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Common and Distinct Brain Regions Support Numerical and Non-numerical Magnitude Processing: A Functional Neuroimaging Meta-Analysis

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A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

COMMON AND DISTINCT BRAIN REGIONS SUPPORT NUMERICAL AND NON-NUMERICAL MAGNITUDE PROCESSING: A FUNCTIONAL NEUROIMAGING META-ANALYSIS

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by

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Abstract

A current debate is whether number is processed using a number-specific system or a general magnitude processing system used for non-numerical magnitudes such as space. Activation likelihood estimation (ALE) was used to conduct the first quantitative meta-analysis of 20 empirical neuroimaging papers examining neural activation during numerical and non-numerical magnitude processing. Foci were compiled to generate probabilistic maps of activation for symbolic numerical magnitudes, nonsymbolic numerical magnitudes and non-numerical magnitudes. Conjunction analyses revealed overlapping activation for symbolic, nonsymbolic and non-numerical magnitudes in frontal and parietal lobes. Contrast analyses revealed specific activation in the left superior parietal lobule (SPL) and right inferior parietal lobule (IPL) for symbolic numerical magnitudes. In contrast, anterior right IPL was specifically activated for nonsymbolic numerical magnitudes. No parietal regions were activated for non-numerical that were not also activated for numerical magnitudes. Therefore, numbers are processed using both a generalized magnitude system and format specific number regions.

Keywords

Numerical Magnitude, Non-numerical Magnitude, Neural Specialization, Functional Magnetic Resonance Imaging, Symbolic, Nonsymbolic

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Chapter 1

1 Introduction

Over the last several decades, the question of how the human brain represents numbers has been addressed through a multitude of neuroimaging experiments. The results from this rapidly growing body of research are consistent with a large body of neuropsychological evidence (Cipolotti, Butterworth, & Denes, 1991; Dehaene, Piazza, Pinel, & Cohen, 2003). Specifically, neuroimaging research, like preceding neuropsychological studies, regularly implicates the bilateral parietal lobes and specifically, the intrapartietal sulcus (IPS) as an important brain region for processing the quantity of a discrete set of items (for reviews see: Ansari, 2008; Brannon, 2006; Dehaene et al., 2003; Nieder, 2005). Hereafter, the quantity of a discrete set of items will be referred to as a numerical magnitude.

1.1 Numerical Magnitude Processing

In the case of numerical magnitudes, humans have the unique ability to represent numbers either symbolically, such as with Arabic symbols (2) or number words (two) or nonsymbolically, appearing as an array of items (••). The system used to process nonsymbolic (••) numbers, referred to as the approximate number system (ANS), is thought to be innate, meaning that infants are born with the ability to process nonsymbolic numerical magnitudes (Cantlon, Libertus, et al., 2009) and have long evolutionary history (Brannon, 2006; Dehaene, Dehaene-Lambertz, & Cohen, 1998). In contrast, the acquisition of the culturally acquired, uniquely human ability to process abstract numerical symbols (2 or two) is a product of learning and development and has emerged recently in human evolution (Ansari, 2008; Coolidge & Overmann, 2012). Because different formats of numerical magnitudes can represent the same quantity, numerical magnitudes are said to have an abstract (i.e. format-independent) quality. As a result, the field of numerical cognition has rested upon the theoretical foundation that symbolic and nonsymbolic numbers have the same underlying representations (Dehaene, Dehaene-Lambertz, & Cohen, 1998). For decades, researchers have canvassed the brain in search of neural responses associated with abstract representations of numerical magnitudes (Brannon, 2006; Cantlon, Libertus, et al., 2009; Dehaene et al., 1998, 2003; Piazza, Pinel, Le Bihan, & Dehaene, 2007).

A large body of research has identified bilateral inferior parietal regions as brain regions that respond to numerical magnitudes across stimulus formats (e.g. Dehaene et al., 2003). This research revealed that the IPS was activated by numerical magnitudes when the numerical information was presented symbolically, either as Arabic digits (Ansari, Garcia, Lucas, Hamon, & Dhital, 2005; Chochon, Cohen, van de Moortele, & Dehaene, 1999; Holloway, Price, & Ansari, 2010; Pesenti, Thioux, Seron, & Volder, 2000) number words (Ansari, Fugelsang, Dhital, & Venkatraman, 2006), or nonsymbolic representations of numerical magnitude, such as dot arrays (Ansari & Dhital, 2006; Holloway, Price, & Ansari, 2010; Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004; Piazza, Pinel, Le Bihan, & Dehaene, 2007; Venkatraman, Ansari, & Chee, 2005). This activation in the IPS during numerical processing was also found when the stimuli were presented across visual and auditory domains (Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003). Together, these results suggest that the IPS hosts a format and modality independent numerical magnitude representation. However, the finding that the

IPS is consistently activated across varying task types and methodologies does not necessarily imply that number is represented using only an abstract format independent system.

In recent years, there has been a growing interest in the distinction between the neural correlates of symbolic processing and nonsymbolic processing (Holloway & Ansari, 2010; Lyons, Ansari, & Beilock, 2014; Shuman & Kanwisher, 2004; Venkatraman et al., 2005). Recent empirical research has highlighted striking differences in the brain activation patterns of numerical stimuli based on stimulus format (Ansari, 2007; Cantlon, Libertus, et al., 2009; Holloway et al., 2010; Piazza et al., 2007; Venkatraman et al., 2005). Right lateralized parietal and frontal regions have been found to show greater activation for nonsymbolic addition compared to symbolic addition (Venkatraman et al., 2005). However, brain regions in the left IPS are more finely tuned to numerical magnitudes presented as Arabic symbols compared to nonsymbolic dot arrays (Piazza et al., 2007). Holloway et al., (2010) directly tested whether the functional neuroanatomy underlying symbolic and nonsymbolic processing is overlapping or distinct. They found overlapping activation in the right IPL, which was activated by both symbolic and nonsymbolic stimuli. They also found that distinct brain regions responded to symbolic and nonsymbolic number respectively. Specifically, symbolic number processing recruited the left angular and left superior temporal gyri while nonsymbolic number processing recruited regions in the right posterior SPL (Holloway et al., 2010). These findings imply that distinct brain regions support format-general and format specific processing of numerical magnitudes.

Although the primary focus in the field of numerical cognition has been on the relationship between activation in the parietal cortex and number processing, converging evidence has shown that brain regions in the bilateral prefrontal and precentral cortex are consistently activated during numerical processing (Ansari et al., 2005; Pinel, Dehaene, Rivière, & LeBihan, 2001). The frontal cortex has been consistently implicated as important for number processing in single-cell recordings from neurons in non-human primates (Nieder, Freedman, & Miller, 2002; Nieder & Miller, 2004). Additionally, developmental imaging studies have documented that brain activation during numerical processing shifts from the frontal cortex to the parietal cortex across development (Ansari et al., 2005; Cantlon, Brannon, Carter, & Pelphrey, 2006; Kaufmann et al., 2006). A quantitative meta-analysis that synthesized studies examining brain regions that are correlated with basic number processing and calculation tasks in adults further support the idea that the frontal cortex is important for number processing in adults (Arsalidou & Taylor, 2011). This meta-analysis revealed that large regions of activation in both the parietal and frontal cortex support basic number and calculation tasks. Results showed that calculation tasks elicited greater activation in the prefrontal cortex compared to basic number tasks. Consequently, these authors concluded that the prefrontal cortices are essential in number and computational tasks (Arsalidou & Taylor, 2011). Together, these studies suggest that a fronto-parietal network may support the processing of numerical information. Although the large body of research examining numerical processing in adults concluded that the parietal lobes support numerical processing, it remains unclear whether frontal activation is as consistent as parietal activation during numerical processing.

1.2 Non-numerical Magnitude Processing

The longstanding predominant view in the field of numerical cognition is that number operates within its own domain (Brannon, 2006; Dehaene et al., 1998, 2003; Piazza et al., 2007). However, researchers have consistently documented striking behavioural similarities between estimating numerical quantities and non-numerical magnitudes such as space and time (Cantlon, Platt, & Brannon, 2009; Cohen Kadosh, Lammertyn, & Izard, 2008; Moyer & Landauer, 1967). Because of this, it has been fiercely debated whether the human brain contains a number module that is specialized for representing numerical magnitudes or if numerical processing operates within a more general system used to process both numerical and non-numerical magnitudes (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008; Simon, 1999; Walsh, 2003). A non-numerical magnitude refers to the size or extent of a continuous dimension such as space, time or luminance.

Recent innovations in neuroimaging techniques have allowed researchers to explicitly test whether number is processed using a generalized magnitude system or a specific number system. Researchers have examined the overlap between neural populations underlying numerical and non-numerical magnitudes. Several studies asked participants to make comparative judgments on different kinds of numerical and non-numerical magnitudes (e.g. Cohen Kadosh et al., 2005; Dormal, Andres, & Pesenti, 2012; Dormal & Pesenti, 2009; Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003; Pinel, Piazza, Le Bihan, & Dehaene, 2004). The majority of these studies have found both distinct and overlapping neural populations for numerical and non-numerical magnitudes (Cohen Kadosh, Lammertyn, et al., 2008). The first empirical paper that studied brain activation during numerical and non-numerical magnitude processing used positron emission tomography (PET) to examine neural activity while subjects compared line lengths, angle size and numerical magnitude of two digit Arabic number symbols (Fias et al., 2003). This study found that the left IPS responded to both numerical and non-numerical magnitude comparison tasks, supporting the hypothesis that different magnitudes are represented by a common mechanism. However, they also found greater activation for number processing in a site anterior to the left IPS (Fias et al., 2003). Similarly, functional magnetic resonance imaging (fMRI) experiments revealed brain activation in a widespread cortical network, including the bilateral IPS, while subjects compared the numerical magnitude, physical size and brightness of Arabic number symbols (Cohen Kadosh et al., 2005; Pinel, Piazza, Le Bihan, & Dehaene, 2004). More specifically, Pinel et al., (2004) found that number and size engaged in a common parietal spatial network and size and luminance shared occipito-temporal perceptual representations. Similarly, Cohen Kadosh et al., (2005) found that regions in the left IPS were activated during processing of number, size and luminance. Number-specific activation was found in the left IPS and right temporal regions (Cohen Kadosh et al., 2005). These pioneering studies, all of which used a symbolic number format, suggest that converging and distinct neural populations support symbolic number processing and non-numerical magnitude processing (Cohen Kadosh et al., 2005; Fias et al., 2003; Pinel et al., 2004).

Distinct and overlapping brain regions for number and non-numerical magnitudes were also revealed when number was represented nonsymbolically, as a discrete array. For instance, Castelli, Glaser, and Butterworth, (2006) found more bilateral IPS activation during processing of discrete stimuli compared to processing of continuous stimuli. In a similar vein, Dormal and Pesenti, (2009) examined brain regions associated with discrete nonsymbolic numbers compared to continuous magnitudes (line length). They found overlapping activation for numerical and non-numerical stimuli in the right IPS. Additionally, they revealed distinct activation in the left IPS during nonsymbolic number processing. The notion that the right IPS underlies a common magnitude system was further supported by Dormal et al., (2012) who examined neural activation during nonsymbolic number processing compared to duration processing. Only one study to date has examined overlapping and distinct neural representations underlying symbolic (positive and negative integers) numbers, nonsymbolic numbers (dot arrays) and non-numerical magnitudes (disk size) (Chassy & Grodd, 2012). Specifically, this study examined the distinction between brain activation patterns during processing of dots and disks compared to symbolic (positive and negative digit) formats. In accordance with previous research, the right IPS was activated during processing of dots and disks, as well as during processing of symbolic numbers. Additionally, symbolic number processing was correlated with activation in the left IPS (Chassy & Grodd, 2012). Taken together, these studies suggest that the right IPS underlies a common magnitude system and additional brain regions, such as the left IPS, are specific to both symbolic and nonsymbolic number.

Another behavioural signature that supports the notion that there is overlap between the systems supporting numerical and non-numerical magnitude processing is the size congruity effect (Algom, Dekel, & Pansky, 1996; Schwarz & Ischebeck, 2003; Tzelgov & Henik, 1983). To evoke this effect, a participant is presented with two Arabic digits or number words that are different physical sizes. The participant must choose which of the two digits has a larger magnitude. The size congruity effect is the outcome that participants are faster and more accurate at determining which of two digits has a larger magnitude in congruent trials (the Arabic numeral with the larger semantic magnitude is also physically larger: 2 vs. 5) compared to incongruent trials (the numeral with the larger semantic magnitude physically smaller: 2 vs. 5) (Algom et al., 1996; Cohen Kadosh, Cohen Kadosh, Linden, et al., 2007; Rubinsten, Henik, Berger, & Shahar-Shalev, 2002; Schwarz & Ischebeck, 2003; Tzelgov & Henik, 1983). The size congruency effect is the conflict that occurs when the physical size of the number is incongruent with the quantity that the number represents. A congruency effect also occurs when the numerical magnitude of an Arabic number (symbol) is congruent or incongruent with luminance level of the symbol. (Cohen Kadosh, Cohen Kadosh, & Henik, 2008). Several neuroimaging studies have demonstrated that the interaction between physical size and numerical magnitude modulates activation in the IPS (Kaufmann et al., 2005; Pinel et al., 2004; Tang, Critchley, Glaser, Dolan, & Butterworth, 2006). However, this relationship between the size congruity effect and IPS activation is inconsistent (Ansari et al., 2006). For example, Ansari et al., (2006) revealed that the bilateral IPS is modulated by numerical distance, but not by size congruency or the interaction between distance and size congruency. This supports the notion that some regions of the IPS are related to number specific processing. Overall, these data lend support to the hypothesis that the bilateral parietal lobes support numerical and non-numerical general magnitude processing.

Taken together, research studying the neural overlap of numerical and non-numerical magnitudes has produced three major findings. First, convergent and distinct brain regions support numerical and non-numerical magnitude processing. Second, the bilateral IPS is implicated as a brain region that supports magnitude processing. Third, regions along the right IPS underlie general magnitude judgments and the left IPS is specialized for processing numerical magnitudes. These conclusions, which arise from studies using magnitude comparison tasks, are further supported by studies using other paradigms such as estimation tasks (Leroux et al., 2009; Vogel, Grabner, Schneider, Siegler, & Ansari, 2013), ordinal tasks (Fulbright, Manson, Skudlarski, Lacadie, & Gore, 2003; Lyons & Beilock, 2013), and identification tasks (Cappelletti, Lee, Freeman, & Price, 2010; Eger et al., 2003).

1.3 Qualitative Meta-Analyses

This consensus, discussed in several review papers (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008; Walsh, 2003) is however *qualitative in nature*. Quantitative statistics that evaluate the consistency across different findings have thus far not been used to probe this conclusion. Two qualitative meta-analyses used Caret software (Van Essen, 2012; Van Essen et al., 2001) to examine brain activation patterns underlying magnitude processing across studies (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008). Caret software is a tool that is widely used to visualize neuroimaging data by projecting the spatial mappings of brain activation patterns onto a population-averaged brain (Van Essen, 2012; Van Essen et al., 2001). Qualitative meta-analysis by Cantlon, Platt, et al., (2009) and Cohen Kadosh, Lammertyn, et al., (2008) used Carat software to depict brain activation patterns from multiple studies that examined different kinds of magnitudes (e.g. number, space, time, luminance, pitch). The spatial distribution of IPS activation across empirical studies illustrates that the IPS hosts overlapping domain-general and domain-specific neural populations for numbers compared to non-numerical magnitudes (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008). This method of merging foci from several experiments into a single figure or table has been the most common approach that researchers have used to combine data across studies (Turkeltaub, Eden, Jones, & Zeffiro, 2002). However, using this technique requires judgments of convergence or divergence across studies that are largely subjective. This subjectivity is undesirable for rigorous evaluation of the convergence of neuroimaging findings. Therefore, quantitative meta-analytic tools, such as activation likelihood estimation (ALE) are critical for synthesizing studies with varying methodologies and inconsistent findings (Eickhoff, Laird, Grefkes, Wang, et al., 2009; Turkeltaub et al., 2012, 2002).

While converging evidence supports the notion that numerical and non-numerical magnitude processing rely on distinct and overlapping brain regions, this evidence has never been quantitatively synthesized. Specifically, previous meta-analyses qualitatively mapped brain activation patterns, but did not statistically test for the convergence of activation reported on these maps. Therefore, it remains unclear which brain areas underlie general magnitude processing and which specifically support number processing. Additionally, previous meta-analyses did not investigate how the brain activation patterns during numerical magnitude processing differ based on number format (i.e. symbolic vs. nonsymbolic). Instead, these qualitative meta-analyses grouped symbolic and nonsymbolic numerical stimuli into a general term: number (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008). However, it is critical to examine symbolic and nonsymbolic numerical stimuli separately since a large body of empirical research highlighted striking differences in the brain activation patterns of symbolic compared to nonsymbolic numerical magnitude processing (Ansari, 2007; Cantlon, Libertus, et al., 2009; Holloway et al., 2010; Piazza et al., 2007; Venkatraman et al., 2005).

1.4 The Current Study

There has been an emergence of quantitative meta-analytic techniques that use coordinate-based approaches to statistically determine concordance across functional imaging studies (Eickhoff, Laird, Grefkes, Wang, et al., 2009; Turkeltaub et al., 2012, 2002). These methods minimize subjectivity of meta-analyses by using statistical models to determine inter-study trends. The present study uses Activation Likelihood Estimation (ALE) to examine brain activation patterns underlying numerical and non-numerical magnitude processing. The aim of an ALE meta-analysis is to quantify the spatial reproducibility of a set of independent fMRI studies. ALE identifies 3D-coordinates (foci) from independent studies and models probability distributions that are centered around foci. The unification of these probability distributions produces statistical whole brain maps (ALE maps) that show statistically reliable activity across independent studies (Eickhoff, Bzdok, Laird, Kurth, & Fox, 2012; Eickhoff, Laird, Grefkes, Wang, et al., 2009; Laird, Lancaster, & Fox, 2005; Turkeltaub et al., 2012, 2002). The quantitative meta-analysis presented in this thesis uses this tool and is the first study to objectively examine brain activity that is overlapping and distinct for numerical and non-numerical magnitudes.

The current study uses ALE to provide a statistically based overview of brain regions that are activated by numerical and non-numerical magnitudes across many empirical neuroimaging papers. Three separate ALE maps were created: two for numerical magnitudes (symbolic number and nonsymbolic number) and one for non-numerical magnitudes. The current study examined brain regions that were active during each of symbolic numerical magnitude processing, nonsymbolic numerical magnitude processing, and non-numerical magnitude processing. Then a conjunction ALE analyses was computed to examine brain regions that were active during symbolic, nonsymbolic and non-numerical magnitude processing. Finally, contrast analyses were computed between each of the ALE maps to determine which brain regions are specifically activated by numerical magnitudes (both symbolic and nonsymbolic), symbolic numerical magnitude, nonsymbolic numerical magnitudes, and non-numerical magnitudes.

These quantitative meta-analyses were used to determine whether number is processed using a specific number processing system or if number is rooted in a general magnitude processing system used to process both numerical and non-numerical magnitudes. This was addressed by examining whether numerical (symbolic and nonsymbolic) and non-numerical magnitudes are processed using the same or distinct brain regions. Additionally, this study examined whether neural representations of numerical magnitudes are format-independent or format-dependent identifying both overlapping and distinct brain regions that are activated by symbolic and nonsymbolic numerical magnitudes.

Chapter 2

2 Method

2.1 Literature Search and Article Selection

A stepwise procedure was used to identify relevant experimental research articles. First, the literature was searched using a standard search in the PubMed (http://www.pubmed.gov) and PsychInfo (http://www.apa.org/psychinfo/) databases. Combinations of the key terms “magnitude”, “number*”, “symbol*”, “nonsymbolic”, “numerical stroop”, “PET”, “positron emission”, “fMRI”, “functional magnetic resonance imaging”, “neuroimaging” and “imaging” were inputted into these databases. Second, the reference list of all relevant papers found in the first step, and all relevant review papers were reviewed. A study was considered for inclusion if it contained at least one non-numerical magnitude task and at least one of either a symbolic numerical task or a nonsymbolic numerical task. This was to ensure consistent methodological paradigms across numerical and non-numerical stimuli. The term ‘study’ refers to a paper and the term ‘experiment’ is defined as an individual contrast reported within a paper.

Additional inclusion/exclusion criteria:

1. Studies had to use at least one of the following tasks: comparison tasks, ordering tasks, passive viewing tasks, numerical estimation tasks, matching tasks, and numerical stroop tasks.
2. Studies had to include a sample of healthy human adults.
3. Brain imaging had to be done using fMRI or PET.

- PET and fMRI studies were included because these imaging methods have comparable spatial uncertainty (Eickhoff, Laird, Grefkes, & Wang, 2009).

4. Studies had to use a whole-brain group analyses with stereotaxic coordinates in Talairach/Tournoux or Montreal Neurological Institute (MNI) space.
    - Experiments that used region of interest analyses were excluded.
    - Experiments that used multivariate statistical approaches were excluded.
5. Studies had to have a sample size > 5 participants.
6. Studies had to be written in English.

Twenty studies met the inclusion criteria, providing data on 337 healthy subjects. All of these studies included at least one numerical and one non-numerical magnitude task. See tables 1-3 for a detailed description of the main characteristics of each selected study. Together, these studies reported 964 activation foci obtained from 142 experiments. The studies were reported in either Talairach or MNI spaces. Studies that reported data in MNI space were transformed into Talairach space using the Lancaster transformation (icbm2tal) (Laird et al., 2010; Lancaster et al., 2007).

2.2 Analysis Procedure

Quantitative, coordinate based meta-analyses were conducted using the revised version of the activation likelihood estimation (ALE) method (Eickhoff et al., 2012; Eickhoff, Laird, Grefkes, Wang, et al., 2009; Turkeltaub et al., 2012). ALE analyses were conducted using GingerALE, a freely available application by Brainmap (http://www.brainmap.org). ALE assesses the overlap between contrast coordinates (i.e. foci) by modeling the coordinates as probability distributions centered on coordinates to create probabilistic maps of activation related to the construct of interest. Specifically, foci reported from experiments were combined for each voxel to create a modeled activation (MA) map. An ALE null-distribution is created by randomly redistributing the same number of foci as in the experimental analysis throughout the brain. To differentiate meaningful convergence of foci from random clustering (i.e. noise) an ALE algorithm empirically determines whether the clustering of converging areas of activity across experiments is greater than chance as shown in the ALE null-distribution. In accordance with Turkeltaub et al., (2012) to prevent subject groups with multiple experiments from influencing the data more than others studies reporting multiple experiments from the same subject group the coordinates were grouped by study rather than by experiment.

2.3 Single Dataset ALE Maps

Three separate ALE meta-analyses were conducted to examine convergence of foci for: 1) symbolic number processing, 2) nonsymbolic number processing and 3) non-numerical magnitude processing. All ALE meta-analyses were conducted using Scribe (version 2.3), Sleuth (version 2.3) and GingerALE (version 2.3). Of the 20 studies, 13 were used to create the symbolic map of activation (236 subjects, 28 experiments, 213 foci) (cf. Table 1), 9 were used to create the nonsymbolic map of activation (150 subjects, 17 experiments, 119 foci) (cf. Table 2), and 9 were used to create the non-numerical map of activation (149 subjects, 26 experiments, 139 foci) (cf. Table 3). All ALE analyses were performed in GingerALE using a cluster-level correction that compared significant cluster sizes in the original data to cluster sizes in the ALE maps that were generated from 1000 threshold permutations. This was in order to correct for false positive clusters that could arise as a result of multiple comparisons within the same voxel. Specifically, these maps had a cluster-level threshold of $p<.05$ and a cluster-forming (uncorrected) threshold of $p<.001$. The ALE maps were transformed into z-scores for display. This recently developed thresholding technique provides a faster more rigorous analytical solution for producing the null-distribution and addresses the issue of multiple-comparison corrections (Eickhoff et al., 2012). All single dataset ALE maps (symbolic, nonsymbolic and non-numerical) were created using this correction.

2.4 Conjunction and Contrast Analyses

Conjunction and contrast analyses were computed to examine overlapping and distinct brain regions for the three ALE maps for symbolic, nonsymbolic and non-numerical magnitude processing (Eickhoff et al., 2011). All conjunction and contrast ALE analyses were performed in GingerALE and used a false discovery rate (FDR) pID threshold of $p<.05$ with 5000 threshold permutations and a minimum volume of 100mm^3. Although the cluster-level correction used to produce the single file ALE maps is the optimal thresholding technique available (Eickhoff et al., 2012), this correction is not yet available for conjunction and contrast analysis. Consequently, the only available correction available to date for conjunction and contrast analysis is FDR thresholding. Therefore, due to methodological constraints cluster-level correction was used for the single file maps and FDR pID thresholding for the conjunction and contrast analyses.

Conjunction analyses were computed to examine similarity of activation between the ALE maps generated by symbolic number processing, nonsymbolic number processing and non-numerical magnitude processing. The voxel-wise minimum value of the input ALE images was used to create the conjunction map. The conjunction was considered to be significant for each voxel if all contributing ALE maps showed significant activation in that voxel at the thresholds described. Conjunction ALE maps were created for 1) symbolic and non-numerical, 2) nonsymbolic and non-numerical and, 3) symbolic and nonsymbolic.

Contrast analyses were computed to compare activation between the ALE maps generated for symbolic number processing, nonsymbolic number processing and non-numerical magnitude processing. Additionally, contrast analyses between numerical magnitude processing and non-numerical magnitude processing was computed. The coordinates of the symbolic map and the nonsymbolic map were pooled to create the numerical magnitude ALE map that was used for this contrast. ALE contrast images are created by directly subtracting one input image from the other. GingerALE creates simulated null data to correct for unequal sample sizes by pooling foci and randomly dividing the foci into two groupings that are equal in size to the original data sets. One simulation dataset is subtracted from the other and compared to the true data. This produces voxel-wise p-value images that show where the true data sit in relation to the distribution of values within that voxel. The p-value images are converted to Z scores. The following ALE contrasts were computed: 1) numerical>non-numerical, 2) non-numerical>numerical, 3) symbolic > non-numerical, 4) non-numerical > symbolic, 5) nonsymbolic > non-numerical, 6) non-numerical>nonsymbolic, 7) symbolic > nonsymbolic, 8) nonsymbolic > symbolic.

Table 1: Studies included in the symbolic meta-analysis

First Author	Year	Journal	N	Imaging Method	Mean Age	Gender	Numerical Magnitude Stimuli	Non-Numerical Magnitude Stimuli	Task(s)	Experiment Name *(name taken from original study)*	Loc
Ansari D	2006	NeuroImage	14	fMRI	21	8F, 6M	Number Words	Font Size	Size Congruity	Main effect of congruity (incongruent > congruent)	2
										Main effect of distance (small > large)	1
										Interaction of congruity and distance effects	2
										Main effect of distance in the neutral condition (small>large)	12
Attout L	2014	PLoS ONE	26	fMRI	21	15F, 11M	Arabic Digit	Luminance	Order Judgment	Conjunction of distance effect for alphabetical order STM and numerical vs. luminance	15
Cappelletti M	2010	Journal of Cognitive Neuroscience	22	fMRI	55	12F, 10M	Arabic Digits	Objects (size)	Answer question	Conceptual Only: Number vs. Object (RT Effects)	7
Chassy P	2012	Cerebral Cortex	16	fMRI	28	16M	Integers, Dots	Disks	Comparison	PI < NI	5
Fias W	2003	Journal of Cognitive Neuroscience	18	PET	23	18M	Two digit numbers	Line length, Angle size	Comparison	Number comparison vs non-numerical Comparison	2
Kadosh R C	2005	Neuro-psychologia	15	fMRI	28	7F, 8M	Arabic Digit	Size, Luminance	Comparison	Numerical vs. Size	1
										Numerical vs. Luminance	4
										Numerical Distance	23
Kadosh RC	2008	Cerebral Cortex	16	fMRI	26	10F, 6M	Arabic Digit	Luminance	Stroop	Size Congruity Effect	2
										Comparison X Congruity	1
Kaufmann L	2005	NeuroImage	17	fMRI	31	7F, 10M	Arabic Digits	Size	Stroop	Numerical comparison > physical comparison	1

										Numerical comparison (Distance 1 > 4, neutral trials)	27
										Numerical comparison (incongruent>congruent trials)	10
Liu X	2006	Journal of Cognitive Neuroscience	23	fMRI		7 F, 5M	Arabic Digits	Decade	Stroop	Incongruent vs. Congruent	3
										Distance of 18 vs. 27	7
Lyons I M	2013	Journal of Cognitive Neuroscience	35	fMRI		16F, 17M	Arabic Digits, Dots	Luminance	Comparison	Symbolic: NumOrd>LumSymbolicOrd	9
										SymOrd>LumOrd(sym) and SymCard>LumCard(Sym)	14
Pinel P	2004	Neuron	15	fMRI	24	18 F, 6M	Arabic Digit	Size, Luminance	Stroop	Number Comparison vs. Size Comparison	2
										Number Comparison Small Distance vs. Number Comparison Large Distance	11
										Incongruent vs. Congruent Trials: Physical Size Interference (Numerical Comparison)	5
Tang J	2006	Journal of Cognitive Neuroscience	20	fMRI	27	&F, 11M	Arabig Digit	Physical Size	Stroop	Numerical > Physical	1
										Numerical Conflict Trials > Numerical Non-Conflict Trials	2
										Numerical Error Trials > Numerical Correct Trials	1
Vogel S E	2013	Neuro-psychologia	14	fMRI	25	7F, 7M	Arabic Digit	Luminance	Number line estimation	Number > Control	8
										Number Specific Activation	3

Hand, handedness of the participants; Loc, number of locations reported in experiment; fMRI, functional magnetic resonance imaging; PET, positron emission tomography.

Table 2: Studies included in the nonsymbolic meta-analysis

First Author	Year	Journal	N	Imaging Method	Mean Age	Gender	Numerical Magnitude Stimuli	Non-Numerical Magnitude Stimuli	Task(s)	Experiment Name *(name taken from original study)*	Loc
Castelli F	2006	PNAS	12	fMRI	24	4F, 8M	Array of discrete squares	Single large square with continuous hues	Discrete analogue response	Estimating Numerosity: In space and time	10
										Difficulty Effect While Estimating Numerosity: In Space	4
										Difficulty Effect While Estimating Numerosity: In Time	2
Chassy P	2012	Cerebral Cortex	16	fMRI	28	16M	Integers, Dots	Disks	Comparison	Dots > Disk	3
Dormal V	2009	Human Brain Mapping	14	fMRI	21	14M	Single black dots presented sequentially	Single black dot presented for varying durations	Numerosity Categorization	Numerosity Processing vs. Ref for N	7
Dormal V	2012	Human Brain Mapping	15	fMRI	21	15M	Single black dots presented sequentially	Single black dot presented for varying durations	Numerosity Categorization	Numerosity vs. Ref for Numerosity	7
										N vs RefN compared to D vs RefD	1
Hayashi M J	2013	Journal of Neuroscience	27	fMRI		14F, 12M	Dot array (numerosity)	Dot array (Duration)	Comparison	Main Effect of Numerosity	1
Jacob S N	2010 9	European Journal of Neuroscience	15	fMRI			Dot array	Line Length	Passive Viewing (Adaptation study)	Dot Proportion full brain analysis	3

										Adaptation to Dot Proportion	9
										Numerosity full brain analysis	5
Leroux G	2009	Developmental Science	9	fMRI	23	9M	Number of dots in a line	Length of Line of dots	Number-length interference	(INT-REFint) AND (COV-REFcov)	13
										(INT-REFint) - (COV-REFcov)	1
										(COV-REFcov) - (INT-REFint)	2
Lyons I M	2013	Journal of Cognitive Neuroscience	33	fMRI		16F, 17M	Arabic Digits, Dots	Luminance	Comparison	Nonsymbolic: Numord>LumNonsymbolicORD	14
										DotOrd>LumOrd(dot) and DotCard>LumCard(Dot)	7
Piazza M	2006	Brain Research	10	fMRI		7M, 3F	Green and Red Squares	High and Low Tones	Estimation, Matching, Counting	Estimation > Matching	7

Hand, handedness of the participants; Loc, number of locations reported in experiment; fMRI, functional magnetic resonance imaging; PET, positron emission tomography.

Table 3: Studies included in the non-numerical meta-analysis

First Author	Year	Journal	N	Imaging Method	Mean Age	Gender	Numerical Magnitude Stimuli	Non-Numerical Magnitude Stimuli	Task(s)	Experiment Name *(name taken from original study)*	Loc
Dormal V	2009	Human Brain Mapping	14	fMRI	21	14M	Linear arrays of dots	Line Length	Comparison	Discrete Length vs. Ref for DL	5
										Continuous Length vs. Ref for CL	5
										Conjunction of Discrete and Continuous LineS	21
Dormal V	2012	Human Brain Mapping	15	fMRI	21	15M	Single black dots presented sequentially	Single black dot presented for varying durations	Numerosity Categorization	Duration vs. Ref for Duration	8
Hayashi M J	2013	Journal of Neuroscience	26	fMRI		14F, 12M	Dot array (numerosity)	Dot array (Duration)	Comparison	Main Effect of Duration	3
Jacob S N	2009	European Journal of Neuroscience	15	fMRI			Dot array	Line Length	Passive Viewing	Line Proportion full brain analysis	9
										Adaptation to Line Proportion	3
Kadosh R C	2005	Neuro-psychologia	15	fMRI	28	7F, 8M	Arabic Digit	Size, Luminance	Comparison	Luminance vs. Numerical	14
										Size vs. numerical	13
										Size vs. luminance	15
										Luminance vs. size	13
										Luminance Distance	2
										Size Distance	1
Kaufmann L	2005	NeuroImage	17	fMRI	31	7F, 10M	Arabic Digits	Size of Arabic digits	Stroop	Physical comparison (Distance 1 > Distance 4, only neutral trials)	1
Pinel P	2004	Neuron	15	fMRI	24	9 F, 6M	Arabic Digit	Physical Size,	Stroop	Size Comparison with numerical stimuli vs	10

								Luminance		Numerical	
										Size with numerical stimuli vs Luminance	5
										Size with numerical stimuli vs size with letter stimuli	13
										Size and Luminance Distance Effects (Close - Far Trials)	6
										Size (numbers) Small Distance vs Size (numbers) Large Distance	1
										Luminance Small Distance vs Luminance Large Distance	18
										Size (letters) small distance vs Size (letters) large distance	7
										Size (all stimuli) small distance vs. Size (all stimuli) large distance	5
										Incongruent vs. Congruent Trials: Physical Size Interference (Luminance Comparison)	2
Tang J	2006	Journal of Cognitive Neuroscience	18	fMRI	25	&F, 11M	Arabig Digit	Physical Size	Stroop	Physical Conflict Trials > Physical Non-Conflict Trials	5
										Physical Error Trials > Physical Correct Trials	3
Vogel S E	2013	Neuro-psychologia	14	fMRI	25	7F, 7M	Arabic Digit	Luminance	Number line estimation	Brightness > Control	10

Hand, handedness of the participants; Loc, number of locations reported in experiment; fMRI, functional magnetic resonance imaging; PET, positron emission tomograpy

Chapter 3

3 Results

This section is organized in the following manner. First, the results will be presented for the three meta-analyses: 1) symbolic numerical magnitude processing, 2) nonsymbolic numerical magnitude processing and 3) non-numerical magnitude processing. This is followed by the results of the conjunction analysis for symbolic and non-numerical magnitude processing, nonsymbolic and non-numerical magnitude processing, and symbolic and nonsymbolic magnitude processing. And finally, the brain regions active for the following contrasts are shown: numerical>non-numerical, non-numerical>numerical, symbolic>non-numerical, non-numerical>symbolic, nonsymbolic>non-numerical, non-numerical>nonsymbolic, symbolic>nonsymbolic, nonsymbolic>symbolic.

3.1 Single Dataset Meta Analysis

3.1.1 Symbolic Numerical Magnitude Processing

This meta-analysis showed activation in a widespread fronto-parietal network of brain areas during symbolic number processing (Fig. 1 and Table 4). The largest clusters of converging brain activation across 13 studies were in the bilateral superior parietal lobules (SPL). Additionally to the SPL, smaller regions in the claustrum, right middle frontal gyrus (MFG), left superior frontal gyrus (SFG) and right inferior frontal gyrus (IFG) exhibited increased activity.

3.1.2 Nonsymbolic Numerical Magnitude Processing

This meta-analysis identified areas where brain activity was consistently positively correlated with nonsymbolic number processing (Fig. 1 and Table 5). Convergent brain activation for 9 studies (Table 2) was found in the right inferior parietal lobe (IPL), a right lateralized frontal network including the SFG, IFG and MFG. A smaller region in the left SPL consistently activated during nonsymbolic number processing. Additional regions including the precuneus, insula, and middle occipital gyrus were also active during nonsymbolic number processing.

3.1.3 Non-numerical Magnitude Processing

This meta-analysis showed that convergent brain activation for non-numerical magnitude processing across 9 studies (Table 3) closely resembled brain regions that were activated during numerical magnitude processing. In the parietal lobe, there was significant clustering in bilaterial IPL and the right SPL. In the frontal lobe, there was activation in the MFG and IFG. Additionally, there was activation in the precentral gyrus, the fusiform gyrus and the insula.

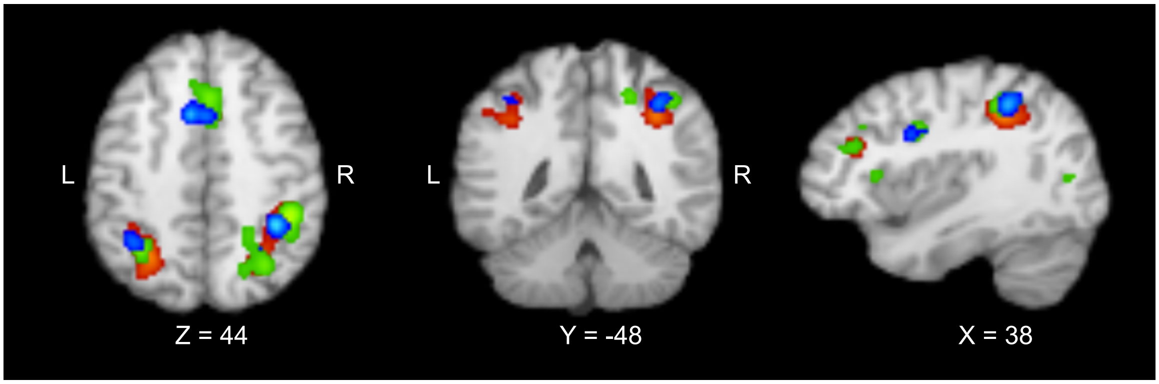

Figure 1: ALE map of single data sets: symbolic (orange), nonsymbolic (green) and non-numerical (blue). The ALE analysis revealed significant clusters of convergence brain clusters (cf., table 4). Activations were identified using a cluster-level threshold of *p*<.05 with 1000 threshold permutations and an uncorrected *p*<.001 Brain slices are shown at coordinates (x, y, z) in Talairach space.

Table 4: Single Dataset Analyses

Hemisphere	Brain Area	BA	X	Y	Z	ALE	Vol/mm^3
Symbolic							
R	Superior Parietal Lobule	7	28	-62	40	0.034346502	6928
L	Superior Parietal Lobule	7	-26	-58	42	0.023388157	3992
R	Claustrum		30	18	4	0.021354228	872
R	Middle Frontal Gyrus	46	40	30	22	0.0212135	584
L	Superior Frontal Gyrus	6	0	10	48	0.016463118	440
R	Inferior Frontal Gyrus	9	46	6	26	0.014979648	384
Nonsymbolic							
R	Superior Frontal Gyrus	6	4	10	48	0.017186532	2664
R	Inferior Parietal Lobule	40	42	-40	44	0.020571694	1872
R	Precuneus	19	30	-64	44	0.015015809	1672
R	Inferior Frontal Gyrus	9	44	2	28	0.026015356	1560
R	Insula	13	32	20	6	0.020576512	1384
L	Superior Parietal Lobule	7	-30	-56	46	0.020028442	928
R	Middle Frontal Gyrus	46	40	32	22	0.012443791	608
R	Middle Occipital Gyrus	18	20	-88	14	0.01507676	336
R	Middle Occipital Gyrus	19	34	-76	8	0.011677275	304
Non-numerical							
L	Medial Frontal Gyrus	32	-6	10	46	0.0180884	1272
L	Precentral Gyrus	6	-44	-6	38	0.015371453	1168
R	Inferior Parietal Lobule	40	36	-44	42	0.020738276	1072
R	Inferior Frontal Gyrus	9	42	4	28	0.019060526	1032
L	Fusiform Gyrus	19	-46	-68	-10	0.015684115	928
R	Insula	13	32	18	8	0.016923757	544
L	Inferior Parietal Lobule	40	-34	-52	44	0.013726167	528
R	Superior Parietal Lobule	7	24	-64	40	0.011744871	488

3.2 Conjunction Analyses

Conjunction analyses were conducted to determine brain regions with convergent clusters of activation between the single dataset ALE maps (Table 5 and Figure 2). Significant clusters of activation for symbolic and non-numerical magnitude processing converged in the bilateral IPL, right SPL, right MFG, left IFG and the claustrum. For nonsymbolic and non-numerical processing, there was significant convergence in the bilateral IPL and SPL as well as the right IFG, right MFG and the insula. Convergent brain activation for symbolic and nonsymbolic numerical processing was found in the bilateral IPL, right SPL, insula, right SFG, right IFG and right MFG.

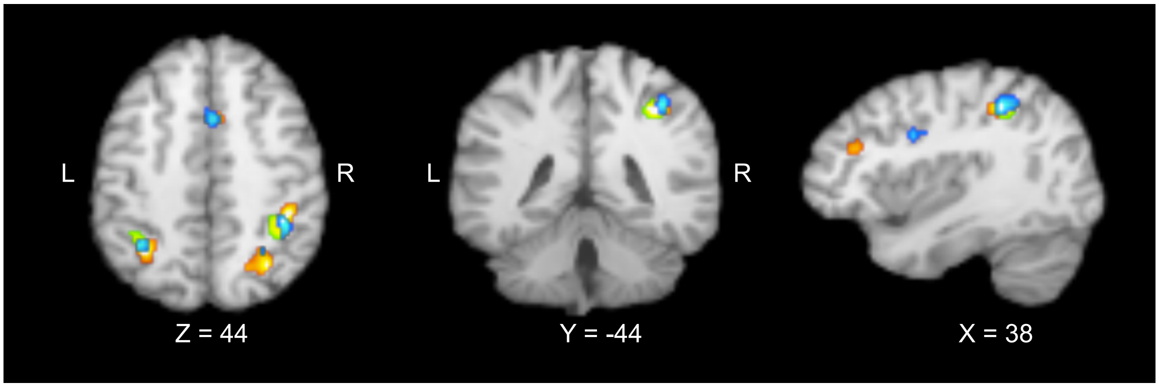

Figure 2: ALE maps for the three conjunction analyses. Conjunction analyses are presented for symbolic and non-numerical (green), nonsymbolic and non-numerical (blue), and symbolic and nonsymbolic (orange). ALE conjunction analysis revealed significant clusters of convergence between single dataset ALE maps (cf., table 5). Activations were identified using a threshold of $p<.05$ (FDR corrected). Brain slices are shown at coordinates (x, y, z) in Talairach space.

Table 5: Conjunction Analyses

Hemisphere	Brain Area	BA	X	Y	Z	ALE	Vol/mm^3
Symbolic and Non-numerical							
R	Inferior Parietal Lobule	40	36	-44	42	0.01993	792
R	Superior Parietal Lobule	7	24	-64	40	0.01174	488
L	Inferior Parietal Lobule	40	-32	-54	44	0.01295	376
R	Claustrum		30	18	8	0.01654	360
R	Medial Frontal Gyrus	32	2	10	46	0.01339	296
L	Inferior Frontal Gyrus	9	44	4	26	0.01356	152
Nonsymbolic and Non-numerical							
R	Inferior Frontal Gyrus	9	42	4	28	0.01906	944
R	Insula	13	32	18	8	0.01692	464
R	Inferior Parietal Lobule	40	38	-42	44	0.01521	424
R	Medial Frontal Gyrus	32	2	10	46	0.01339	328
L	Inferior Parietal Lobule	40	-34	-54	44	0.01327	192
R	Superior Parietal Lobule	7	22	-64	42	0.01056	128
R	Superior Parietal Lobule	7	28	-58	44	0.00899	16
R	Superior Parietal Lobule	7	28	-60	42	0.00976	16
Symbolic and Nonsymbolic							
R	Superior Parietal Lobule	7	30	-64	44	0.01502	712
R	Inferior Parietal Lobule	40	40	-40	42	0.01851	664
L	Inferior Parietal Lobule	7	-30	-56	44	0.01697	592
R	Insula	13	30	20	6	0.01937	520
R	Superior Frontal Gyrus	6	2	10	48	0.01515	352
R	Inferior Frontal Gyrus	9	46	6	26	0.01498	264
R	Middle Frontal Gyrus	46	40	32	22	0.01244	256

3.3 Contrast Analyses

To assess which brain regions were specifically activated for symbolic, nonsymbolic and non-numerical magnitude processing, contrast analyses were conducted to compare numerical and non-numerical, symbolic and non-numerical, nonsymbolic and non-numerical, and symbolic and nonsymbolic. The numerical map included the foci of the symbolic and nonsymbolic maps. All regions of activation from the contrast analyses are reported in Table 6 and depicted in Figure 3. Significant clusters of activation were found in the right IPL and left SPL for numerical>non-numerical (Fig. 3A). The contrast non-numerical>numerical revealed significant activation in the left cingulate gyrus, left fusiform gyrus, left precuneus and left precentral gyrus (Fig. 3A). Significant clusters of activation were found in the right supramarginal gyrus and the left SPL for symbolic > non-numerical magnitude processing (Fig. 3B). Small regions in the left cingulate gyrus and left fusiform gyrus were found for non-numerical>symbolic magnitude processing (Fig. 3C). For nonsymbolic compared to non-numerical magnitude processing the right IPL was found for nonsymbolic>non-numerical processing (Fig. 3C) No brain regions were specifically activated during non-numerical >nonsymbolic numerical processing. When comparing symbolic and nonsymbolic numerical clusters the contrast analysis revealed significant clusters of activation in the right IPL and the left supramarginal gyrus for symbolic>nonsymbolic (Fig. 3D). There were significant clusters of activation in the right precentral gyrus, right IPL, right SFG, right IFG and left MFG for nonsymbolic>symbolic (Fig. 3D).

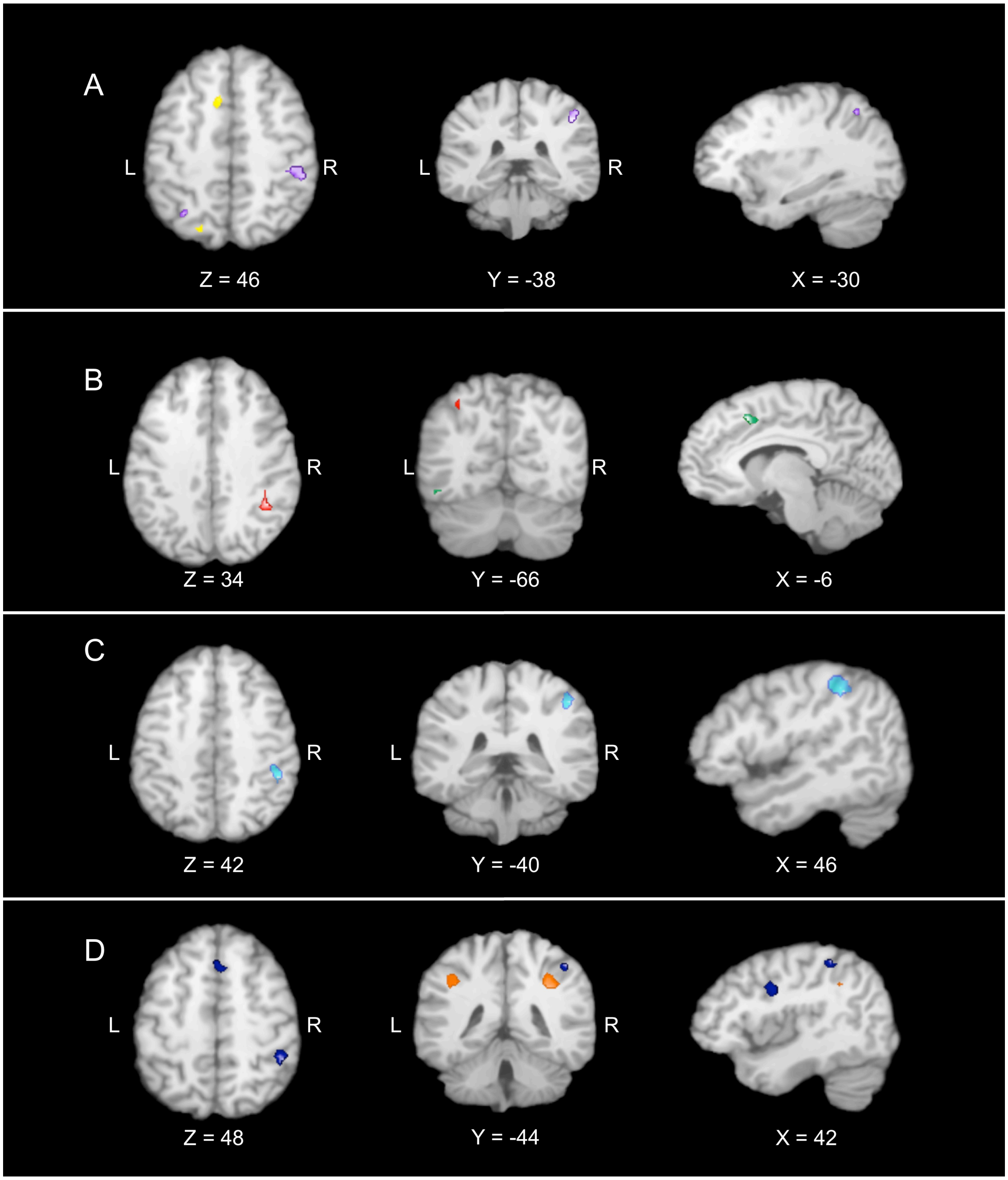

Figure 3: ALE maps of the contrast analyses between symbolic, nonsymbolic and non-numerical using (cf., table 6). A) Activation in purple indicated stronger activation for numerical>non-numerical and activation in yellow indicated stronger activation for non-numerical>numerical. B) Activation in red indicated stronger activation for symbolic>non-numerical and activation in green indicated stronger activation for non-numerical>symbolic. C) Activation in light blue indicated

stronger activation for nonsymbolic>non-numerical. No regions were significantly activated for non-numerical>nonsymbolic. D) Activation in orange indicated stronger activation for symbolic>nonsymbolic and activation in navy blue indicated stronger activation for nonsymbolic>symbolic. Activations were identified using a threshold of p<.05 (FDR corrected). All brain slices are shown at coordinates (x, y, z) in Talairach space.

Table 6: Contrast Analyses

Hemisphere	Brain Area	BA	X	Y	Z	ALE	Vol/mm^3
Numerical>Non-numerical							
R	Inferior Parietal Lobule	40	48	-40	40	2.2571292	768
L	Superior Parietal Lobule	7	-30	-62	42	2.0537488	232
Non-numerical>Numerical							
L	Cingulate Gyrus	32	-6	14	42	2.6520698	400
L	Fusiform Gyrus	19	-48	-72	-10	2.0295727	160
L	Precuneus	7	-20	-73	44	1.9172987	144
L	Precentral Gyrus	6	-45	-8	39	1.7915816	112
Symbolic>Non-numerical							
R	Supramarginal Gyrus	40	42	-48	34	2.1700904	240
L	Superior Parietal Lobule	7	-30	-62	44	2.0705593	232
Non-numerical>Symbolic							
L	Cingulate Gyrus	32	-7	14	43	2.2571292	248
L	Fusiform Gyrus	19	-43	-69	-13	1.8867052	168
Nonsymbolic>Non-numerical							
R	Inferior Parietal Lobule	40	46	-42	42	2.3739276	752
Non-numerical>nonsymbolic (No regions found)							
Symbolic>Nonsymbolic							
R	Inferior Parietal Lobule	40	32	-50	34	3.540084	1832
L	Supramarginal Gyrus	40	-37	-42	35	2.5005517	816
Nonsymbolic>Symbolic							
R	Precentral Gyrus	6	44	-4	30	2.5491042	576
R	Inferior Parietal Lobule	40	46	-44	48	2.4275784	432
R	Superior Frontal Gyrus	8	4	18	50	2.2262118	280
R	Inferior Frontal Gyrus	45	32	26	8	1.9809222	144
L	Medial Frontal Gyrus	8	-2	24	44	2.0455568	104

Chapter 4

4 Discussion

The current study examined the neural bases of the ability to process numerical and non-numerical magnitudes. Quantitative meta-analytic techniques were used to address two important questions. First, the study examined whether number is processed using a specific number processing system or if number is rooted in a general magnitude processing system used to process both numerical and non-numerical magnitudes. This question was addressed through an examination of whether numerical and non-numerical magnitudes are processed using the same or distinct brain regions. Second, the study examined whether neural representations of numerical magnitudes are format-independent or format-dependent. This question was addressed by identifying both overlapping and distinct brain regions that are activated by symbolic and nonsymbolic numerical magnitudes.

The current study was the first in a rapidly evolving field to conduct quantitative meta-analyses in order to examine the neural correlates of numerical and non-numerical magnitude processing. Activation likelihood estimation (ALE) was used to identify the neural correlates of numerical (symbolic and nonsymbolic) and non-numerical magnitude processing. Specifically, three ALE meta-analyses were computed to identify the neural correlates of: 1) symbolic, 2) nonsymbolic and, 3) non-numerical magnitudes. These meta-analyses revealed that brain regions in the fronto-parietal network were associated with symbolic, nonsymbolic and non-numerical magnitude processing across studies.

In the frontal cortex, the MFG and IFG were activated during symbolic, nonsymbolic and non-numerical magnitude processing whereas the SFG was activated during symbolic and nonsymbolic magnitude processing. In the parietal cortex, bilateral SPL activation was correlated with symbolic numerical magnitude processing while regions along the bilateral IPL and left SPL were correlated with nonsymbolic numerical magnitude processing and non-numerical magnitude processing. The spatial distributions of the single dataset quantitative ALE maps that were generated for symbolic, nonsymbolic and non-numerical magnitudes suggest that both overlapping and distinct brain regions are associated with numerical and non-numerical magnitudes.

The finding that overlapping and distinct brain regions (particularly in regions along the IPS) support numerical and non-numerical magnitude processing provide statistically quantified support for previous qualitative meta-analyses (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008). In particular, Cantlon, Platt, et al., (2009) concluded that the IPS is recruited during both numerical and non-numerical magnitude processing. Similarly, Cohen Kadosh, Lammertyn, et al., (2008) concluded that the IPS hosts overlapping domain general and domain specific neural populations associated with numerical and non-numerical magnitudes. However, these previous conclusions were inferred by spatially mapping coordinates onto a template brain (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008; Van Essen, 2012). In contrast, the current quantitative meta-analysis rigorously evaluated the data using sophisticated statistical techniques. Importantly, the results from the current quantitative meta-analysis were convergent with results from previous qualitative meta-analyses (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008). The current coordinate-based meta-analysis provides stronger evidence for the theory that numbers are processed using a general magnitude system that is instantiated in the parietal cortex. Additionally to this quantitative replication of previous qualitative meta-analyses, tools used in the current study allowed for the implementation of conjunction and contrast analyses to quantitatively evaluate overlapping and distinct brain regions that support symbolic, nonsymbolic and non-numerical magnitude processing. In what follows, this discussion will outline several important research findings that arose from these conjunction and contrast analyses and discuss how these findings relate to prominent theoretical frameworks. A brief introduction is suggested here.

4.1 Numerical vs. Non-numerical

A prominent view in the field of numerical cognition is that numbers are represented using an approximate number system that is specifically used to process numerical magnitudes. An alternative hypothesis, that numbers are processed using a general magnitude system used to process both numerical and non-numerical magnitudes, has been proposed several times during the expansion of the field of numerical cognition (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008; Simon, 1999; Walsh, 2003). In the current study, conjunction analyses were used to quantitatively identify regions that were overlapping for the three ALE maps in order to determine whether brain regions used to process number are specifically associated with number or if these regions process magnitude more generally. Conjunction analyses revealed that regions along the bilateral IPL, right SPL, IFG and MFG were activated for the conjunction of symbolic and non-numerical, nonsymbolic and non-numerical, and symbolic and nonsymbolic. These quantitative conjunction analyses highlighted brain regions that were consistently activated by both numerical and non-numerical stimuli. Therefore, these findings support the hypothesis that regions along the parietal and frontal cortex host a general magnitude processing system used to process both numerical and non-numerical numbers.

It is important to acknowledge that ALE methodology does not discriminate between patterns of activation within the overlapping regions of a conjunction analysis. The limitation of coarse spatial resolution is often noted in empirical studies that use univarate analysis techniques. In these empirical studies, researchers have addressed this limitation of course spatial resolution by implementing multivariate techniques often referred to as Multi-Voxel Pattern Analysis (MVPA) (e.g. Bulthé, De Smedt, & Op de Beeck, 2014; Damarla & Just, 2013; Eger et al., 2009; Lyons & Beilock, 2013). However, no empirical study has used MVPA to compare patterns of activation for numerical and non-numerical magnitudes in overlapping regions. An important implication of this limitation is that the overlapping regions in the brain may be overlapping due to domain general processes such as decision-making or response selection rather than magnitude representations. Therefore, although the current study supports the theory that there are regions in the brain that are engaged in general magnitude processing (i.e. both numerical and non-numerical), current available meta-analytic methods cannot determine whether the overlapping brain regions use the same mechanism to process numerical and non-numerical magnitudes.

Additionally to using conjunction analyses to examine the overlap of numerical and non-numerical magnitudes, contrast analyses were used to reveal brain regions that were specifically activated by numerical (symbolic and nonsymbolic) versus non-numerical magnitude processing. Subtracting the non-numerical map from the symbolic and nonsymbolic numerical maps respectively, revealed activation in regions typically associated with number processing (Ansari, 2008; Cantlon, 2012; Dehaene et al., 2003; Nieder & Dehaene, 2009). Specifically, the contrast symbolic>non-numerical showed that activation in the right supramarginal gyrus and left SPL is correlated with symbolic numbers. Relatedly, contrasting nonsymbolic>non-numerical revealed that specific activation in the right IPL is correlated with nonsymbolic numbers. Importantly, no brain regions that are typically associated with number processing were specifically activated in non-numerical magnitude processing. Specifically, the contrast non-numerical>symbolic revealed that activation in the fusiform gyrus and cingulate gyrus related to non-numerical magnitude processing. The left fusiform gyrus has been implicated in the identification of object properties as well as the categorization of objects (Allison, McCarthy, Nobre, Puce, & Belger; Martin, 2007) and the left cingulate is often activated during domain-general conflict processing (Botvinick, Cohen, & Carter, 2004; Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999). Thus, activation in the left fusiform and cingulate gyri may not have been related to the magnitude processing. Rather, activation in the left fusiform and cingulate gyri was likely correlated with domain general processes such as the identification of a non-numerical object. Overall, the results of the non-numerical>symbolic contrast showed that symbolic numbers activated all number related brain regions that were correlated with the processing of non-numerical magnitudes. In a similar vein, there were no regions specifically activated by the contrast non-numerical>nonsymbolic. Again, this implied that nonsymbolic numbers activated all regions that were activated by non-numerical magnitudes, as well as additional regions that were specifically correlated with nonsymbolic numbers. Together these findings suggest that symbolic and nonsymbolic numbers are processed using the entirety of a general magnitude processing system used to process non-numerical magnitudes. Moreover, symbolic and nonsymbolic numbers are correlated with additional number specific brain regions that are related to the format of the numerical magnitude (i.e symbolic or nonsymbolic).

The finding that symbolic and nonsymbolic numbers activate the same neural regions as non-numerical magnitudes lends support to the neuronal recycling hypothesis (Dehaene & Cohen, 2007). The neuronal recycling hypothesis states that culturally acquired skills such as reading and math use a set of evolutionarily ancient circuits that are sufficiently similar to the required function and have sufficient neural plasticity to support processing of novel cultural abilities (Dehaene & Cohen, 2007). In accordance with this hypothesis, the data from the current meta-analysis indicates that the culturally acquired ability to process numbers may have invaded cortical regions dedicated to the evolutionarily older general magnitude processing system in order to process non-numerical magnitudes.

The contrasts of symbolic and nonsymbolic numerical magnitudes compared to non-numerical magnitudes suggested that symbolic and nonsymbolic numbers activate a general magnitude system as well as additional seemingly format-specific regions. Interestingly, symbolic numbers specifically activated superior bilateral regions of the parietal cortex and nonsymbolic numbers specifically activated anterior regions of the right IPL. This suggested that the brain regions that are format-dependent (i.e. differentially activated by symbolic and nonsymbolic numbers) were distinct and lateralized within the parietal cortex. Given the involvement of the left temporal and parietal cortex in language abilities (Price, 2000), it is possible that the regions along the left parietal lobule that are specifically activated by symbolic numbers may reflect the verbal semantic processing of number symbols. Therefore, it is likely that symbolic numerical representations are processed using general magnitude processing regions as well as adjacent language areas that may support the mapping of symbols onto numerical magnitudes. This suggestion is in accordance with the neuronal recycling hypothesis (Dehaene & Cohen, 2007). The analogous nonsymbolic contrast, namely nonsymbolic>non-numerical, revealed that the region in the IPL that is specifically activated by nonsymbolic numbers is right lateralized and anterior. A large body of research has implicated the anterior IPS as important for tactile and visual object processing in both humans and macaques (For a review see: Grefkes & Fink, 2005). Consequently, it is likely that the specific nonsymbolic activation in the right IPL was related to the processing of the objects in a nonsymbolic array. In a similar vein, it has been suggested that activation in the postcentral gyrus and regions adjacent to the anterior IPS was important for the link between finger counting and basic number processing (Butterworth, 2005; Kaufmann et al., 2008). It is possible that the discrete and iconic nature of nonsymbolic numbers elicits activation typically associated with finger counting strategies. Overall, these contrasts supported the idea that both symbolic and nonsymbolic numbers are processed using a general magnitude system as well as format specific number regions, rather than an approximate number system. Still, a comparison of symbolic and nonsymbolic numerical magnitude processing is critical to determine whether these number specific regions process numbers abstractly using a numerically specific approximate number system (ANS) or whether activation in these regions is related to number format.

4.2 Symbolic vs. Nonsymbolic

In order to address whether numbers are represented abstractly or if the human brain hosts format dependent representations for number, quantitative analyses were computed to examine whether overlapping or distinct neural populations correlated with symbolic and nonsymbolic numerical magnitudes. Specifically, conjunction and contrast analyses were conducted to compare symbolic and nonsymbolic ALE maps. Conjunction analyses revealed that regions along the bilateral IPL and right SPL as well as the IFG, MFG and SFG were specifically activated by the conjunction of symbolic and nonsymbolic numerical magnitudes. Contrast analyses revealed that the right IPL and left supramarginal gyrus were specifically activated for symbolic compared to the nonsymbolic numbers. A right lateralized frontal parietal network including the right IPL, precentral gyrus, SFG, IFG as well as the left MFG were specifically activated for nonsymbolic compared to symbolic numbers. These findings are consistent with empirical research suggesting that numbers are processed using both overlapping and distinct neural mechanisms (e.g. Holloway et al., 2010; Lyons & Beilock, 2013; Piazza et al., 2007).

Additionally to replicating the finding that overlapping and distinct neural populations support different number formats, these conjunction and contrast analyses provide valuable insights into the highly debated question of whether number is processed abstractly (e.g. Ansari, 2007; Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Cohen Kadosh & Walsh, 2009; Dehaene et al., 1998; Nieder & Dehaene, 2009;

Piazza et al., 2007). The finding that several neural regions were activated by the conjunction of symbolic and nonsymbolic numerical magnitude maps supports the notion that the human brain represents numbers abstractly. This finding implicates the bilateral IPL, right SPL, right IFG, MFG and SFG and the insula as candidate regions that may support abstract number processing. However, the nature of the overlap between symbolic and nonsymbolic numerical maps is unclear because the statistical algorithms that underlie ALE do not evaluate patterns of activation within an overlapping region. Therefore, while it is possible that the overlap could represent common semantic processing, it could also represent common task demands such as response-selection. In empirical studies, researchers addressed this limitation of coarse spatial resolution by implementing MVPA to examine patterns of activation for symbolic and nonsymbolic numbers in the IPS (Damarla & Just, 2013; Eger et al., 2009; Lyons et al., 2014) and at the whole brain level (Bulthé et al., 2014). These studies consistently reported a lack of association between patterns of activation for symbolic and nonsymbolic numbers. Such findings challenge the idea that overlapping activation for symbolic and nonsymbolic numerical processing implies that numbers are processed abstractly. It is important to interpret overlapping activation with caution until an algorithm that can analyze patterns of activation between ALE maps is available.

Meta-analytic contrast analyses revealed that distinct neural mechanisms are activated by symbolic compared to nonsymbolic numbers and supported the theory that numerical representations are dependent on format (Cohen Kadosh, Cohen Kadosh, Kaas, et al., 2007; Cohen Kadosh & Walsh, 2009; Cohen Kadosh et al., 2011). In particular, the contrast symbolic>nonsymbolic revealed that symbolic numerical magnitude processing specifically relates to activation in the right IPL and left supramarginal gyrus. Conversely, the contrast nonsymbolic>symbolic showed that nonsymbolic numbers specifically correlate with activation in an anterior region of the right IPL. Interestingly, stimulus format seemed to be lateralized within the parietal cortex. Specifically, the right parietal lobule supported both symbolic and nonsymbolic processing, while activation in the left parietal lobule was specific to symbolic number processing. Importantly, even though symbolic and nonsymbolic maps both show activation in the right parietal cortex, the localization in the right IPS is different. Specifically, activation is more dorsal for nonsymbolic and more ventral for symbolic. In other words, the contrast analyses comparing symbolic and nonsymbolic ALE maps suggest that within the right IPS symbolic and nonsymbolic are associated with different spatial patterns of activation. The findings that symbolic numbers activated the bilateral SPL while nonsymbolic numbers activated the right lateralized anterior IPL conflicted with the notion that the brain possesses a number module that is indifferent to number format. Instead, regions that are format specific may imply differential semantic processing of symbolic and nonsymbolic numerical magnitudes. Had the format specific regions been located in the visual or frontal cortex, it could have been argued that these format specific regions were related to differences in perceptual processing of the visual stimuli or differential task related processes. However, since the format specific regions were in the parietal cortex, which is typically associated with the semantic processing numerical magnitudes (e.g. Holloway, Battista, Vogel, & Ansari, 2013), it is unlikely that the format-specific regions are entirely asemantic and just format related. Ultimately, this question of format specificity in the human brain calls for further investigation in order to understand the process of how the brain represents symbols compared to nonsymbolic numbers.

The concept of hemispheric specialization within the parietal lobes is supported by developmental studies (Holloway & Ansari, 2010). For example, researchers revealed increasing specialization of the left IPS for processing of symbolic numbers across development (e.g. Vogel, Goffin, & Ansari, 2014) but consistent activation across children and adults in the right IPS for nonsymbolic numbers (e.g. Cantlon et al., 2006). The notion that this hemispheric asymmetry in the parietal cortex is a result of developmental specialization is further supported by a developmental quantitative meta-analysis that identified brain regions supporting symbolic and nonsymbolic number processing in children (Kaufmann, Wood, Rubinsten, & Henik, 2011). The results of this meta-analysis showed that the notation of the number (symbolic vs. nonsymbolic) influenced the location of neural activation patterns both within and outside the parietal lobes (Kaufmann et al., 2011). In accordance with the current meta analyses, Kaufmann et al., (2011) showed that symbolic number magnitude processing was correlated with bilateral parietal activation (in the left SPL and right IPS) while activation during nonsymbolic number processing was lateralized to the right parietal lobe (in the anterior right IPS). Together, these findings challenge the notion that the parietal cortex hosts a single system that processes number abstractly. Instead, it is probable that the parietal cortex develops hemispheric specialization for number formats during cortical maturation.

The triple code model (Dehaene & Cohen, 1995; Dehaene, 1992) is a theoretical model that predicts that three distinct systems of representation are recruited for basic numerical processing and calculation tasks. These systems include a quantity system (which processes abstract numerical representations that are not related to number format), a verbal system (which represents numbers as words) and a visual system (which encodes numbers as strings of Arabic digits). Dehaene et al., (2003) used three-dimensional visualization software to examine how parietal activation related to this model. Using these data, they proposed that that three distinct but functionally related networks coexist in the parietal lobes, and these networks were used to support numerical processing (Dehaene et al., 2003). Briefly, the triple code model suggests that the bilateral horizontal segments of the IPS subserves the quantity system, the left angular gyrus is related to the verbal system, and the posterior SPL is related to the visual system and specifically attention processes (Dehaene et al., 2003). For over a decade, this model has driven researchers to examine the neural underpinnings of basic number processing and calculation. This influential model has been both supported and challenged by empirical research (Chassy & Grodd, 2012; Eger et al., 2003; Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004; Piazza et al., 2007; Price & Ansari, 2011). Results of the current quantitative meta-analysis challenge several aspects of the triple code model. In particular, two findings from the current study contradict the idea that IPS processes number specifically and abstractly. First, the finding that the IPL is activated by the conjunction of numerical and non-numerical stimuli (Figure 2, Table 5) suggests that the IPL processes all magnitudes and is therefore not a number specific region. Second, the current study revealed notation specific activation for symbolic compared to nonsymbolic numbers in the IPS. The right IPL and left supramarginal gyrus were specifically activated for the symbolic numbers, while the anterior right IPL showed greater activation for nonsymbolic numbers (Figure 3, Table 6). This indicates that the IPS may process numbers in a format dependent rather than abstract manner. Together, these findings question the notion put forward by Dehaene et al., (2003) that "the horizontal segment of the intraparietal sulcus (HIPS) appears as a plausible candidate for domain specificity" (p.487). Additionally, findings from the current meta-analysis both support and challenge the idea that activation in the SPL is a consequence of attending to visual dimensions of numbers. Evidence from the conjunction analyses of the current meta-analyses found that the right SPL was activated for the conjunction of symbolic and non-numerical magnitude processing as well as the conjunction of nonsymbolic and non-numerical magnitude processing. This convergence of activation could be due to a visual attention orienting response as proposed by Dehaene et al., (2003). However, the fact that symbolic>non-numerical was correlated with activation in the left SPL conflicts with the idea that the SPL supports visual attention processes. Instead, these findings reveal hemispheric asymmetry in the bilateral SPL that mirrors the IPL. Namely, that the right parietal lobule is related to the processing of all magnitudes and the left parietal lobule supports acquisition of symbolic numerical representations. Ultimately, these meta-analytic findings challenge the idea that the SPL solely supports visual attentional processing.

It has been over a decade since the initial proposal of the triple code model. The results of the current quantitative meta-analysis do not converge with the data that supports the triple code model (Dehaene et al., 2003). On the bases of these discrepancies, it is recommended that the triple code model should be updated. In particular, the system used to process number should be conceptualized as a general magnitude system rather than a number specific approximate number system, which processes numbers abstractly. This recommendation is in accordance with other theoretical perspectives (Cantlon, Platt, et al., 2009; Cohen Kadosh, Lammertyn, et al., 2008; Walsh, 2003). The parietal lobules should be canvassed in search of regions that support both format dependent and format independent numerical representations. This will illuminate the extent to which format-specific regions reflect various components of format-specific processing including semantic, perceptual and decision making processing. Furthermore, the examination of brain regions that support format dependent and format independent numerical representations will clarify which regions in the IPS and SPL are associated with various aspects of basic magnitude processing. This should ultimately illuminate the mechanism underlying magnitude processing in the parietal lobes.

4.3 Frontal vs. Parietal

During the last decade, there has been an intense focus on the parietal lobes as brain regions involved in number processing (e.g. Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Cohen Kadosh & Walsh, 2009; Dehaene et al., 2003; Eger et al., 2003; Fias et al., 2003). However, many neuroimaging studies reported activation in regions of the frontal cortex during number processing (e.g. Cohen Kadosh et al., 2007; Cohen Kadosh & Walsh, 2009; Dormal, Dormal, Joassin, & Pesenti, 2012; Dormal & Pesenti, 2009; Eger et al., 2003; Franklin & Jonides, 2008; Hayashi et al., 2013). The importance of the frontal cortex in number processing was revealed in research that used single-cell recording in animals as well as in pediatric neuroimaging studies. Specifically, invasive single-cell recording in non-human primates identified putative ‘number neurons’ in the parietal as well as the prefrontal cortex; these neurons responded to specific quantities (such as two dots) while an animals performed a number discrimination task (Nieder, Freedman, & Miller, 2002; Nieder, 2013). These findings suggested that regions of the frontal cortex may host pure magnitude representations. Similarly, pediatric neuroimaging studies showed that young children recruited the prefrontal cortex more than adults during number discrimination tasks. In contrast, IPS activation during number comparison increased across development (Ansari et al., 2005; Kaufmann et al., 2006). Researchers suggested that this frontal to parietal shift from childhood to adulthood may reflect a decrease in the need for domain general cognitive resources such as working memory and attention as children begin to process number symbols automatically (Cantlon et al., 2006; Cantlon, Libertus, et al., 2009; Venkatraman et al., 2005). The notion that regions in the frontal cortex are important for number and calculation tasks is further supported by a quantitative meta-analysis that identified brain regions supporting number processing and calculation in adults (Arsalidou & Taylor, 2011). Unlike the current meta-analysis, Arsalidou and Taylor, (2011) focused on calculation tasks such as arithmetic and subtraction tasks. Their meta-analysis showed that prefrontal regions are essential for number and calculation. Moreover, they revealed that activation in regions along the prefrontal cortex was related to the difficulty of the task. Specifically, IFG was activated during the processing of simple numerical tasks while the MFG and SFG were involved in more complex calculation problems (Arsalidou & Taylor, 2011). In view of this, Arsalidou and Taylor, (2011) suggested that this activation in the prefrontal cortex was a result of domain general processes, such as working memory, that are essential for number and calculation tasks. A common explanation for the consistent activation reported in the frontal cortex during number and calculation tasks was that the frontal cortex is activated in response to general cognitive processes associated with the task (e.g. Arsalidou & Taylor, 2011; Cantlon et al., 2006). However, it has also been argued that frontal activation is supporting numerical magnitude representations rather than general cognitive processes (for a review see: Nieder & Dehaene, 2009).

The current meta-analysis lends additional support to the idea that frontal activation is important for general cognitive processes associated with basic number tasks. Results revealed consistent activation in frontal regions during symbolic, nonsymbolic and non-numerical magnitude processing. Moreover, results showed that neural activation in response to magnitude processing is no less consistent in the frontal cortex compared to the parietal cortex. In particular, the single dataset ALE maps revealed that the MFG and IFG were activated during symbolic, nonsymbolic and non-numerical magnitude processing and the SFG was activated during symbolic and nonsymbolic magnitude processing. In a similar vein, the conjunction of symbolic and non-numerical as well as nonsymbolic and non-numerical showed activation in the IFG and MFG and the conjunction of symbolic and nonsymbolic revealed activation in the IFG, MFG and SFG. Together, these results support the notion the frontal cortex is important for the processing of basic number tasks. This frontal activation could be related to underlying magnitude representations or general cognitive processing associated with the tasks. The current meta-analysis deliberately included only basic magnitude processing tasks in order to minimize the recruitment of additional cognitive resources typically needed for complex calculation tasks. Additionally to this, all experiments included in the current meta-analysis were contrasted against control conditions. These attributes make it likely that the activation revealed in the current meta-analyses is related, at least in part, to magnitude representations. Further evidence for the idea that frontal regions may support magnitude representations is that contrast analyses revealed that the right IFG and SFG and left MFG were specifically activated by nonsymbolic numerical magnitudes but not by symbolic numerical magnitudes. The specificity of frontal activation for nonsymbolic numbers suggests that these right lateralized frontal regions may be essential for identifying the number of objects within a set. Therefore, similarly to activation in the parietal cortex, the activation patterns within the frontal cortex vary as a function of format (symbolic vs. nonsymbolic). Together, the data from the current meta-analysis indicate that there is no reason to think that the parietal cortex is more specialized for number than the frontal cortex. Consequently, this meta-analysis does not support the argument that frontal regions are involved in task demands while parietal regions are involved in semantic processing. Instead, these data indicate that both the frontal cortex and the parietal cortex may be involved in general cognitive processes associated with number tasks and magnitude representations. A meta-analytic contrast analysis comparing studies that used active compared to passive tasks would help to illuminate which brain regions are activated by responding to a task. In a similar vein, a meta-analytic contrast comparing number activation and executive functioning activation would illuminate which regions are specifically correlated with numerical representations. Ultimately, the field of numerical cognition needs to acknowledge that frontal regions are consistently engaged, even during basic number processing, and in accordance with this, reduce biases towards parietal activation.

4.4 Limitations

The present study focused on brain regions that support symbolic and nonsymbolic numerical magnitude processing as well as non-numerical magnitude processing by quantitatively synthesizing results from empirical papers. This study identified brain regions that were consistently activated across studies with varying methodologies and contrasts for numerical and non-numerical magnitudes. Importantly, the symbolic and nonsymbolic ALE maps were generated using a set of contrasts that were homogeneous. The majority of the contrasts used data from number discrimination paradigms where the participant compared either Arabic digits for symbolic numbers or dot arrays for nonsymbolic numbers. However, the contrasts that comprise the non-numerical magnitude ALE map were relatively heterogeneous. For example, contrasts comparing physical size, duration, and luminance were all included as contrasts in the non-numerical magnitude ALE map. Although ALE is a valuable methodology that can synthesize many different studies with different methods and techniques, it is important to be cognizant of the fact that the homogeneity of the contrasts within the three maps being compared are not equivalent. Additionally to this, ALE methodology has several specific limitations such as difficulty accounting for differences in statistical thresholding approaches across studies and difficulty determining the spatial extent and magnitude of the activation for each foci (for a more detailed discussion these limitations: Arsalidou & Taylor, 2011; Christ, Van Essen, Watson, Brubaker, & McDermott, 2009; Di Martino et al., 2009; Ellison-Wright, Glahn, Laird, Thelen, & Bullmore, 2008). Despite these limitations, ALE has several important advantages as a tool for synthesizing neuroimaging data. Particularly, the algorithms that underlie ALE allow for the quantification of foci among empirical papers with varying methodologies. For example, this method can account for differences in the number of runs, the duration of the presentation of the stimuli and the type of design (e.g. block vs. event related). It is likely that this diversity in methodologies is one of the main drivers of conflicting findings often reported between studies. Additionally, because neuroimaging research is so costly, the majority of empirical studies have small sample sizes. ALE groups different studies with varying methodologies by domains in order to increase sample sizes and ultimately address broader theoretical questions. Overall, ALE is a valuable meta-analytic tool that can quantitatively integrate large amounts of neuroimaging data to reveal converging patterns of findings.

Chapter 5

5 Conclusions

In conclusion, this meta-analysis has reaffirmed the well-known concept that the ability to process numerical magnitudes relies on a large number of brain regions. This study shows that overlapping and distinct regions in the frontal and parietal lobes are activated by symbolic, nonsymbolic and non-numerical magnitudes, revealing the specific roles of parietal and frontal regions supporting numerical magnitude processing. Based on the finding that all forms of magnitudes activate the right IPL, a general magnitude processing system may be located in the right IPL. Additionally, the contrasts symbolic>non-numerical and nonsymbolic>non-numerical revealed no specific non-numerical areas of activation. This suggests that while there is specialization for symbolic and nonsymbolic numerical magnitude processing, the areas involved in non-numerical magnitude processing completely overlap with those engaged by non-numerical magnitude processing. This study also illuminates the lateralization of symbolic compared to nonsymbolic number processing within the parietal lobes. Specifically, the left parietal lobe is potentially important for the mapping of symbols onto nonsymbolic or non-numerical magnitudes, while the right anterior IPL may be important for processing nonsymbolic sets of items. The lateralization of symbolic and nonsymbolic number is an intriguing avenue for future research. Additionally, this research highlights the consistency of frontal activation during numerical magnitude processing. The issue of whether this consistent frontal activation is due to general cognitive processes or numerically specific processes is an important empirical question that remains unanswered. Ultimately, the current meta-analysis extends our understanding of the brain regions associated with basic number processing and initiates future research on the neural mechanisms that underlie our essential ability to comprehend numbers.

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Curriculum Vitae

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Post-secondary Education and Degrees:

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2013-Present, M.Sc.

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2009-2013, B.Sc. (Honours)

Honours and Awards:

NSERC Alexander Graham Bell Canada Graduate Scholarship (CGS-D)
2015-2018

Western Graduate Research Scholarship
2013-2014, 2014-2015,

NSERC Alexander Graham Bell Canada Graduate Scholarship (CGS-M)
2013-2014

Clark and Mary J. Wright Scholarship
April, 2013

Deans Honour List
2010-2013

Institute of Medical Sciences Best Poster Presentation Award
August, 2013

Summer Undergraduate Research Scholarship ($2400)
Summer, 2013

Summer Undergraduate Research Scholarship ($2400)
Summer, 2012

Summer Undergraduate Research Scholarship ($2400)
Summer, 2010

University of Western Ontario Entrance Scholarship ($2000)
2009-2010

David Oucherlony Leadership Award ($50)

2007-2008,2008-2009

Related Work Experience:

Teaching Assistant
The University of Western Ontario
2013-2014, 2014-2015

Research Assistant in Maternal Behavioural Neuroscience Laboratory
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Summer, 2011, 2012, 2013

Research Assistant in the Numerical Cognition Laboratory
The University of Western Ontario
2012-2013

Research Assistant in the Cerebral Systems Laboratory
The University of Western Ontario
2011-2012

Research Assistant in the Molecular Neuroscience of Schizophrenia Laboratory
The Center for Addiction and Mental Health,
Summer, 2010

Research Assistant in the Insect Cold Tolerance Laboratory,
University of Western Ontario
2009-2010

Refereed Publications:

Sokolowski, H. M., Clouston, B. J., Gill, G., Kim, C. & Worgan, R. (2013) Grass type, vegetation cover, and predation affect abundance of *Microtus californicus* and *Thomomys bottae* in costal Mediterranean ecosystem. Immediate Science Ecology. 2: 11-7. DOI: 10.7332/ise2013.2.2.dsc.

Menon, M., Quilty, L. C., Zawadzki, J. A., Woodward, T. S., Sokolowski, H. M., Boon, H. S. & Wong, A. H. (2013). The role of cognitive biases and personality variables in subclinical delusional ideation. *Cognitive Neuropsychiatry.* 18(3):208-218. DOI: 10.1080/13546805.2012.692873.

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Non-refereed Publications:

Sokolowski, H. M. (2014) Child and brain development program meeting: Brain development, cognition and education. Report for the 30th program meeting for the Canadian Institute for Advanced Research. London, UK.

Sokolowski, H. M., Matejko, A., & Ansari, D. (2012) Training of early numeracy skills in preschool and kindergarten: An iPad training study. (Unpublished Honours Bachelor's dissertation). University of Western Ontario, London Ontario.

Poster Presentations:

Sokolowski. H. M., Fias, W., & Ansari, D. (2014, January) Are numbers specialized or grounded in a general magnitude system? A quantitative meta-analysis. Poster at the LOVE conference, Niagara Falls, Ontario Canada.

Matejko, A., Sokolowski, H. M., & Ansari, D. (2013, April). Early numeracy skills in preschool and kindergarten children: an iPad pilot study. Poster at the Biennial Meeting of the Society for Research in Child Development, Seattle, WA, USA.

Sokolowski, H. M., Matejko, A., & Ansari, D. (2013, April) Training of early numeracy skills in preschool and kindergarten: An iPad training study. Poster presented at the University of Western Ontario Honours Thesis Poster Day, London Ontario.

Matejko, A., Erdeg, B., Lefcoe, A., Sokolowski, H. M., & Ansari, D. (2012, September). Training early numeracy skills in Kindergarten children: and iPad pilot study. Poster presented at the Connought Global Challenge Symposium, Institute for Human Development, Toronto, Ontario. *Award Winning Poster

Browne, D.T., Agrati, D., Akbari, E., de Medeiros, C., Sokolowski, H.M., Sokolowski, M.B., Kennedy, J., Meaney, M., Steiner, M & Fleming, A.S. (2012, September) Maternal anxiety from pregnancy to two years post-partum: Examining the interactive roles of 5-HTTLPR and early child trauma. Presented at Connaught Global Challenge International Symposium, Institute for Human Development, Toronto Ontario.

Sokolowski, H.M., Mileva-Seitz V., Kennedy, J.L., Meaney, M. J. Sokolowski, M. B., & Fleming, A. S. (2012, August) Corticotrophin Releasing Hormone Receptor 1 (CRHR1), life events and maternal behavior: A MAVAN Project. Presented at the University of Toronto Institute of Medical Sciences Research Day, Toronto Ontario. *Award Winning Poster

Wonch, K.E., Steiner, M, de Medeiros, C.B., Barrett, J.A., Sokolowski, HM., Fleming, A.S. & Hall, G. (2012) The neural correlates of responsiveness to infant cues in mothers with and without postpartum depression. University of Toronto, Psychology. Presented at McMaster Brain and Body Conference, Hamilton, Ontario.

Zawadzki, J.A., Menon, M., Quilty, L.C., Woodward, T.S., Sokolowski, H.M., Boon, H.S. & Wong, A.H.C. (2012, July) Predictors of Sub-clinical delusional ideation in the general population. Center for Addiction and Mental Health. Presented at the Gordon Conference on the neurobiology of cognition, Lucca (Barga), Italy.

Sokolowski, H.M., Wonch, K., De Medeiros, D., Barrett, J., Hall, G., Steiner, M. & Fleming, A.S. (2011, August) fMRI activation patterns in new mothers suffering from post-partum depression in response to infant pictures. Presented at the University of Toronto Institute of Medical Sciences Research Day, Toronto Ontario.

Sokolowski, H.M., John Zawadzki, Heather Boon, Mahesh Menon and Albert H. C. Wong (2010, August) Cognitive factors associated with belief formation in the general population. Presented at the University of Toronto Institute of Medical Sciences Research Day, Toronto Ontario.

Oral Presentations:

Sokolowski, H. M., Ansari, D. (2013) A theory of magnitude. Lab Retreat Presentation, Bayfield, Ontario.

Sokolowski, H. M., Sokolowski, M. B. & Fleming, A. (2013, December) Gene-Environment Interplay: A MAVAN Study, University of Toronto.

Sokolowski, H. M. (2014) Language Development. Guest Lecture in Course 2043A Exceptional Child: Developmental Disorders, University of Western Ontario, London Ontario.

Sokolowski, H. M., Ansari, D. (2013) A theory of magnitude. Developmental Brownbag London, Ontario.

Sokolowski, H. M. (2013) The development of early numeracy. Guest Lecture in Course 2043A Exceptional Child: Developmental Disorders, University of Western Ontario, London Ontario.

Sokolowski, H.M., & Matejko, A. (2012) Early development of numeracy skills through technology. Presentation for teachers at London District School Board Professional Development Day.