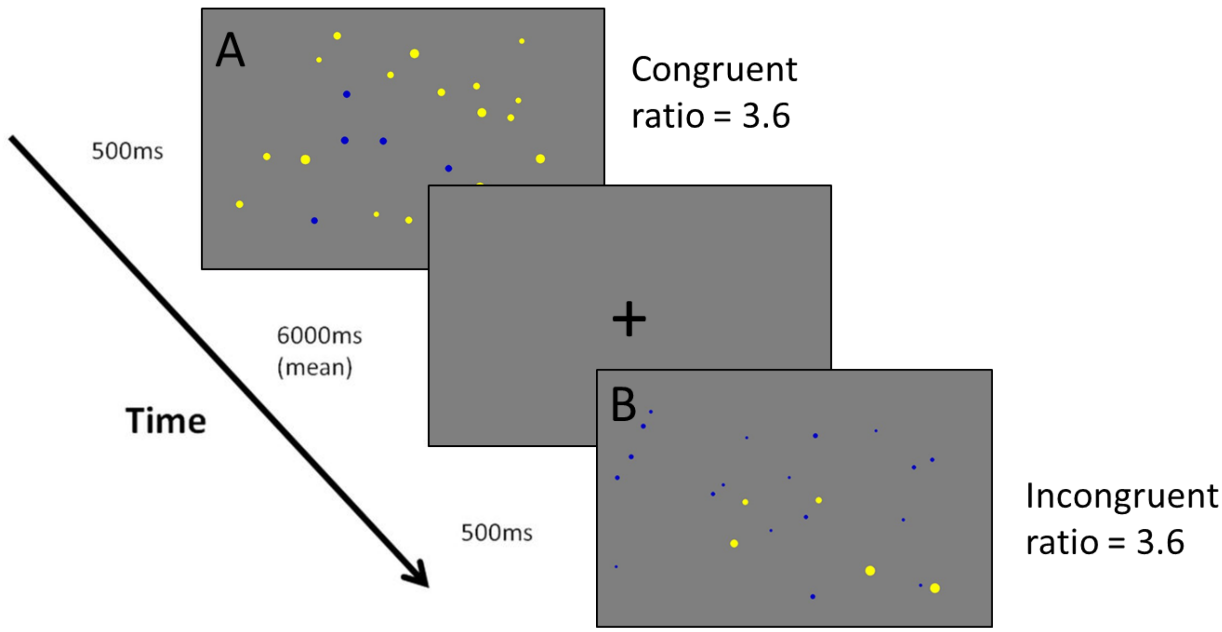


Figure 3.1. Nonsymbolic number comparison stimuli and paradigm timing. (top) Incongruent trial example of ratio 3.6 (larger number dot set/smaller number dot set, 18/5 = 3.6). (bottom) Congruent trial example, also of ratio 3.6.

Preliminary Scholastic Aptitude Test (PSAT)

As our measure of mathematical competence, we used standard scores from the PSAT math subtest sat during grade 10. The PSAT math subtest is part of a nationally administered test taken by over 3.5 million high school students in the USA each year as reported by "College Board" ("College Board," 2017). It is designed to reliably predict college entrance exam scores and serves as the qualifying test for the U.S. Merit-Based Scholarship Program, and it is thus also known at the National Merit Scholarship Qualifying Test (PSAT/NMSQT). Therefore, performance on the PSAT is highly relevant to higher education success among students in the U.S. Most individuals who take the PSAT are 10th graders, and in most states (including Maryland, where most of the participants resided) 10th graders are enrolled in a mathematics course. Beginning in 11th grade, some students choose not to pursue elective coursework (Updegraff, Eccles, Barber, & O'brien, 1996). Thus, 10th grade PSAT math subtest was chosen as a measure of broad achievement outcomes at the latest school grade during which all participants were receiving ongoing math instruction.

The PSAT math subtest contains 38 items, including word problems, geometry, algebraic equations, and complex arithmetic (no single-digit simple calculations), and it therefore represents a broad test of mathematical competence of significant importance to an individual's academic success. As a control measure for broad academic achievement, we used standard scores from the Grade 10 PSAT critical reading subtest. The PSAT reading subtest includes reading comprehension, questions about full-length and paragraph-length passages, such as speculating on the origin of the passage, as well as questions requiring students to fill in missing words from a range of sentences. Standard scores were used for all analyses, but percentile ranks are reported to characterize the sample since they are more readily interpretable. PSAT math and reading scores were correlated at r (31) = .54 (p = .001, n = 33).

MRI Acquisition Parameters

All MR imaging was acquired with a 3T Phillips MRI scanner using an 8-channel head coil with parallel imaging capability. Using multi-slice 2D SENSE T2* gradient-echo, echo planar imaging (EPI) pulse sequence, functional images were obtained in the axial plane. Higher order shimming was applied to the static magnetic field (B0). The EPI parameters were as follows: echo time, 30ms; TR, 2000ms; flip angle, 75°; acquisition matrix, 80 X 80 voxels; field of view, 240mm; SENSE factor of 2. This protocol acquired 34 axial brain slices per TR (3mm thickness with 1 mm slice gap, achieving a resolution of 3mm isotropic) and a time course of 176 temporal whole brain image volumes after discarding the first five volumes to ensure steady state. Anatomical scan parameters were performed using an 8-channel head coil, 240 mm field of view, and a 1 mm isotropic MP-RAGE (magnetization-prepared rapid acquisition with gradient echo), which takes 6 minutes with SENSE factor 2.

fMRI Analyses

Images were analyzed using Brainvoyager QX 2.8 (Goebel, Esposito, & Formisano, 2006). Functional images were corrected for differences in slice time acquisition, head motion, and linear trends, spatially smoothed with a 6mm FWHM Gaussian kernel, and aligned to T1 structural images, manually fine-tuned and then transformed into Talairach space (Talairach, J., & Tournoux, 1988). Functional data were analyzed using a random effects general linear model covering the whole brain and corrected for serial correlations using the AR(2) model implemented in BrainVoyager. Analyses were masked based on a group-level anatomical image to include all cortical grey matter (including the cerebellum), excluding white matter, ventricles, subcortical, and midbrain structures, as the theoretical focus of the current analysis was limited to cortical structures directly related to higher level semantic/representational processing and to reduce the number voxel-wise comparisons not relevant for the current level of analysis. Experimental events were convolved with a standard two-gamma HRF to model the expected BOLD signal (Friston, Josephs, Rees, & Turner, 1998) corresponding to regressors of interest. All analyses were run as whole-brain contrasts modeling correct trials from each of the 4 ratio bins. Baseline was modeled as fixation time between trials. Incorrect trials were modeled as separate predictors and excluded from further analyses. Additionally, a parametric regressor was created to model the relationship between ratio and BOLD response by weighting trials with the log-transformed ratio values (i.e. the neural ratio effect). Log-transformed ratio weights were utilized because previous studies of nonsymbolic number paradigms indicate that both behavioral responses (i.e. response time and accuracy rates) and fMRI % signal change in number-sensitive regions of the brain display a relationship to numerical ratio that is logarithmically compressed (Halberda et al., 2008; Jacob & Nieder, 2009; Piazza et al., 2004). Non-transformed ratios accounted for 49% of the variance in accuracy rates and 22% of the variance in response times in the current data. Log-transformed ratios predicted 55% and 25% respectively. Further, using log-transformed ratio predictors, residual standard errors of each model decreased from .57 to .26 for accuracy rates and from .70 to .34 for response times, indicating an overall improvement in the model fits for task behaviors. Parametric weights were de-meaned in order to orthogonalize regressors in the GLM and avoid multi-collinearity since main effects and parametric effects are inherently related. A negative relationship was modeled between ratio and BOLD activity because previous research indicates that brain regions processing numerical information increase in activity with ratios that are closer together (i.e. more difficult to compare). In this study, ratio is calculated as *ratio = larger number / smaller number*. Therefore, the smaller ratio trials are generally more difficult and are expected to elicit a greater BOLD response. Modeled linearly, we expected a negative parametric relationship between ratio and BOLD response in several brain regions and thus reverse-coded the results such that a ratio effect in the expected direction (i.e. greater activity with more difficult ratios being compared) would result in a positive β-weight and thus a positive t-statistic would indicate a better fit for the expected ratio effect. This reverse-coding practice was utilized for all results associated with the parametric regressor in the current study. All statistical results were thresholded at $p < .005$ and corrected for multiple comparisons at $p < .05$ using the cluster-level correction toolbox in Brainvoyager (Goebel et al., 2006), which estimates a cluster-level, false-positive rate based on a Monte Carlo simulation of 1,000 trials. Anatomical labels of results were defined by manually entering MNI converted peak coordinates into Jülich atlas' probability maps within the Anatomy Toolbox v2.0 in SPM8 (Eickhoff et al., 2005) and using the Talairach Daemon (Lancaster et al., 1997; Lancaster et al., 2000), prioritizing the method that allowed for greater specificity of anatomical label.

Nonsymbolic number comparison and the effect of congruency. To investigate differences in neural activity during nonsymbolic numerical comparison related to visual control conditions (i.e. congruent vs. incongruent), we first tested for a ratio effect across the whole-brain by performing a conjunction of random effects analysis of (a) a main effect of task vs. baseline and (b) a ratio effect (using the parametrically modeled ratio effect regressor). The conjunction revealed regions in which task-related activity was above baseline, but also increased proportional to the ratio-related difficulty of the trials (i.e. the ratio effect). Beta weights, separated by congruency condition, were then extracted from regions showing significant ratio effects and compared using within-subject t-tests to assess whether ratio-dependent activity within these regions differed according to congruency condition. A second, whole-brain random effects analysis was conducted directly comparing the parametric ratio effect between congruency conditions to reveal differential ratio effects that may not have shown a parametric ratio effect averaged across all task trials, but only within a congruency condition. Third, we investigated differences in activation according to congruency condition by contrasting congruent trials and incongruent trials irrespective of a ratio effect by performing a conjunction of random effects analysis of (a) a main effect of task vs. baseline and (b) a main effect of congruency (i.e. congruent > incongruent).

The neural ratio effect and math achievement. To assess the relation between the neural mechanisms underlying numerical magnitude processing and math achievement, we extracted mean beta weights of the ratio effect from clusters resulting from the previous conjunction of (a) a main effect of task vs. baseline and (b) a ratio effect and correlated participant beta weights with PSAT math scores. A subsequent correlation between the parametric ratio regressor and PSAT math scores was run at the whole-brain level to test for correlations that did not satisfy the conditions of the conjunction. It is possible that, in areas of the brain other than the four clusters resulting from the conjunction, some individuals demonstrated a parametric neural ratio effect and others did not, leading to null results for the conjunction, despite the presence of individual differences in beta weights potentially relevant for the correlation with math achievement. This whole-brain correlation was intended to test for individual differences in areas that were not significant for the conjunction at the group level. Subsequently, to control for domain-general academic achievement factors driving the behavioral correlation, the same analyses were repeated while controlling for reading achievement. To do this, PSAT math scores were entered into a linear regression with PSAT reading scores and the resulting unstandardized residuals were used for further analysis, thus removing variance associated with reading achievement. These scores are referred to as *residualized PSAT math scores* when utilized in an analysis and *PSAT math scores* otherwise.

The neural ratio effect and math achievement by congruency. To explore the relationship between the neural ratio effect and math achievement as a function of congruency condition, we ran whole-brain correlations between the parametric ratio regressor and math scores independently for each congruency condition with both PSAT math scores and residualized PSAT math scores.

3.3 Results

Behavioral Results

The two behavioral variables of interest from the fMRI task were response time (ms) for correct responses and percent accuracy across all trials. To assess the effect of ratio on each of these variables we conducted two repeated-measures ANOVA with ratio (4 levels) and congruency (2 levels) as factors. To correct for multiple hypothesis testing, the critical *p*-values for each set of correlations were adjusted using the Benjamini-Hochberg's (B-H) False Discovery Rate method with α_{FDR} = .05 (Benjamini & Hochberg, 1995), which provides a good balance between controlling for false positives and power for detecting weaker, but significant relationships. Raw *p*-values are reported, but significance is interpreted in terms of Benjamini-Hochberg corrected *p*-values. Results for accuracy revealed a main effect of ratio [$F(3, 105) = 208.73$, $p < .001$, partial-$\eta^2 = 0.856$], a main effect of congruency [$F(1, 35) = 10.33$, $p = .0003$, partial-$\eta^2 = 0.228$], and a ratio x congruency interaction [$F(3, 105) = 5.46$, $p = .002$, partial-$\eta^2 = 0.135$]. Greater ratios and congruent trials were each associated with more accurate performance (Figure 3.2A). Individuals were more accurate during congruent trials only during ratio bins 1.32 [$t(35) = 3.59$, $p = .001$, Cohen's $d = 0.74$] and 1.99 [$t(35) = 3.60$, $p = .001$, Cohen's $d = 0.67$], but not during the smallest ratio bin, 1.21 [$t(35) = -0.59$, $p = .558$, Cohen's $d = -0.13$], or largest ratio bin, 3.21 [$t(35) = 1.64$, $p = .110$, Cohen's $d = 0.21$], after adjusting for multiple comparisons. Results for response time revealed a main effect of ratio [$F(3, 105) = 94.45$, $p < .001$, partial-$\eta^2 = 0.730$], a main effect of congruency [$F(1, 35) = 99.61$ $p < .001$, partial-$\eta^2 = 0.359$], and a ratio x congruency interaction [$F(3, 105) = 3.72$, $p = .014$, partial-$\eta^2 = 0.096$]. Response times were faster for larger ratios than smaller ratios and for congruent vs. incongruent trials (Figure 3.2B). Individuals responded faster during congruent trials only during larger ratio bins 1.99 [$t(35) = 5.08$, $p < .001$, Cohen's $d = 0.46$] and 3.2 [$t(35) = 4.45$, $p < .001$, Cohen's $d = 0.84$], but not during the smallest ratio bins, 1.21 [$t(35) = 0.47$, $p = .558$, Cohen's $d = 0.05$] and 1.32 [$t(35) = 1.01$, $p = .320$ Cohen's $d = 0.09$], after adjusting for multiple comparisons.

To assess the relation between number comparison performance and math competence, we correlated PSAT math scores and residualized PSAT math scores with mean accuracy and response time, as well as the slopes of accuracy and response time by ratio. Mean accuracy rate did not correlate with PSAT math [$r(31) = .18$, $p = .524$]. When split by congruency condition, mean accuracy on congruent trials was not correlated with PSAT math [$r(31) = .11$, $p = .524$] nor was mean accuracy for incongruent trials [$r(31) = .18$, $p = .321$]. Mean accuracy rate did not correlate with residualized PSAT math scores [$r(31) = .07$, $p = .711$], nor did the accuracy rate for congruent [$r(31) = -.06$, $p = .739$] or incongruent trials [$r(31) = .16$, $p = .374$]. Mean response time did not correlate with PSAT math across all trials [$r(31) = -.35$, $p = .049$], during congruent trials [$r(31) = -.35$, $p = .048$], or incongruent trials [$r(31) = -.34$, $p = .056$], after correcting for multiple comparisons, though the effect size was very similar to previously reported effect sizes from meta-analyses (Chen & Li, 2014; Schneider et al., 2017). Mean response times correlated with residualized PSAT math scores across all trials [$r(31) = -.48$ ($p = .005$)], congruent trials [$r(31) = -.49$, $p = .001$], and incongruent trials [$r(31) = -.46$, $p = .008$] after controlling for multiple comparisons, indicating that slower response time overall, and within congruency conditions, was correlated with lower PSAT math scores after controlling for PSAT reading. The slopes for mean accuracy and reaction time did not correlate with either PSAT math or residualized PSAT math scores (all p-values's $> .11$).

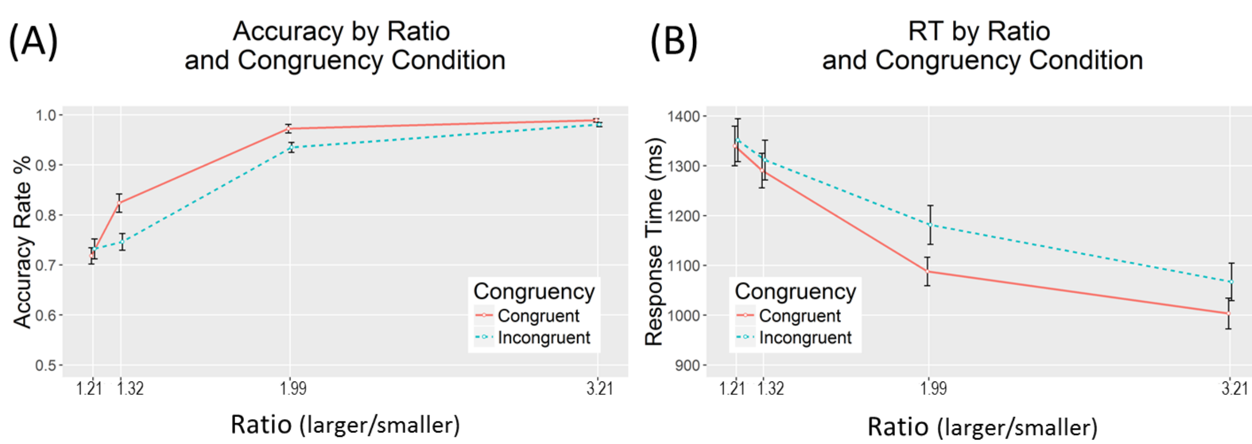


Figure 3.2. Nonsymbolic comparison behavioral data from fMRI task showing (A) accuracy rate (total % correct) split by congruency condition (B) and response time (RT) split by congruency condition, by ratio.

fMRI Results

Nonsymbolic number comparison and the effect of congruency. The conjunction of the main effect of task and parametric effect of ratio revealed four clusters that showed a parametric increase with increasingly difficult ratios, including the anterior cingulate cortex (ACC) extending into the supplementary motor area (SMA), the left precentral gyrus, the left intraparietal sulcus (hIP1), and a superior/medial portion of the right superior parietal lobule (SPL) with peak activation in the precuneus, which sits superior and medial to the IPS (Figure 3.3, Table 3.1). A comparison of mean beta weights for the parametric ratio predictor extracted from these four regions did not show any differences according to congruency condition (results of all within-sample t-tests $p > .258$), indicating that in areas demonstrating a ratio effect at the whole-brain level, the ratio effect did not differ as a function of congruency condition. It is possible, however, that areas of the brain in which the parametric ratio effect was significant in only the congruent or incongruent visual control condition were not revealed when the neural ratio effect was modeled as an average of the two conditions. Therefore, we directly contrasted the parametric effect of ratio between the two congruency conditions at the whole-brain level. Results revealed that there were no brain regions showing a significant difference between the congruent and incongruent ratio effects.

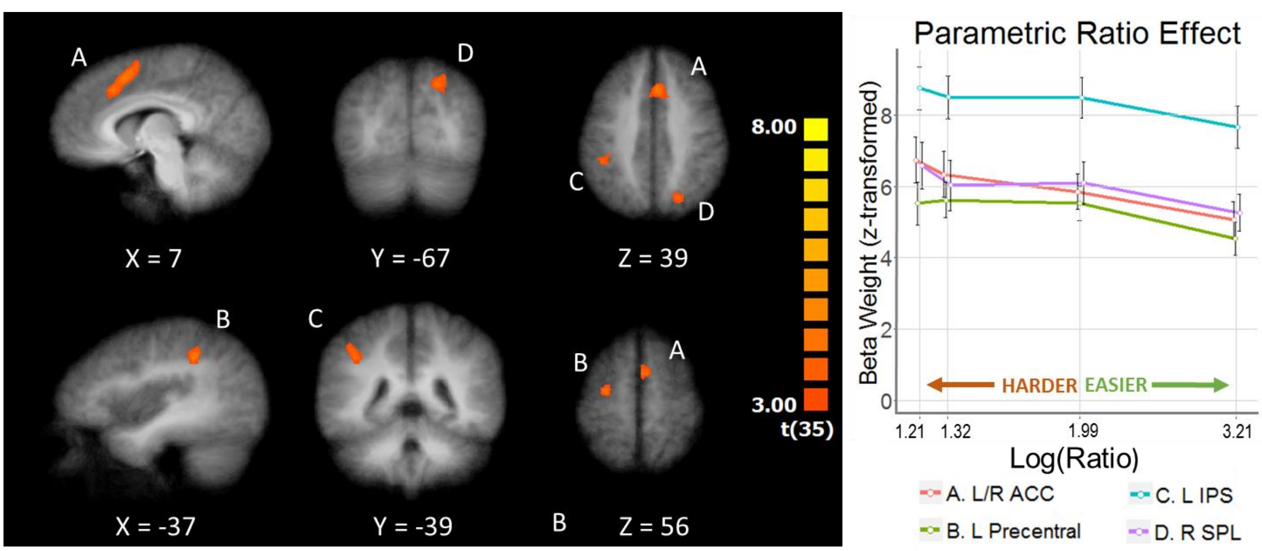


Figure 3.3. Results from the whole brain conjunction analysis of main effect of task and ratio effect. Analysis was performed on de-meaned ratios but is presented here as above baseline for visualization purposes. Slices labeled in Talairach space. Lettered labels of clusters correspond to beta weight plots in line graph. Images are presented in neurological convention, whereby right is right.

Table 3.1. Significant clusters for conjunction of task effect (main effect) and parametric ratio effect.

Cluster	Peak TAL (x y z)	Voxels	Peak *t*	BA	Anatomical Description
A	(-2 8 49)	4210	5.94	32	L/R Anterior Cingulate
B	(-24 -10 52)	619	5.08	6	L Precentral Gyrus
C	(-39 -37 34)	663	4.84	40	L Intraparietal Sulcus (hIP1)
D	(18 -67 40)	836	4.42	7	R Superior Parietal Lobule (Precuneus)

Note. $n = 36$. All results cluster corrected at p <0.05, uncorrected p <0.005 (clusters > 391 voxels, 1mm iso). TAL = talairach coordinates; BA = Brodmann area.

The comparison of overall activation (i.e. main effects as opposed to ratio effects) between congruency conditions revealed four regions where activity is greater for incongruent trials (Figure 3.4, Table 3.2), suggesting that incongruent trials generally recruit more neural resources in the rAG, right inferior frontal gyrus (IFG), right fusiform gyrus (rFG), and right parahippocampal gyrus. No regions were more active for congruent trials.

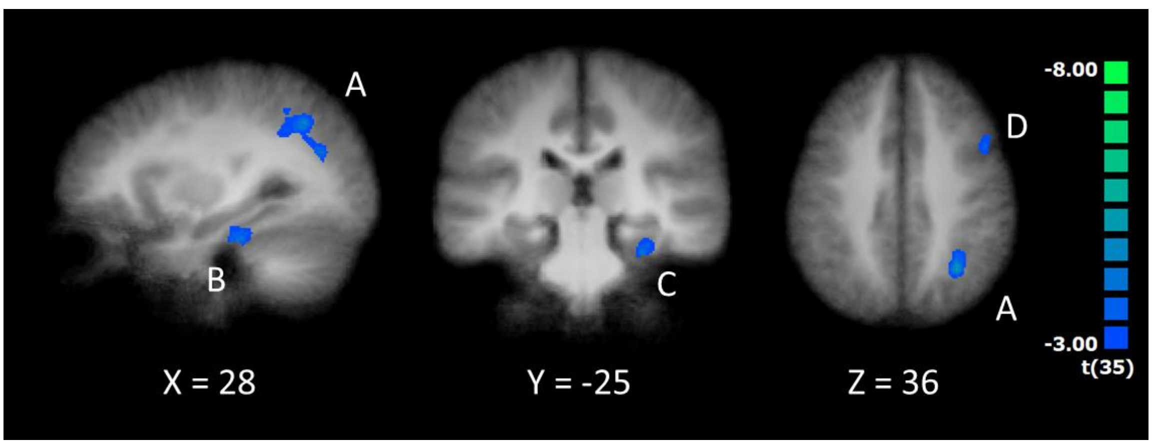


Figure 3.4. Results from the whole brain conjunction analysis of main effect of task and a main effect of congruency condition. Negative t-statistics indicate BOLD response for incongruent trials is greater than for congruent trials. Slices labeled in Talairach space. Lettered labels of clusters correspond Table 3.2. Images are presented in neurological convention, whereby right is right.

Table 3.2. Significant clusters for conjunction analysis of main effect of task and a main effect of congruency condition.

Cluster	Peak TAL (x y z)	Voxels	Peak *t*	CON *β*	CON se	INC *β*	INC se	BA	Anatomical Description
A	(30 -67 22)	1621	6.24	7.62	0.23	8.32	0.23	39	R Angular Gyrus
B	(51 -46 -8)	1250	4.80	3.62	0.24	4.58	0.24	37	R Fusiform Gyrus
C	(27 -25 -20)	708	4.60	3.09	0.27	3.98	0.27	35	R Parahippocampal Gyrus
D	(45 14 31)	864	4.29	3.50	0.23	4.31	0.23	9	R Inferior Frontal Gyrus

*All results cluster corrected at $p < .05$, uncorrected $p < .005$ (clusters > 339 voxels, 1mm iso). TAL = talairach coordinates; CON = congruent; INC = incongruent; BA = Brodmann area.

The neural ratio effect and math achievement. To assess the relation between the ratio effect and math competence, we first correlated PSAT math scores and residualized PSAT math scores with the parametric ratio effect beta weights from the four regions reported in our whole-brain ratio effect analysis. These analyses revealed no significant associations. We subsequently correlated the neural ratio effect with PSAT math scores and residualized PSAT math scores across the whole brain. Before controlling for reading, this analysis revealed two significant associations in the left and right insula whereby a greater ratio effect was associated with lower math competency (Table 3.3). When controlling for reading, this association was present in the left insula at the same corrected threshold ($p < .05$) but not in the right insula.

The neural ratio effect and math achievement by congruency. To assess the relation between the ratio effect and math competence when congruent and incongruent trials were considered separately, independent whole-brain correlations between PSAT math scores and the ratio effect were run for each congruency condition, followed by the same analysis run with residualized scores. Before controlling for reading, the ratio effect correlated negatively with PSAT math scores in a left-lateralized portion of the insula during congruent trials (Table 3.3). For incongruent trials, the ratio effect was negatively correlated with PSAT math in the left precuneus, right insula, and the right culmen of the cerebellum. Both of these results indicated lower PSAT math scores were associated with a greater ratio effect. When controlling for reading, residualized PSAT math scores correlated positively with the ratio effect during congruent trials in the right supramarginal gyrus extending into the superior temporal gyrus (Figure 3.5, Table 3.3). However, during incongruent trials, residualized PSAT math scores correlated negatively with the ratio effect in the left angular gyrus extending into the superior temporal gyrus and the left precuneus extending into the posterior cingulate cortex (Figure 3.6, Table 3.3).

Table 3.3. Clusters showing a significant correlation between the ratio effect and PSAT math scores or residualized PSAT math scores.

Condition	Math	Peak TAL (x y z)	Voxels	Peak *r*	Mean *r*	BA	Anatomical Description
CON & INC	PSAT math	(45 8 1)	392	-.59	-.51	13	R Insula
		(-42 -7 1)	1924	-.78	-.56	13	L Insula
CON & INC	*res*. PSAT math	(-42 -7 4)	608	-.62	-.54	13	L Insula
CON	PSAT math	(-45 -1 7)	917	-.61	-.52	13	L Insula
INC	PSAT math	(-12 -52 43)	769	-.65	-.53	7	L Precuneus
		(45 8 10)	454	-.62	-.52	44	R Insula
		(-27 -52 -26)	421	-.62	-.51	-	L Cerebellum, Culmen
CON	*res*. PSAT math	(54 -37 19)	649	.60	.51	40, 22	R SMG / STG
INC	*res*. PSAT math	(-60 -37 22)	1548	-.61	-.51	39, 22	L AG / STG
		(-9 -49 40)	1101	-.67	-.53	7, 31	L Precuneus / Posterior Cingulate

Note. $n = 33$. All results cluster corrected at $p < 0.05$, uncorrected $p < 0.005$. TAL = talairach coordinates; CON = congruent; INC = incongruent; BA = Brodmann area; R = right; L = Left; SMG = supramarginal gyrus; STG = superior temporal gyrus; AG = angular gyrus; *res*. = residualized.

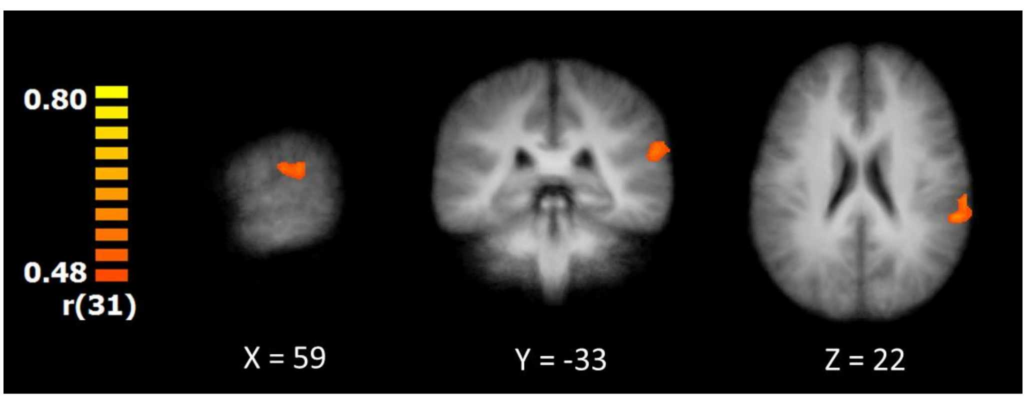


Figure 3.5. Supramarginal gyrus / superior temporal gyrus cluster resulting from whole-brain correlation with residualized PSAT math scores for congruent trials. Images are presented in neurological convention, whereby right is right.

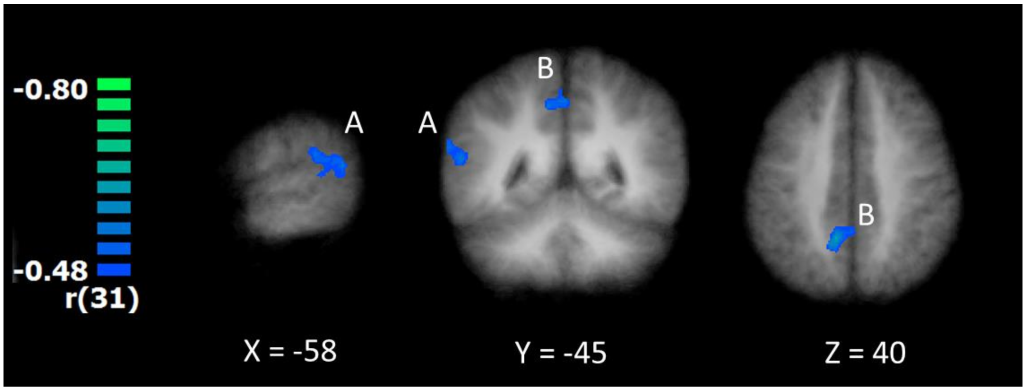


Figure 3.6. (Left) (A) Left angular gyrus / superior temporal gyrus and (B) left precuneus / posterior cingulate cluster resulting from whole-brain correlation with residualized PSAT math scores for incongruent trials. Images are presented in neurological convention, whereby right is right.

3.4 Discussion

A growing body of recent research indicates that performance on the nonsymbolic comparison task is heavily influenced by visual control parameters such that the relationship between math achievement and nonsymbolic comparison is driven by performance on trials with incongruent visual cues in preschoolers (Fuhs & McNeil, 2013), children in primary school (Gilmore et al., 2013), and in individuals with dyscalculia (Bugden & Ansari, 2015). Further, the one neuroimaging study to investigate this issue thus far indicates that recruitment of neural resources also differs as a function of congruency condition (Leibovich et al., 2015). This earlier work suggests that the relation between nonsymbolic comparison performance and math achievement may not be driven solely by domain-specific numerical processing mechanisms. Furthermore, only a handful of neuroimaging studies have demonstrated a link between BOLD activation during nonsymbolic number processing and math achievement, and almost exclusively by way of comparison between typically developing and dyscalculic populations (Dinkel et al., 2013; Kovas et al., 2009; Kucian et al., 2011; Moeller, Neuburger, Kaufmann, Landerl, & Nuerk, 2009; Price et al., 2007). Among those studies, there is little consensus about which cognitive mechanisms drive the relationship between the neural system used to encode numerical magnitudes (i.e. the ANS) and math skills. Only one study to date has investigated this question in a typically developing population with nonsymbolic stimuli (Gullick et al., 2011). That study did not, however, examine the influence of non-numerical visual control parameters on the observed relation. Thus, the question of whether the neural correlates of nonsymbolic magnitude processing and their relation to math competency are influenced by visual parameters in a manner similar to recent behavioral studies remains open. The present study is the first to empirically investigate this question.

Our results indicate that BOLD response was modulated by ratio in brain regions previously shown to exhibit a neural ratio effect when calculated from the average of congruent and incongruent trials, as it is in most studies, and that the ratio effect within those regions did not differ as a function of congruency condition. In other words, the effect was not driven by either condition. Further confirmation that regions of the brain sensitive to changes in numerical magnitude did not differ as a function of congruency came from the whole-brain direct contrast of the incongruent and congruent ratio effects, which did not reveal any regions that differed. This lends support to the idea that regions of the brain previously found to encode numerical magnitude, such as the IPS and SPL, do so consistently when other visual cues are congruent or incongruent with judgement about numerical magnitudes. In other words, the ratio-dependent activation during nonsymbolic number comparison does not appear to be the product of cognitive processes specific to either congruent or incongruent task conditions. In contrast, there were significant differences in overall task-related activation according to congruency condition when compared at the whole-brain level in fronto-parietal areas known to be important for encoding numerical magnitude and other mathematical computations. The neural ratio effect correlated with PSAT math in the left insula before and after controlling for reading achievement. When the relationship between the neural ratio effect and PSAT math scores was investigated independently for congruent and incongruent trials separately, results indicated a left-lateralized correlation in the insula during congruent trials and right-lateralized correlation in the insula during incongruent trials. The whole-brain correlation controlling for reading, and thus specific to math, resulted in correlations that were again in opposite hemispheres, but also opposite in the directionality of their relationship to math.

The first steps in our analysis largely confirmed previous results of nonsymbolic number tasks.

Our findings of a neural ratio effect in several frontal and parietal regions replicates existing evidence from fMRI studies showing increased activity with increasingly difficult magnitude comparisons (Ansari & Dhital, 2006; Gullick et al., 2011; Price et al., 2007), and is in line with the results of previous meta-analyses showing nonsymbolic number processing is subserved by the intraparietal sulcus and regions extending into superior parietal lobule (Arsalidou & Taylor, 2011; Sokolowski et al., 2016). The increase in activity of the anterior cingulate cortex and supplementary motor areas are likely a result of increasing task difficulty that covaries with ratio, as this trend is a frequently observed consequence of increased cognitive demand across a wide range of tasks (for a review, see Paus, 2001). In contrast, the same pattern of activity in the right superior parietal lobules (SPL) and the anterior portion of the left IPS (hIP1) are likely to represent the encoding of numerical information. Electrocorticography studies of both experimental and naturalistic settings (Daitch et al., 2016; Dastjerdi, Ozker, Foster, Rangarajan, & Parvizi, 2013), fMRI adaptation studies of numeric versus non-numeric stimuli (Cantlon, Brannon, Carter, & Pelphrey, 2006; Piazza, Izard, Pinel, Bihan, & Dehaene, 2004) and multi-modal numerical stimuli (Vogel et al., 2017), neurological case studies of superior parietal lesions (McCloskey, 1992; Takayama, Sugishita, Akiguchi, & Kimura, 1994), and other fMRI studies demonstrating numerical ratio effects (Gullick et al., 2011; Vogel, Goffin, & Ansari, 2015) all indicate that a bilateral region extending from the IPS to the superior parietal lobule is involved in numerical magnitude processing. There is considerable variability in the literature in regards to the anatomical labeling of the IPS, likely due to the fact that the shape of the IPS varies greatly among individuals and that it is a large structure that extends from the occipital lobe to the postcentral sulcus. Despite this variability, the lIPS (hIPS) and rSPL structures from the current results overlap with regions identified in a large meta-analysis of number-related fMRI studies, indicating their likely involvement in magnitude-related processing. However, the increase in parietal activation may also reflect a response to the increased attention demands of more difficult trials. Several studies show that numerical magnitude encoding, visuo-spatial attention, and working memory function converge in the superior parietal lobe (Dumontheil & Klingberg, 2012; Zago et al., 2008; Zago & Tzourio-Mazoyer, 2002). Given the limited degree of control over visual factors in stimulus design and the degree of anatomical overlap in attentional mechanisms in the parietal lobe, future studies should utilize multivariate techniques together with analyses of nuanced visual parameters in order to further investigate whether there are indeed differences not captured by the current analysis.

Comparison of task-related, non-ratio-specific neural response according to congruency condition revealed four regions that were more active for incongruent than congruent trials, including the rAG, rFG, rIFG, and right parahippocampal gyrus. By nature of the contrast, the same ratios are involved in congruent and incongruent trials, and therefore necessarily reflect differences in neural recruitment that are not dependent on the dimension of numerical magnitude. Nonetheless, several of these regions have been frequently implicated in research of numerical magnitude encoding and magnitude processing. The IFG is thought to work with parietal regions to encode numerical magnitude but has been shown to respond differentially under various working memory and inhibitory control demands (Dumontheil & Klingberg, 2012; Eiselt & Nieder, 2013). With single-cell recordings in primates, Jacob and Nieder (2014) showed that the lateral prefrontal cortex, a potential homologue of the IFG and MFG in humans, was a selection stage for goal-directed number processing that represented behaviorally relevant as well as transiently irrelevant numerical information, whereas distractor-resistant working memory representations were maintained in the parietal cortex. If both discrete and continuous quantity are processed in superior parietal regions, parietal magnitude neurons may rely on their connection to the IFG, which acts as part of a global neuronal workspace, to resolve competition among representations for selecting an appropriate rule-based response. Comparing competing aspects of the stimuli (i.e. numerical magnitude and visual cues) would increase both working memory and inhibitory control demands. If this is the case, it would stand to reason that the IFG would be more active during cases of conflict. The source of this same pattern of results in the AG is less clear since the AG is widely active in a variety of tasks, serving to integrate multisensory information and reorient attention to relevant information (Seghier, 2012). One possible explanation is that the AG may be involved in integrating stimulus information from the SPL and IFG/MFG, since it is known that the AG serves as a hub that connects to the SPL with the superior, middle, and inferior frontal gyri (Seghier, 2012). Similarly, as part of the orienting network (S.E Petersen & Posner, 2012), the AG may be involved in orienting attentional resources from parietal systems involved in object size to parietal systems involved in numerical magnitude representation. Though the AG has often been implicated in arithmetic fact retrieval (Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002; Yang et al., 2017), this activity is usually left-lateralized and specific to symbolic representation of number (Holloway, Price, & Ansari, 2010; Gavin R. Price & Ansari, 2011). Therefore, it is likely that the present right-lateralized AG finding is more related to attention than magnitude perception. Interpretation of increased activity in the right parahippocampal gyrus and rFG is more speculative, but may be related to the increased need during incongruent trials for a detailed and complete processing of the visual scene (for a review, see Aminoff, Kveraga, & Bar, 2013). There is evidence that these regions are associated with processing scenes with high spatial frequency (Rajimehr, Devaney, Bilenko, Young, & Tootell, 2011). Given the short stimulus duration of the task and complexity of the dot arrays, participants are unlikely to foveate on each object, and processing the stimulus as a whole is necessary for a successful response. Given that the visual association between numerical quantity and many visual cues is reversed during incongruent trials, a more detail processing of visual associations is likely required. In sum, the present study provides evidence that congruent and incongruent trials differentially recruit neural resources in regions that support stimulus processing but are not directly involved in the encoding magnitudes.

A further aim of the current study was to investigate the relationship between patterns of activity associated with the processing of numerical magnitude and individual differences in math achievement. Our hypotheses were limited due to inconsistent findings in previous studies of dyscalculic populations and there being only one study of typically developing individuals. To date, two studies have found greater activation in various parietal areas for children with dyscalculia compared to controls (Dinkel et al., 2013; Kaufmann et al., 2009), two found weaker parietal activity in dyscalculic children (Kucian et al., 2006, 2011), another found no group differences in parietal regions (Kovas et al., 2009), and one study found less ratio-dependent modulation in dyscalculic individuals compared to controls (Price et al., 2007). Gullick et al. (2011) showed a negative correlation between the neural distance effect in bilateral perisylvian areas and math achievement in college-aged adults. Results from the current study revealed very similar findings to the study by Gullick and colleagues (2011), showing an inverse correlation between PSAT math scores and the neural ratio effect, such that individuals with a weaker ratio effect in the left insula and right insula had higher math scores. It is important to note that individual beta weights within this region ranged from negative to positive indicating that some people had greater activity for "easier" ratios and thus a negative beta or "inverse ratio effect". It was these individuals who scored highest in math competency. Though left and right insular activity correlated with math performance, only activity in the right insula remained significant after controlling for PSAT reading. This suggests that ratio-dependent activity in the left insula did not specifically relate to math skills but reflected task-related processes relevant for domain-general academic achievement., A decrease in the neural ratio effect has been suggested to indicate an increase in task-related processing efficiency (Gullick et al., 2011). If more difficult trials elicit a higher BOLD response, then it would follow that individuals with better performance (those who found difficult trials less difficult) would not show as large of a ratio-dependent increase. The current results appear to support this interpretation, albeit in regions of the brain not typically associated with magnitude processing. Further, it should be noted that the ratio effect in areas of the brain previously associated with the encoding of numerical magnitudes did not correlate with math achievement as we hypothesized. This calls into question the idea that magnitude processing efficiency, as measured by the neural ratio effect in the parietal lobe, relates to math achievement in typically developing populations of the age of participants in the present study. Indeed, the weak relationship of the behaviors measured in the current study, $r = .18$ for accuracy rates and $r = -.35$ for response times across all ratios, is supported by recent meta-analyses that estimate the strength of this behavioral relationship to be $r = .20$ and $r = .241$ (Chen & Li, 2014; Schneider et al., 2017) compared to a correlation of $r = .302$ with symbolic stimuli (Schneider et al., 2017).

As discussed, recent research has suggested that performance on incongruent trials during nonsymbolic number comparison tasks is more strongly related to math ability than performance on congruent trials. Therefore, the final aim of this study was to explore whether the relation between the neural ratio effect and math competency differed as a function of congruency condition. After controlling for general academic achievement, results revealed diverging patterns of association such that the ratio effect positively correlated with math competency in the rSMG during congruent trials (greater BOLD response for more difficult ratios correlated with higher math scores), but negatively correlated with math competency in the lAG during incongruent trials (greater BOLD response for easier ratios correlated with higher math scores). Interpretation of this finding should be tempered by the fact that these two correlations were not significant before controlling for reading. Though multicollinearity among PSAT reading and PSAT math is not a likely factor (r = .54) the relation between reading and math does factor into the relationship in the current findings and may be less generalizable than the right insula correlation, which was significant before and after controlling for reading. Increases in activity with increased trial difficulty likely reflect increased recruitment of cognitive resources for discrimination between and manipulation of numerical magnitude information that work in cooperation with brain regions that directly encode numerical magnitudes under differing congruency conditions. Increased activity of the SMG has been reported in response to magnitude perception even in the absence of response selection (Ansari, Dhital, & Siong, 2006). Further, children with dyscalculia have shown reduced modulation due to task-complexity during arithmetic problems in the SMG compared to typically developing peers (Ashkenazi, Rosenberg-Lee, Tenison, & Menon, 2012). Therefore, this positive correlation between the ratio effect and math competency may indicate that increased recruitment of the SMG during comparison is important for efficient processing of numerical information when multiple dimensions of magnitude are aligned with numerical magnitude. The negative correlation between math competency and the neural ratio effect in the left angular gyrus may represent a trend in the processing of numerical information, however, it may also reflect the processing of conflicting visual information. The angular gyrus is activated by a large variety of tasks with the common themes of combining and integrating information, manipulating mental representations, and reorienting attention to relevant information (Seghier, 2012). Differences in the correlation between math competency and activation according to congruency may be due to the fact that for incongruent trials, the degree of visual conflict increases as ratios become easier to compare. This feature is a product of the way visual controls and trials ratios are necessarily linked. For incongruent trials, the surface area of each dot set within a trial is matched. Therefore, a numerically larger dot set necessarily has smaller dots. For example, when comparing 18 dots and 5 dots in the incongruent condition, as exemplified in Figure 3.1, dots belonging to the 18 dot set are smaller than the dots of the 5 dots set. Further, across trials, the degree of the difference in dot size covaries with ratio such that the greater the ratio is, the more visually incongruent the visual information. For example, if 40 dots compared to 5 dots in the incongruent condition, the 40 dots would need to be even smaller than the 18 dots in Figure 3.1 in order to equate surface area. Given these two examples, the second example 40 vs 5 is an easier numerical ratio to compare than 18 vs 5, but the degree of visual conflict in average dot size is more extreme. Therefore, it may be that individuals with higher math competency are appropriately engaging mechanisms in the angular gyrus to resolve conflicting visual cues as ratios get easier (i.e. but more visually incongruent).

Further, although both the left AG and right SMG have been more commonly associated with symbolic number and verbally mediated numerical information (Sokolowski et al., 2016), the current findings relating their activity during a nonsymbolic number comparison task to math competency suggests that their role is not limited to symbolic magnitude processing and requires further investigation. For example, it is well established that acquisition of exact, verbal number representation enhances acuity of nonsymbolic number representation (Manuela Piazza, Pica, Izard, Spelke, & Dehaene, 2013; Pica, Lemer, Izard, & Dehaene, 2004). And, an emerging body of literature suggests that symbolic number processing may mediate the influence of nonsymbolic magnitude processing on math development (Fazio, Bailey, Thompson, & Siegler, 2014; Lyons, Ansari, & Beilock, 2012; Gavin R. Price & Fuchs, 2016). The current results demonstrating a relationship between ratio-dependent activity in the lAG and rSMG and PSAT math score may reflect the increased relation between symbolic and verbal magnitude systems with nonsymbolic magnitude systems towards the end of math development in the current sample. However, only developmental imaging studies following the link between nonsymbolic magnitude representation and math skills over the course of acquiring symbolic math skills will be able to disentangle the feedback mechanisms responsible for such findings.

Future Directions

Several limitations exist in the current study that should be noted. First, the current study used the most frequently utilized method for controlling for visual parameters of dot sets in order to make results relevant to an existing body of behavioral literature. However, this method of control is not ideal for the long-term project of understanding the interaction of congruency of visual parameters and perception of numerical magnitude, and their relation to math. Behavioral studies have provided in-depth analyses of more extensive visual properties of dot sets than those mentioned in the current study (Gebuis & Reynvoet, 2012; Leibovich & Henik, 2013). Though it is impossible to rid the nonsymbolic comparison task of the influence of visual cue congruency, two practices may be employed in future studies to further elucidate the nuanced effects presented by controlling congruency of stimulus properties. First, stimuli in future studies should tightly control as many visual parameters as possible, including surface area, density, convex hull, dot size, and luminance. Secondly, since degree of congruency and ratio are inherently related in the visual control method used in the present study, the two cannot be separated in any analysis. Future studies should provide the opportunity to analyze degree of congruency as ratio is held constant as well as the converse by designing stimuli with such properties.

Secondly, performance on the nonsymbolic comparison task is not related to all math measures equally. This may be true of neural correlate results as well. Meta-analyses indicate that the correlation for nonsymbolic comparison to early math abilities, such as mental arithmetic, has an effect size of r = .454 compared to an effect size of r = .288 for written arithmetic and curriculum-based measures (Schneider et al., 2016), such as the one used in the current study. Importantly, all three of the studies that show a difference between incongruent and congruent trials on the nonsymbolic comparison task and math achievement utilize measures of math mostly targeting mental arithmetic (Bugden & Ansari, 2015; Fuhs & McNeil, 2013; Gilmore et al., 2013). Given that the current task shows robust differences in neural activation according to visual control condition only for overall task activity, and not the neural ratio effect, the current preliminary findings about their relation to math achievement should not be considered conclusive and further studies are needed with a larger sample size and various measures of math achievement, including mental arithmetic. It may be the case that various aspects of mathematical competencies are differentially associated with number processing. Investigating these nuances may provide insight to the heterogeneity of individuals differences associated with math difficulties. Moreover, developmental differences are also likely, particularly as proficiency of mental calculations has a protracted and varied trajectory in the early school years.

Lastly, task difficulty has been shown to greatly influence the neuroimaging results of studies measuring individual differences in task-related competency. Often, more proficient individuals show lower task-related brain activation (Dunst et al., 2014). In the current study, where we found a negative correlation between the neural ratio effect and math achievement, accuracy rate was approximately 10 percent lower than in the studies of Ansari & Dhital (2006) (decreased ratio effect in children compared to adults) or of Price et al. (Gavin R. Price et al., 2007) (decreased rIPS modulation in dyscalculic children compared to control children). Unfortunately, difficulty and ratio are inextricably linked, making their comparison difficult. Future studies will need to explore paradigms that control for subject-level difficulty while allowing for a wide enough range in ratio to investigate both dimensions, ratio and subject-level difficulty.

Conclusion

In sum, the present results show that visual control parameters often utilized in the nonsymbolic comparison task, originally intended to serve as a control against non-numeric task strategies, significantly influence the degree of general task-related neural activity in multiple brain regions but do not influence neural activity modeled according to the ratio of number comparisons. There was a consistent neural ratio effect in the right superior parietal lobule and left IPS that did not differ by congruency, suggesting that parietal results from previous studies collapsing across congruent and incongruent trials likely captured activity related to numerical encoding mechanisms rather than inhibitory control. Incongruent trials elicited a greater overall response in several regions implicated in previous literature focused on magnitude perception, including the right inferior frontal gyrus. Further, response time in this task correlated with PSAT math scores while controlling for reading (but did not reach significance before controlling) as did neural activation modeled according to trial ratios. This finding aligns with previous research. Additionally, the directionality of the neural ratio effect related to higher math scores was opposite for congruent and incongruent trials when controlling for reading achievement. Together, these findings support the idea that performance on the nonsymbolic comparison task relates to math competency, that traditionally cited parietal mechanisms used for numerosity extraction do not differ as a function of congruency condition, but that congruent and incongruent trials generally recruit different neural mechanisms. Further, results from the current study show that the correlation between ratio-sensitive neural activation and math achievement differs as a function of the congruency of non-numeric visual cues. This suggests that behavioral measures aimed at capturing math-relevant magnitude perception deficits should attend to, rather than simply control for, individual differences related to the influence of non-numeric visual information. Further, interventions aimed at training this approximate number system, should they prove successful, may find greater efficacy by intentionally manipulating the congruency of non-numeric visual cues.

3.5 Acknowledgments

Eric D. Wilkey performed the research, analyzed the data, and wrote the paper. Jordan C. Barone aided in data analysis. Michelle M. M. Mazzocco, Stephan E. Vogel, and Gavin R. Price designed the original study, collected the data, and provided feedback for preparation of the manuscript. This work has been been published in *NeuroImage:*

Wilkey, E. D., Barone, J. C., Mazzocco, M. M. M., Vogel, S. E., & Price, G. R. (2017). The effect of visual parameters on neural activation during nonsymbolic number comparison and its relation to math competency. *NeuroImage*, *159*(August), 430–442. http://doi.org/10.1016/j.neuroimage.2017.08.023

CHAPTER 4

ATTENTION TO NUMBER: A NEUROCOGNITIVE FOUNDATION FOR MATHEMATICAL COMPETENCE

4.1 Introduction

The current study aims to investigate the relation between three neural mechanisms (i.e. numerical magnitude processing, attention, and attention to number) and mathematical competence. Based on the behavioral literature to date, it is clear that magnitude processing tasks relate to mathematical competence (Chen & Li, 2014; Schneider et al., 2017), but it is unclear what underlying neural mechanisms are responsible for this relation. To investigate this question, neural activity was measured via functional MRI while children 8 to 11 years of age completed a nonsymbolic number comparison task and an Eriksen flanker task. Contrasts were designed to capture magnitude processing (i.e. ratio effect) and attention to number during the number comparison task (i.e. numerical congruency effect) and attention in a non-numerical context during the flanker task (i.e. flanker congruency effect). Providing a neural measure of response to increased attentional demand in a numerical (number comparison) and non-numerical context (Flanker) allowed us to separate attentional components that have previously been considered principally as a singular, domain-general neurocognitive construct. Therefore, we specified a fourth contrast corresponding to the double subtraction of attention to number minus attention in a non-numeric context. Individual differences in neural measures of each construct were then related to mathematics achievement.

All three neurocognitive mechanisms specified in the current study may contribute to the acquisition of mathematical skills. Accordingly, fMRI measures of all three constructs may correlate with math achievement. However, if numerical magnitude processing acuity alone predicts mathematics achievement, we expect to see individual differences in the neural ratio effect alone correlate with achievement. If differences in non-numerical, domain-general attention mechanisms alone predict mathematics achievement, we expect to see a correlation of achievement with individual differences in the flanker congruency effect alone. However, behavioral research investigating the issue of congruency in number comparison tasks would suggest that attentional mechanisms are a critical component of the relation between numerical acuity and mathematics. Therefore, we hypothesized a strong relationship between attention to number as captured by neural measures of the numerical congruency effect and mathematics in fronto-parietal attention and magnitude processing mechanisms. Comparing each of the three constructs may provide and understanding of their unique contribution to individual differences in handling numerical information, a critical step in identifying the origins of math learning deficits.

4.2 Method

Participants

Fifty-two typically developing children completed the current study. Of those, seven children were excluded from all analyses based on MRI quality assessment techniques (i.e. motion and signal artifacts, *see fMRI Analyses below for details*), two due to unavailable behavioral data during MRI acquisition, two due to accuracy on fMRI tasks below chance, and one was excluded due to misalignment of the bounding box which resulted in missing slices. The final sample thus consisted of 40 children (8.02-10.76 years, *M* = 9.27, 19 female). All participants were either in 3rd or 4th grade with the youngest participants beginning the summer after completing 2nd grade. The following exclusionary criteria were applied during the initial recruitment phase: 1) parent report of major health concerns, 2) parent report of developmental disability, 3) known existing neurological or psychiatric problems including seizures and migraines, 4) known, uncorrected visual impairment, and 5) language other than English learned as primary language. Individuals with reported diagnoses of ADHD (n = 2) were not excluded from participation and were instructed to maintain typical schedule of medications. All procedures conducted in this experiment were approved by the Institutional Review Board.

Procedure

The study consisted of two testing sessions, a behavioral testing session with a mock scan and an MRI session. In the first, behavioral session we assessed performance on a range of academic, intelligence, and cognitive measures (Table 4.1) and concluded with a 20-min training session in the mock scanner to familiarize children with the scanner environment and experimental tasks. They then returned for the MRI scans on a second visit. Scans included a structural scan, three task-based fMRI scans, resting state, and a diffusion-weighted scan if time allowed.

Behavioral Assessment

Mathematics achievement. Mathematical achievement was assessed using the Applied Problems, Math Fluency, and Calculation subtests of the Woodcock-Johnson III Tests of Achievement (WCJ-III) (Woodcock et al., 2001). The Applied Problems subtest is an untimed verbal and picture-based measure of a student's ability to analyze and solve math problems, beginning with the application of basic number concepts. The Math Fluency subtest requires participants to answer as many simple addition, subtraction, and multiplication problems as possible within a 3-minute period. The Calculation subtest, on the other hand, is untimed, and requires participants to complete as many calculation items as possible that increase in difficulty, ranging from simple arithmetic to calculus. Grade-normed standard scores were used for all analyses. A composite mathematics achievement scores was created by taking the mean of the three grade-normed standard scores to capture a wide range of mathematics skills. Kolmogorov-Smirnov test of normality with Lilliefors significance correction demonstrated that all the math measures were normally distributed (all p-values > 0.072).

IQ. Nonverbal IQ, Verbal IQ, and Composite IQ estimates were obtained for each participant based on the Kaufman Brief Intelligence Test, second edition (Kaufman & Kaufman, 2004). The KBIT-II Verbal IQ is a comprised of a picture vocabulary section and a riddles section, while the nonverbal IQ includes a single section of matrix reasoning questions. Composite IQ is used to describe the sample and Verbal IQ is used as a control measure of domain-general intelligence theoretically unrelated to the spatial reasoning factors measured during the nonsymbolic comparison and flanker task.

Table 4.1. Sample descriptive statistics, $n = 40$

	Mean	SD	Range
Age (years)	9.3	0.66	(8.0 – 10.8)
WCJ-III Calculation (grade-normed)	111.7	16.1	(81 – 145)
WCJ-III Math Fluency (grade-normed)	100.8	14.5	(75 – 145)
WCJ-III Applied Problems (grade-normed)	112.4	13.8	(78 – 137)
Mathematics Achievement (average of WCJ-III math measures)	108.3	12.6	(84 – 142)
Verbal IQ (KBIT-2)	114.1	13.6	(80 – 137)

WCJ-III = Woodcock Johnson III; KBIT-2 = Kaufman Brief Intelligence Test, 2nd edition.

MRI Session

On the second visit, children were rebriefed on MRI procedures and practiced the in-scanner tasks for 10 minutes before their MRI. During scanning, children's head were stabilized with headphones, foam padding, and medical tape. A research assistant, present during the first testing session, accompanied the child into the scan room for the duration of each imaging session. During each MRI session, children completed reference and anatomical scans, followed by two functional runs each of a symbolic number comparison task, a nonsymbolic number comparison task, and a flanker task with event-related designs. The order of tasks was counterbalanced across participants with all six possible task orders. Stimuli order within tasks were consistent across participants. Only data from the nonsymbolic comparison task and the flanker task are analyzed in the current study. All tasks utilized left and right thumb buttons for responses.

fMRI tasks.

Nonsymbolic Number Comparison. Participants were presented with two sets of dots simultaneously and asked to indicate via button press which set was more numerous (i.e., which set contained more dots)(Figure 4.1). A button box was placed on each hand and participants responded with the thumb button of each box. Light grey dots (RGB value of 50, 50, 50) were presented on a dark grey background (RGB value of 230, 230, 230) divided by a vertical, black fixation line for a duration of

1250ms followed by a screen with just the fixation line for inter-stimulus intervals of 3250, 4250, 5250, or 6250ms (*M* = 4750ms). Two ranges of ratios were presented, small and large (ratio = smaller number of dots divided by larger number). Small (easier) ratios ranged from 0.286 to 0.375 and large (more difficult) ratios ranged from 0.625 to 0.714. The number of dots in a given set ranged from 5 to 21. 40 small ratio and 40 large ratio trials were presented for a total of 80 trials. Response side, inter-stimulus interval, ratio, and congruency were counterbalanced. To control for the possibility that participants might choose a response based on visual cues rather than number of dots, the following visual properties of dot sets were varied using a modified version of the MATLAB code recommended by Gebuis & Reynvoet (2011) to generate stimuli: convex hull (area extended by a stimulus), total surface area (aggregate value of dot surfaces), average dot diameter, and density (convex hull divided by total surface area). In half of all trials convex hull, total surface area, and dot diameter were greater for the greater of the two numerosities presented (i.e. congruent), with the same parameters being incongruent for incongruent trials. Convex hull and surface area have demonstrated the greatest effect on behaviors (Clayton et al., 2015; Gilmore, Cragg, Hogan, & Inglis, 2016). Across the two runs, there were 20 trials of each of the following conditions: (1) congruent large ratio, (2) incongruent large ratio, (3) congruent small ratio, (4) incongruent small ratio.

Flanker Task. Participants were presented with a horizontal array of five arrows with the middle arrow pointing either in the same direction as the flanking arrows (i.e. congruent condition) or in the opposite direction as the flanking arrows (i.e. incongruent condition) and asked to indicate via button press which direction the middle arrow was pointed (Figure 4.1). Arrows were presented in the same light grey as the dots in the number comparison task against a background of dark grey for a duration of 1250 ms followed by a blank dark grey screen for inters-stimulus intervals of 3250, 4250, 5250, or 6250 ms. 40 incongruent and 40 congruent trials were presented for a total of 80 trials. Response side, inter-stimulus interval, and congruency were counterbalanced across trials. In order to encourage saccadic eye movement similar to the number comparison tasks and prevent focusing only on the center of the screen, the array of arrows pseud-randomly appeared centered on either the left or right side of the screen.

Arrows were preceded by 200ms by a fixation box that encompassed the arrows, allowing time for the children to orient to the stimulus with enough remaining time to successfully complete the task. Luminance across Flanker stimuli (the same for each trial) was equated with mean luminance across the nonsymbolic comparison task (different across trials).

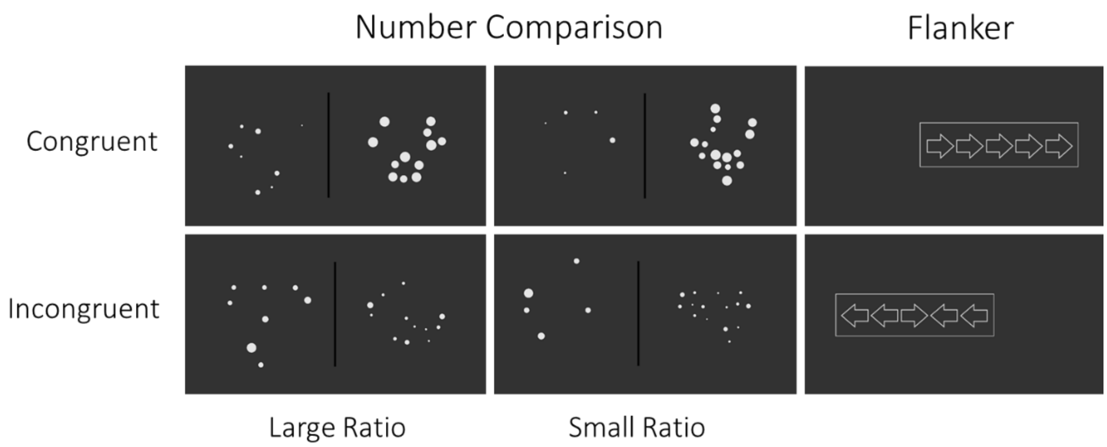


Figure 4.1. Example stimuli from the nonsymbolic number comparison (left and center) and flanker (right) tasks. Number comparison stimuli on the left are large ratio trials (i.e. more difficult ratios) and number comparison stimuli in the center are small ratio trials (i.e. easier ratios). Congruent trials from each task and condition are in the top row.

MRI acquisition parameters. All MR imaging was acquired with a Phillips Achieva 3T MR scanner using an 32-channel head coil. Using multislice 2D SENSE T2* gradient-echo, echo planar imaging (EPI) pulse sequence. Functional images were obtained in the axial plane with the following parameters: Repetition time (TR) = 2000ms; Echo Time (TE) = 25ms; inter-slice gap = 0.25 mm; voxel size = 2.5 × 2.5 x 3 mm with an inter-slice gap of 0.25mm; field of view = 240 × 129.75 × 240 mm; imaging matrix = 96 x 96; flip angle = 90°; SENSE factor = 2.5. The whole brain was acquired in 40 slices with a slice thickness of 3mm isotropic. To allow for steady-state magnetization to be reached before acquiring the functional data, 5 dummy volumes were added at the beginning of each scan, which were subsequently discarded. For the two nonsymbolic comparison runs, 133 volumes were collected for each run and each run had a duration of 279.9 seconds. For the two flanker task runs, 137 volumes were collected for each run and each run had a duration of 288.4 seconds. Inter-stimulus intervals were set at 3.25, 4.25, 5.25, or 6.25 seconds (mean = 4.75) for all runs. In the same session, a high-resolution T1-

weighted, three-dimensional Magnetization Prepared Rapid Gradient Recalled Echo (MP-Rage) sequence was also acquired according to the following specifications: TR = 8.929 s; TE = 4.61 ms; flip angle = 8°; 170 sagittal slices with no inter-slice gap; voxel size = 1 x 1 x 1 mm; imaging matrix = 256 × 256; acquisition time = 264.8s. Scans were oriented in the anterior-posterior commissure plane.

fMRI Preprocessing. Images were analyzed using BrainVoyager Version 20.6.2.3266 (Goebel et al., 2006) with preprocessing steps performed in BrainVoyager and outlying volume detection using the Artifact Detection Tools (ART) toolbox as implemented in CONN toolbox (v17, www.nitrc.org/projects/conn, RRID:SCR_009550) (Whitfield-Gabrieli & Nieto-Castanon, 2012). Structural images were skull-stripped, corrected for inhomogeneities, and then normalized to MNI space (MNI-ICBM 152). Preprocessing of functional images consisted of slice scan time correction (cubic splice interpolation), motion correction with respect to the first volume in each run (tri-linear/sinc interpolation), and linear trend removal in the temporal domain (cutoff: 3 cycles). Functional images were aligned to T1 structural images using gradient-driven affine transformation in native space, with manual adjustments when needed, normalized into MNI space using transformation matrices based on the transformation of structural images, and them spatially smoothed with a 6mm FWHM Gaussian kernel.

fMRI Analyses. Functional data were analyzed using a general linear model (GLM) and a random effect analysis for the group-level data. Experimental events were convolved with a standard two-gamma hemodynamic response function (HRF). Baseline was implicitly modeled as fixation time between trials. The GLM included 6 regressors of no interest that corresponded to the six motion parameters obtained during preprocessing. An additional covariate of no interest was created to account for variance associated with outlying volumes with volume-to- volume motion exceeding 1.5mm or a mean volume intensity of 4 SD's beyond the z-normalized global signal across runs as determined by the ART toolbox. Individuals with greater than 25% of volumes flagged as outliers across both runs of each task (n = 6) were excluded from further analysis. One additional individual was excluded due to a large wraparound artifact identified through visual inspection of data. Incorrect trials in all tasks were modeled as separate predictors and excluded from subsequent analyses. Anatomical labels of results were defined by manually entering MNI converted peak coordinates into Jülich atlas probability maps within the Anatomy Toolbox v2.2b in SPM12 (Eickhoff et al., 2005).

Number, attention to number, and attention. The first set of analyses consisted of three whole-brain statistical contrasts of experimental conditions designed to capture neural activity related to (1) numerical magnitude processing, (2) attention to numerical magnitude, and (3) attention in a non-numerical context. First, to investigate neural activity related to the processing of numerical magnitudes, we contrasted large ratio trials with small ratio trials of the number comparison task. Second, to investigate neural activity related to attentional demands in a numerical context, we contrasted incongruent trials with congruent trials of the number comparison task. Third, to investigate activity related to attentional demands in a non-numerical context, we contrasted incongruent trials with congruent trials in the flanker task. All statistical results were thresholded at $p < .005$ and corrected for multiple comparisons at $p < .05$ using the cluster-level correction toolbox in BrainVoyager (Goebel et al., 2006), which estimates a cluster-level, false-positive rate based on a Monte Carlo simulation of 1,000 iterations.

Attention to number, controlling for non-numeric attention. To further investigate attention mechanisms specifically associated with numerical magnitude processing, a double subtraction was performed whereby the congruency effect in the flanker task was subtracted from the congruency effect in the number comparison task [(incongruent number comparison > congruent number comparison) - (incongruent flanker > congruent flanker)]. Incongruent trials on both tasks are thought to engage top-down, fronto-parietal inhibitory control mechanisms in order to direct attention to the relevant stimulus dimension, numerical magnitudes and orientation of the arrows respectively (Amso & Scerif, 2015; Gilmore et al., 2013). Therefore, this subtraction should capture neural activity specifically involved in attending to numerical magnitudes beyond activity related to attentional demands in a similar, but non-numerical task.

Relation to Mathematics Achievement. To investigate how individual differences in neural measures of each construct related to mathematical competence, average β-weights from significant clusters in each of the three single contrasts were extracted at the subject level and correlated with the composite measure of mathematics achievement, controlling for verbal IQ utilizing partial correlations. Additionally, to investigate the relation of attention to number while controlling for non-numerical attention, beta weights from the double-subtraction were extracted and then correlated with mathematics achievement across the whole brain, controlling for verbal IQ and performance in the flanker task. To investigate if other regions of the brain demonstrated individual differences in this specific contrast that were not significant at the group level, correlation was run with mathematics achievement as the covariate in a whole-brain ANCOVA. Similar to single contrast controls, Verbal IQ was controlled for by entering mathematics scores into a linear regression as the dependent variable with verbal IQ as a predictor and using unstandardized residuals as the covariate in a whole-brain ANCOVA. To control for verbal IQ and flanker performance simultaneously, both measures were included in the regression to compute residuals. To correct for multiple comparisons, correlations use the Bonferroni method adjusting for the number of tests within in each set of neural contrasts (i.e. alpha for 4 cluster's = .05/4 = .0125). Corrected and adjusted *p*-values are presented.

4.3 Results

Behavioral Performance in MRI Tasks

Effects of ratio and congruency. Behavioral variables of interest from the fMRI tasks were response time (ms) for correct responses and percent accuracy across all trials in both the nonsymbolic comparison task and the flanker task. In line with previous results from similar nonsymbolic comparison tasks (Inglis & Gilmore, 2014; Merkley & Ansari, 2010; Price, Palmer, Battista, & Ansari, 2012; Price & Wilkey, 2017), individuals were more accurate for small ratio trials than large ratio trials [$t(39) = 11.35$, $p < .001$, Cohen's $d = 1.98$] and for congruent trials than incongruent trials [$t\ (39) = 6.25$, $p < .001$, Cohen's $d = 1.02$]. Response times were greater for small ratios than large ratios [$t\ (39) = 8.08$, $p < .001$, Cohen's $d = 1.34$] and greater for incongruent trials than congruent trials [$t\ (39) = 9.34$, $p < .001$, Cohen's $d = 1.71$] (within-subject adjusted Cohen's *d;* Morris & DeShon, 2002). In the flanker task, children were also more accurate for congruent trials [$t\ (39) = 7.25$, $p < .001$, Cohen's $d = 1.26$] and had greater response times for incongruent trials [$t\ (39) = 12.38$, $p < .001$, Cohen's $d = 2.02$]. Effect sizes indicate that the size of the behavioral congruency effect was similar, but slightly larger for the flanker task as compared to the number comparison task.

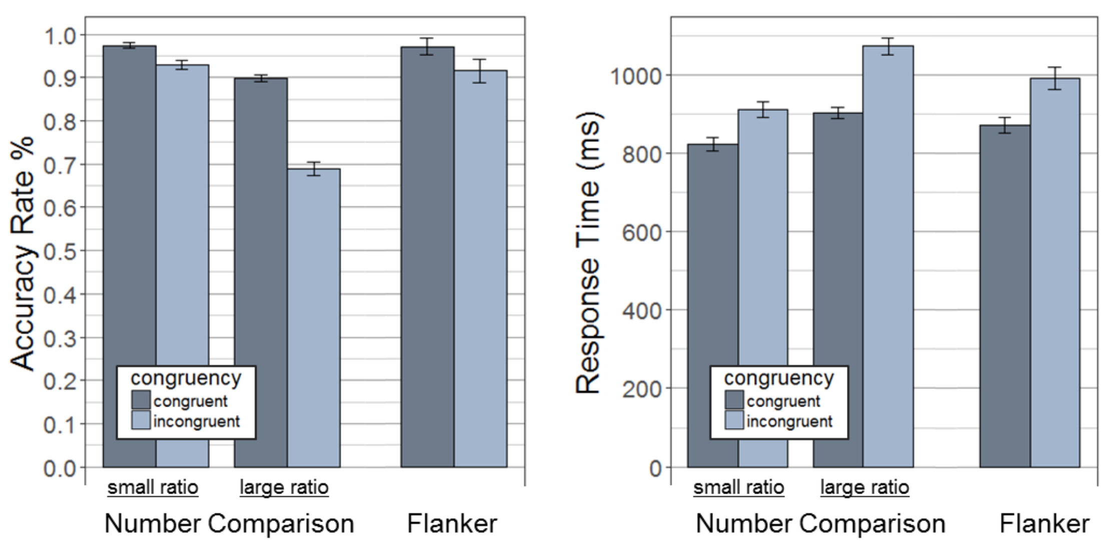


Figure 4.2. Nonsymbolic comparison and flanker behavioral data from fMRI tasks showing (left) accuracy rate (total % correct) and (right) response time, split by ratio bin (left/right) and congruency condition (light/dark blue).

Task performance and mathematics achievement correlations. Bivariate correlations were computed to assess the relation between fMRI task performance, mathematics achievement, and verbal IQ (Table 4.2). Of note, mathematics achievement was significantly correlated with verbal IQ, accuracy on number comparison, and accuracy on the flanker task. However, when separated by congruency, only the relationship between incongruent trials on the number comparison task and mathematics achievement reached significance. In contrast, performance on congruent trials in the flanker task, and not incongruent trials, was significantly related to mathematics achievement. For significant bivariate correlations, partial correlations were also computed between mathematics achievement and task performance while controlling for Verbal IQ. All four task performance measures remained significant [number comparison, all trials $r(37) = .375$, $p = .019$; number comparison, incongruent trials $r(37) = .328$, $p = .042$; flanker, all trials $r(37) = .338$, $p = .035$; flanker, congruent trials $r(37) = .397$, $p = .012$]. Behavioral ratio effects (e.g. large ratio accuracy – small ratio accuracy) and congruency effects (incongruent mean accuracy – congruent mean accuracy) were also computed for both accuracy and response times in both tasks and correlated with mathematics achievement. No ratio effect or congruency effect correlations with mathematics were significant [all *p*'s > .277].

Table 4.2. Correlations between behavioral measures and MRI task performance.

Measure (n = 40)	**1**	**2**	**3**	**4**	**5**	**6**	**7**
7. Mathematics Achievement							
8. Verbal IQ (KBIT-2)	.331*						
9. Number Comparison (all trials, accuracy)	.366*	.038					
10. Number Comparison (incongruent trials, accuracy)	.324*	.045	.876***				
11. Number Comparison (congruent trials, accuracy)	.237	.007	.662***	.219			
12. Flanker (all trials, accuracy)	.378*	.196	.526***	.429*	.398*		
13. Flanker (incongruent trials, accuracy)	.279	.126	.505**	.413*	.380*	.946***	
14. Flanker (congruent trials, accuracy)	.447**	.259	.447**	.363*	.341*	.869***	.662***

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

fMRI Results

Number comparison ratio effect. The contrast of large ratio trials (i.e. more difficult ratios) compared to small ratio trials revealed four regions with significantly greater activity for large ratio trials including the right middle frontal gyrus (rMFG), right inferior frontal gyrus *pars trangularis* (rIFG), right IPS, and right superior medial gyrus (Figure 4.3a, Table 4.3). All four of these regions were task-positive (i.e. above the implicit baseline activation level) on average. Three regions showed significantly greater activity for small ratio trials, including the right angular gyrus (rAG), left middle temporal gyrus (lMTG), and left supramarginal gyrus (lSMG). The rAG was below baseline across conditions, but the lMTG and lSMG were below baseline in large trials and slight above baseline during small ratio trials.

Table 4.3. Significant clusters for contrast of large ratio > small ratio trials in number comparison task.

Cluster	Peak MNI (x, y, z)	Voxels	Peak *t* (Mean *t*)	Large β	Large se	Small β	Small se	BA	Anatomical Description
positive effects = (large ratio > small ratio)									
A	(48, 38, 19)	902	4.74 (3.43)	1.16	0.19	0.51	0.21	46	R MFG
B	(42, 20, 4)	2,298	4.55 (3.54)	1.44	0.19	0.69	0.20	45	R IFG (*p. Triangularis*)
C	(3, 23, 46)	1,480	4.08 (3.23)	1.36	0.24	0.72	0.23	8	R Sup. Med. Gyrus
D	(27, -49, 3)	1,160	3.88 (3.19)	1.77	0.27	1.14	0.23	7	R IPS (*hIP1*)
negative effects = (small ratio > large ratio)									
E	(51, -67, 2)	808	-4.22 (-3.28)	-0.51	0.17	-0.16	0.19	39	R AG (*PGp*)
-	(-60, -58, 4)	1,177	-4.38 (-3.43)	-0.45	0.21	0.07	0.19	39	L MTG
-	(-69, -31, 8)	1,143	-3.93 (-3.24)	-0.10	0.19	0.43	0.18	40	L SMG (*PF*)

*All results cluster corrected at p <.05, uncorrected p <.005 (clusters > 740 voxels, 1mm iso). MNI = peak coordinates in MNI-ICBM 152; Large = large ratio (more difficult) trials; Small = small ratio (easier) trials; BA = Brodmann area. β values are means extracted at the cluster level. R = right; L = left. Clusters with letters are represented in Figure 4.3. Anatomical description abbreviations in italics refer to Juelich atlas labels.

Number comparison congruency effect. The contrast of incongruent trials in the number comparison task (i.e. those where visual parameters conflicted with greater numerosity) compared to congruent trials revealed one region with greater activity for incongruent trials, the rIFG, and three regions with greater activity for congruent trials, in the bilateral fusiform gyrus and right primary visual cortex (Figure 4.3b, Table 4.4). Activity was above baseline in all regions, on average, but showed below baseline activity for congruent trials in the rIFG, as indicated by mean β-weights.

Table 4.4. Significant clusters for contrast of incongruent > congruent trials in number comparison task.

Cluster	Peak MNI (x, y, z)	Voxels	Peak *t* (Mean *t*)	INC β	INC se	CON β	CON se	BA	Anatomical Description
positive effects = (incongruent > congruent)									
A	(45, 23, 10)	1,216	5.25 (3.49)	0.37	0.18	-0.26	0.18	45	R IFG (*p. Triangularis*)
negative effects = (congruent > incongruent)									
-	(11, -103, -2)	1,169	-4.87 (-3.43)	1.83	0.25	2.31	0.25	17	R Primary Visual (*V1, hOc1*)
B	(24, -46, -17)	725	-4.20 (-3.33)	0.63	0.21	1.04	0.18	37, 20	R Fusiform Gyrus (*FG3*)
C	(-21, -49, -14)	2,128	-4.23 (-3.33)	0.85	0.22	1.38	0.19	37, 20	L Fusiform Gyrus (*FG3*)

*All results cluster corrected at p <.05, uncorrected p <.005 (clusters > 598 voxels, 1mm iso). MNI = peak coordinates in MNI-ICBM 152; INC= incongruent trials; CON = congruent trials; BA = Brodmann area. R = right; L = left. β values are means extracted at the cluster level. Clusters with letters are represented in Figure 4.3. Anatomical description abbreviations in italics refer to Juelich atlas labels.

Flanker congruency effect. The contrast of incongruent trials in the flanker task (i.e. trials with flanking arrows in opposite directions from the central arrow) compared to congruent trials revealed seven regions with greater activity for incongruent trials (Figure 4.3b, Table 4.5). These regions included large portions of the bilateral superior parietal lobe (SPL) centered in each hemisphere’s IPS, bilateral early visual processing areas in the occipital lobe, the right insula, right middle frontal gyrus (rMFG), and the right inferior temporal gyrus (rITG). Of note, the cluster in the right anterior insula is medial to both rIFG clusters resulting from the number comparison ratio effect and congruency effect contrasts. However, the flanker congruency effect does partially overlap with the number comparison congruency effect where the rIFG and right insula meet. There is no overlap between the flanker congruency effect with the ratio effect contrast in the rIFG.

Table 4.5. Significant clusters for contrast of incongruent > congruent trials in flanker task.

Cluster	Peak MNI (x, y, z)	Voxels	Peak *t* (Mean *t*)	INC β	INC se	CON β	CON se	BA	Anatomical Description
A	(39, -82, -5)	3,364	5.77 (3.58)	3.99	0.36	3.53	0.35	19	R Inferior Occipital Gyrus (*hOc4lp*)
B	(30, 17, 10)	1,420	5.52 (3.67)	1.12	0.19	0.61	0.20	13	R Insula
C	(30, -64, 55)	8,230	5.38 (3.52)	2.02	0.21	1.39	0.18	7	R SPL (*7A*, *hIP3*)
D	(-33, -91, 7)	3,805	5.33 (3.48)	3.91	0.31	3.42	0.28	18	L Middle Occipital Gyrus (*hOc4lp*)
E	(-24, -61, 37)	1,291	4.44 (3.36)	1.52	0.22	1.02	0.20	7	L IPS (*hIP3, hIP1*)
F	(36, 2, 55)	1,288	4.40 (3.34)	1.87	0.21	1.41	0.20	6	R MFG
G	(45, -55, -11)	1,988	4.37 (3.35)	2.34	0.20	1.79	0.17	37, 20	R ITG (*FG4*)

*All results cluster corrected at p <.05, uncorrected p <.005 (clusters > 740 voxels, 1mm iso). MNI = peak coordinates in MNI-ICBM 152; INC= incongruent trials; CON = congruent trials; BA = Brodmann area. R = right; L = left. β values are means extracted at the cluster level. Clusters with letters are represented in Figure 4.3. Anatomical description abbreviations in italics refer to Juelich atlas labels.

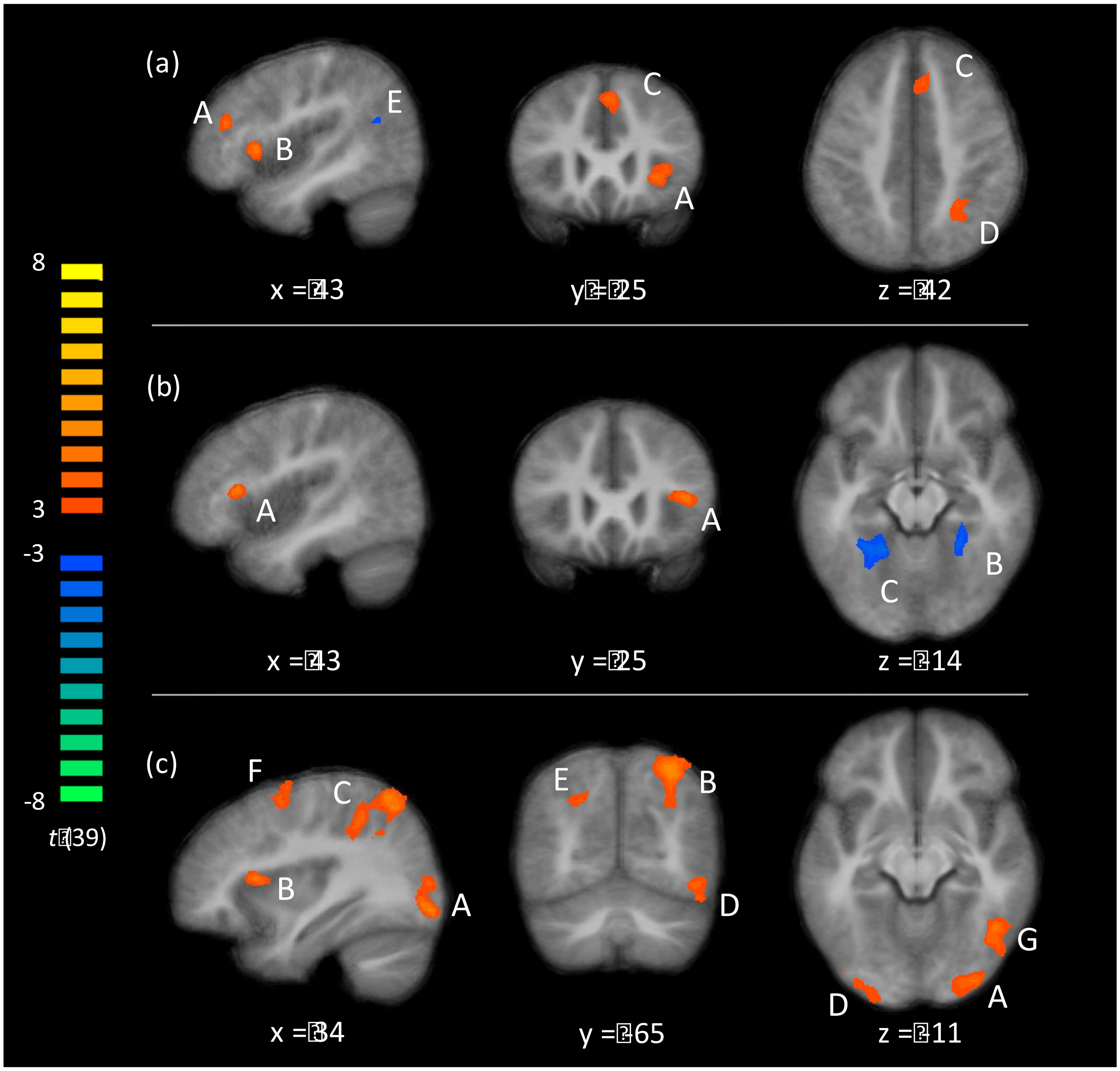


Figure 4.3. Results from contrasts of (a) number comparison large ratios > small ratios, (b) number comparison incongruent > congruent, and (c) flanker incongruent > congruent. All maps are cluster corrected at p <.05, uncorrected p <.005. Cluster details are presented in Tables 4.3, 4.4, and 4.5 respectively. Slices labeled in MNI space and presented in neurological convention.

Number comparison congruency effect minus flanker congruency effect. The double subtraction of the congruency effect in the number comparison task minus the congruency effect in the flanker task, designed to capture neural activity relate to attending to numerical magnitudes beyond non-numerical attentional demands, revealed five regions with a significant effect (Figure 4.4, Table 4.6). Three of the regions were similar to (i.e. largely overlapping with) those present in the single subtraction of incongruent compared to congruent conditions of the number comparison task (i.e. also present in Table 4.4): the right IFG [mean t = 3.60, voxels = 1,000], the right primary visual cortex [mean t = -4.89, voxels = 2,110], and left fusiform gyrus [mean t = -3.82, voxels = 587]. As in the single subtraction, the resulting t-statistic in each of these three regions continued to be positive for the rIFG and negative for the right fusiform and occipital regions. One region, the left inferior occipital gyrus (V2) [mean t = -3.46, voxels = 1,399], largely overlaps with the left middle occipital gyrus of the congruency effect in the flanker task, with the double subtraction resulting in a negative t-statistic. Further, one region in the precentral gyrus [mean t = -3.16, voxels = 583] was unique to the double subtraction.

Table 4.6. Significant clusters for double subtraction of congruency effect in number comparison > congruency effect in flanker task.

Cluster	Peak MNI (x, y, z)	Voxels	Peak *t*	Mean *t*	BA	Anatomical Description
positive effects						
B	(45, 23, 10)	1,000	5.58	3.60	45	R IFG (*p. Triangularis*)
positive effects						
C	(21, -100, 1)	2,110	-4.89	-3.53	17	R Primary Visual (*V1*)
D	(-24, -100, -11)	1,399	-4.82	-3.46	18	L Inferior Occipital Gyrus (*V2*)
-	(-27, -49, -14)	587	-3.82	-3.22	37, 20	L FG (*FG3*)
A	(45, -22, 58)	583	-3.69	-3.16	4	R Postcentral Gyrus

*All results cluster corrected at p <.05, uncorrected p <.005 (clusters > 598 voxels, 1mm iso). MNI = peak coordinates in MNI-ICBM 152; BA = Brodmann area. R = right; L = left. Clusters with letters are represented in Figure 4.4. Anatomical description abbreviations in italics refer to Juelich atlas labels.

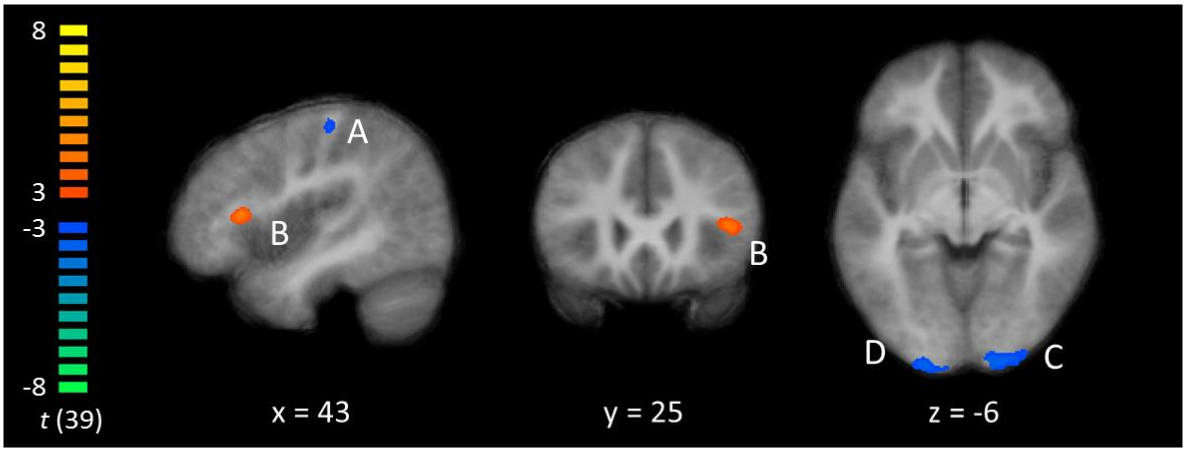


Figure 4.4. Results from double subtraction contrast of congruency effect in number comparison > congruency effect in flanker task. All maps are cluster corrected at p <.05, uncorrected p <.005. Cluster details are presented in Table 4.6. Slices labeled in MNI space and presented in neurological convention.

Correlation of single contrasts with mathematics achievement. To investigate the relation between individuals differences in neural measures of (1) numerical magnitude processing (i.e. ratio effect), (2) attention to numerical magnitude (i.e. number comparison congruency effect), and (3) attention in a non-numerical context (i.e. flanker congruency effect) and mathematics achievement, cluster-level β-weights from the significant regions in each of the contrasts were extracted for each subject and correlated with the composite mathematics achievement score. Results indicated that individual differences in each of the seven regions in Table 4.3 showing a significant ratio effect did not correlate with mathematics achievement before controlling for verbal IQ [all p's > .453] or after [all p's > 0.279], even before controlling for multiple comparisons. For the four regions demonstrating a significant congruency effect in the number comparison task in Table 4.4, only the rIFG demonstrated a significant correlation with mathematics achievement [$r(38) = -.468$, $p = .002$, Bonferroni-adjusted $p = .008$; all other p's > .292, unadjusted]. The correlation with activity in the rIFG was negative, meaning that higher mathematics scores correlated with less difference in neural activation between incongruent and congruent trials of the number comparison task. The relation in the rIFG remained essentially unchanged [$r(37) = -.474$, $p = .002$, Bonferoni-adjusted $p = .008$)] after controlling for verbal IQ and stronger after controlling for both verbal IQ and mean accuracy on the flanker task [$r(36) = -.537$, $p = .001$, Bonferonniadjusted $p = .004$]. Regarding the last neural contrast, the flanker congruency effect, correlation results indicated that individual differences in one of the seven clusters in Table 4.5, the middle occipital gyrus, significantly related to mathematics achievement. Similar to the congruency effect in the number comparison task, a lesser difference between incongruent and congruent β-weights correlated with higher mathematics scores [$r(38) = -.450$, $p = .004$, Bonferroni-adjusted $p = .028$] which remained significant after controlling for verbal IQ [$r(37) = -.450$, $p = .004$, Bonferroni-adjusted $p = .028$]. The flanker effect in one other region, the right middle frontal gryus, showed a marginal correlation with mathematics achievement, but did not survive correction for multiple comparisons before controlling for verbal IQ [$r(38) = -.315$, $p = .048$, Bonferroni-adjusted $p = .336$] or after [$r(37) = -.360$, $p = .025$, Bonferroni-adjusted $p = .175$]. All other regions showed uncorrected correlation p's > .061, unadjusted].

Correlation of attention to number with mathematics achievement. To investigate the relation between individual differences in neural measures of attention to numerical magnitude while controlling for the neural response to attentional demands in a similar, but non-numeric task, cluster-level β-weights from the significant regions in the double subtraction of the number comparison congruency effect minus the flanker congruency effect were extracted for each subject and correlated with the composite mathematics achievement score. Of the five regions showing a significant group-level effect in Table 4.6, only activity in the rIFG showed a correlation that approached significance [$r(38) = -.369$, $p = .019$, Bonferroni-adjusted $p = .095$; all other p's > .528 unadjusted]. The correlation had a similar effect size after controlling for verbal IQ [$r(37) = -.370$, $p = .020$, Bonferroni-adjusted $p = .10$] and for verbal IQ and flanker accuracy rate [$r(36) = -.365$, $p = .024$, Bonferroni-adjusted $p = .12$]. Considering the single contrast of the numerical congruency effect correlated with mathematics achievement at $r = -.468$, we interpret the current effect size of $r = -.370$ to continue to indicate a meaningful relation while acknowledging that the conservatively corrected *p-value* does not reach significance.

Further, to test if individual differences in the construct of *attention to number* correlated with mathematics achievement in regions that may not have demonstrated a group-level effect, a whole-brain correlation was run with the double subtraction as the neural contrast of interest and the composite measure of mathematics achievement as the behavioral measure of interest. This analysis was repeated while controlling for verbal IQ, and then again controlling for verbal IQ and accuracy rate on the flanker task, in an effort to control for factors related to general academic achievement unspecific to mathematics. Results indicate a significant negative correlation in another region of the rIFG, *pars orbitalis* (Table 4.7, top section), which remains significant after controlling for verbal IQ and also mean accuracy on the flanker task (Table 4.6, middle and bottom sections). Figure 4.5 displays results from the correlation controlling for verbal IQ in order to display all regions present in the correlation. The resulting region in the rIFG, *pars orbitalis,* does not overlap with rIFG clusters demonstrating a neural ratio effect and numerical congruency effect though a smaller cluster in the *pars triangularis* does, but does not survive cluster correction (overlay of maps detailed in Supp. Figure 4.6. at uncorrected $p < .005$).

Table 4.7. Correlation of double subtraction of congruency effect in number comparison greater than congruency effect in flanker task with composite mathematics achievement score.

Cluster	Peak MNI (x, y, z)	Voxels	Peak *r*	Mean *r*	BA	Anatomical Description
correlation with math achievement						
-	(30, 35, -14)	1,034	-0.55	-0.48	47	R Inferior Frontal Gyrus (*p. Orbitalis*)
correlation with math achievement controlling for verbal IQ						
A	(39, 35, -8)	1,471	-0.61	-0.49	47	R Inferior Frontal Gyrus (*p. Orbitalis*)
B	(-12, 38, 1)	1,025	-0.52	-0.46	33	L Anterior Cingulate Cortex
C	(-36, 35, 34)	1,291	-0.58	-0.48	9	L Middle Frontal Gyrus
correlation with math achievement controlling for verbal IQ and flanker accuracy						
-	(39, 35, -11)	1,356	-0.60	-0.48	47	R Inferior Frontal Gyrus (*p. Orbitalis*)
-	(-36, 35, 34)	1,706	-0.62	-0.49	9	L Middle Frontal Gyrus

*All results cluster corrected at p <.05, uncorrected p <.005 (clusters > 598 voxels, 1mm iso). MNI = peak coordinates in MNI-ICBM 152. BA = Brodmann area. R = right; L = left. Anatomical description abbreviations in italics refer to Juelich atlas labels.

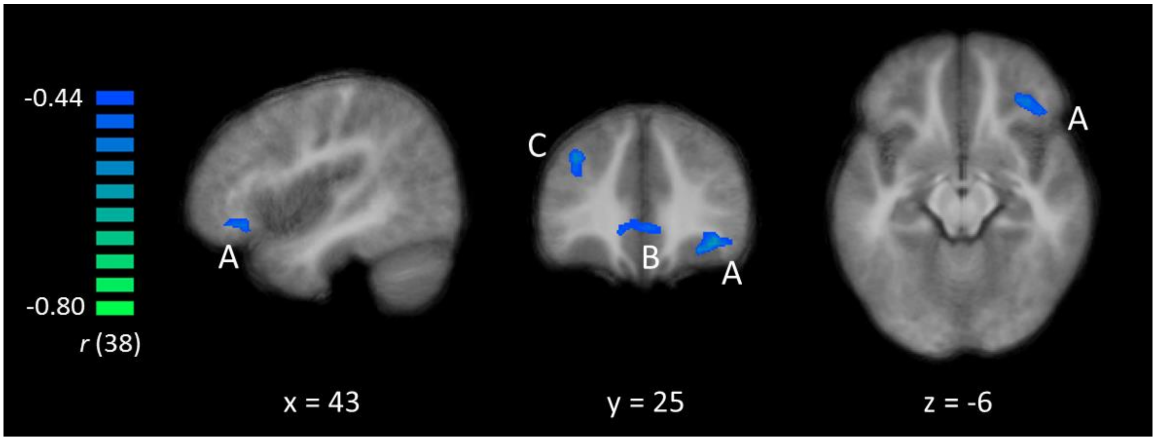


Figure 4.5. Results from contrasts of correlation of mathematics achievement composite score with double subtraction of congruency effect in number comparison greater than congruency effect in flanker task. All maps are cluster corrected at $p < .05$, uncorrected $p < .005$. Cluster details are presented in Table 4.6. Slices labeled in MNI space and presented in neurological convention.

4.4 Discussion

Deficits in attention and the processing of numerical magnitudes have both been linked to difficulties in acquiring numeracy (Fias, Menon, & Szucs, 2013; Geary, Hoard, Nugent, & Bailey, 2013; Mazzocco et al., 2011; Mazzocco & Thompson, 2005; Szucs, Devine, Soltesz, Nobes, & Gabriel, 2013). However, little is known about the neural mechanisms that support their integration and how they relate to mathematical behaviors. The current study tested the hypothesis that *attention to number*, a construct representing this integration, achieved through the biological interaction of attentional mechanisms with numerical magnitude processing mechanisms, is a source of individual differences important for the development of mathematical skills. As previous studies have reported, accuracy rates on incongruent trials of the nonsymbolic number comparison task correlated with mathematics achievement, while accuracy rates on congruent trials did not. Further, while the neural ratio effect, a potential measure of magnitude processing efficiency, did not relate to mathematical achievement, the numerical congruency effect negatively correlated with achievement in the right IFG after controlling for verbal IQ and performance on the flanker task. This relation continued to show a moderate to small correlation after subtracting out activation related to the congruency effect in the flanker task. Therefore, behavioral and neuroimaging results support our hypothesis that there are specific neural substrates associated with *attention to number*, the activity of which relates to math competence over and above numerical acuity or domain-general attention alone. These finding calls into question previously held assumptions about the relation between magnitude processing mechanisms and mathematical competence, detail an alternative explanation for the relation between nonsymbolic number comparison task performance and mathematics achievement, and build the groundwork for future research investigating neural mechanisms related to *attention to number* as a potential source of difficulties related to math-specific learning disabilities.

Attention to Number and Spontaneous Focusing on Number

Before further discussion, it should be noted that a substantial body of research originating with Hannula-Sormunen and colleagues has identified the spontaneous, self-initiated attentional focus on numerosity (SFON) as a strong predictor of math development (for a review, see Rathé, Torbeyns, Hannula-Sormunen, De Smedt, & Verschaffel, 2016). However, the construct of *attention to number* differs from SFON in several regards. For example, while attention to number refers to the neurocognitive mechanisms controlling attention to numerosity, SFON may be thought of a disposition towards exact number that an individual carries into any given scenario. Accordingly, any measure of SFON must be taken in the absence of explicitly numerical task demands (Rathé et al., 2016). In contrast, neurocognitive mechanisms underlying attention to number may be utilized spontaneously or under explicit instruction. To measure the efficacy of these mechanisms, the current study does explicitly instruct participants to attend to numerosity. As a second point of difference, SFON research focuses on smaller numerosities that children are capable of counting quickly and exactly (Hannula et al., 2010) whereas numerical magnitude processing often requires approximation of larger quantities. In other words, SFON refers to the tendency of an individual to notice numerical features of a given scene, while attention to number to refers to an individual's ability to upregulate number specific neural processes, or inhibit non-numerical neural representations, in order to extract numerical information from a specific stimulus, especially in the case of competing information.

Numerical Magnitude Processing, Attention to Number, and Attention

Results from the three single contrasts of interest in the current results largely support previously published results. Areas of the ventrolateral prefrontal cortex, medial anterior cortex, and rIPS demonstrated task-positive ratio effects, similar to meta-analyses of number processing tasks (Sokolowski et al., 2016), indicating their functional role in numerical magnitude perception. Results for incongruent > congruent trials are similar to the only two previous studies to execute a comparable contrast with the nonsymbolic number comparison task (Leibovich, Vogel, Henik, & Ansari, 2015; and Study 2 from the current work: Wilkey, Barone, Mazzocco, Vogel, & Price, 2017) in that all three showed significantly greater activity during incongruent trials in the rIFG and Wilkey et al. (2017) also showed similar effects in the fusiform gyrus, although those previous studies involved adults and adolescents respectively. A large body of work supports the notion that a right-lateralized portion of the inferior frontal cortex is critical for inhibiting response tendencies more generally and orienting to behaviorally relevant stimuli (reviewed in Aron & Poldrack, 2005; Aron, Robbins, & Poldrack, 2014; for meta-analysis see Levy & Wagner, 2011). However, in the current results, the numerical congruency effect in the rIFG is significant in the single contrast and continues to be significant at the group level when subtracting out activity related to the flanker effect in the double subtraction. The flanker task was designed to elicit response inhibition and task interference effects similar to the numerical congruency effect, but in a non-numerical context. Therefore, if modulation of the rIFG were a generalizeable effect of inhibition, we would expect the effect to significantly diminish or disappear. Results report a similar, but slightly greater peak and mean *t*-values in the rIFG, indicating that the relation is specific to the number comparison task. Further, the contrasts of large > small ratio and incongruent > congruent trials of the number comparison task overlap in the rIFG, *pars triangularis,* suggesting the location is involved in numerical magnitude encoding. This interpretation fits with previous studies reporting a numerical ratio effect in both symbolic and nonsymbolic numerical formats (Ansari & Dhital, 2006; Cantlon et al., 2009) in the rIFG, particularly in children. Therefore, increased activity in the rIFG, *par triangularis,* during incongruent trials may reflect the allocation of more attentional resources, and therefore greater BOLD response, to a region of the cortex encoding numerical information. Alternatively, this increase in rIFG may also be representative of the increased allocation to numerical magnitudes itself. In other words, this region may be involved in the upregulation of neural representations of numerical magnitude elsewhere in the cortex or it may be the region encoding numerical magnitudes. In either case, we would expect a significant ratio effect and congruency effect. In contrast, decreased activity to the bilateral fusiform gyri and primary visual cortex may represent a suppression of activity related to non-numerical visual factors of the stimuli such as overall surface area and convex hull.

Lastly, results for the congruency effect in the flanker task showed similar results to three previous analyses of the flanker effect in children, which demonstrated greater activity for incongruent than neutral trials in the rIPS (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Vaidya et al., 2005) and bilateral occipital gyri (Konrad et al., 2005), though a similar lateralization in the lIFG and left insula to Bunge et al. (2002) was not replicated. As in all three studies of the flanker effect in children compared to adults, the anterior cingulate in the current study did not show a significant congruency effect, which is typical of response interference tasks in adults (Houdé, Rossi, Lubin, & Joliot, 2010; van Veen, Cohen, Botvinick, Stenger, & Carter, 2001). In short, results indicate a strong congruency effect consistent with previous studies, and therefore provide justification for the use of this contrast as a method of controlling for non-numerical attentional allocation associated with inhibition and interference control.

Relations to Mathematical Competence

Most studies relating neural correlates of numerical magnitude processing to mathematical competence have focused on group comparisons between typically developing children or adults and individuals with dyscalculia (Dinkel, Willmes, Krinzinger, Konrad, & Koten, 2013; Kovas et al., 2009; Kucian, Loenneker, Martin, & von Aster, 2011; Price et al., 2007), and provide little consensus about which neurocognitive mechanisms drive the number comparison task's relation to mathematics. The two studies relating a similar neural contrast to math achievement in typically developing young adults and high school students (Gullick, Sprute, & Temple, 2011; Wilkey et al., 2017) found inverse ratio effects correlated with math achievement in bilateral insula, and inferior parietal regions, regions not canonically associated with the processing of numerical information. With the recent array of behavioral data indicating that incongruent trials drive the relation between task performance and mathematics achievement (Bugden & Ansari, 2015; Fuhs & McNeil, 2013; Gilmore et al., 2013; Prager, Sera, & Carlson, 2016), evidence is mounting in favor of the importance of executive function mechanisms and their interaction with magnitude processing mechanisms as a foundation for mathematical competence. The current results lend support to this interpretation in that none of the neural contrasts associated with magnitude processing alone (i.e. balanced for congruency) correlate with mathematics achievement, while the numerical congruency effect in the rIFG*, pars triangularis,* an area which demonstrated a significant ratio effect and numerical congruency effect, does correlate with mathematics achievement. The negative correlation, showing individuals with a lesser congruency effect are better at mathematics, could indicate a more effortful response in the inhibition process or protracted development of inhibitory control mechanisms.

The whole-brain correlation of mathematics achievement with the double-subtraction of the numerical congruency effect minus the flanker congruency effect similarly indicated the importance of attentional components of the task. However, the strongest correlation at the whole-brain level was an inverse correlation between a more inferior and anterior portion of the rIFG, the *pars orbitalis,* which did not overlap with the *pars triangularis* region displaying a significant ratio and congruency effect. The presence of two regions in the rIFG with a numerical congruency effect that negatively correlated with mathematics achievement, one of which demonstrates a ratio effect, may indicate that the rIFG is responsible for an array of mathematically relevant inhibition functions. Multiple aspects of executive function are thought to be orchestrated by the rIFG and its cortico-thalamic connections. A meta-analysis of neuroimaging data of cognitive control tasks by Levy and Wagner (2011) suggests that specific forms of cognitive control, such as the detection of relevant stimulus parameters and decision uncertainty, are subserved by distinct subregions of the rIFG. The current results, at the ROI level and in the whole-brain analysis, show that neural response of attention to number relates to mathematical competence in two regions of the rIFG, both the *pars triangularis* and *pars orbitalis*. Therefore, it may be that multiple attentional components dedicated to numerical magnitude processing are subserved by distinct subregions of the rIFG.

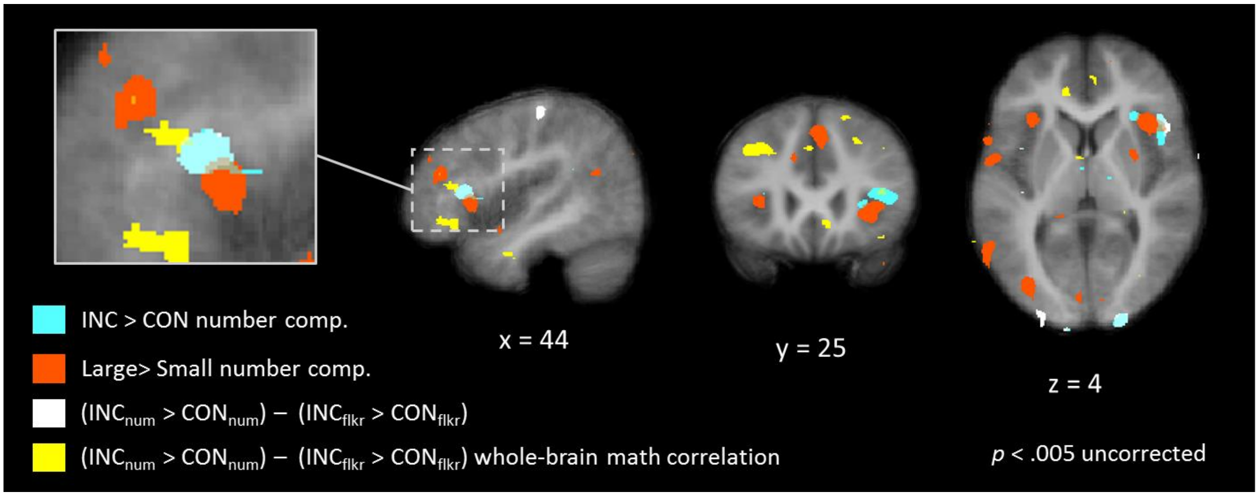
Future Directions

The current study utilizes a contrast based on numerical ratio in the number comparison task to identify areas of the brain associated with magnitude processing and then assumes that individual differences in this contrast would capture individual differences the associated neural substrate. However, little evidence exists that neural measures at standard resolutions of fMRI during the number comparison task are capable of indexing a neural measure of numerical acuity that is thought to be captured by behavioral indices of numerical acuity, such as accuracy or weber fraction. A greater neural ratio effect has been argued to indicate greater efficiency (Bugden et al., 2012) and also lesser efficiency (Gullick et al., 2011) of numerical magnitude processing mechanisms, but the underlying biological origin of each of these effects remains poorly understood. Only one study to date has related acuity of neural representation (i.e. neural tuning curves in the IPS) to behaviors measuring perceptual sensitivity, but this study did not include a measure of math achievement and largely avoided the confound of inhibitory control with the use of an adaptation paradigm with sequential presentation of stimuli (Kersey & Cantlon, 2016). However, the approach taken by Kersey and Cantlon may provide more information for a detailed account of numerical acuity in the future.

Two further issues should be taken into account in future studies of this topic. First, an exploration of both structural and functional connectivity between neural structures that support executive function and magnitude processing may provide an explanation of the role of subregions in the IFG. This may elucidate the actual role of the IFG *pars triangularis* as either a substrate for direct encoding of numerical information or as a region involved in the regulation of regions that encode numerical information. Second, executive function and numerical magnitude processing are both known to undergo substantial development during the early elementary school years (Ansari, Garcia, Lucas, Hamon, & Dhital, 2005; Davidson, Amso, Anderson, & Diamond, 2006). Executive function is known to increasingly involve the integration of a fronto-parietal and cingulo-opercular network (Fair et al., 2007, 2009). Therefore, in the current study, individual differences may be a result of naturally varying neural development or the development of mathematical skills. More research across development is needed to draw the link between differences in neural signatures and biologically plausible accounts of their corresponding behavioral significance.

Conclusions

The present findings support previous behavioral studies suggesting that attentional components of the nonsymbolic number comparison task are an important factor for its relation to mathematical competence (Bugden, & Ansari, 2015; Fuhs & McNeil, 2013; Gilmore et al., 2015), as indicated by a stronger correlation between mathematics achievement and performance on incongruent trials of the number comparison task than congruent trials. Further, fMRI results suggest that individual differences in neural activity in the rIFG specifically involved in numerical magnitude processing measured during incongruent versus congruent trials of the number comparison task, our construct of *attention to number*, correlate with mathematics achievement. In contrast, neural activity in frontal and parietal regions associated with differences in ratio difficulty, our construct for numerical magnitude processing, does not correlate with mathematics achievement. Therefore, behavioral and neuroimaging evidence from the current study suggest that *attention to number*, or the ability to upregulate number specific neural representations or inhibit non-numerical neural representations, are an important predictor of mathematical competence, over and above numerical magnitude processing or domain-general attention alone.



Supplementary Figure 4.6. Overlay of results from the congruency contrast in the number comparison task (teal), the ratio effect contrast (red), and the whole-brain correlation of math with the double subtraction of the congruency effect during number comparison minus the congruency effect in the flanker task (yellow). Voxels from the math correlation with no control, verbal IQ, and verbal IQ + flanker performance are all pictured as yellow voxels. All maps are uncorrected at $p < .005$. Cluster-corrected details are presented in Table 4.3, 4.4, and 4.6. Slices labeled in MNI space and presented in neurological convention.

4.5 Acknowledgments

Eric D. Wilkey designed and performed the research, analyzed the data, and wrote the paper. Gavin R. Price provided feedback for preparation of the manuscript.

CHAPTER 5

DISCUSSION AND INTEGRATION OF FINDINGS

5.1 Introduction

A lack of competence in basic mathematics increases an individual's risk for unemployment (Parsons & Bynner, 2005; Rivera-Batiz, 1992), poverty (Gross et al., 2009), and negative health outcomes (Duncan et al., 2007; Hibbard et al., 2007). For many, even with adequate resources, becoming numerate is extremely difficult (Butterworth & Laurillard, 2010). It requires mastery of a large range of skills over the course of years of schooling. As their foundation, mathematical skills require the training and cooperation of a range of neurocognitive mechanisms that may also be the source of learning difficulties or, in atypical development, the source of a math specific learning disability. One such proposed mechanism used for the processing of numerical magnitudes, often referred to as the approximate number system (ANS) (Halberda et al., 2008) or number sense (Dehaene, 2011) has been the focus of a substantial body of research. Behavioral measures of ANS acuity relate to mathematics achievement across development and levels of mathematics achievement (Chen & Li, 2014; Schneider et al., 2017) and neural measures of magnitude processing substrates have also been associated with mathematical learning disabilities (Iuculano, Tang, Hall, & Butterworth, 2008; Mazzocco, Feigenson, & Halberda, 2011; Mazzocco, Feigenson, & Halberda, 2011; Mejias, Mussolin, Rousselle, Grégoire, & Noël, 2012; Mussolin, Mejias, Noël, & Noel, 2010; Price, Holloway, Räsänen, Vesterinen, & Ansari, 2007; Szkudlarek & Brannon, 2017; Wilson & Dehaene, 2007).

However, despite this large confluence of evidence, recent findings indicate that those same measures of numerical acuity, and their subsequent relation to mathematics, may not be driven by magnitude processing mechanisms alone. Rather, the relation may depend on executive function demands introduced via visual properties of numerical stimuli, such as surface area or object size, that compete with discrete quantity for visual saliency (Gilmore et al., 2013) in the dot arrays being compared. Specifically, inhibitory control has been shown to either account for a significant amount of variance in the relation between number comparison performance and mathematics achievement (Gilmore et al., 2015; Keller & Libertus, 2015) or explain the relation altogether (Fuhs & McNeil, 2013; Gilmore et al., 2013). As a result, the influence of visual parameter congruency may be acting as a confound that invalidates theoretical accounts of the relation between the nonsymbolic number comparison task and ANS theory and their subsequent relation to mathematical competence. Therefore, the studies presented in Chapters 2-4 investigated the attentional factors that interact with numerical magnitude processing mechanisms by asking three basic questions. First, does *attention to number* relate to mathematics development beyond acuity of magnitude representation and domain-general executive function factors? Second, how are neural substrates of numerical magnitude processing affected by incongruent visual cues in the nonsymbolic number comparison tasks? And third, how do individual differences in *attention to number*, as indexed by neural activity related to the numerical congruency effect, relate to the development of mathematical competence?

5.2 Summary of findings

In Study 1, we investigated the relations between performance on congruent and incongruent trials of the nonsymbolic number comparison task and mathematics achievement, both as a continuous variable related to mathematics across the full spectrum of achievement and in terms of how it relates to group differences in mathematics achievement groups (i.e. DD, low achievement, and typical achievement). The major contribution from this study was the inclusion of measures of different components of executive function in non-numerical contexts, including visuo-spatial working memory, inhibitory control, and shifting behaviors. Previous research had investigated the intersection of magnitude processing mechanisms with inhibitory control *or* visuo-spatial working memory, but no study to date had included both measures, along with the third major component of executive function (Miyake et al., 2000), task-switching. Where most previous studies have framed the correlation between performance in nonsymbolic number comparison tasks as being driven by either executive function *OR* magnitude processing acuity (with the exception of Gilmore (2013, 2015) and Prager et al. (2016)), the inclusion of these additional measures in our first study allowed for a detailed analysis of attentional components of magnitude processing beyond what is associated with either construct alone. Further, the large-scale and longitudinal nature of this data allowed for the classification of mathematics achievement groups based on six continuous years of stable math achievement, including three years at school entry and three years at the beginning of middle school (5^{th} to 7^{th} grade). Defining a DD group based on stable low achievement rather than a discrepancy criterion allowed for an analysis that controlled for executive function factors issues rather than exclude them. As hypothesized, both the regression results in the full sample and the achievement group comparison results indicated that performance on incongruent trials of the number comparison task correlate with mathematics achievement after controlling for inhibitory control, task switching, visuospatial working memory, and reading achievement. In contrast, congruent trials did not relate to achievement group differences or math achievement more broadly, even before controlling for additional factors. These results indicate that behavioral correlates of number-specific attention mechanisms, or *attention to number*, are related to mathematics while behavioral correlates of ANS acuity with low attentional demands were not.

Study 2 used fMRI in a typically developing high school sample to investigate two principal issues: (1) the influence of congruency of non-numerical visual cues during the nonsymbolic number comparison task on the neural mechanisms supporting numerical magnitude perceptions, and (2) the influence of congruency on the relation between mathematics achievement, as measured by the preliminary scholastic aptitude test (PSAT), and the neural ratio effect, a neural proxy for acuity of the ANS. The task elicited ratio-dependent activity in canonical fronto-parietal brain regions (Sokolowski et al., 2016), but a comparison of the ratio effect during congruent versus incongruent trials within those regions showed no significant differences. A whole-brain contrast of these effects also found no differences, supporting the idea that regions of the brain previously found to encode numerical magnitude, such as the IPS and SPL, do so consistently when non-numerical visual cues are congruent or incongruent with numerical magnitudes. Therefore, ratio-dependent activation during nonsymbolic number comparison does not appear to be the product of cognitive processes specific to either congruent or incongruent task conditions. The main effect of congruency, which was not ratio-dependent, did show that four regions had significantly greater activity for incongruent trials, including the right IFG, right angular gyrus, right fusiform gyrus, and right parahippocampal gyrus. Congruency also affected the tasks relation to math, but not in canonical magnitude processing regions. The neural ratio effect did not correlate with math in any regions showing a ratio effect. However, in the whole-brain analysis an inverse correlation between PSAT math and the neural ratio effect appeared consistently in the left insula for both congruency conditions considered together, even after controlling for reading achievement. However, when the correlation was split by congruency condition, different patterns emerged, whereby a positive correlation was found between PSAT math scores and the neural ratio effect in the right supramarginal gyrus and a negative correlation in the left angular gyrus and left precuneus. First, the lack of any correlation between the neural ratio effect and math achievement in regions showing a ratio effect calls into question whether the relation between nonsymbolic number comparison performance and mathematics achievement is driven by ANS acuity. Second, a divergence in correlation patterns by congruency condition indicates that the task's relation to math is more complicated than magnitude perception alone. Instead, correlations between task-related activation and mathematical competence in non-ANS substrates suggests the involvement of alternative, or at least complementary, neural mechanisms.

Finally, Study 3 used fMRI to examine whether neural correlates of *attention to number* could be isolated, and whether they correlate with math competence in children. Study 3 built upon the findings of Study 2 in that participants again completed a nonsymbolic number comparison task which was analyzed by congruency condition, but also completed an Erickson flanker task. The Flanker task was designed to mirror the attentional demands of the congruency effect in the nonsymbolic number comparison task, but in a non-numeric domain. As in Study 1, accuracy rates on the incongruent trials, but not congruent trials, correlated with mathematics achievement. Neural contrasts of interest included the neural ratio effect and congruency effect in the nonsymbolic comparison task and the flanker congruency effect. Each of these contrasts elicited activity in line with previously published results, engaging a network of fronto-parietal regions commonly associated with both number-specific number processing substrates and generalized attentional allocation and cognitive control networks. However, the neural ratio effect in regions resulting from those contrasts did not correlate with math scores in any region. In contrast, there was a strong, inverse correlation between the numerical congruency effect (incongruent – congruent trials of nonsymbolic number comparison) in the right IFG that strengthened after controlling for Verbal IQ and performance on the flanker task (i.e. accuracy rate) and continued to show a moderate correlation after subtracting out neural response in the right IFG cluster (incongruent – congruent trials of flanker task). Since this region in the right IFG overlapped with a region with a significant ratio effect, results indicate that activity associated with numerical magnitude processing and attentional allocation converge in the inferior frontal gyrus, and further, that individual differences in the activity of this region during nonsymbolic magnitude comparison correlate specifically with a mathematics achievement.

5.3 Behavioral correlations between nonsymbolic comparison and mathematics achievement

Across studies, behavioral results from the nonsymbolic number comparison task in Studies 1 and 3 lend support for both the concept *attention to number* and its role in the relation between nonsymbolic number comparison performance and mathematics achievement. Results from Study 1 resemble the behavioral results in Study 3 in that accuracy rates on incongruent trials of the in-scanner version of the nonsymbolic number comparison task correlate with mathematics achievement, while performance on congruent trials does not. However, both of these correlations differ from Study 2, where response times in the nonsymbolic comparison task correlated with PSAT math scores across congruency condition, but accuracy rates did not. These differences across studies could be due to at least two principal factors. First, each sample is a different age. Study 3 has the youngest children (ages 8-11 yo), followed by Study 1 (11-13 yo) and Study 2 (17-19 yo). Effect sizes of the correlation between incongruent trials of the nonsymbolic number comparison task and mathematics achievement decrease with age of the samples from $r = .324$ in Study 3 to $r = .226$ in Study 1 to $r = .180$ in Study 2. This decrease of the effect size with age could be driven by developmental differences in the coupling between executive function and mathematics achievement. It may be that early in development, there are widespread differences in children's ability to up-regulate relevant, numerical information and suppress irrelevant distractors but that by high school, the neurocognitive systems that regulate this behavior could be fully developed for all typically developing individuals. In step with this account, age has been shown to be a mediating factor between nonsymbolic number comparison tasks and mathematics achievement across congruency conditions (Schneider et al., 2017). Secondly, differences in measures of mathematics may account for differences across studies. Meta-analyses also show that nonsymbolic number comparison performance is more highly correlated with measures of mathematics achievement that index mathematical fluency in basic arithmetic rather than higher-level mathematics achievement (Chen & Li, 2014; Schneider et al., 2017). Our composite measure of mathematics achievement in Study 3, the study with the youngest participants, includes mostly measures of basic numeracy and applied arithmetic, including a timed measure of math fluency. In Study 1, the outcome measure of mathematics achievement, the KeyMath3, involved basic algebra, geometry, and principles of numeracy commensurate with a 6^{th}-grade mathematics curriculum, which builds on arithmetic fluency but is several steps abstracted from more basic mathematical operations. Study 2 included the oldest sample and also utilized a measure of mathematics achievement, the PSAT, that involved trigonometry, more advanced geometry, and high school algebra. As a result, mathematics achievement as measured by the PSAT is the furthest measure from arithmetic fluency across studies, and therefore least likely to show a strong relation to nonsymbolic number comparison performance based on the moderator analysis presented in Schneider et al.'s meta-analysis (2017). Unfortunately, the current set of studies cannot make a distinction between the influence of developmental age and type of mathematics achievement measure. To do so, future studies will need to measure both arithmetic fluency as well as more advanced mathematics in the same sample across multiple age groups.

5.4 The neural ratio effect

Just as behavioral performance during the nonsymbolic number comparison task has been used in previous research to measure acuity of the ANS, the neural ratio effect has been used as a measure of individual differences in neural mechanisms related to magnitude processing of the ANS (Ansari et al., 2006; Gullick et al., 2011; Price et al., 2007). However, before the current studies, it was unknown how the ratio effect was influenced by executive function demands due to interference from incongruent visual cues. Therefore, Studies 2 and 3 investigated this issue as well as how the neural ratio effect's relation to math was influenced by congruency of visual stimulus parameters. Results indicated that number comparison in both studies elicited ratio effects at the group-level in regions previously reported in meta-analyses of number processing tasks (Sokolowski et al., 2016), including the IPS (left IPS for Study 2 and right IPS for Study 3) and superior medial gyrus extending into the anterior cingulate cortex. One difference between Study 2 and Study 3 was that children in Study 3 (3rd to 4th grade) showed ratio effects in the rIFG and rMFG, indicating a greater reliance on frontal regions compared to the high school students in Study 2, who showed a ratio effect in one additional cluster in the right superior parietal lobule bordering the precuneus. Previous research utilizing a mental arithmetic task has shown increasing reliance on parietal structures over the course of development coupled with a decrease in frontal activation (Ansari et al., 2005; Rivera et al., 2005). The current findings from Study 2 and Study 3 may reflect this developmental shift. However, it should be noted that a main effect for congruency (i.e. not ratio-dependent) was reported in the rIFG in Study 2, indicating increased reliance on the rIFG for incongruent trials of the number comparison task. Therefore, taken together, the younger children in Study 3 showed significant group-level ratio effects in frontal regions as well as group-level congruency effect, while adolescents in Study 2 group-level congruency effect in frontal regions only for congruency effects. This indicates that the proposed developmental shift is specific to the processing of numerical information, but not inhibitory control mechanisms, an interpretation that fits well with prior studies which have reported a fronto-parietal shift in both nonsymbolic number comparison (Ansari & Dhital, 2006) and symbolic number comparison tasks (Ansari et al., 2005; Kaufmann et al., 2006).

Given the similarities between Study 2 and 3, it should also be noted that they took slightly different approaches to the correlation between the neural ratio effect and mathematics achievement. In Study 2, beta-weights were extracted from regions showing a group-level ratio effect and then correlated with math. None of those correlations were significant, but to check for correlations with the ratio effect in regions that did not show a group-level effect, the correlation was conducted at the whole brain, which results in correlations that differed by congruency outside of canonical ANS substrates. In Study 3, again, no regions showed a correlation between the neural ratio effect and mathematics achievement in regions showing a group-level ratio effect. However, in Study 3, the cluster-level analysis was not followed by a whole-brain analysis in order to investigate the influence of congruency manipulations in a specific set of neural substrates. Therefore, it should be underscored that no region showing a group-level ratio effect in either study had subject-level beta values that correlated with mathematics achievement. This provides support against the argument that individual differences in neural mechanisms supporting nonsymbolic numerical magnitude processing relate to mathematics competence, insofar as they are captured by the neural ratio effect. Further, it calls into question the broader, dominant theoretical view that ANS acuity is a major factor predicting math achievement (Justin Halberda & Feigenson, 2008) that has initiated a host of interventions (Fuhs et al., 2016; Park & Brannon, 2014; Wang, Odic, Halberda, & Feigenson, 2016) and diagnostic tools (Butterworth, 2012; Nosworthy et al., 2013) that target ANS acuity.

One further aspect of the results from Study 2 that should be made explicit is the lack of difference between congruent and incongruent neural ratio effects in any of these regions showing a group-level ratio effect. In other words, the neural ratio effect was not driven by either congruency condition alone. This is important for the interpretation of previous results in the field, which draw implications from their findings from analyses that collapse across congruency conditions in the nonsymbolic number comparison task. This lack of difference means that the confound of visual cue congruency does not necessarily invalidate inference drawn from previous studies that rely on this task to measure numerical magnitude processing mechanisms. The fact that activation in those same regions does not correlate with math, however, does call into question what drives the relation nonsymbolic number comparison performance and mathematics achievement. For example, Gullick et al. (2011) report an inverse correlation between the distance effect and SAT scores in bilateral perisylvian structures, peaking in the insula. This relation, collapsed across congruency conditions, may very well be driven by number-specific attentional demands, even if the result is derived from a magnitude specific neural contrast. Correlations between the neural ratio effect and PSAT math scores in Study 2 underscore this point, showing that inverse ratio effects in the left and right insula have the strongest relationship to PSAT math, areas not previously considered as principle components of any magnitude processing network.

5.5 Differing methods of controlling for visual parameters of nonsymbolic stimuli

One important difference in design among the current collection of studies is the method used for controlling visual parameters of the dot arrays. Studies 1 and 3 utilized a code generated by Gebuis and Reynvoet (2011), which allow for the control of four visual properties: (1) area extended by the entire dot array (convex hull), (2) total surface area (aggregate of dot surfaces), (3) item size, and (4) density (area extended/surface area). In this way, it is ensured that visual properties are not significant predictors of numerosity. Further, the degree of incongruency/congruency is not tightly related to trial ratio. Most previous studies before the publication of Gebuis & Reynvoet (2011) have utilized a method whereby extrinsic variable were equated (e.g. total surface area of the dot sets) and intrinsic variables varied randomly (e.g., the diameter and size of each dot) in half the trials, with the reverse on the other half of trials (Ansari & Dhital, 2006; Halberda et al., 2008; Manuela Piazza et al., 2010; Price et al., 2007) using the method detailed by Dehaene et al. (2005). However, in the method suggested by Dehaene, the issue of congruency is inextricably linked to trial ratio. For example, consider two trials of differing ratios, 3.2 (5 vs. 16) and 1.2 (5 vs. 6). For the congruent version of these ratios, average dot size is equated and thus the surface area of the more numerous dot set is greater in each trial (i.e. surface area is visually congruent with the larger numerosity). However, the degree of the difference in surface area also covaries with ratio; the greater the ratio, the greater the difference in surface area, and thus, more visually congruent information. Conversely, for the incongruent trials, the surface area of each dot set within each trial is equivalent and the numerically larger dot set necessarily has smaller dots. Further, the degree of the difference in dot size between dot sets covaries with ratio such that the greater the ratio is, the more visually incongruent the visual information. In the present example, the degree of dot size difference is more exaggerated in the 5 vs. 16 than 5 vs. 6 ratio, and thus, there is greater conflicting visual information in the larger ratio trial. As a result, the degree of congruent and incongruent visual information may be driving the differing trends in the neural ratio effect and behavioral ratio effects.

These two control methods also lead to differing hypotheses about ratio x congruency interactions that were born out in differences between Study 2 and Study 3, which were not the principle focus of our analyses but are important to mention nonetheless. For example, if the degree of incongruency decreases with increasing ratio difficulty, as the Dehaene method specifies, one would expect to see a greater congruency effect for easier trials. And, in fact, easier ratios show a greater ratio effect and there is no significant difference in response time or accuracy rates between congruent and incongruent trials of the most difficult ratio in Study 2. However, if ratio and degree of congruency are not linearly related, we would expect the effect of congruency to either be equal across ratios, or perhaps increase as ratios become more difficult (i.e. compounding the difficulty of comparing numerosities with interfering visual cues). In line with this hypothesis, Study 3 does show a greater congruency effect for more difficult ratios. For this reason, the effects of congruency and ratio are more separable in Study 3 than in Study 2. In effect, Study 3 utilizes a superior, but less common way of controlling for the influence of visual parameters. Therefore, the influence of ratio difficulty and congruency are confounded in a majority of the literature to date in a way that does not allow for an investigation of their respective contributions for behavioral performance on the nonsymbolic number comparison task or associated neural activation. As such, a more nuanced distinction across all visual parameters and their interaction with ratio would be a ripe area for future research.

5.6 Neural mechanisms associated with attention to number

While Study 1 indicated the relevance of *attention to number* as a construct of interest for the development of mathematical competence through behavioral data, Studies 2 and 3 lend support for a specific set of neural substrates related to *attention to number*. Study 2 indicated that individual differences in canonical numerical magnitude processing substrates do not relate to math achievement in high school, a similar finding to previous results (Gullick et al., 2011). Instead, a smaller ratio effect in the left insula, left posterior cingulate, and left angular gyrus, as well as a greater ratio effect in the right supramarginal gyrus correlated with math. In particular, the left posterior cingulate correlation was specific to incongruent trials of the nonsymbolic number comparison task before and after controlling for PSAT reading scores. Though these results are difficult to interpret due to their lack of group-level task effect, it is evident that congruency manipulations affect what individual differences in neural response correlate with mathematics achievement.

Study 3, with 3rd and 4th grade children, included tighter controls of visual parameters, a more comprehensive measure of mathematics achievement, and a comparable non-numerical response inhibition/task interference task (i.e. the flanker task). Results from Study 3 largely mirrored the numerical congruency effects from Study 2, demonstrating an effect of congruency in the right fusiform gyri and rIFG. However, Study 2 had no way of indicating if these results were magnitude-specific or merely related to shifts in attention more broadly. In contrast, Study 3 indicated that these regions demonstrated a congruency effect specific to attentional demands in a numerical context by subtracting out the flanker congruency effect. Specifically, three findings in Study 3 indicate of the importance of the rIFG as a locus of individual differences in *attention to number*. First, this region demonstrates a group-level ratio effect and a numerical congruency effect, even with the double-subtraction. Second, individual differences in this effect correlate with mathematics achievement, even after controlling for verbal IQ and performance in the flanker task (indicating a highly specific relation). And third, the whole-brain correlation of the double subtraction [(incongruent number comparison – congruent number comparison) > (incongruent flanker – congruent flanker)] revealed another region of the rIFG, the *pars orbitalis,* that correlated with mathematics achievement with the same control variables. The *pars orbitalis* is anterior and inferior to the *pars triangularis*, but their functions are not well-differentiated, especially in regards to their role in inhibition (Aron et al., 2014; Levy & Wagner, 2011). The three most probable roles for either of these regions are their involvement in (a) the upregulation of areas of the cortex dedicated to numerical magnitude processing, (b) the suppression of non-numerical, incongruent visual cues, or (c) magnitude processing itself. Since *attention to number* is likely to involve the upregulation in processing numerical information to increase saliency as well as the suppression of non-numerical, visual cue information, activation in these areas of the cortex may be *either the cause or of effect* attention to number. Future dynamic causal modeling or psycho-psychological interaction modeling analyses should be performed to evaluate the role of the IFG in attention to number.

5.7 Future Directions

In many ways, the current collection of studies represent a move away from a domain-specific vs domain-general framing of cognitive mechanisms linked to math development and math specific learning disabilities. Instead, building a more complex model of the biological interaction between numerical magnitude processing and executive function mechanisms should provide additional theoretical support to integrate seemingly disparate findings common across current neuroimaging studies of the foundations of math competence. In regards to attention and the mathematics learning disability DD, much of the conversation has been dominated by whether DD is caused by a core domain-specific deficit such as numerical magnitude processing and symbolic number mapping or domain-general deficits such as attention deficits or working memory deficits (e.g., Butterworth, Varma, & Laurillard, 2011; Geary & Moore, 2016; Szucs, Devine, Soltesz, Nobes, & Gabriel, 2013). From a biological standpoint, attention necessarily involves *attending to something* and working memory involves the *maintaining of something.* Manifestations of DD are heterogeneous, sometimes presenting as comorbid with attention deficits and reading disabilities, and sometimes being isolated to mathematics. Research into the interaction of attention mechanisms or working memory mechanisms with perceptual information relevant for particular types of academic skills (and relevant for specific learning disabilities) may provide a framework for understanding the biological framework for these heterogeneous deficits and their comorbidities. Therefore, the current collection of studies should not be taken to advocate for the study of *attention to number* as another core deficit associated with DD or the one neurocognitive mechanism educators need to train in order to improve math abilities, but rather a step in framing specific cognitive deficits in a more dynamic framework that involves the interaction of multiple biological mechanisms.

In addition to the general framework of the current collection, two points should be made about the scope of the experiments. First, the current studies rely exclusively on visual information to study a multi-modal perceptual phenomenon. To be functionally numerate is to interact with number successfully in a variety of contexts, often through spoken word or in other physical forms. Some work has been done on the multi-modal nature of numerical magnitude representations in IPS substrates (Abboud, Maidenbaum, Dehaene, & Amedi, 2015; Arrighi, Togoli, & Burr, 2014; Damarla, Cherkassky, & Just, 2016; Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003), but currently the field is dominated by visual experiments. The current collection is no exception. Second, most numerical information we encounter in modern society is symbolic and exact in nature. Whether it be through Arabic digits or spoken number words, most behaviorally relevant interactions with number beyond early childhood are not with nonsymbolic numerical stimuli of the type presented in the current collection of studies, but rather number in a symbolic form. Further, a growing body of research suggests that processing of symbolic number is a greater predictor of mathematics achievement than processing of number in its nonsymbolic form (De Smedt et al., 2013; Price & Wilkey, 2017). Therefore, stemming from these two points, natural next steps from the current studies would be to expand *attention to number* to incorporate more complicated representation of number that involve multiple sensory modalities and also symbolic frameworks.

5.8 Conclusion

Studies 1 through 3 investigated the neurocognitive mechanisms associated with ANS acuity, executive function, and attention to number. On the whole, they provide little evidence that individual differences in ANS acuity relate to competence in mathematics, either at the behavioral or neural level. In contrast, executive function is an important element of math competence across age ranges and types of measures. The current studies provide evidence that *attention to number*, which can be described as the dynamic interplay of executive function and magnitude processing mechanisms, is a foundation of math competence appearing at least as early as second grade and having a measurable relation to mathematics achievement through middle and high school. Together, these findings suggest a need to reframe existing models of the relation between basic number processing and math competence and that educational interventions built on those models are premature and may be misdirected.

REFERENCES

Abboud, S., Maidenbaum, S., Dehaene, S., & Amedi, A. (2015). A number-form area in the blind. *Nature Communications, 6*, 1–9. http://doi.org/10.1038/ncomms7026

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5*. Washington, D. C.: Washington, D. C. American Psychiatric Association.

Aminoff, E. M., Kveraga, K., & Bar, M. (2013). The role of the parahippocampal cortex in cognition Elissa. *Trends in Cognitive Sciences, 17*(8), 379–390.

Amso, D., & Scerif, G. (2015). The attentive brain : insights from developmental cognitive neuroscience. *Nature Reviews, 16*(10), 606–619. http://doi.org/10.1038/nrn4025

Anobile, G., Stievano, P., & Burr, D. C. (2013). Visual sustained attention and numerosity sensitivity correlate with math achievement in children. *Journal of Experimental Child Psychology*, *116*(2), 380–391. http://doi.org/10.1016/j.jecp.2013.06.006

Ansari, D. (2008). Effects of development and enculturation on number representation in the brain. *Nature Reviews Neuroscience*, *9*(4), 278–291. http://doi.org/10.1038/nrn2334

Ansari, D., & Dhital, B. (2006). Age-related changes in the activation of the intraparietal sulcus during nonsymbolic magnitude processing: an event-related functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience*, *18*(11), 1820–8. http://doi.org/10.1162/jocn.2006.18.11.1820

Ansari, D., Dhital, B., & Siong, S. C. (2006). Parametric effects of numerical distance on the intraparietal sulcus during passive viewing of rapid numerosity changes. *Brain Research*, *1067*(1), 181–188. http://doi.org/10.1016/j.brainres.2005.10.083

Ansari, D., Garcia, N., Lucas, E., Hamon, K., & Dhital, B. (2005). Neural correlates of symbolic number processing in children and adults. *Neuroreport*, *16*(16), 1769–1773. http://doi.org/10.1097/01.wnr.0000183905.23396.f1

Aron, A. R., & Poldrack, R. a. (2005). The cognitive neuroscience of response inhibition: relevance for genetic research in attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *57*(11), 1285–92. http://doi.org/10.1016/j.biopsych.2004.10.026

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex : one decade on. *Trends in Cognitive Sciences*, *18*(4), 177–185. http://doi.org/10.1016/j.tics.2013.12.003

Arrighi, R., Togoli, I., & Burr, D. C. (2014). A generalized sense of number. *Proceedings of the Royal Society B: Biological Sciences, 281*(1797), 20141791–20141791. http://doi.org/10.1098/rspb.2014.1791

Arsalidou, M., & Taylor, M. J. (2011). Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations. *NeuroImage*, *54*(3), 2382–2393. http://doi.org/10.1016/j.neuroimage.2010.10.009

Ashkenazi, S., Black, J. M., Abrams, D. A., Hoeft, F., & Menon, V. (2013). Neurobiological Underpinnings of Math and Reading Learning Disabilities. *Journal of Learning Disabilities, 46*(6), 549–569. http://doi.org/10.1177/0022219413483174

Ashkenazi, S., Rosenberg-Lee, M., Tenison, C., & Menon, V. (2012). Weak task-related modulation and stimulus representations during arithmetic problem solving in children with developmental dyscalculia. *Developmental Cognitive Neuroscience*, *2*(SUPPL. 1), S152–S166. http://doi.org/10.1016/j.dcn.2011.09.006

Ashkenazi, S., Rubinsten, O., & Henik, A. (2009). Attention, automaticity, and developmental dyscalculia. *Neuropsychology*, *23*(4), 535–540. http://doi.org/10.1037/a0015347

Batchelor, S., Inglis, M., & Gilmore, C. (2015). Spontaneous focusing on numerosity and the arithmetic advantage. *Learning and Instruction*, *40*, 79–88. http://doi.org/10.1016/j.learninstruc.2015.09.005

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society*. http://doi.org/10.2307/2346101

Bisley, J. W. (2011). The neural basis of visual attention. *The Journal of Physiology*, *589*(Pt 1), 49–57. http://doi.org/10.1113/jphysiol.2010.192666

Blair, C., & Razza, R. P. (2007). Relating effortful control, executive function, and false belief understanding to emerging math and literacy ability in kindergarten. *Child Development*, *78*(2), 647–663. http://doi.org/10.1111/j.1467-8624.2007.01019.x

Bugden, S., & Ansari, D. (2011). Individual differences in children's mathematical competence are related to the intentional but not automatic processing of Arabic numerals. *Cognition*, *118*(1), 32–44. http://doi.org/10.1016/j.cognition.2010.09.005

Bugden, S., & Ansari, D. (2015a). Probing the nature of deficits in the "Approximate Number System" in children with persistent Developmental Dyscalculia. *Developmental Science*, 1–17. http://doi.org/10.1111/desc.12324

Bugden, S., & Ansari, D. (2015b). Probing the nature of deficits in the "Approximate Number System" in children with persistent Developmental Dyscalculia. *Developmental Science*, *5*, 1–17. http://doi.org/10.1111/desc.12324

Bugden, S., Bugden, S., & Ansari, D. (2015). Probing the nature of deficits in the " Approximate Number System " in children with persistent Developmental Dyscalculia Probing the nature of deficits in the " Approximate Number System " in children with persistent Developmental Dyscalculia, (July). http://doi.org/10.1111/desc.12324

Bugden, S., Price, G. R., McLean, D. A., & Ansari, D. (2012). The role of the left intraparietal sulcus in the relationship between symbolic number processing and children's arithmetic competence. *Developmental Cognitive Neuroscience*, *2*(4), 448–57. http://doi.org/10.1016/j.dcn.2012.04.001

Bull, R., & Scerif, G. (2001). Executive Functioning as a Predictor of Children's Mathematics Ability: Inhibition, Switching, and Working Memory. *Developmental Neuropsychology*, *19*(3), 273–293. http://doi.org/10.1207/S15326942DN1903_3

Bull, R., & Scerif, G. (2001). Executive functioning as a predictor of children's mathematics ability: inhibition, switching, and working memory. *Developmental Neuropsychology*, *19*(3), 273–293. http://doi.org/10.1207/S15326942DN1903_3

Bunge, S. A., Dudukovic, N. M., Thomason, M. E., Vaidya, C. J., & Gabrieli, J. D. E. (2002). Immature Frontal Lobe Contributions to Cognitive Control in Children: Evidence from fMRI. *Neuron*, *33*(2), 301–311. http://doi.org/10.1016/S0896-6273(01)00583-9

Butterworth, B. (2012). Dyscalculia Screener. http://doi.org/10.1037/t05204-000

Butterworth, B., & Kovas, Y. (2013). Understanding Neurocognitive Developmental Disorders Can Improve Education for All. *Science*, *340*(6130), 300–305. http://doi.org/10.1126/science.1231022

Butterworth, B., & Laurillard, D. (2010). Low numeracy and dyscalculia: identification and intervention. *ZDM*, *42*(6), 527–539. http://doi.org/10.1007/s11858-010-0267-4

Butterworth, B., Varma, S., & Laurillard, D. (2011). Dyscalculia: from brain to education. *Science (New York, N.Y.)*, *332*(6033), 1049–53. http://doi.org/10.1126/science.1201536

Bynner, J., Parsons, S., Bynner, J., & Parsons, S. (2006). *Does Numeracy Matter More? National Research and Development Centre for Adult Literacy and Numeracy*. London: The Basic Skills Agency. Retrieved from http://www.nrdc.org.uk/publications_details.asp?ID=16#

Cantlon, J. F., Brannon, E. M., Carter, E. J., & Pelphrey, K. a. (2006). Functional imaging of numerical processing in adults and 4-y-old children. *PLoS Biology*, *4*(5), 844–854. http://doi.org/10.1371/journal.pbio.0040125

Cantlon, J. F., Libertus, M. E., Pinel, P., Dehaene, S., Brannon, E. M., & Pelphrey, K. A. (2009). The Neural Development of an Abstract Concept of Number. *Journal of Cognitive Neuroscience*, *21*(11), 2217–2229. http://doi.org/10.1162/jocn.2008.21159.The

Chen, Q., & Li, J. (2014). Association between individual differences in non-symbolic number acuity and math performance: a meta-analysis. *Acta Psychologica*, *148*, 163–72. http://doi.org/10.1016/j.actpsy.2014.01.016

Clayton, S., & Gilmore, C. (2014). Inhibition in dot comparison tasks. *Zdm*, 1–12. http://doi.org/10.1007/s11858-014-0655-2

Clayton, S., Gilmore, C., & Inglis, M. (2015). Dot comparison stimuli are not all alike: The effect of different visual controls on ANS measurement. *Acta Psychologica*, *161*, 177–184. http://doi.org/10.1016/j.actpsy.2015.09.007

College Board. (2017). Retrieved January 19, 2017, from https://research.collegeboard.org/programs/psat/data/cb-jr/archived/2010

Connolly, A. J. (2007). KeyMath-3 Diagnostic Assessment. San Antonio, TX: Pearson.

Corsi, P. (1972). Human memory and the medial temporal region of the brain. *Dissertation Abstracts International*, *34*(2).

Cragg, L., Keeble, S., Richardson, S., Roome, H. E., & Gilmore, C. (2017). Direct and indirect influences of executive functions on mathematics achievement. *Cognition*, *162*, 12–26. http://doi.org/10.1016/j.cognition.2017.01.014

Czamara, D., Tiesler, C. M. T., Kohlb??ck, G., Berdel, D., Hoffmann, B., Bauer, C. P., … Heinrich, J.

(2013). Children with ADHD Symptoms Have a Higher Risk for Reading, Spelling and Math Difficulties in the GINIplus and LISAplus Cohort Studies. *PLoS ONE*, *8*(5). http://doi.org/10.1371/journal.pone.0063859

Daitch, A. L., Foster, B. L., Schrouff, J., Rangarajan, V., Kaşikçi, I., Gattas, S., & Parvizi, J. (2016). Mapping human temporal and parietal neuronal population activity and functional coupling during mathematical cognition. *Proceedings of the National Academy of Sciences*, 201608434. http://doi.org/10.1073/pnas.1608434113

Damarla, S. R., Cherkassky, V. L., & Just, M. A. (2016). Modality-independent representations of small quantities based on brain activation patterns. *Human Brain Mapping*, *37*(4), 1296–1307. http://doi.org/10.1002/hbm.23102

Dark, V. J., & Benbow, C. P. (1994). Type of Stimulus Mediates the Relationship Between Working-Memory Performance and Type of Precocity. *Intelligence*, *19*, 337–357. http://doi.org/10.1016/0160-2896(94)90006-X

Dastjerdi, M., Ozker, M., Foster, B. L., Rangarajan, V., & Parvizi, J. (2013). Numerical processing in the human parietal cortex during experimental and natural conditions. *Nature Communications*, *4*, 2528. http://doi.org/10.1038/ncomms3528

Davidson, M. C., Amso, D., Anderson, L. C., & Diamond, A. (2006). Development of cognitive control and executive functions from 4 to 13 years: Evidence from manipulations of memory, inhibition, and task switching. *Neuropsychologia*, *44*(11), 2037–2078. http://doi.org/10.1016/j.neuropsychologia.2006.02.006

De Smedt, B., Noël, M.-P., Gilmore, C., & Ansari, D. (2013). How do symbolic and non-symbolic numerical magnitude processing skills relate to individual differences in children's mathematical skills? A review of evidence from brain and behavior. *Trends in Neuroscience and Education*, *2*(2), 48–55. http://doi.org/10.1016/j.tine.2013.06.001

Dehaene, S. (1997). *The Number Sense*. Oxford: Oxford University Press.

Dehaene, S. (2011). *The number sense: How the mind creates mathematics.* Oxford University Press.

Dehaene, S., & Cohen, L. (1997). Cerebral pathways for calculation: double dissociation between rote verbal and quantitative knowledge of arithmetic. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *33*(2), 219–250. http://doi.org/10.1016/S0010-9452(08)70002-9

Dehaene, S., Izard, V., & Piazza, M. (2005). *Control over non-numerical parameters in numerosity experiments*.

Delazer, M., & Benke, T. (1997). Arithmetic facts without meaning. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *33*(4), 697–710. http://doi.org/10.1016/S0010-9452(08)70727-5

Diamond, A. (2014). Executive Functions. *Annual Review of Clinical psychologyPsychol.*, *64*, 135–168. http://doi.org/10.1146/annurev-psych-113011-143750.Executive

Dinkel, P. J., Willmes, K., Krinzinger, H., Konrad, K., & Koten, J. W. (2013). Diagnosing developmental dyscalculia on the basis of reliable single case FMRI methods: promises and limitations. *PloS One*, *8*(12), e83722. http://doi.org/10.1371/journal.pone.0083722

Dumontheil, I., & Klingberg, T. (2012). Brain activity during a visuospatial working memory task predicts arithmetical performance 2 years later. *Cerebral Cortex*, *22*(May), 1078–1085. http://doi.org/10.1093/cercor/bhr175

Duncan, G. J., Dowsett, C. J., Claessens, A., Magnuson, K., Huston, A. C., Klebanov, P., … Japel, C. (2007). School readiness and later achievement. *Developmental Psychology*, *43*(6), 1428–46. http://doi.org/10.1037/0012-1649.43.6.1428

Dunst, B., Benedek, M., Jauk, E., Bergner, S., Koschutnig, K., Sommer, M., … Neubauer, A. C. (2014). Neural efficiency as a function of task demands. *Intelligence*, *42*(1), 22–30. http://doi.org/10.1016/j.intell.2013.09.005

Eger, E., Sterzer, P., Russ, M. O., Giraud, A.-L., & Kleinschmidt, A. (2003). A supramodal number representation in human intraparietal cortex. *Neuron*, *37*(4), 719–25. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12597867

Eickhoff, S. B., Stephan, K. E., Mohlberg, H., Grefkes, C., Fink, G. R., Amunts, K., & Zilles, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *NeuroImage*, *25*(4), 1325–1335. http://doi.org/10.1016/j.neuroimage.2004.12.034

Eiselt, A.-K., & Nieder, A. (2013). Representation of abstract quantitative rules applied to spatial and numerical magnitudes in primate prefrontal cortex. *J Neurosci*, *33*(17), 7526–34. http://doi.org/10.1523/JNEUROSCI.5827-12.2013

Espy, K. A., McDiarmid, M. M., Cwik, M. F., Stalets, M. M., Hamby, A., & Senn, T. E. (2004). The contribution of executive functions to emergent mathematic skills in preschool children. *Developmental Neuropsychology*, *26*(1), 465–486. http://doi.org/10.1207/s15326942dn2601_6

Fair, D. A., Cohen, A. L., Power, J. D., Dosenbach, N. U. F., Church, J. A., Miezin, F. M., … Petersen, S. E. (2009). Functional brain networks develop from a "local to distributed" organization. *PLoS Computational Biology*, *5*(5), 14–23. http://doi.org/10.1371/journal.pcbi.1000381

Fair, D. A., Dosenbach, N. U. F., Church, J. A., Cohen, A. L., Brahmbhatt, S., Miezin, F. M., … Schlaggar, B. L. (2007). Development of distinct control networks through segregation and integration. *Proceedings of the National Academy of Sciences*, *104*(33), 13507–13512. http://doi.org/10.1073/pnas.0705843104

Fazio, L. K., Bailey, D. H., Thompson, C. A., & Siegler, R. S. (2014). Relations of different types of numerical magnitude representations to each other and to mathematics achievement. *Journal of Experimental Child Psychology*, *123*(1), 53–72. http://doi.org/10.1016/j.jecp.2014.01.013

Feigenson, L., Dehaene, S., & Spelke, E. (2004). Core systems of number. *Trends in Cognitive Sciences*, *8*(7), 307–314. http://doi.org/10.1016/j.tics.2004.05.002

Fias, W., Menon, V., & Szucs, D. (2013). Multiple components of developmental dyscalculia. *Trends in Neuroscience and Education*, 1–5. http://doi.org/10.1016/j.tine.2013.06.006

Friston, K. J., Josephs, O., Rees, G., & Turner, R. (1998). Nonlinear Event-Related Responses in. *Magnetic Resonance in Medicine*, 41–52.

Fuchs, D., Morgan, P. L., Young, C. L., & Rise, T. (2003). Responsiveness-to-Intervention : Definitions , Evidence , and Implications for the Learning Disabilities Construct, *18*(3), 157–171.

Fuhs, M. W., Kelley, K., O'Rear, C., & Villano, M. (2016). The Role of Non-Numerical Stimulus Features in Approximate Number System Training in Preschoolers from Low-Income Homes. *Journal of Cognition and Development*, *17*(5), 737–764. http://doi.org/10.1080/15248372.2015.1105228

Fuhs, M. W., & McNeil, N. M. (2013). ANS acuity and mathematics ability in preschoolers from low-income homes: contributions of inhibitory control. *Developmental Science*, *16*(1), 136–48. http://doi.org/10.1111/desc.12013

Geary, D. C. (2004). Mathematics and learning disabilities. *Journal of Learning Disabilities*, *37*(1), 4–15. http://doi.org/10.1177/00222194040370010201

Geary, D. C., Hoard, M. K., Byrd-craven, J., & Nugent, L. (2007). Cognitive Mechanisms Underlying Achievement Deficits in Children With Mathematical Learning Disability, *78*(4), 1343–1359.

Geary, D. C., Hoard, M. K., Nugent, L., & Bailey, D. H. (2013). Adolescents' Functional Numeracy Is Predicted by Their School Entry Number System Knowledge. *PLoS ONE*, *8*(1). http://doi.org/10.1371/journal.pone.0054651

Geary, D. C., & Moore, A. M. (2016). Cognitive and brain systems underlying early mathematical development. In *The Mathematical Brain Across the Lifespan* (1st ed., pp. 75–103). Elsevier B.V. http://doi.org/10.1016/bs.pbr.2016.03.008

Gebuis, T., & Reynvoet, B. (2011). Generating nonsymbolic number stimuli. *Behavior Research Methods*, *43*(4), 981–6. http://doi.org/10.3758/s13428-011-0097-5

Gebuis, T., & Reynvoet, B. (2012). Continuous visual properties explain neural responses to nonsymbolic number. *Psychophysiology*, *49*(11), 1649–1659. http://doi.org/10.1111/j.1469-8986.2012.01461.x

Gilmore, C., Attridge, N., Clayton, S., Cragg, L., Johnson, S., Marlow, N., … Inglis, M. (2013). Individual differences in inhibitory control, not non-verbal number acuity, correlate with mathematics achievement. *PloS One*, *8*(6), e67374. http://doi.org/10.1371/journal.pone.0067374

Gilmore, C., Attridge, N., & Inglis, M. (2011). Measuring the approximate number system. *Quarterly Journal of Experimental Psychology (2006)*, *64*(11), 2099–109. http://doi.org/10.1080/17470218.2011.574710

Gilmore, C., Cragg, L., Hogan, G., & Inglis, M. (2016). Congruency effects in dot comparison tasks: convex hull is more important than dot area. *Journal of Cognitive Psychology*, *28*(8), 923–931. http://doi.org/10.1080/20445911.2016.1221828

Gilmore, C., Keeble, S., Richardson, S., & Cragg, L. (2015). The role of cognitive inhibition in different components of arithmetic. *Zdm*, 1–12. http://doi.org/10.1007/s11858-014-0659-y

Göbel, S. M., Johansen-Berg, H., Behrens, T., & Rushworth, M. F. S. (2004). Response-selection-related parietal activation during number comparison. *Journal of Cognitive Neuroscience*, *16*(9), 1536–1551. http://doi.org/10.1162/0898929042568442

Goebel, R., Esposito, F., & Formisano, E. (2006). Analysis of Functional Image Analysis Contest (FIAC) data with BrainVoyager QX: From single-subject to cortically aligned group General Linear Model analysis and self-organizing group Independent Component Analysis. *Human Brain Mapping*, *27*(5), 392–401. http://doi.org/10.1002/hbm.20249

Goodman, M., Sands, A., & Coley, R. (2015). *America's Skills Challenge: Millennials and the Future*. Retrieved from papers2://publication/uuid/E2D8945E-D15E-4719-BFB0-DD9392524065

Grabner, R. H., Ansari, D., Koschutnig, K., Reishofer, G., & Ebner, F. (2013). The function of the left angular gyrus in mental arithmetic: Evidence from the associative confusion effect. *Human Brain Mapping*, *34*(5), 1013–1024. http://doi.org/10.1002/hbm.21489

Gross, J., Hudson, C., & Price, D. (2009). The long term costs of numeracy difficulties. *London (UK): Every Child a Chance Trust and KPMG*, (January 2009). Retrieved from http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:The+long+term+costs+of+numeracy+difficulties#0

Gullick, M. M., Sprute, L. A., & Temple, E. (2011). Individual differences in working memory, nonverbal IQ, and mathematics achievement and brain mechanisms associated with symbolic and nonsymbolic number processing. *Learning and Individual Differences*, *21*(6), 644–654. http://doi.org/10.1016/j.lindif.2010.10.003

Halberda, J., & Feigenson, L. (2008). Developmental change in the acuity of the "Number Sense": The Approximate Number System in 3-, 4-, 5-, and 6-year-olds and adults. *Developmental Psychology*, *44*(5), 1457–65. http://doi.org/10.1037/a0012682

Halberda, J., Mazzocco, M., & Feigenson, L. (2008). Individual differences in nonverbal number acuity correlate with maths achievement. [supplement]. *Nature*, 8–11. http://doi.org/10.1038/nature

Halberda, J., Mazzocco, M. M. M. M., & Feigenson, L. (2008). Individual differences in non-verbal number acuity correlate with maths achievement. *Nature*, *455*(October), 8–11. http://doi.org/10.1038/nature07246

Hannula, M. M., Lepola, J., & Lehtinen, E. (2010). Spontaneous focusing on numerosity as a domain-specific predictor of arithmetical skills. *Journal of Experimental Child Psychology*, *107*(4), 394–406. http://doi.org/10.1016/j.jecp.2010.06.004

Henik, A., Rubinsten, O., & Ashkenazi, S. (2011). The "where" and "what" in developmental dyscalculia. *The Clinical Neuropsychologist*, *25*(6), 989–1008. http://doi.org/10.1080/13854046.2011.599820

Hibbard, J. H., Peters, E., Dixon, A., Tusler, M., Peters, E., & Dixon, A. (2007). Consumer Competencies and the Use of Comparative Quality Information: It Isn't Just about Literacy. *Medical Care Research and Review*, *64*(4), 379–394. http://doi.org/10.1177/1077558707301630

Hillyard, S. a, Vogel, E. K., & Luck, S. J. (1998). Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *353*(1373), 1257–1270. http://doi.org/10.1098/rstb.1998.0281

Hoard, M. K., Geary, D. C., Byrd-craven, J., & Nugent, L. (2008). Mathematical Cognition in Intellectually Precocious First Graders. *Developmental Neuropsychology*, *33*(3), 251–276.

http://doi.org/10.1080/87565640801982338

Hofer, K. G., Lipsey, M. W., Dong, N., & Farran, D. C. (2013). *Results of the Early Math Project – Scale-Up Cross-Site Results*. Nashville, TN.

Holloway, I. D., Price, G. R., & Ansari, D. (2010). Common and segregated neural pathways for the processing of symbolic and nonsymbolic numerical magnitude: An fMRI study. *NeuroImage*, *49*(1), 1006–1017. http://doi.org/10.1016/j.neuroimage.2009.07.071

Houdé, O., Rossi, S., Lubin, A., & Joliot, M. (2010). Mapping numerical processing, reading, and executive functions in the developing brain: an fMRI meta-analysis of 52 studies including 842 children. *Developmental Science*, *13*(6), 876–885. http://doi.org/10.1111/j.1467-7687.2009.00938.x

Inglis, M., & Gilmore, C. (2014). Indexing the approximate number system. *Acta Psychologica*, *145*, 147–55. http://doi.org/10.1016/j.actpsy.2013.11.009

Ipata, A. E., Gee, A. L., Gottlieb, J., Bisley, J. W., & Goldberg, M. E. (2006). LIP responses to a popout stimulus are reduced if it is overtly ignored. *Nature Neuroscience*, *9*(8), 1071–1076. http://doi.org/10.1038/nn1734

Iuculano, T. (2016). *Neurocognitive accounts of developmental dyscalculia and its remediation. Progress in brain research* (1st ed., Vol. 227). Elsevier B.V. http://doi.org/10.1016/bs.pbr.2016.04.024

Iuculano, T., Tang, J., Hall, C. W. B., & Butterworth, B. (2008). Core information processing deficits in developmental dyscalculia and low numeracy. *Developmental Science*, *11*(5), 669–680. http://doi.org/10.1111/j.1467-7687.2008.00716.x

Jacob, S. N., & Nieder, A. (2009). Tuning to non-symbolic proportions in the human frontoparietal cortex. *European Journal of Neuroscience*, *30*(7), 1432–1442. http://doi.org/10.1111/j.1460-9568.2009.06932.x

Jacob, S. N., & Nieder, A. (2014). Complementary roles for primate frontal and parietal cortex in guarding working memory from distractor stimuli. *Neuron*, *83*(1), 226–237. http://doi.org/10.1016/j.neuron.2014.05.009

Kaufman, A., & Kaufman, N. (2004). Kaufman Brief Intelligence Test-2. London: Pearson.

Kaufmann, L., Koppelstaetter, F., Siedentopf, C., Haala, I., Haberlandt, E., Zimmerhackl, L.-B., … Ischebeck, A. (2006). Neural correlates of the number???size interference task in children. *NeuroReport*, *17*(6), 587–591. http://doi.org/10.1097/00001756-200604240-00007

Kaufmann, L., Mazzocco, M. M., Dowker, A., von Aster, M., Göbel, S. M., Grabner, R. H., … Nuerk, H.-C. (2013). Dyscalculia from a developmental and differential perspective. *Frontiers in Psychology*, *4*(August), 516. http://doi.org/10.3389/fpsyg.2013.00516

Kaufmann, L., Vogel, S. E., Starke, M., Kremser, C., Schocke, M., & Wood, G. (2009). Developmental dyscalculia: compensatory mechanisms in left intraparietal regions in response to nonsymbolic magnitudes. *Behavioral and Brain Functions : BBF*, *5*, 35. http://doi.org/10.1186/1744-9081-5-35

Keller, L., & Libertus, M. (2015). Inhibitory control may not explain the link between approximation and math abilities in kindergarteners from middle class families. *Frontiers in Psychology*, *6*(May), 1–11.

http://doi.org/10.3389/fpsyg.2015.00685

Kerlin, J. R., Shahin, A. J., & Miller, L. M. (2010). Attentional Gain Control of Ongoing Cortical Speech Representations in a "Cocktail Party." *Journal of Neuroscience*, *30*(2), 620–628. http://doi.org/10.1523/JNEUROSCI.3631-09.2010

Kersey, A. J., & Cantlon, J. F. (2016). Neural tuning to numerosity relates to perceptual tuning in 3- to 6-year-old children. *Journal of Neuroscience*, *37*(3), 512–522. http://doi.org/10.1523/JNEUROSCI.0065-16.2016

Konrad, K., Neufang, S., Thiel, C. M., Specht, K., Hanisch, C., Fan, J., … Fink, G. R. (2005). Development of attentional networks: An fMRI study with children and adults. *NeuroImage*, *28*(2), 429–439. http://doi.org/10.1016/j.neuroimage.2005.06.065

Kovas, Y., Giampietro, V., Viding, E., Ng, V., Brammer, M., Barker, G. J., … Plomin, R. (2009). Brain correlates of non-symbolic numerosity estimation in low and high mathematical ability children. *PLoS ONE*, *4*(2). http://doi.org/10.1371/journal.pone.0004587

Kucian, K., Loenneker, T., Dietrich, T., Dosch, M., Martin, E., & von Aster, M. (2006). Impaired neural networks for approximate calculation in dyscalculic children: a functional MRI study. *Behavioral and Brain Functions : BBF*, *2*, 31. http://doi.org/10.1186/1744-9081-2-31

Kucian, K., Loenneker, T., Martin, E., & von Aster, M. (2011). Non-symbolic numerical distance effect in children with and without developmental dyscalculia: a parametric fMRI study. *Developmental Neuropsychology*, *36*(February 2015), 741–762. http://doi.org/10.1080/87565641.2010.549867

Lancaster, J. L., Rainey, L. H., Summerlin, J. L., Freitas, C. S., Fox, P. T., Evans, A. C., … Mazziotta, J. C. (1997). Automated labeling of the human brain: A preliminary report on the development and evaluation of a forward-transform method. *Human Brain Mapping*, *5*(4), 238–242. http://doi.org/10.1002/(SICI)1097-0193(1997)5:4<238::AID-HBM6>3.0.CO;2-4

Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., … Fox, P. T. (2000). Automated Talairach Atlas labels for functional brain mapping. *Human Brain Mapping*, *10*(3), 120–131. http://doi.org/10.1002/1097-0193(200007)10:3<120::AID-HBM30>3.0.CO;2-8

Landerl, K., Bevan, A., & Butterworth, B. (2004). Developmental dyscalculia and basic numerical capacities: a study of 8–9-year-old students. *Cognition*, *93*(2), 99–125. http://doi.org/10.1016/j.cognition.2003.11.004

Landerl, K., Göbel, S. M., & Moll, K. (2013). Core deficit and individual manifestations of developmental dyscalculia (DD): The role of comorbidity. *Trends in Neuroscience and Education*, *2*(2), 38–42. http://doi.org/10.1016/j.tine.2013.06.002

Leibovich, T., & Henik, A. (2013). Magnitude processing in non-symbolic stimuli. *Frontiers in Psychology*, *4*(June), 375. http://doi.org/10.3389/fpsyg.2013.00375

Leibovich, T., Vogel, S. E., Henik, A., & Ansari, D. (2015). Asymmetric Processing of Numerical and Nonnumerical Magnitudes in the Brain: An fMRI Study. *Journal of Cognitive Neuroscience*, 1–11. http://doi.org/10.1162/jocn

Lemer, C., Dehaene, S., Spelke, E., & Cohen, L. (2003). Approximate quantities and exact number words: Dissociable systems. *Neuropsychologia*, *41*(14), 1942–1958. http://doi.org/10.1016/S0028-3932(03)00123-4

Levy, B. J., & Wagner, A. D. (2011). Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. *Annals of the New York Academy of Sciences*, *1224*(1), 40–62. http://doi.org/10.1111/j.1749-6632.2011.05958.x

Lewis, C., Hitch, G. J., & Walker, P. (1994). The prevalence of specific arithmetic difficulties and specific reading difficulties in 9- to 10-year-old boys and girls. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *35*(2), 283–292. http://doi.org/10.1111/j.1469-7610.1994.tb01162.x

Lyons, I. M., Ansari, D., & Beilock, S. L. (2012). Symbolic estrangement: evidence against a strong association between numerical symbols and the quantities they represent. *Journal of Experimental Psychology. General*, *141*(4), 635–41. http://doi.org/10.1037/a0027248

Lyons, I. M., & Beilock, S. L. (2011). Numerical ordering ability mediates the relation between number-sense and arithmetic competence. *Cognition*, *121*(2), 256–61. http://doi.org/10.1016/j.cognition.2011.07.009

Lyons, I. M., Nuerk, H.-C., & Ansari, D. (2015). Rethinking the implications of numerical ratio effects for understanding the development of representational precision and numerical processing across formats. *Journal of Experimental Psychology. General*, *144*(5), 1021–35. http://doi.org/10.1037/xge0000094

Mangun, G. R., Hopfinger, J. B., Kussmaul, C. L., Fletcher, E. M., & Heinze, H. (1997). Covariation in ERP and PET measures of Spatial Selective Attention in Human Extrastriate Cortex. *Human Brain Mapping*, *5*, 273–279.

Mazzocco, M. M. M., Feigenson, L., & Halberda, J. (2011). Impaired Acuity of the Approximate Number System Underlies Mathematical Learning Disability (Dyscalculia). *Child Development*, *82*(4), 1224–1237. http://doi.org/10.1111/j.1467-8624.2011.01608.x

Mazzocco, M. M. M., Feigenson, L., & Halberda, J. (2011). Preschoolers' Precision of the Approximate Number System Predicts Later School Mathematics Performance. *PLoS ONE*, *6*(9), e23749. http://doi.org/10.1371/journal.pone.0023749

Mazzocco, M. M. M., & Myers, G. F. (2003). Complexities in identifying and defining mathematics learning disability in the primary school-age years. *Annals of Dyslexia*. http://doi.org/10.1007/s11881-003-0011-7

Mazzocco, M. M. M., & Thompson, R. E. (2005). Kindergarten Predictors of Math Learning Disability. *Learning Disabilities Research & Practice : A Publication of the Division for Learning Disabilities, Council for Exceptional Children*, *20*(3), 142–155. http://doi.org/10.1111/j.1540-5826.2005.00129.x

Mazzocco, M., & Rasanen, P. (2013). Contributions of longitudinal studies to evolving definitions and knowledge of developmental dyscalculia. *Trends in Neuroscience and Education*. Elsevier. http://doi.org/10.1016/j.tine.2013.05.001

McCloskey, M. (1992). Cognitive mechanisms in numerical processing: evidence from acquired dyscalculia. *Cognition*, *44*(1–2), 107–157. http://doi.org/10.1016/0010-0277(92)90052-J

McLean, J. F., & Hitch, G. J. (1999). Working memory impairments in children with specific arithmetic learning difficulties. *Journal of Experimental Child Psychology*, *74*(3), 240–260. http://doi.org/10.1006/jecp.1999.2516

Mejias, S., Mussolin, C., Rousselle, L., Grégoire, J., & Noël, M.-P. (2012). Numerical and nonnumerical estimation in children with and without mathematical learning disabilities. *Child Neuropsychology*, *18*(6), 550–575. http://doi.org/10.1080/09297049.2011.625355

Merkley, R., & Ansari, D. (2010). Using eye tracking to study numerical cognition: the case of the ratio effect. *Experimental Brain Research. Experimentelle Hirnforschung. Expérimentation Cérébrale*, *206*(4), 455–60. http://doi.org/10.1007/s00221-010-2419-8

Merkley, R., Thompson, J., & Scerif, G. (2016). Of huge mice and tiny elephants: Exploring the relationship between inhibitory processes and preschool math skills. *Frontiers in Psychology*, *6*(JAN), 1–14. http://doi.org/10.3389/fpsyg.2015.01903

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex “Frontal Lobe” tasks: a latent variable analysis. *Cognitive Psychology*, *41*(1), 49–100. http://doi.org/10.1006/cogp.1999.0734

Moeller, K., Neuburger, S., Kaufmann, L., Landerl, K., & Nuerk, H. C. (2009). Basic number processing deficits in developmental dyscalculia: Evidence from eye tracking. *Cognitive Development*, *24*(4), 371–386. http://doi.org/10.1016/j.cogdev.2009.09.007

Morris, S. B., & DeShon, R. P. (2002). Combining effect size estimates in meta-analysis with repeated measures and independent-groups designs. *Psychological Methods*, *7*(1), 105–125. http://doi.org/10.1037//1082-989X.7.1.105

MOYER, R. S., & LANDAUER, T. K. (1967). Time required for Judgements of Numerical Inequality. *Nature*, *215*(5109), 1519–1520. http://doi.org/10.1038/2151519a0

Mussolin, C., De Volder, A., Grandin, C., Schlögel, X., Nassogne, M.-C., & Noël, M.-P. (2010). Neural correlates of symbolic number comparison in developmental dyscalculia. *Journal of Cognitive Neuroscience*, *22*(5), 860–874. http://doi.org/10.1162/jocn.2009.21237

Mussolin, C., De Volder, A., Grandin, C., Schlogel, X., Nassogne, M. C., & Noel, M. P. (2009). Neural Correlates of Symbolic Number Comparison in Developmental Dyscalculia. *Journal of Cognitive Neuroscience*, (Early Access), 1–15.

Mussolin, C., Mejias, S., Noël, M.-P., & Noel, M. P. (2010). Symbolic and nonsymbolic number comparison in children with and without dyscalculia. *Cognition*, *115*(1), 10–25. http://doi.org/10.1016/j.cognition.2009.10.006

Nieder, A. (2012). Supramodal numerosity selectivity of neurons in primate prefrontal and posterior parietal cortices. *Proceedings of the National Academy of Sciences*, *109*(29), 11860–11865. http://doi.org/10.1073/pnas.1204580109

Nieder, A. (2016). The neuronal code for number. *Nature Reviews Neuroscience*, *advance on*. http://doi.org/10.1038/nrn.2016.40

Nieder, A., & Dehaene, S. (2009). Representation of Number in the Brain. *Annual Review of Neuroscience*, *32*(1), 185–208. http://doi.org/10.1146/annurev.neuro.051508.135550

Nieder, A., & Miller, E. K. (2004). A parieto-frontal network for visual numerical information in the monkey. *Proceedings of the National Academy of Sciences*, *101*(19), 7457–7462. http://doi.org/10.1073/pnas.0402239101

Nosworthy, N., Bugden, S., Archibald, L., Evans, B., & Ansari, D. (2013). A Two-Minute Paper-and-Pencil Test of Symbolic and Nonsymbolic Numerical Magnitude Processing Explains Variability in Primary School Children's Arithmetic Competence. *PLoS ONE*, *8*(7), e67918. http://doi.org/10.1371/journal.pone.0067918

Odic, D., Hock, H., & Halberda, J. (2014). Hysteresis affects approximate number discrimination in young children. *Journal of Experimental Psychology. General*, *143*(1), 255–65. http://doi.org/10.1037/a0030825

Odic, D., Libertus, M. E., Feigenson, L., & Halberda, J. (2013). Developmental Change in the Acuity of Approximate Number and Area Representations. *Developmental Psychology*, *49*(6), 1103–1112. http://doi.org/10.1037/a0029472

Park, J., & Brannon, E. M. (2014). Improving arithmetic performance with number sense training: An investigation of underlying mechanism. *Cognition*, *133*(1), 188–200. http://doi.org/10.1016/j.cognition.2014.06.011

Park, J., & Brannon, E. M. (2016). How to interpret cognitive training studies: A reply to Lindskog & Winman. *Cognition*, *150*, 247–251. http://doi.org/10.1016/j.cognition.2016.02.012

Parsons, S., & Bynner, J. (2005). *Does Numeracy Matter More? NRDC (National Research and Development Centre for adult literacy and numeracy).[aRCK]*. London.

Paus, T. (2001). Primate anterior cingulate cortex: where motor control, drive and cognition interface. *Nature Reviews. Neuroscience*, *2*(6), 417–424. http://doi.org/10.1038/35077500

Petersen, S. ., & Posner, M. (2012). The Attention System of the Human Brain: 20 Years After. *Annual Review of Neuroscience*, *21*(35), 73–89. http://doi.org/10.1146/annurev-neuro-062111-150525.The

Petersen, S. E., & Posner, M. I. (2012). The Attention System of the Human Brain: 20 Years After. *Annual Review of Neuroscience*, *21*(35), 73–89. http://doi.org/10.1146/annurev-neuro-062111-150525.The

Piazza, M., Facoetti, A., Trussardi, A. N., Berteletti, I., Conte, S., Lucangeli, D., … Zorzi, M. (2010). Developmental trajectory of number acuity reveals a severe impairment in developmental dyscalculia. *Cognition*.

Piazza, M., Facoetti, A., Trussardi, A. N., Berteletti, I., Conte, S., Lucangeli, D., … Zorzi, M. (2010). Developmental trajectory of number acuity reveals a severe impairment in developmental dyscalculia. *Cognition*, *116*(1), 33–41. http://doi.org/10.1016/j.cognition.2010.03.012

Piazza, M., Izard, V., Pinel, P., Le Bihan, D., & Dehaene, S. (2004). Tuning Curves for Approximate Numerosity in the Human Intraparietal Sulcus. *Neuron*, *44*(3), 547–555. http://doi.org/10.1016/j.neuron.2004.10.014

Piazza, M., Pica, P., Izard, V., Spelke, E. S., & Dehaene, S. (2013). Education enhances the acuity of the nonverbal approximate number system. *Psychological Science*, *24*(6), 1037–43. http://doi.org/10.1177/0956797612464057

Pica, P., Lemer, C., Izard, V., & Dehaene, S. (2004). Exact and approximate arithmetic in an Amazonian indigene group. *Science (New York, N.Y.)*, *306*(5695), 499–503. http://doi.org/10.1126/science.1102085

Pinel, P., Dehaene, S., Rivière, D., & LeBihan, D. (2001). Modulation of parietal activation by semantic distance in a number comparison task. *NeuroImage*, *14*(5), 1013–1026. http://doi.org/10.1006/nimg.2001.0913

Posner, M. I., & Petersen, S. E. (1990). The Attention System Of The Human Brain. *Annual Review of Neuroscience*, *13*(1), 25–42. http://doi.org/10.1146/annurev.neuro.13.1.25

Prager, E. O., Sera, M. D., & Carlson, S. M. (2016). Executive function and magnitude skills in preschool children. *Journal of Experimental Child Psychology*, *147*, 126–139. http://doi.org/10.1016/j.jecp.2016.01.002

Price, G. R., & Ansari, D. (2011). Symbol processing in the left angular gyrus: Evidence from passive perception of digits. *NeuroImage*, *57*(3), 1205–1211. http://doi.org/10.1016/j.neuroimage.2011.05.035

Price, G. R., & Fuchs, L. S. (2016). The Mediating Relation between Symbolic and Nonsymbolic Foundations of Math Competence. *Plos One*, *11*(2), e0148981. http://doi.org/10.1371/journal.pone.0148981

Price, G. R., Holloway, I., Räsänen, P., Vesterinen, M., & Ansari, D. (2007). Impaired parietal magnitude processing in developmental dyscalculia. *Current Biology*, *17*(24), R1042–R1043. http://doi.org/10.1016/j.cub.2007.10.013

Price, G. R., Mazzocco, M. M. M., & Ansari, D. (2013). Why mental arithmetic counts: brain activation during single digit arithmetic predicts high school math scores. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *33*(1), 156–63. http://doi.org/10.1523/JNEUROSCI.2936-12.2013

Price, G. R., Palmer, D., Battista, C., & Ansari, D. (2012). Nonsymbolic numerical magnitude comparison: Reliability and validity of different task variants and outcome measures, and their relationship to arithmetic achievement in adults. *Acta Psychologica*, *140*(1), 50–57. http://doi.org/10.1016/j.actpsy.2012.02.008

Price, G. R., & Wilkey, E. D. (2017). Cognitive mechanisms underlying the relation between nonsymbolic and symbolic magnitude processing and their relation to math. *Cognitive Development*, *44*(September), 139–149. http://doi.org/10.1016/j.cogdev.2017.09.003

Price, G. R., & Wilkey, E. D. (2017). Cognitive mechanisms underlying the relation between nonsymbolic and symbolic magnitude processing and their relation to math. *Cognitive Development*, *44*. http://doi.org/10.1016/j.cogdev.2017.09.003

Price, G. R., Wilkey, E. D., Yeo, D. J., & Cutting, L. E. (2016). The relation between 1st grade grey matter volume and 2nd grade math competence. *NeuroImage*, *124*, 232–237.

http://doi.org/10.1016/j.neuroimage.2015.08.046

Rajimehr, R., Devaney, K. J., Bilenko, N. Y., Young, J. C., & Tootell, R. B. H. (2011). The "' Parahippocampal Place Area '" Responds Preferentially to High Spatial Frequencies in Humans and Monkeys. *PLoS Biology*, *9*(4). http://doi.org/10.1371/journal.pbio.1000608

Ramani, G. B., & Siegler, R. S. (2008). Promoting broad and stable improvements in low-income children's numerical knowledge through playing number board games. *Child Development*, *79*(2), 375–394. http://doi.org/10.1111/j.1467-8624.2007.01131.x

Ranpura, A., Isaacs, E., Edmonds, C., Rogers, M., Lanigan, J., Singhal, A., … Butterworth, B. (2013). Developmental trajectories of grey and white matter in dyscalculia. *Trends in Neuroscience and Education*, *2*(2), 56–64. http://doi.org/10.1016/j.tine.2013.06.007

Räsänen, P., Salminen, J., Wilson, A. J., Aunio, P., & Dehaene, S. (2009). Computer-assisted intervention for children with low numeracy skills. *Cognitive Development*, *24*(4), 450–472. http://doi.org/10.1016/j.cogdev.2009.09.003

Rathé, S., Torbeyns, J., Hannula-Sormunen, M. M., De Smedt, B., & Verschaffel, L. (2016). Spontaneous focusing on numerosity: A review of recent research. *Mediterrean Journal for Research in Mathematics Education*, *15*(January), 1–25.

Ritchie, S. J., & Bates, T. C. (2013). Enduring Links From Childhood Mathematics and Reading Achievement to Adult Socioeconomic Status. *Psychological Science*, *24*(7), 1301–1308. http://doi.org/10.1177/0956797612466268

Rivera-Batiz, F. L. (1992). Quantitative Literacy and the Likelihood of Employment among Young Adults in the United States. *The Journal of Human Resources*, *27*(2), 313–328. Retrieved from http://www.jstor.org/stable/145737

Rivera, S. M., Reiss, a L., Eckert, M. a, & Menon, V. (2005). Developmental changes in mental arithmetic: evidence for increased functional specialization in the left inferior parietal cortex. *Cerebral Cortex (New York, N.Y. : 1991)*, *15*(11), 1779–90. http://doi.org/10.1093/cercor/bhi055

Rosenberg-Lee, M., Ashkenazi, S., Chen, T., Young, C. B., Geary, D. C., & Menon, V. (2015). Brain hyper-connectivity and operation-specific deficits during arithmetic problem solving in children with developmental dyscalculia. *Developmental Science*, *18*(3), 351–372. http://doi.org/10.1111/desc.12216

Rotzer, S., Kucian, K., Martin, E., Aster, M. Von, Klaver, P., & Loenneker, T. (2008). Optimized voxel-based morphometry in children with developmental dyscalculia. *NeuroImage*, *39*(1), 417–422. http://doi.org/10.1016/j.neuroimage.2007.08.045

Rotzer, S., Loenneker, T., Kucian, K., Martin, E., Klaver, P., & von Aster, M. (2009). Dysfunctional neural network of spatial working memory contributes to developmental dyscalculia. *Neuropsychologia*, *47*(13), 2859–2865. http://doi.org/10.1016/j.neuropsychologia.2009.06.009

Rourke, B. P., & Conway, J. A. (1997). Disabilities of arithmetic and mathematical reasoning perspectives from neurology and neuropsychology. *Journal of Learning Disabilities*, *30*(1), 34–46.

Rousselle, L., & Noël, M.-P. (2007). Basic numerical skills in children with mathematics learning disabilities: a comparison of symbolic vs non-symbolic number magnitude processing. *Cognition*, *102*(3), 361–95. http://doi.org/10.1016/j.cognition.2006.01.005

Rykhlevskaia, E., Uddin, L. Q., Kondos, L., & Menon, V. (2009). Neuroanatomical correlates of developmental dyscalculia: combined evidence from morphometry and tractography. *Frontiers in Human Neuroscience*, *3*(November), 51. http://doi.org/10.3389/neuro.09.051.2009

Schneider, M., Beeres, K., Coban, L., Merz, S., Susan Schmidt, S., Stricker, J., & De Smedt, B. (2017). Associations of non-symbolic and symbolic numerical magnitude processing with mathematical competence: a meta-analysis. *Developmental Science*, *20*(3), e12372. http://doi.org/10.1111/desc.12372

Schwenk, C., Sasanguie, D., Kuhn, J. T., Kempe, S., Doebler, P., & Holling, H. (2017). (Non-)symbolic magnitude processing in children with mathematical difficulties: a meta-analysis. *Research in Developmental Disabilities*, *64*, 152–167. http://doi.org/10.1016/j.ridd.2017.03.003

Seghier, M. (2012). The Angular Gyrus: Multiple Functions and Multiple Subdivisions. *The Neuroscientist*, *19*(1), 43–61. http://doi.org/10.1177/1073858412440596

Shalev, R. S. (2004). Developmental dyscalculia. *Journal of Child Neurology*, *19*(10).

Shalev, R. S., Auerbach, J., & Gross-Tsur, V. (1995). Developmental dyscalculia behavioral and attentional aspects: a research note. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *36*(7), 1261–8. http://doi.org/10.1111/j.1469-7610.1995.tb01369.x

Shalev, R. S., Auerbach, J., Manor, O., & Gross-Tsur, V. (2000). Developmental dyscalculia: prevalence and prognosis. *European Child & Adolescent Psychiatry*, *9*(S2), S58–S64. http://doi.org/10.1007/s007870070009

Siegel, L. S., & Ryan, E. B. (1989). The Development of Working Memory in Normally Achieving and Subtypes of Learning Disabled Children. *Child Development*, *60*(4), 973. http://doi.org/10.2307/1131037

Simon, O., Mangin, J. F., Cohen, L., Le Bihan, D., & Dehaene, S. (2002). Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. *Neuron*, *33*(3), 475–487. http://doi.org/10.1016/S0896-6273(02)00575-5

Sokolowski, H. M., Fias, W., Mousa, A., & Ansari, D. (2016). Common and distinct brain regions in both parietal and frontal cortex support symbolic and nonsymbolic number processing in humans: A functional neuroimaging meta-analysis. *NeuroImage*, (February), 0–1. http://doi.org/10.1016/j.neuroimage.2016.10.028

Starkey, P., Spelke, E. S., & Gelman, R. (1990). Numerical abstraction by human infants. *Cognition*, *36*(2), 97–127. http://doi.org/10.1016/0010-0277(90)90001-Z

Swanson, H. L., & Sachse-Lee, C. (2001). Mathematical problem solving and working memory in children with learning disabilities: both executive and phonological processes are important. *Journal of Experimental Child Psychology*, *79*(3), 294–321. http://doi.org/10.1006/jecp.2000.2587

Szkudlarek, E., & Brannon, E. M. (2017). Does the Approximate Number System Serve as a Foundation for Symbolic Mathematics? *Language Learning and Development*, *13*(2), 171–190.

http://doi.org/10.1080/15475441.2016.1263573

Szucs, D., Devine, A., Soltesz, F., Nobes, A., & Gabriel, F. (2013). Developmental dyscalculia is related to visuo-spatial memory and inhibition impairment. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *49*(10), 2674–88. http://doi.org/10.1016/j.cortex.2013.06.007

Szűcs, D., & Goswami, U. (2013). Developmental dyscalculia: Fresh perspectives. *Trends in Neuroscience and Education*, *2*(2), 33–37. http://doi.org/10.1016/j.tine.2013.06.004

Szűcs, D., & Myers, T. (2016). A critical analysis of design, facts, bias and inference in the approximate number system training literature: a systematic review. *Trends in Neuroscience and Education*. http://doi.org/10.1016/j.tine.2016.11.002

Szűcs, D., Nobes, A., Devine, A., Gabriel, F. C., & Gebuis, T. (2013). Visual stimulus parameters seriously compromise the measurement of approximate number system acuity and comparative effects between adults and children. *Frontiers in Psychology*, *4*(July), 444. http://doi.org/10.3389/fpsyg.2013.00444

Takayama, Y., Sugishita, M., Akiguchi, I., & Kimura, J. (1994). Isolated acalculia due to left parietal lesion. *Archives of Neurology*, *51*(3), 286–91. http://doi.org/10.1001/archneur.1994.00540150084021

Talairach, J., & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain. 3-Dimensional proportional system: an approach to cerebral imaging.

Updegraff, K. A., Eccles, J. S., Barber, B. L., & O'brien, K. M. (1996). Course enrollment as self-regulatory behavior: Who takes optional high school math courses? *Learning and Individual Differences*. http://doi.org/10.1016/S1041-6080(96)90016-3

Vaidya, C. J., Bunge, S. A., Dudukovic, N. M., Zalecki, C. A., Elliott, G. R., & Gabrieli, J. D. E. (2005). Altered neural substrates of cognitive control in childhood ADHD: Evidence from functional magnetic resonance imaging. *The American Journal of Psychiatry*, *162*(9), 1605–1613. http://doi.org/162/9/1605 [pii]\n10.1176/appi.ajp.162.9.1605

van Veen, V., Cohen, J. D., Botvinick, M. M., Stenger, V. A., & Carter, C. S. (2001). Anterior Cingulate Cortex, Conflict Monitoring, and Levels of Processing. *NeuroImage*, *14*(6), 1302–1308. http://doi.org/10.1006/nimg.2001.0923

Verguts, T., & Fias, W. (2004). Representation of number in animals and humans: a neural model. *Journal of Cognitive Neuroscience*, *16*(9), 1493–504. http://doi.org/10.1162/0898929042568497

Viarouge, A., Courtier, P., Hoppe, M., Melnik, J., Houdé, O., & Borst, G. (2017). Spontaneous orientation towards irrelevant dimensions of magnitude and numerical acuity. *Learning and Instruction*, 1–8. http://doi.org/10.1016/j.learninstruc.2017.09.004

Viswanathan, P., & Nieder, A. (2013). Neuronal correlates of a visual "sense of number" in primate parietal and prefrontal cortices. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(27), 11187–92. http://doi.org/10.1073/pnas.1308141110

Vogel, S. E., Goffin, C., & Ansari, D. (2015). Developmental specialization of the left parietal cortex for the semantic representation of Arabic numerals: An fMR-Adaptaton study. *Developmental*

Cognitive Neuroscience, *12*(2015), 61–73. http://doi.org/10.1016/j.dcn.2014.12.001

Vogel, S. E., Goffin, C., Bohnenberger, J., Koschutnig, K., Reishofer, G., Grabner, R. H., & Ansari, D. (2017). Parietal adaptation to symbolic number in both the visual and auditory modality: evidence from fMRI adaptation. *NeuroImage*, *153*(March), 16–27. http://doi.org/10.1016/j.neuroimage.2017.03.048

Wang, J., Odic, D., Halberda, J., & Feigenson, L. (2016). Changing the precision of preschoolers' approximate number system representations changes their symbolic math performance. *Journal of Experimental Child Psychology*, *147*, 82–99. http://doi.org/10.1016/j.jecp.2016.03.002

Warrington, E. K. (1982). The fractionation of arithmetical skills: a single case study. *The Quarterly Journal of Experimental Psychology. A, Human Experimental Psychology*, *34*(Pt 1), 31–51. http://doi.org/10.1080/14640748208400856

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn : A Functional Connectivity Toolbox for Correlated and Anticorrelated Brain Networks. *Brain Connectivity*, *2*(3), 125–141. http://doi.org/10.1089/brain.2012.0073

Wilkey, E. D., Barone, J. C., Mazzocco, M. M. M., Vogel, S. E., & Price, G. R. (2017). The effect of visual parameters on neural activation during nonsymbolic number comparison and its relation to math competency. *NeuroImage*, *159*(August), 430–442. http://doi.org/10.1016/j.neuroimage.2017.08.023

Wilkey, E. D., Barone, J. C., Mazzocco, M. M. M., Vogel, S. E., & Price, G. R. (2017). The effect of visual parameters on neural activation during nonsymbolic number comparison and its relation to math competency. *NeuroImage*, *159*. http://doi.org/10.1016/j.neuroimage.2017.08.023

Willcutt, E. G., Petrill, S. A., Wu, S., Boada, R., DeFries, J. C., Olson, R. K., & Pennington, B. F. (2013). Comorbidity Between Reading Disability and Math Disability. *Journal of Learning Disabilities*, *46*(6), 500–516. http://doi.org/10.1177/0022219413477476

Wilson, A. J., & Dehaene, S. (2007). Human behavior, learning, and the developing brain: Atypical development. In *Number sense and developmental dyscalculia.* (pp. 212–238).

Wilson, A. J., Andrewes, S. G., Struthers, H., Rowe, V. M., Bogdanovic, R., & Waldie, K. E. (2015). Dyscalculia and dyslexia in adults: Cognitive bases of comorbidity. *Learning and Individual Differences*, *37*, 118–132. http://doi.org/10.1016/j.lindif.2014.11.017

Woodcock, R. W., McGrew, K. S., & Mather, N. (2001). Woodcock–Johnson III Tests of Achievement. Itasca, IL: Riverside.

Wright, A., & Diamond, A. (2014). An effect of inhibitory load in children while keeping working memory load constant. *Frontiers in Psychology*, *5*(MAR), 1–9. http://doi.org/10.3389/fpsyg.2014.00213

Xu, F., & Spelke, E. S. (2000). Large number discrimination in 6-month-old infants. *Cognition*, *74*(1), B1–B11. http://doi.org/10.1016/S0010-0277(99)00066-9

Yang, Y., Zhong, N., Friston, K., Imamura, K., Lu, S., Li, M., … Hu, B. (2017). The functional architectures of addition and subtraction: Network discovery using fMRI and DCM. *Human Brain*

Mapping, *0*(January). http://doi.org/10.1002/hbm.23585

Zago, L., Petit, L., Turbelin, M. R., Andersson, F., Vigneau, M., & Tzourio-Mazoyer, N. (2008). How verbal and spatial manipulation networks contribute to calculation: An fMRI study. *Neuropsychologia*, *46*(9), 2403–2414. http://doi.org/10.1016/j.neuropsychologia.2008.03.001

Zago, L., & Tzourio-Mazoyer, N. (2002). Distinguishing visuospatial working memory and complex mental calculation areas within the parietal lobes. *Neuroscience Letters*, *331*(1), 45–49. http://doi.org/10.1016/S0304-3940(02)00833-9

Zamarian, L., Ischebeck, A., & Delazer, M. (2009). Neuroscience of learning arithmetic-Evidence from brain imaging studies. *Neuroscience and Biobehavioral Reviews*, *33*(6), 909–925. http://doi.org/10.1016/j.neubiorev.2009.03.005