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The Neurocognitive Underpinnings of Arithmetic in Children and Adults: Examining the Roles of Domain General and Domain Specific Abilities

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Abstract

What are the cognitive underpinnings of arithmetic and how do they contribute to individual differences in children's calculation abilities? Behavioural research has provided insights into which domain general (e.g., working memory) and domain specific (e.g., symbol-quantity associations) competencies are important for the acquisition of arithmetic skills. However, how domain general and domain specific skills are related to arithmetic at the neural level remains unclear. This thesis investigates the interplay between arithmetic and both domain general and specific competencies in the brain.

In Chapter 2 I examine how visuo-spatial working memory (VSWM) networks overlap with those for arithmetic in children and adults. While both children and adults recruited the intraparietal sulcus (IPS) for VSWM and arithmetic, children showed more focal activation within the right IPS, whereas adults recruited the bilateral IPS. These findings indicate that the regions underlying VSWM and arithmetic undergo age-related changes and become more left-lateralized in adults.

Chapter 3 provides evidence that basic number processing networks overlap with those for arithmetic in adults and children. Number processing and arithmetic elicited conjoint activity in the IPS in children and adults. Their overlap was also related to arithmetic problem size (i.e., how demanding the problems were of time-intensive procedural strategies); both arithmetic and basic number processing recruited the IPS when the problems relied on procedural strategies that likely involve the manipulation of numerical quantities.

In Chapter 4 I investigate how individual differences in domain general and domain specific competencies relate to the recruitment of the IPS during arithmetic. Both VSWM and symbolic number skills correlated with brain activity in the IPS, however, the relationships depended on the index of brain activity used. VSWM was related to a neural index of arithmetic complexity (neural problem size effect), whereas symbolic number skills were related to overall arithmetic activity (small and large problems).

The present thesis provides the first empirical evidence that shows how domain general and domain specific abilities are related to the neural basis of arithmetic in children and adults. Moreover, this thesis suggests the IPS plays a multifaceted role during arithmetic and cannot be attributed to one function.

Keywords

Arithmetic, domain general, domain specific, visuo-spatial working memory, number processing, fMRI, individual differences, children

Co-Authorship Statement

The work presented in this doctoral thesis was designed and written in collaboration with my advisor, Dr. Daniel Ansari. For each of the studies within this thesis Dr. Ansari contributed to the design, analysis, and interpretation of the findings. Though this thesis is my own work, it should be acknowledged that Dr. Ansari contributed to the revising and editing of each of the chapters.

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Chapter 1

1 General Introduction

The acquisition of fluent arithmetic skills in not only an important milestone in the development of mathematical thinking, but it is also critical for academic and economic success (Bynner, 1997; Parsons & Bynner, 2005). Indeed, children's school-entry math skills have been found to be the strongest predictor of later academic achievement (Duncan et al., 2007). Arithmetic and mathematical skills are also becoming increasingly important in today's economy where jobs routinely require a level of functional numeracy (math competencies related to economic outcomes and employability). In Canada, high school students are falling behind other OECD countries on measures of mathematics (OECD PISA study: Brochu, Deussing, Houme, & Chuy, 2012). Fifty-five percent of Canadian university graduates have numeracy skills below average, and those with the lowest scores are less likely to hold professional and managerial positions even after holding other factors constant (Statistics Canada: Hango, 2014). In other countries, measures of math proficiency (e.g., arithmetic, word problems, algebra and measurement) also predict wages and employability (Bynner, 1997; Hanushek & Woessmann, 2008; Parsons & Bynner, 1997). Strikingly, a recent study found that individuals with poorer basic calculation skills were more likely to default on their mortgage, even after controlling for cognitive and sociodemographic variables (Gerardi, Goette, & Meier, 2013). This is likely a consequence of poor saving, spending, and investing patterns in individuals with lower calculation abilities (James & Oldfield, 2007; Lusardi & Mitchell, 2009).

The trajectories for poor numeracy skills likely begin early, and numerical competencies measured in the first years of school predict later success in math (Duncan et al., 2007; LeFevre et al., 2010; Schneider et al., 2016). Children's early numerical skills have been found to predict later success in arithmetic irrespective of age, gender, intelligence, and socio-economic status (Vanbinst, Ceulemans, Ghesquière, & De Smedt, 2015). Early numerical skills in kindergarten are also related to functional numeracy skills six years later in adolescence (Geary, Hoard, Nugent, & Bailey, 2013). These findings highlight that basic numeracy and arithmetic skills learned early in elementary school may have life-long effects. Therefore, it is important to better understand the development and acquisition of arithmetic by exploring its neurocognitive foundations. This research can constrain our understanding of how children learn arithmetic and could in turn be used to inform and tailor educational practices.

Arithmetic is a complex skill and it is likely that multiple cognitive factors influence individual differences in arithmetic proficiency. Research has begun to uncover the behavioural and neural contributions to the acquisition of arithmetic skills, although many questions remain unexplored. In this thesis I examine the neurocognitive underpinnings of arithmetic by exploring how working memory and basic number processing skills share common neural circuits with arithmetic in adults and children. I also explore whether individual differences in multiple cognitive abilities relate to how children recruit different regions of the brain during arithmetic. Below, I provide an overview of the behavioural literature that examines the cognitive determinants of arithmetic abilities. This literature has greatly informed which skills are important for the acquisition of arithmetic, and has guided much of the existing neuroimaging research. Next, I provide a summary of the neuroimaging literature that investigates the neural correlates of arithmetic in adults and children and how different cognitive skills may underpin the components of the arithmetic network. Finally, I discuss limitations with the existing neuroimaging literature and how the present thesis aims to address these gaps.

1.1 Behavioural Predictors of Arithmetic Skills

The cognitive predictors of arithmetic skills have been extensively studied using behavioural methods. Much research has focused on the domain specific and domain general determinants of arithmetic skills (Vanbinst & De Smedt, 2016). Domain specific abilities refer to skills that are exclusively related to mathematical competencies (e.g., knowledge of number symbols or numerical quantities), whereas domain general abilities are skills that are important for information processing across domains (e.g., working memory or attention) (Vanbinst & De Smedt, 2016). A better understanding of how these factors are related to calculation can provide some insights into which early-developing skills are markers of later success or difficulties in arithmetic. In the sections below I review which domain specific and domain general predictors are related to the acquisition of arithmetic skills and how these predictors may shift over development. This literature provides an important background for the present thesis because it indicates which cognitive abilities are most important for arithmetic. It has also informed much of the current neuroimaging literature investigating the neurocognitive development of calculation.

1.1.1 Domain Specific Predictors of Arithmetic

1.1.1.1 Symbolic and nonsymbolic skills

Before children can become fluent with arithmetic, they first need to develop an understanding of symbolic numbers (Arabic digits such as 2 or 5) and the quantities they represent. For example, a child needs to be able to be able to identify that four apples can be enumerated and can also be represented with the symbolic digit “4”. Research examining the domain specific predictors of arithmetic skills has overwhelmingly focused on how fluency with symbolic and nonsymbolic (i.e., dots) quantities relates to concurrent and later arithmetic skills. Children’s symbolic and nonsymbolic skills are typically assessed using a number comparison task, where they are presented with two symbolic or nonsymbolic quantities and are asked to identify which is numerically larger. Children who are better able to discriminate between numerical quantities score higher on tests of arithmetic (Bartelet, Vaessen, Blomert, & Ansari, 2014; De Smedt, Verschaffel, & Ghesquière, 2009; Holloway & Ansari, 2009; Nosworthy, Bugden, Archibald, Evans, & Ansari, 2013; Schneider et al., 2016), and children with specific deficits in arithmetic (developmental dyscalculia) perform poorly on these measures (Butterworth, 2010; Landerl, Bevan, & Butterworth, 2004; Mussolin, Mejias, & Noël, 2010). The relationship between quantity discrimination tasks and arithmetic is thought to be related to individual differences in the precision of symbolic and nonsymbolic number representations; individuals who have more precise number representations are able to calculate more rapidly and efficiently (Feigenson, Libertus, & Halberda, 2013). Though both symbolic and nonsymbolic skills correlate with arithmetic abilities, the relationship between symbolic comparison and arithmetic is generally stronger and more robust (De Smedt, Noël, Gilmore, & Ansari, 2013; Schneider et al., 2016).

1.1.1.2 Mapping between symbolic and nonsymbolic formats

Infants and non-human primates are thought to have a rudimentary number sense because they can discriminate between nonsymbolic quantities if the difference between the quantities is sufficiently large (Cantlon, 2012; Nieder & Dehaene, 2009; Xu & Spelke, 2000). Because nonsymbolic representations of number develop early, it has been hypothesized that they provide a scaffold onto which symbolic numbers are learned (Dehaene, 2007; Piazza, 2010). Increasingly, research has revealed that the ability to link symbolic and nonsymbolic quantities is correlated with individual differences in arithmetic and math abilities (Bartelet et al., 2014; Brankaer, Ghesquière, & De Smedt, 2014; Kolkman, Kroesbergen, & Leseman, 2013; Mundy & Gilmore, 2009). The ability to map between different number formats has been found to predict unique variance in children's arithmetic skills, even after accounting for other basic number processing skills such as number comparison abilities (Brankaer et al., 2014). Symbolic-to-nonsymbolic mapping may also mediate the development from informal to formal math abilities (Göbel, Watson, Lervåg, & Hulme, 2014; Purpura, Baroody, & Lonigan, 2013), suggesting that it may have an important role in the acquisition of formal arithmetic skills. Though much of this literature is still in its infancy, these findings converge to suggest that a fluent understanding of symbol-quantity relationships is particularly important for arithmetic and mathematical skills.

1.1.1.3 Symbolic ordering

Though most of the research examining domain specific predictors of arithmetic has concentrated on number comparison, there has been an increasing focus on symbolic ordering and how understanding the relationships between numbers and their relative position is related to arithmetic abilities (Goffin & Ansari, 2016; Lyons & Ansari, 2015; Lyons & Beilock, 2011; Lyons, Price, Vaessen, Blomert, & Ansari, 2014). Tests of symbolic ordering often involve the presentation of three digits, and the participant is required to identify whether the numbers are in the correct ascending order not (e.g., " 2 3 4" vs "3 4 2"). Performance on symbolic ordering tasks is highly predictive of arithmetic performance in childhood and adulthood (Goffin & Ansari, 2016; Lyons & Ansari, 2015; Lyons et al., 2014). However, there are developmental changes in the importance of symbolic ordering skills. Cross sectional studies have found that symbolic ordering becomes more strongly related to arithmetic skills over development (Lyons & Ansari, 2015; Lyons et al., 2014), and it is not until Grade 4 that it becomes one of the strongest domain specific predictors of arithmetic skills (Lyons et al., 2014). As children become more fluent with arithmetic, an understanding of the relative magnitudes of numbers (assessed through symbolic comparison) may become less important for calculation, whereas ordinal information may become more critical (Lyons et al., 2014).

1.1.2 Domain General Predictors of Arithmetic

1.1.2.1 Working memory

Abilities such as holding information in mind and manipulating that information (working memory), ignoring distracting information (inhibition), and flexible thinking (shifting), have all been associated with calculation skills (Cragg & Gilmore, 2014). However, there has been a large focus on the role of working memory in calculation because it may facilitate the solution of more difficult arithmetic problems by manipulating numbers and holding intermediate steps (DeStefano & LeFevre, 2004; Menon, 2016). Visuo-spatial working memory (VSWM) and verbal working memory are both strong predictors of arithmetic skills (Peng, Namkung, Barnes, & Sun, 2015; Raghubar, Barnes, & Hecht, 2010). Many studies have also demonstrated that children with developmental dyscalculia have poorer VSWM abilities (Fias, Menon, & Szucs, 2013; McLean & Hitch, 1999; Menon, 2016; Rotzer et al., 2009), and that it may be one of the strongest predictors of math learning disabilities (Szucs, Devine, Soltesz, Nobes, & Gabriel, 2013).

The relative importance of VSWM and verbal working memory for arithmetic may change over development. VSWM may be more important for arithmetic problem solving earlier in development and verbal working memory may become increasingly important later in development (McKenzie, Bull, & Gray, 2003; Rasmussen & Bisanz, 2005). However, developmental decreases in the recruitment of VSWM have not been observed in all studies. For example, a meta-analysis examining the relationship between arithmetic and different components of working memory found no age-related decreases (Peng et al., 2015). The authors of this meta-analysis contend that the role of working memory may be dependent on task difficulty, and studies examining the relationship between these skills tend to select more difficult and developmentally appropriate tasks as children get older. Therefore, if the arithmetic task is kept constant, the working memory demands are likely to gradually decrease as children use fewer strategies that require effortful calculation. This may indicate that working memory remains important for arithmetic across development as long as the problem is calculated rather than retrieved and requires effortful processing (e.g., manipulating quantities or calculating intermediate steps).

1.1.2.2 Verbal and phonological skills

The domain general skills that support the acquisition of and fluency with arithmetic are not limited to working memory, but also include verbal and language skills (Durand, Hulme, Larkin, & Snowling, 2005; Fuchs et al., 2006; LeFevre et al., 2010; Vukovic & Lesaux, 2013). It has been suggested that linguistic skills (e.g., vocabulary, verbal reasoning, phonological awareness) may be indirectly related to arithmetic through symbolic number skills, and that verbal abilities influence the way children understand and reason with numbers (LeFevre et al., 2010; Vukovic & Lesaux, 2013). However, more direct pathways may also exist. In particular, phonological processing has been found to be directly related to arithmetic performance (De Smedt, Taylor, Archibald, & Ansari, 2010; Vukovic & Lesaux, 2013). Individual differences in phonological processing have been related to small arithmetic problems or problems that were more likely to be solved by retrieving the solution from memory (De Smedt, Taylor, et al., 2010). Therefore, better phonological representations are associated with more efficient and verbally-mediated arithmetic strategies in children (De Smedt, Taylor, et al., 2010). Together, this literature points to a role for verbal abilities in the acquisition and fluency of arithmetic.

1.1.3 Combining Domain Specific and Domain General Predictors of Arithmetic.

As illustrated in the review above, arithmetic is a complex skill and the cognitive predictors of arithmetic are multifaceted. Most of the aforementioned studies focused on either domain general or domain skills as predictors of arithmetic, and few studies have simultaneously examined how both of these abilities predict future arithmetic performance. By using measures of either domain general or domain specific predictors of arithmetic, but not both, it is unclear whether they each contribute equal variance to children's arithmetic skills or whether they interact. Studies examining multiple predictors of arithmetic have begun to disentangle how domain specific and domain general skills simultaneously contribute to calculation. For example, Fuchs and colleagues (2010) found that the domain general and domain specific predictors differ depending on how arithmetic problems are assessed in 5-7 year old children. Domain specific number processing skills were more closely related to measures of arithmetic fluency (problems such as 5 + 7) and domain general variables did not add any significant unique variance. In contrast, both domain specific and domain general measures predicted performance on word problems that also involved arithmetic. In slightly older children, Szucs et al. (2014) found that domain general skills, such as verbal intelligence, phonology, spatial skills, planning, and visuo-spatial short term and working memory were the strongest predictors of arithmetic. None of the domain specific measures (such as symbolic and nonsymbolic comparison) emerged as significant unique predictors. Therefore, there still appears to be no consensus on the strongest predictors once all domain general and domain specific measures are considered. These studies, however, do highlight that the type of arithmetic measure and the age at which arithmetic is being assessed will likely play a role in which domain general or domain specific predictors are the strongest.

1.2 Neural Basis of Arithmetic

The behavioural literature discussed above presents a complex picture of the domain general and domain specific contributions to arithmetic skills. Even though cognitive processes cannot be directly inferred from brain imaging, understanding the neural correlates of arithmetic, how they develop, and how they are related to other brain networks can provide an additional level of explanation (Vanbinst & De Smedt, 2016). Importantly, neuroimaging can also provide neurobiologically plausible hypotheses that can then be used to inform other behavioural research (De Smedt, Ansari, et al., 2010; Poldrack, 2000).

Numerous investigations have examined the neural basis of calculation and have revealed a bilateral fronto-parietal network of brain regions that are commonly activated during arithmetic tasks (see Figure 1.1b, Arsalidou and Taylor, 2011). Many inferences have been made about the functions of each region within the arithmetic network. Activation in the bilateral middle and inferior frontal gyri as well as the left superior frontal gyrus is thought to reflect more domain general factors related to attention, working memory, task difficulty, and goal monitoring (Arsalidou & Taylor, 2011; Delazer et al., 2005; Ischebeck et al., 2006; Metcalfe, Ashkenazi, Rosenberg-Lee, & Menon, 2013). In contrast, activation in the intraparietal sulcus (IPS) as well as the superior and inferior parietal cortex have been thought to reflect more domain specific skills required for calculation such as numerical magnitude processing (see Figure 1.1a; Arsalidou & Taylor, 2011; Bugden et al., 2012; Menon, Rivera, White, Glover, & Reiss, 2000). To test how different components of the fronto-parietal network are driven by particular cognitive demands, some studies have attempted to isolate activity related to task difficulty or calculation specific skills. Task difficulty has been shown to increase the engagement of the inferior frontal cortex, whereas calculation specific skills have been associated with activation in the inferior parietal cortex, particularly in the IPS, as well as the angular and supramarginal gyri (Gruber, Indefrey, Steinmetz, & Kleinschmidt, 2001; Kong et al., 2005; Menon et al., 2000; Menon, Mackenzie, Rivera, & Reiss, 2002).

The literature examining the neural correlates of arithmetic has shown that brain activity is modulated by a number of factors including the difficulty of the problem, the type of arithmetic operation, the kind of strategy used, and experience. Research has moved beyond localizing regions related to calculation and has now provided several insights into how different components of the network are related to the cognitive demands underpinning arithmetic problem solving. Below, I provide an overview of how the arithmetic network changes with experience and development, and how different arithmetic strategies are reflected in the brain. I will also provide a more detailed account of how domain specific (e.g., basic number processing) and domain general (e.g., VSWM) abilities are related to the arithmetic network. This research has informed the present thesis by providing insights into how the neural networks for arithmetic develop and how different components of this network might be related to different cognitive demands.

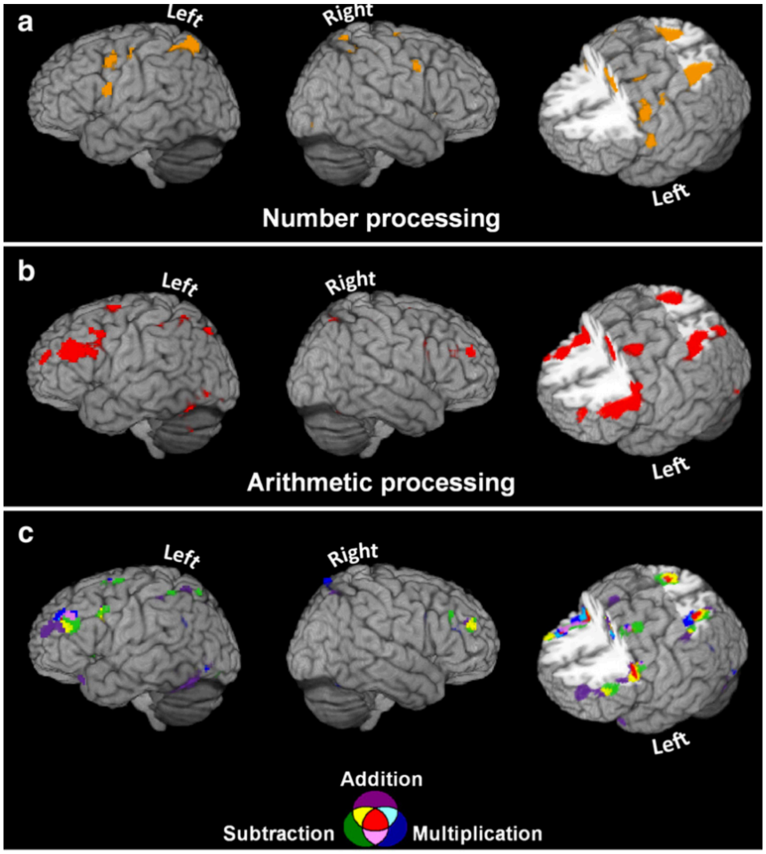

Figure 1.1 Brain activity during number processing (a), overall arithmetic (b), and different arithmetic operations (c). This figure is adapted from Arsalidou and Taylor (2011)

1.2.1 Developmental Changes in the Arithmetic Network

The cognitive demands of arithmetic problem solving change over development (e.g., McKenzie et al., 2003; Rasmussen & Bisanz, 2005; Alloway & Passolunghi, 2011), and this is thought to be related to a fronto-parietal shift in brain activation as children get older. Several studies have shown increasing engagement of brain regions related to number processing and decreases in brain regions related to domain general processes (Kucian, Von Aster, Loenneker, Dietrich, & Martin, 2008; Rivera, Reiss, Eckert, & Menon, 2005; Rosenberg-Lee, Barth, & Menon, 2011). In a seminal paper, Rivera et al. (2005) found that brain activity during an arithmetic verification task was positively correlated with age in the left supramarginal gyrus, anterior IPS, and lateral occipitotemporal cortex. In contrast, brain activity was negatively correlated with age in the dorsolateral and ventrolateral prefrontal cortex, as well as the basal ganglia and hippocampus. These findings indicate that younger children rely on prefrontal brain regions to a greater degree than older children. Furthermore, they also suggest that the left inferior parietal cortex becomes increasingly specialized for mental arithmetic over developmental time. Other research has largely confirmed these findings. Similar age-related changes have been documented when comparing arithmetic networks in children and adults (Kucian et al., 2008), and when comparing children who are one year apart (Rosenberg-Lee et al., 2011). During an arithmetic task, third grade students showed greater activity when compared to second grade students in the superior parietal lobule, IPS, angular gyrus, ventral visual areas, and the dorsolateral prefrontal cortex. In contrast, second grade students only showed greater activity in the right ventromedial prefrontal cortex when compared to third grade students (Rosenberg-Lee et al., 2011). This literature converges to suggest a dynamic fronto-parietal shift in the arithmetic network over development that has been largely attributed to decreasing demands on cognitive control during arithmetic. Learning arithmetic is therefore similar to how other skills are acquired: a change from more general-purpose (domain general) to task-specific (domain specific) processing (Poldrack, 2000). However, developmental changes in strategy use likely also contribute to the fronto-parietal shift and to the brain regions used to solve arithmetic problems.

1.2.2 How Strategies Impact the Calculating Brain

Different cognitive strategies are implemented depending on the type of arithmetic problem (i.e., addition vs. subtraction) and the difficulty of the problem. Some problems are solved by retrieving the solution from memory, whereas others are solved by using more procedural and time intensive strategies such as counting or decomposing the problem into smaller parts. The problem size effect refers to the phenomenon where problems with smaller operands are more likely to be retrieved (sums < 10), whereas problems with larger operands (sums > 10) are more likely to be solved by calculation, resulting in longer response times for large compared to small problems (Campbell & Xue, 2001; LeFevre et al., 1996). Verbal strategy reports or manipulations of problem size have been used to investigate the functional correlates of arithmetic strategies. Smaller problems, or problems that are solved using retrieval, have been shown to activate perisylvian language regions in the left hemisphere, particularly the left angular and supramarginal gyri (Grabner et al., 2009; Kong et al., 2005). In contrast, larger problems, or problems solved using calculation, tend to activate a large fronto-parietal network including the IPS (Grabner et al., 2009).

Individual differences in math proficiency also modulate the recruitment of these regions; individuals who are higher performers on standardized tests of arithmetic recruited the left angular gyrus more than lower performers during a multiplication task (Grabner et al., 2007). These findings indicate that individuals who are more proficient in mathematics may rely on fact-retrieval and automatic verbally-mediated strategies. Converging evidence from Price, Mazzocco, and Ansari (2013) also highlights how individual differences in math proficiency can have an impact on the regions that are recruited during simple arithmetic. They found that individuals with lower high-school math scores had greater activity in right IPS during an arithmetic task, potentially indicating the use of more procedural based strategies. In contrast, higher math performers recruited brain regions that are more commonly associated with retrieval-based strategies including the left supramarginal gyrus and anterior cingulate cortex.

Children also exhibit a neural problem size effect when solving arithmetic problems. In a study with 10-12 year old children, De Smedt and colleagues (2010) found that large problems activated a fronto-parietal network more than small problems, suggesting that difficult problems are associated with greater use of the fronto-parietal network. The authors also found that subtraction problems elicited more activity within the fronto-parietal network than addition problems, which might be related to subtraction problems relying more procedural strategies than addition (Campbell & Xue, 2001). Training studies have also indicated that experience and practice with arithmetic changes the types of strategies that are utilized, and this is reflected in the underlying neural networks (for a review see Zamarian, Ischebeck, & Delazer, 2009). These studies have pointed to a shift in activation from the IPS to the angular and supramarginal gyri following training of arithmetic problems (Delazer et al., 2003, 2005; Ischebeck et al., 2006). Therefore, as adults or children become more familiar with arithmetic problems, they increasingly rely on retrieval strategies, which is related to a shift in brain activity from the IPS to the angular and supramarginal gyri. Together, these findings provide evidence that the cognitive operations being performed on arithmetic problems modulate brain activity within the arithmetic network. Greater fluency with arithmetic is also reflected in a shift from regions that are commonly associated with effortful calculation (IPS) to regions that support verbally-mediated retrieval strategies (angular and supramarginal gyri).

1.2.3 The Role of Domain General and Domain Specific Abilities in the Arithmetic Network

Even though many studies have made the distinction between domain general processes in the frontal cortex versus domain specific processes in the parietal cortex, most of this work has relied on reverse inferences, comparisons across studies, or brain-behaviour correlation to understand these associations. For example, a common reverse inference in the literature is that activation in the parietal cortex arithmetic is related to numerical magnitude processing. This is assumed because other literature has found that number processing tasks elicit brain activity within this region (Arsalidou & Taylor, 2011; Dehaene, Piazza, Pinel, & Cohen, 2003). Such assumptions are problematic because different functions can be attributed to the same brain structures (Poldrack, 2012), and it is likely that a more complex picture exists of how domain general and domain specific skills relate to arithmetic. With this caveat in mind, I provide an overview of the literature on how arithmetic brain networks overlap with those for domain specific and domain general processes. In particular, I focus on basic number processing skills (such as number comparison) and VSWM due to their strong association with arithmetic in the behavioural literature.

1.2.3.1 Arithmetic and basic number processing

Several key pieces of evidence from behavioural and neuroimaging literature point to arithmetic skills being scaffolded on earlier basic numerical competencies, and indicate that they may have shared neural circuits within the IPS. In an fMRI meta-analysis that included studies on both number processing and arithmetic tasks, overlapping activity was observed in the superior and inferior parietal lobules in addition to a number of other regions (Figure 1.1a) (Arsalidou & Taylor, 2011). Regions that are activated for both basic number processing (such as number comparison) and calculation may serve as a neuroanatomical scaffold, where basic number processing skills form the basis from which arithmetic skills are learned. Though few studies have simultaneously examined the overlapping activation for basic numerical tasks and arithmetic in the same sample of participants, some evidence points to common neural substrates. For instance, Knops and Willmes (2014) examined the neural overlap between symbolic ordering and addition and subtraction. They found that ordering and arithmetic had shared neural substrates in a network of regions including the bilateral IPS, however, they found that brain activity between ordering and arithmetic was most similar in the right IPS. They further hypothesized that subtraction might rely more on symbolic ordering than addition due to its greater demand on basic number concepts. Indeed, they found that the spatial patterns of activation were more similar in the right IPS between ordering and subtraction than with addition. This provides strong evidence that basic number processing and arithmetic share common neural substrates localized within the IPS, and this relationship may depend on the cognitive demands of the arithmetic problem.

Similar research has explored how magnitude processing skills overlap with networks involved in arithmetic in adults. Number comparison and multiplication were found to have shared neural circuits in the bilateral occipital cortices, left precentral gyrus, and supplementary motor area, but not in the parietal cortex (Dehaene et al., 1996; Rickard et al., 2000). This lack of overlap in the parietal cortex, particularly in the IPS, may largely be due to the kinds of strategies that are used to solve multiplication problems: single digit multiplication problems are predominantly solved by retrieval and are therefore not highly demanding of strategies that rely on the manipulation of quantities (for a more detailed discussion of how strategies modulate the arithmetic network see section 1.2.2 above). Operations such as subtraction, which are more often calculated and require a greater manipulation of quantities, may show greater overlap with magnitude processing skills. Therefore, the literature that has concurrently examined brain networks involved in basic number processing tasks and arithmetic is mixed, and no studies to date have simultaneously examined these processes in children.

Brain-behaviour correlations have also been used to infer relationships between basic number processing tasks and arithmetic, and several studies have documented relationships between parietal brain activity during number comparison tasks and measures of arithmetic proficiency. For instance, Bugden et al. (2012) found that children who recruited the left IPS more during a symbolic number comparison task had higher scores on a standardized test of arithmetic. Similarly, Haist and colleagues (2014) demonstrated that the neural response to a nonsymbolic comparison task was related to measures of arithmetic and math achievement in a number of brain regions. This included, but was not limited to, the right superior, inferior, and intraparietal cortex. Studies have also indicated that arithmetic proficiency is not only associated with activity in isolated brain regions, but is also related to the connectivity between those regions. Emerson and Cantlon (2012) found that brain connectivity in neural networks associated with symbolic-to-nonsymbolic mapping predicted children's math performance. These findings suggest that individual differences in children's arithmetic proficiency are related to basic number processing skills, and that the parietal cortex may be a particularly critical region for this relationship. They also provide some converging evidence that the parietal cortex, particularly the IPS, is related to both basic numerical processes and arithmetic. However, this has largely been inferred by making comparisons across studies or by using brain-behaviour correlations, hence this literature cannot directly determine whether arithmetic and number processing have the same neural basis within the IPS.

1.2.3.2 Arithmetic and visuospatial working memory skills

VSWM recruits a distinctly similar fronto-parietal network to arithmetic which includes superior frontal brain regions and parietal regions, such as the intraparietal sulcus (IPS) (see Figure 1.2). Both adults and children recruit a front-parietal network for VSWM (Scherf, Sweeney, & Luna, 2006), and there are linear increases in the recruitment of these regions with age (Klingberg, Forssberg, & Westerberg, 2002; Kwon, Reiss, & Menon, 2002; Scherf et al., 2006). VSWM capacity has been correlated with the recruitment of the left superior frontal sulcus and the IPS within this network (Klingberg et al., 2002). Because arithmetic and VSWM rely on a fronto-parietal network of brain regions, there may be considerable overlap in the neural circuitry that underlies these abilities. The shared neural substrates for arithmetic and VSWM may provide a neurobiologically plausible explanation for the close relationship between the two skills, especially if they are correlated with activity in the same neuronal populations.

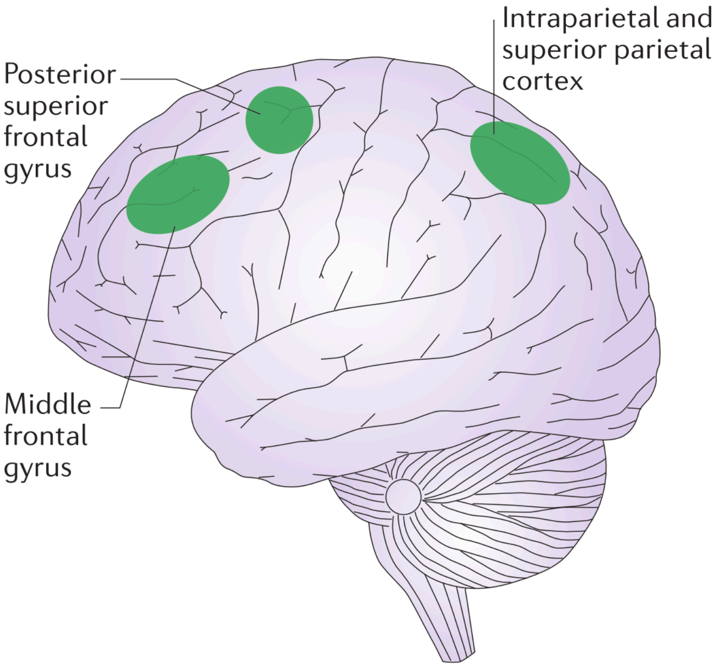

Figure 1.2 Brain regions associated with VSWM. Figure adapted from Constantinidis and Klingberg (2016).

Some limited research has examined whether VSWM and arithmetic have common neuronal circuits adults. VSWM and arithmetic have been found to have overlapping activation in the bilateral IPS, right middle frontal gyrus/superior frontal sulcus, right superior parietal lobule, and the left supramarginal gyrus (Zago et al., 2008). Similar patterns have been observed by comparing tasks across participants as well (Zago & Tzourio-Mazoyer, 2002). Though no research has simultaneously investigated these processes in children, some studies have examined how brain activity is associated with behavioural performance on either VSWM or arithmetic tasks. For instance, one study demonstrated that greater recruitment of the left, but not the right, IPS during VSWM predicted children's arithmetic scores 2 years later (Dumontheil & Klingberg, 2012). Children with dyscalculia have also been found to recruit the right IPS, insula, and inferior frontal cortex for VSWM less than typically developing children (Rotzer et al., 2009). Together, these findings suggest a link between the recruitment of VSWM networks and individual differences in arithmetic proficiency. Other studies have also demonstrated that the recruitment of the arithmetic network is related to behavioural measures of VSWM. Children with higher VSWM scores recruited several frontal and parietal brain regions more during an arithmetic task (Ashkenazi, Rosenberg-Lee, Metcalfe, Swigart, & Menon, 2013; Demir, Prado, & Booth, 2014; Metcalfe et al., 2013), indicating that the neural basis of arithmetic is modulated by children's VSWM capacities. However, the relationship between individual differences in VSWM abilities and brain activity during arithmetic is not observed in children with dyscalculia, even in the same regions where relationships are observed in typically developing children (Ashkenazi et al., 2013). This indicates that children with poor math skills seem to recruit VSWM resources differently than typically developing children (Ashkenazi et al., 2013). As a whole, the literature examining brain-behaviour correlations in children has demonstrated a close relationship between VSWM and arithmetic performance within fronto-parietal brain regions and has consistently demonstrated these relationships within the IPS.

When surveying the neuroimaging literature on VSWM and arithmetic, the role of the parietal cortex in arithmetic is unclear. VSWM elicits brain activity in the parietal cortex, including the IPS (e.g., Klingberg, 2006), and brain-behaviour relationships have shown associations between these skills within this region. Therefore, the recruitment of the IPS during calculation could be associated with domain specific processes related to number representations, but it could also be elicited by the activation of domain general processes such VSWM. A within-subjects approach is thus necessary to determine whether arithmetic and VSWM have common underlying neural substrates in adults and children, and to disentangle the precise cognitive origins of brain activity within IPS during arithmetic. The present thesis uses such an approach by examining VSWM, number processing, and arithmetic in the same sample of participants to explicitly test whether they have a common neural basis.

1.3 Summary, Outstanding Questions, and Overview of the Current Thesis

The literature reviewed above reveals an incomplete picture of the neurocognitive underpinnings of arithmetic and how they change over development. Though the behavioural literature has provided some consensus on the domain specific and domain general predictors of arithmetic abilities in children, our understanding of how these skills are interrelated at the neural level is still poor. Neuroimaging can help disentangle the relationships between arithmetic, domain general, and domain specific skills, and further clarify some of the relationships observed in the behavioural literature by providing evidence for similarities and differences in processing at the neurobiological level.

Several assumptions have been made about the role of domain specific and domain general factors in the arithmetic network. First, it is often assumed that that the IPS is recruited during the solution of arithmetic problems due to its role in manipulating quantities. However, very few studies have empirically tested this hypothesis in the *same sample of participants*. The studies that have examined these relationships have only examined them in adults and have often used arithmetic tasks that are unlikely to be demanding on magnitude systems (e.g., multiplication). The overlap between basic number processing networks and arithmetic is likely to be strongest in childhood, when children have not yet mastered arithmetic and are using computationally intensive strategies such as calculation.

A second common assumption relates to the role of domain general processes in the arithmetic network. Previous literature has demonstrated that brain networks involved in arithmetic undergo a fronto-parietal shift in brain activity over development (Rivera et al., 2005). This has been interpreted as evidence for reductions in the frontally-mediated, domain general processes of arithmetic over time. However, skills such as VSWM rely on a superior fronto-parietal network that has been found to overlap with arithmetic in the bilateral IPS and in superior frontal brain regions in adults (Zago & Tzourio-Mazoyer, 2002; Zago et al., 2008). Therefore, domain general processes likely exert an influence on arithmetic outside of the frontal cortex. Brain activity in the IPS may not exclusively be related to basic number processes alone, but could also be related to VSWM. Using a developmental approach will be imperative to understanding how VSWM are related to one another, particularly while children are actively acquiring arithmetic skills and are still using cognitively demanding calculation strategies.

In summary, our understanding of the neural relationships between arithmetic, and domain specific and domain general skills has predominantly been based on reverse inferences, comparisons across studies, and brain-behaviour correlations. Moreover, we have a poor understanding of how these processes are related at the neural level in children, when some of these relationships might be expected to be the strongest. The present thesis aims to address these outstanding questions by using a developmental within-subjects approach to investigate the role of VSWM and basic number processing skills in the neural basis of arithmetic. The structure of this thesis is described below.

In Chapter 2, I present a study that examines the common neural substrates of VSWM and arithmetic in children and adults. The objectives were to: (1) examine how VSWM and arithmetic brain networks overlap in the same sample of children and adults; and (2) determine whether there are age-related changes in the neural association between VSWM and arithmetic. For this chapter (and the following chapters) I selected a sample of 7-10 year old children (Canadian Grades 2-4) who are in the process of becoming fluent in arithmetic, but have not yet fully mastered it. This study, therefore, captures an important developmental period in which VSWM and arithmetic may be closely related.

Chapter 3 of this thesis describes a second study that investigates how basic number processing and arithmetic brain networks overlap. The objectives for this study were to: (1) determine whether the parietal cortex is recruited for both symbol-quantity associations and arithmetic within the same sample of children and adults; (2) examine whether the neural association between basic number processing and arithmetic is modulated by the cognitive demands of the arithmetic problem (i.e., problems that are predominantly calculated versus retrieved); and (3) whether adults and children show similar patterns of activation for arithmetic and number processing when the cognitive demands of the arithmetic task are comparable. This study directly tests whether the IPS is involved in the processing of both symbol-quantity associations and arithmetic, and how this relationship changes depending on how demanding the arithmetic problems are of procedural problem solving strategies.

Finally, in Chapter 4 of this thesis, I describe a study that explores how individual differences in domain general and domain specific competencies are related to brain activity in the IPS. Previous studies examining brain-behaviour associations have been somewhat fragmented and have only investigated one domain general or domain specific measure at a time. These studies have revealed that the bilateral IPS is related to VSWM, basic number processing, and arithmetic. To expand on this literature, this study simultaneously examined multiple domain general (verbal & non-verbal skills, and VSWM) and domain specific measures (nonsymbolic & symbolic comparison, and symbolic ordering) to determine how they are related to the recruitment of the IPS during arithmetic in children. The goals of this chapter were to: (1) examine which domain specific and domain general measures are related to the recruitment of the IPS during arithmetic problem solving; and (2) determine whether the nature of these relationships differ depending on which index is used to assess brain activity (e.g., the neural problem size effect).

Together, this thesis uncovers how domain general and domain specific abilities contribute to the neural basis of arithmetic in adults and in children. It specifically tests several long-held assumptions within the literature by using a developmental within-subjects approach to probe the nature of the relationships between these competencies.

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Chapter 2

2 Age-related changes in the neural processing of visuo-spatial working memory and arithmetic

2.1 Introduction

Arithmetic is a complex skill that is not process-pure. A large body of research has focused on which domain general competencies predict arithmetic skills. Working memory (the ability to hold and manipulate task-relevant information for brief periods of time) has been shown to be an important predictor of mathematical skills in both children and adults (for a review see Raghubar, Barnes, & Hecht, 2010). Though working memory is found to correlate with a range of mathematical skills, there has been particular focus on how it relates to arithmetic (Peng, Namkung, Barnes, & Sun, 2015). Individual differences in working memory capacity are correlated with arithmetic proficiency (Alloway & Passolunghi, 2011; Dumontheil & Klingberg, 2012), and longitudinal studies have shown that working memory abilities predict later success in mathematics (Bull, Espy, & Wiebe, 2008). Working memory is thought to contribute to arithmetic by storing and processing intermediate steps involved in finding a solution to a problem (Peng et al., 2015). More difficult arithmetic problems that have multiple intermediary steps are thought to be more demanding of working memory resources (DeStefano & LeFevre, 2004). These problems also tend to be solved using calculation-based strategies as opposed to retrieval-based strategies (where the solution is recalled from memory). It has been argued that demands on working memory may be greater when children are learning new mathematical skills or when children are doing more complex mathematical problems (Raghubar et al., 2010). Therefore, working memory may be an essential component of learning arithmetic and mathematical concepts at all stages of development.

Working memory is thought to be comprised of multiple systems (for a review see Baddeley, 2003) and many studies make distinctions between working memory for verbal or visuospatial information. Both visuospatial working memory (VSWM) and verbal working memory have been shown to predict mathematical abilities (Peng et al., 2015). However, their relative contributions may depend on the task and the age of the participants. Several studies, for instance, have demonstrated developmental changes in how arithmetic relates to these domains of working memory (Alloway & Passolunghi, 2011; Rasmussen & Bisanz, 2005). Younger children have been found to predominantly rely on VSWM to solve arithmetic problems (McKenzie, Bull, & Gray, 2003; Rasmussen & Bisanz, 2005), whereas older children use both verbal and VSWM (McKenzie et al., 2003). These age-related changes may be related to the kinds of strategies children are using to solve the problems and how familiar they are with the procedures and concepts. The importance of VSWM in the development of arithmetic has also been highlighted in literature examining children with math learning disabilities (developmental dyscalculia). Children with developmental dyscalculia have marked impairments in VSWM and visuo-spatial short term memory, which may be even more significant than their impairments in magnitude processing skills (Szucs, Devine, Soltesz, Nobes, & Gabriel, 2013). The aforementioned behavioural literature has suggested a strong relationship between VSWM, and arithmetic. It is possible that the established behavioural relationship between VSWM and arithmetic could be a product of overlapping neural networks underlying these abilities. Neuroimaging can therefore provide additional evidence to elucidate the neural mechanisms underlying the relationship between VSWM and arithmetic. Little work, however, has detailed the neurocognitive processes by which VSWM and arithmetic interact in adults and children and whether there are age-related changes in the underlying neural networks.

Numerous investigations have examined the neural basis of calculation and have revealed a bilateral fronto-parietal network of brain regions that are commonly activated during arithmetic tasks (for a meta-analysis see Arsalidou & Taylor, 2011). Activation in the frontal cortex, particularly in the bilateral middle and inferior frontal gyri, as well as the left superior frontal gyrus are thought to reflect more domain general factors such as working memory (Arsalidou & Taylor, 2011; Delazer et al., 2005; Ischebeck et al., 2006; Metcalfe, Ashkenazi, Rosenberg-Lee, & Menon, 2013). Task difficulty has been shown to increase the engagement of the inferior frontal cortex, whereas calculation specific skills engage the inferior parietal cortex, particularly in the IPS, and the angular and supramarginal gyri (Gruber, Indefrey, Steinmetz, & Kleinschmidt, 2001; Kong et al., 2005; Menon et al., 2000; Menon, Mackenzie, Rivera, & Reiss, 2002). Like arithmetic, VSWM has also been shown to recruit a remarkably similar fronto-parietal network that includes superior frontal regions as well as the intraparietal sulcus (IPS) (Klingberg, 2006). This network shows increases in activation with age, and activity within the left superior frontal sulcus and IPS have been shown to correlate with VSWM capacity (Klingberg, Forssberg, & Westerberg, 2002). Because both arithmetic and VSWM rely on a fronto-parietal network of brain regions, there may be considerable overlap in the neural circuitry that underlies these abilities. Yet, VSWM and arithmetic are rarely studied in the same sample of participants, therefore any inferences about the common neural substrates are largely inferred by comparing across studies. Determining how these networks interact is important for understanding arithmetic development; the development of arithmetic skills are likely a product of interactions within and between large-scale networks subserving multiple cognitive processes (Bressler & Menon, 2010; Fias, Menon, & Szucs, 2013).

Though many studies have separately investigated the brain networks involved in these abilities, little research has simultaneously examined the VSWM and arithmetic networks in the same sample of participants. To our knowledge, only one study to date has directly investigated the distinct and overlapping networks for VSWM and arithmetic. Zago and colleagues (2008) demonstrated that VSWM and arithmetic were characterized by overlapping activation in the bilateral IPS, right middle frontal gyrus/superior frontal sulcus, left supramarginal gyrus, and right superior parietal lobule in a sample of adults. Because working memory may be particularly important when children are learning arithmetic skills for the first time (and are using time-intensive calculation strategies), using a developmental approach to understand how VSWM and arithmetic neural networks relate to one another could provide additional insights into their relationship. However, to date only indirect evidence has been provided to suggest a relationship between VSWM and arithmetic at the neural level in children; Dumontheil and Klingberg (2012) demonstrated that activation in the left, but not right, IPS for a

VSWM task significantly predicted individual differences in future arithmetic performance. Individual differences in activation within frontal and parietal regions during an arithmetic task have also been found to correlate with behavioural measures of VSWM in typically developing children (Ashkenazi, Rosenberg-Lee, Metcalfe, Swigart, & Menon, 2013; Demir, Prado, & Booth, 2014; Metcalfe et al., 2013). These findings suggest that individual differences in children's VSWM capacities can modulate the neural basis of arithmetic. Children with math learning disabilities also seem to recruit VSWM resources differently than typically developing children. In the same regions that typically developing children show correlations between VSWM capacity and brain activity during arithmetic problem solving, children with math learning disabilities fail to show such a relationship (Ashkenazi et al., 2013). Children with dyscalculia also do not engage the right IPS to the same degree as typically developing children during a non-numerical VSWM task (Rotzer et al., 2009). These brain-behaviour correlations suggest there is a strong relationship between VSWM and arithmetic and that children with math learning disabilities do not appropriately use VSWM resources. However, such data do not imply that VSWM and arithmetic share an underlying neuronal basis. To ascertain this one needs to study the neural correlates of VSWM and arithmetic concurrently.

The present study aims to expand on the above-mentioned literature by examining whether there are common underlying neural substrates for VSWM and arithmetic in children and adults. Our sample of school-aged children (Grades 2-4) was specifically selected to capture a developmental period where children are learning and becoming more fluent with arithmetic facts (Ashcraft, 1982). We identified VSWM and arithmetic networks in the same sample of participants to identify how they overlap. Given the large body of literature that has independently identified fronto-parietal networks for VSWM and arithmetic (e.g., Arsalidou & Taylor, 2011; Klingberg, 2006), we predicted overlap in superior frontal regions and the IPS. Because research has demonstrated that the association between VSWM and arithmetic changes with age, we also examined whether there are age-related changes in the regions subserving arithmetic and VSWM. Given the research that has shown a developmental shift in the role of VSWM to verbal working memory in arithmetic problem solving (McKenzie et al., 2003; Rasmussen & Bisanz, 2005), it is possible that the networks involved in VSWM and arithmetic may become less associated over time or their anatomical localization could shift. Literature examining the developmental changes in the localization of numerical processing and arithmetic has suggested that there is a shift towards more left lateralized activation within the parietal cortex (Emerson & Cantlon, 2014; Rivera, Reiss, Eckert, & Menon, 2005; Vogel, Goffin, & Ansari, 2015). On the other hand, the bilateral dorso-lateral prefrontal, superior fontal, and parietal cortex show age-related increases for VSWM (Klingberg et al., 2002; Klingberg, 2006; Kwon, Reiss, & Menon, 2002). Therefore, there may be a shift from right or bilateral activation for VSWM and arithmetic in children, to greater left-lateralized activation in adults due to the left-lateralization of arithmetic and number processing. Characterizing how these networks overlap and change with age will further elucidate the neurocognitive mechanisms by which VSWM and arithmetic interact with one another.

2.2 Method

2.2.1 Participants

Twenty-six adults and 59 typically developing children were recruited to participate in this fMRI experiment. Two of the children did not complete the MRI session and eight children were removed from analyses due to head motion that exceeded 1.5 mm between volumes or more than 3mm over the entire scan. Ten additional children were removed due to poor accuracy on the fMRI tasks (less than 50% total accuracy on either of the fMRI tasks) and one was removed due to atypical neurological signs. No adults were excluded from the analysis. The final sample of participants included 26 adults (12 females, all right-handed) and 38 children (17 females, 2 left-handed). Adults were undergraduate and graduate students between 19.5-26.3 years of age (M = 22.2), and children were between 7.7- and 10.4-years of age (M = 9.2). All participants were fluent English speakers and had normal or corrected to normal vision. The Health Sciences Research Ethics Board at the University of Western Ontario approved all methods and procedures in this study, and participants were reimbursed for their participation. All participants (or children's caregivers) gave informed consent.

2.2.2 Procedure

This study consisted of two testing sessions. In the first session, participants completed a battery of standardized tests of math achievement, working memory, and intelligence. During this session children also completed a mock scanning session to familiarize them with the MRI environment and procedures. Children practiced keeping their head still while completing a short arithmetic verification task in the mock scanner. Approximately between 1-66 days following the first session (M=15.3), participants returned for the second session to complete the MRI component of the study. During the MRI session, participants completed arithmetic and visuo-spatial working memory tasks. Children also completed an additional 2-3 tasks in the scanner and adults completed an additional 4 tasks that are not discussed here. The task order was counterbalanced using a Latin square design.

2.2.3 Experimental Tasks & Design

2.2.3.1 Arithmetic task

To investigate neural processing associated with arithmetic problem solving, participants completed two runs of a single-digit arithmetic verification task that consisted of three conditions: (1) Small Problems; (2) Large Problems; and (3) Plus 1 Problems. For all conditions, an addition problem with two addends was presented along with a solution. Participants were asked to identify if the solution was correct or incorrect. Small problems had a solution less than or equal to 10, Large problems had a solution of greater than 10, and Plus 1 problems were always a single digit plus 1 (Figure 2.1a). Tie problems (e.g., 3 + 3) and problems containing a 0 were excluded from the problem list. In half of the trials the solution was incorrect and on the other half of trials the solution was correct. If the solution was incorrect, the presented solution was the correct solution +1 or +2. Each run consisted of 36 unique problems (12 problems per condition), resulting in 72 trials across both runs (see Appendix B for the problem list). For the small and large problem conditions, half the trials had the larger number presented on the left (4 + 2) and in the other half of the trials the larger number was presented on the right (3 + 5). If the larger number was presented on the left for a specific problem in run 1, it was presented on the right in the second run (e.g., Run 1 [4 + 2]; Run 2 [2 + 4]). All adults and most children had above chance performance and good motion on the two arithmetic runs (30/38 children had 2 usable arithmetic runs). If a child did not pass our selection criteria for either motion or accuracy on one of the runs, it was excluded from the analysis and the other run was included.

2.2.3.2 Visuo-spatial working memory task

To isolate networks involved in VSWM, we adapted a dot matrix task from Klingberg et al. (2002)[1]. This task was specifically selected because it does not include any symbolic numbers (for an example of a VSWM task that uses symbolic numbers see Dumontheil and Klingberg, 2012). Therefore, any overlap in the arithmetic and VSWM networks cannot be attributed to the processing of symbolic numbers. The VSWM task consisted of a VSWM condition and a control condition. In the VSWM condition, the participant was instructed to remember which squares the red dots passed through in a 4 x 4 grid (Figure 2.1b). Once the target stimulus was presented (an empty red circle), the participant was asked to identify if this was where one of the previous dots had appeared. On half the trials the dot was in a correct location that corresponded to one of the dots in the prior sequence, and on the other half of the trials the dot was in an incorrect location. If the target was presented in an incorrect location, it was presented in a square adjacent to a potentially correct solution. Either 2 or 4 dots were presented, with 6 trials for each load. For all analyses we collapsed across both loads resulting in 12 trials for the WM condition. The control condition was identical to the VSWM condition, except that the dots were blue and participants were instructed to watch the dots and did not need to remember their locations. When the target stimulus appeared (an empty blue circle), the

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[1] It is important to acknowledge that there are terminological inconsistencies for the dot-matrix task in the literature. Some studies refer to the dot matrix task as a visuo-spatial short-term memory task whereas others refer to it as a visuo-spatial working memory task. To remain consistent with the fMRI literature, I refer to this task as a visuo-spatial working memory task throughout this thesis. Though there are likely to be distinctions between the two, both visuo-spatial short term and working memory measures load onto the same factor in a factor analysis (Miyake et al., 2001), and they are both related to individual differences in arithmetic (Szucs et al. 2014).

participants always responded with their index finger regardless of where the circle was located. Consequently, the VSWM condition and the control conditions were identical in the stimulus presentation, except that participants were instructed to remember the spatial locations in the VSWM condition, and to watch the dots and wait for the target in the control condition. The control condition also had 2 or 4 dots which we collapsed across in the analyses, resulting in 12 trials in total for the control condition (6 trials for each load).

2.2.3.3 Task Design

Both arithmetic and VSWM tasks were presented using a block design with an initial fixation of 6500 ms and end fixation of 12000 ms (see Figure 2.1c for a schematic of the timing and design). Each block consisted of 6 trials and the duration of each trial and the number of blocks per run depended on the task. The inter-trial interval (ITI) was 1500 ms on average (duration was 1000, 1500, and 2000 ms). For the arithmetic task, each problem was presented for a total of 4500ms, and participants could also respond during the ITI screen. For the WM task the duration of the trial depended on the load. Each dot was presented for 500ms followed by a blank grid of 500 ms. After all dots had been presented a wait screen appeared for 1500ms followed by the target screen, which appeared for 1500 ms. The trial duration for a 2-dot trial was therefore 5000 ms whereas a 4-dot trial was 7000 ms. The duration of the inter-block interval (IBI) averaged to 9 seconds across the runs in both tasks. The conditions were randomly presented.

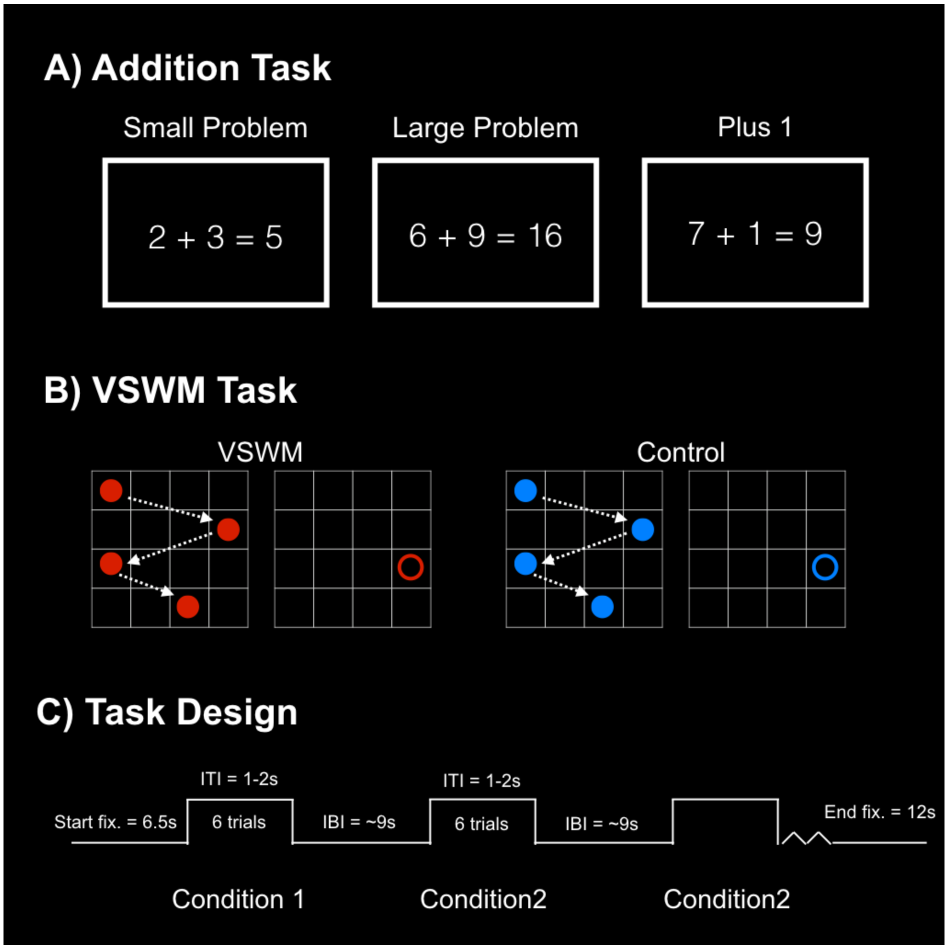

Figure 2.1 Tasks performed during the scanning session a) Examples of the three conditions in the arithmetic verification task. Participants were asked to identify if the solution was correct or incorrect. b) Examples of the VSWM condition and the control condition. Participants were instructed to remember the spatial locations in the VSWM condition, and identify if the target was in the same spatial location as one of the previous dots. The control condition was identical except that the participants did not need to remember the spatial locations of the dots, and responded to the target stimulus in the same way regardless of where it was located c) Schematic of the timing in the block design for both tasks.

2.2.4 MRI data acquisition

MRI data were acquired on a 3T Siemens Prisma Fit whole-body scanner, using a 32-channel receive-only headcoil (Siemens, Erlangen, Germany). A whole-brain high resolution T1-weighted anatomical scan was collected using an MPRAGE sequence with 192 slices, a resolution of 1x1x1 mm voxels, and a scan duration of 5 minutes and 21 seconds (TR = 2300 ms; TE = 2.98 ms; TI = 900 ms; flip angle = 9°). The in-plane resolution was 256x256 pixels. Functional MRI data were acquired during the arithmetic and VSWM tasks using a T2* weighted single-shot gradient-echo planar sequence (TR = 2000 ms, TE = 30 ms, FOV 210 x 210 mm, matrix size =70 x 70, flip angle = 78°). Thirty-five slices were obtained in an interleaved ascending order with a slice thickness of 3 mm, an in-plane resolution of 3 x 3 mm, and a .75 mm gap. There were 2 runs of the arithmetic task with 144 volumes and 1 run of the VSWM task with 117 volumes. Padding was used around the head to reduce head motion. The total scan duration was approximately 40 minutes for children and 1.5 hours for adults (more tasks and runs were obtained for adults that are not discussed here).

2.2.5 Analyses

Brain imaging data were analyzed using Brain Voyager QX 2.8.4 (Brain Innovation, Maastricht, Netherlands). Functional data were corrected for differences in slice-time acquisition, head motion, linear trends, and low frequency noise. Functional images were spatially smoothed with a 6mm FWHM Gaussian smoothing kernel. The functional images were then coregistered to the T1 weighted anatomical images and transformed into Talairach Space (Talairach & Tournoux, 1988). Though using an adult-template to spatially normalize pediatric populations can lead to systematic differences in anatomy and anatomical variability in children, such methods do not result in spurious findings when comparing fMRI data across groups (Burgund et al. 2002). A 2-gamma hemodynamic response function was used to model the expected BOLD signal. A random-effects GLM was then performed on the data. Whole-brain contrasts were first thresholded at a voxelwise *p*-value of 0.005, uncorrected and then corrected for multiple-comparisons using Monte-Carlo simulation procedure to determine a minimum cluster threshold (Goebel, Esposito, & Formisano, 2006), resulting in an overall $\alpha < .05$. This cluster thresholding method estimates and accounts for spatial smoothness and spatial correlations within the data (estimates of spatial smoothness are based on the formula discussed in Forman et al., 1995).

First, we separately investigated arithmetic and VSWM networks in adults and children. We isolated regions associated with calculation using the neural problem size effect (*Large problems* > *Small problems*). This comparison has been previously used by numerous studies to identify regions involved in calculation (e.g., De Smedt, Holloway, & Ansari, 2010; Grabner et al., 2007; Stanescu-Cosson et al., 2000). Investigating the problem size effect is particularly important in relation to VSWM because Large problems are more likely to rely on VSWM resources (DeStefano & LeFevre, 2004). To identify regions recruited for VSWM we compared the VSWM condition to its control condition (*VSWM* > *Control*), which is a contrast that has commonly been used in previous research (e.g., Dumontheil & Klingberg, 2012; Klingberg et al., 2002). To investigate regions that are common to both tasks we conducted a conjunction analysis between the arithmetic and VSWM tasks [(*Large problems* > *Small problems*) ∩ (*VSWM* > *Control*)]. To determine how the overlapping networks for arithmetic and VSWM differ between adults and children, a fixed effects GLM was conducted for each subject after which individual conjunction maps were calculated. These individual conjunction maps were then combined into two group-average maps, one for adults and one for children. A random-effects *t*-test comparison determined differences in the conjunction between the two groups.

2.3 Results

2.3.1 Behavioural Performance

Two separate mixed design ANOVAs were conducted on reaction time (RT) and accuracy data, with task (arithmetic, VSWM) and condition (large/small problems, VSWM/Control) as within subjects factors and group (children, adults) as a between subjects factor (see Figure 2.2 for RT and accuracy data).

The 2x2x2 mixed ANOVA with RT as the dependent variable revealed a main effect of group, where adults were significantly faster than children, $F(1,62) = 1167.2$, $p < .001$ and a main effect of task indicating that participants were significantly faster on the VSWM task $F(1,62) = 443.8$, $p < .001$. This analysis also revealed a main effect of condition where participants were slower on the Large arithmetic problems and VSWM problems, $F(1,62) = 155.4$, $p < .001$. We found an interaction between task and group, $F(1,62) = 84.2 < .001$, and post-hoc tests revealed that children showed greater differences in RT between the arithmetic and VSWM tasks than adults ($t(60.8) = 10.1$, $p < .001$). We also observed an interaction between condition and group $F(1,62) = 6.43$, $p = .014$, where the differences between conditions was greater in children than in adults ($t(62) = 2.5$, $p = .014$). Finally, the mixed ANOVA also revealed a Task x Condition x Group interaction, $F(1,62) = 4.13$, $p = .046$. Post-hoc analyses revealed that the magnitude of the difference between the VSWM and control conditions was greater for children than for adults ($t(62) = 5.3$, $p < .001$), but the difference between the large and small arithmetic problems was equivalent across groups ($t(62) = .12$, $p = .896$).

The 2x2x2 mixed ANOVA with accuracy as the dependent variable revealed a similar pattern of findings. There was a main effect of group with adults performing better on the tasks than children $F(1,62) = 8090.1$, $p < .001$, a main effect of task that showed participants were more accurate on the VSWM task than the arithmetic task $F(1,62) = 26.2$, $p < .001$, and a main effect of condition, where participants were less accurate on the Large arithmetic problems and VSWM problems $F(1,62) = 18.1$, $p < .001$. We also found an interaction between task and group, where children performed better on the VSWM task than the arithmetic task ($t(37) = 6.0$ $p < .001$) however adults showed no significant differences in performance between the two tasks (t $(25) = 1.2$, $p = .24$). We also observed an interaction between group and condition $F(1,62) = 11.7$, $p < .001$, with post-hoc tests revealing that children showed significant differences in the conditions for both tasks (t $(37) = -5.1$, $p < .001$), however adults performed equally well in both conditions ($t(25) = -.835$, $p =.44$). We did not find a Task x Condition x Group interaction.

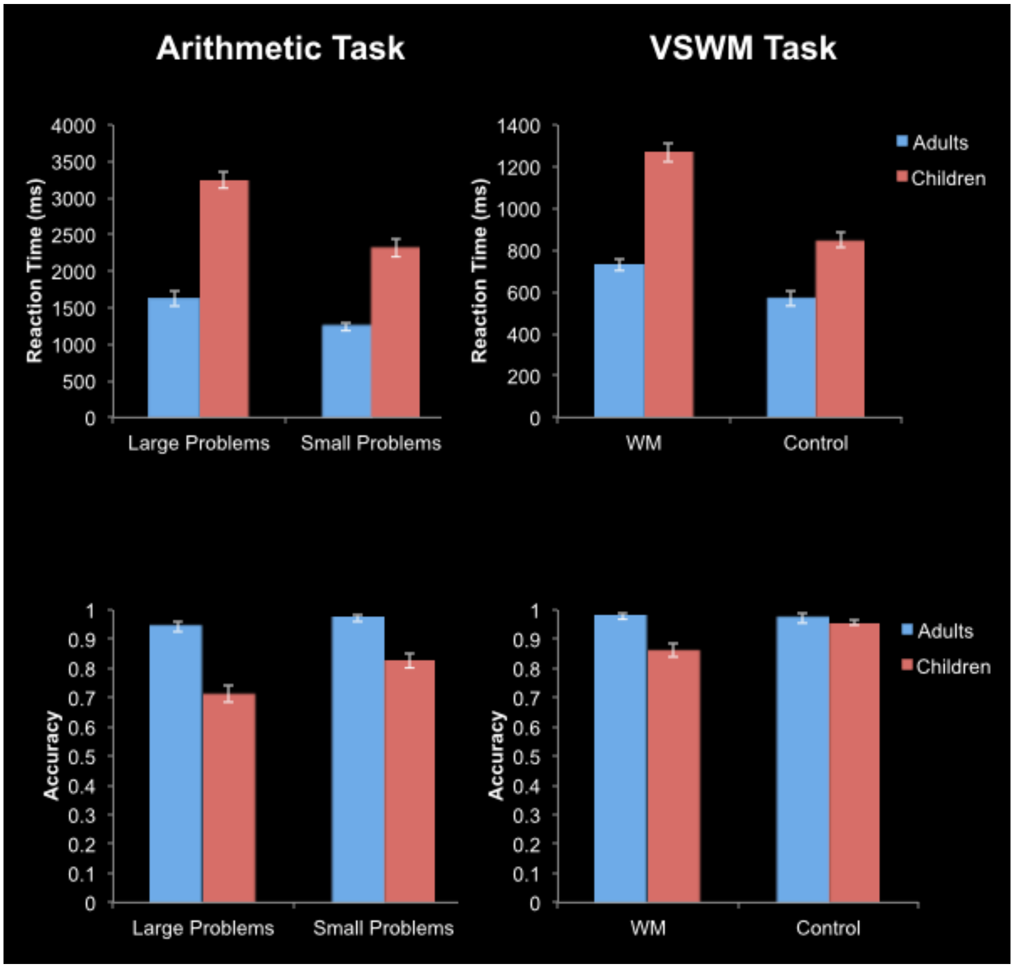

Figure 2.2 Reaction time and accuracy on the arithmetic and VSWM tasks between adults and children.

2.3.2 Brain Imaging

2.3.2.1 Adults

To isolate regions involved in calculation we contrasted Large problems with Small problems (*Large problems* > *Small problems*). This revealed a largely fronto-parietal network that included regions such as the bilateral IPS, superior frontal gyri (SFG), middle frontal gyri (MFG), left inferior frontal gyrus (IFG), and right insula (see regions in cold colors in Figure 2.3a, and Table 2.1). Similarly, a fronto-parietal network was also identified when comparing the VSWM task to its control (*VSWM* > *Control*) (see regions in hot colors in Figure 2.3a, and Table 2.1). This included regions such as the bilateral IPS, superior and inferior parietal lobules (SPL/IPL), MFG, precentral gyri, the right insula, and left SFG. We superimposed these networks in Figure 2.3a, which illustrates considerable overlap including in the bilateral IPS, left MFG and post-central gyrus, and the left insula.

To statistically examine whether VSWM and arithmetic activate the same brain regions, we conducted a conjunction analysis with the two contrasts used to identify the VSWM and arithmetic networks [(*Large problems* > *Small problems*) ∩ (*VSWM* > *Control*)]. Adult participants showed activation for both arithmetic and VSWM in the bilateral IPS, right SPL, right insula, left MFG, and superior frontal sulcus (see Figure 2.4a and Table 2.1).

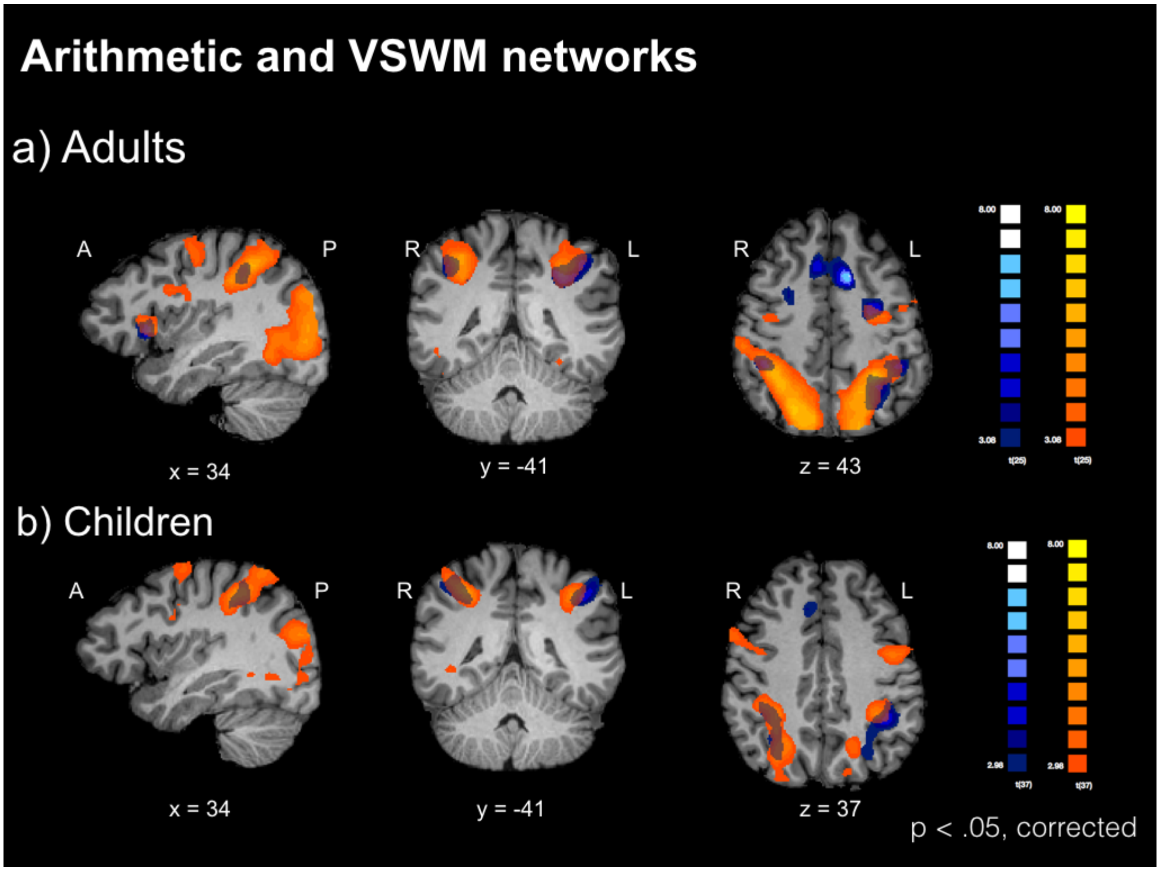

Figure 2.3 Statistical maps illustrating networks for arithmetic and VSWM in (a) adults and (b) children. The arithmetic network (*Large>Small problems*) is displayed in cold colors and the VSWM network (*VSWM>control*) is shown in hot colors.

2.3.2.2 Children

The arithmetic network (identified by the *Large problems* > *Small problems* contrast) also consisted of fronto-parietal regions in children. This included the bilateral IPS, superior frontal gyri, and right insula (see cold colors in Figure 2.3b and Table 2.1 for a full list of regions). The VSWM task (*VSWM* > *Control*) elicited activation in a similar set of regions. This network was comprised of regions that included the bilateral IPS, SPL, IPL, MFG, precentral sulci, superior frontal sulci, right IFG, and regions within the occipital cortex (see hot colors in Figure 2.3b and Table 2.1 for a full list of regions).

Similar to the adults, children had considerable overlap in their arithmetic and VSWM networks. We also conducted a conjunction analysis to statistically examine whether the VSWM and arithmetic tasks activated the same neuroanatomical regions [(*Large problems* > *Small problems*) ∩ (*VSWM* > *Control*)]. Only the right IPS was found to be active to be active for both VSWM and arithmetic tasks in children (see Figure 2.4b and Table 2.1).

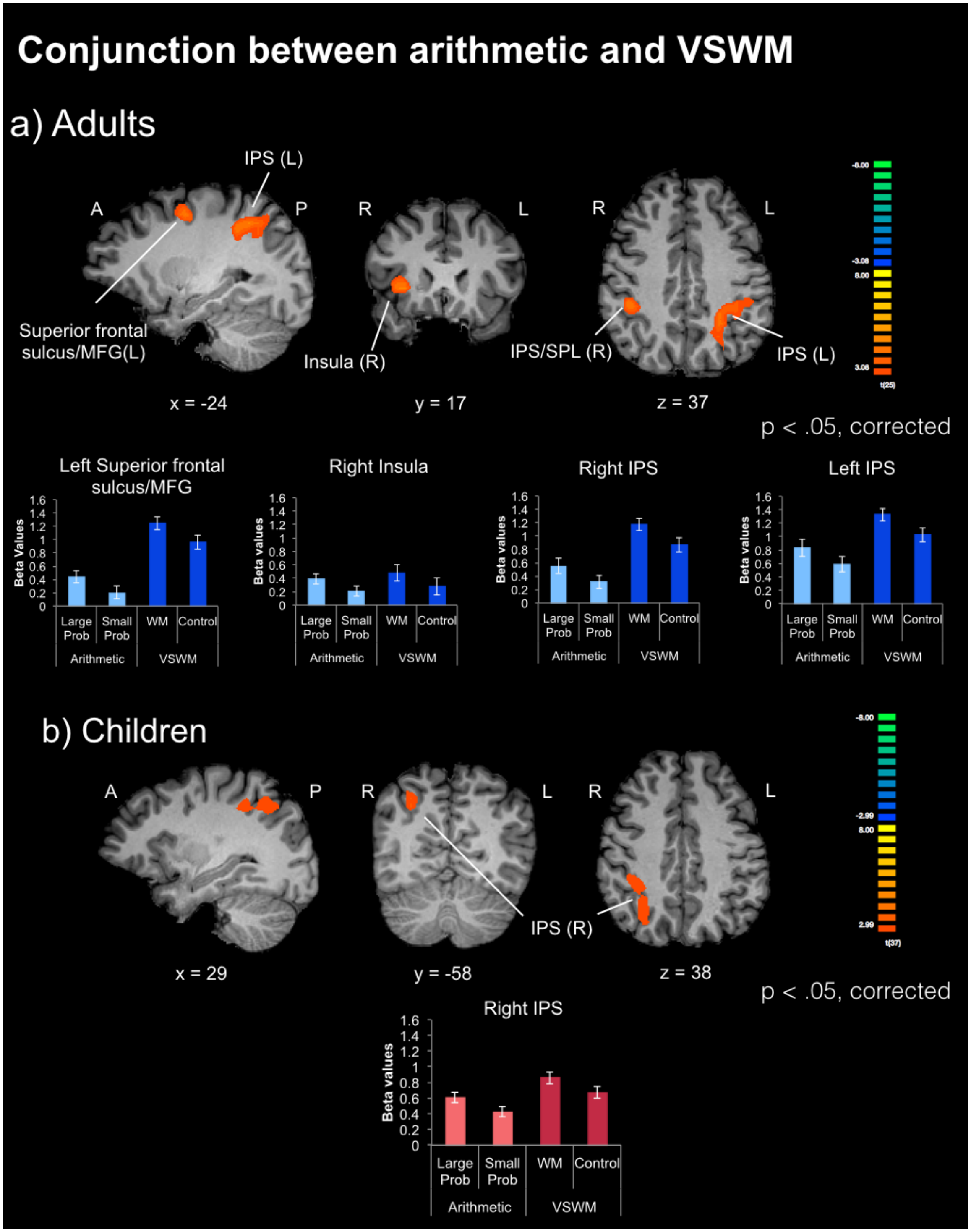

Figure 2.4 Statistical maps illustrating the conjunction between arithmetic and VSWM in (a) adults and (b) children. Also shown are beta values corresponding to each statistically significant cluster of activation where clusters extracted from adults are shown in blue and clusters extracted from children are shown in red.

2.3.2.3 Age-related changes

Both arithmetic and VSWM tasks were found to rely on fronto-parietal networks in adults and children. However, the conjunction analyses (conducted separately in each group) suggested that there might be relative differences in the regions that children and adults recruit. In adults, for instance, a number of regions were co-activated for VSWM and arithmetic, whereas children only showed co-activation in the right IPS. To further investigate these age-related changes we tested whether there were group differences in the conjunction between the arithmetic and VSWM tasks. The group comparison of the conjunctions revealed that adults recruited the left IPS, IPL, MFG, superior frontal sulcus, and bilateral middle occipital gyri for arithmetic and VSWM to a greater degree than children. In contrast, children recruited the right middle temporal and supramarginal gyri more than adults (see Figure 2.5 and Table 2.1 for a list of regions and beta values). An examination of the beta values from this region (Figure 2.5b) revealed that the age-related changes were driven by relatively less deactivation in this region for children. These findings indicate that though both adults and children recruit similar networks for arithmetic and VSWM, there are age-related changes in the engagement of these regions.

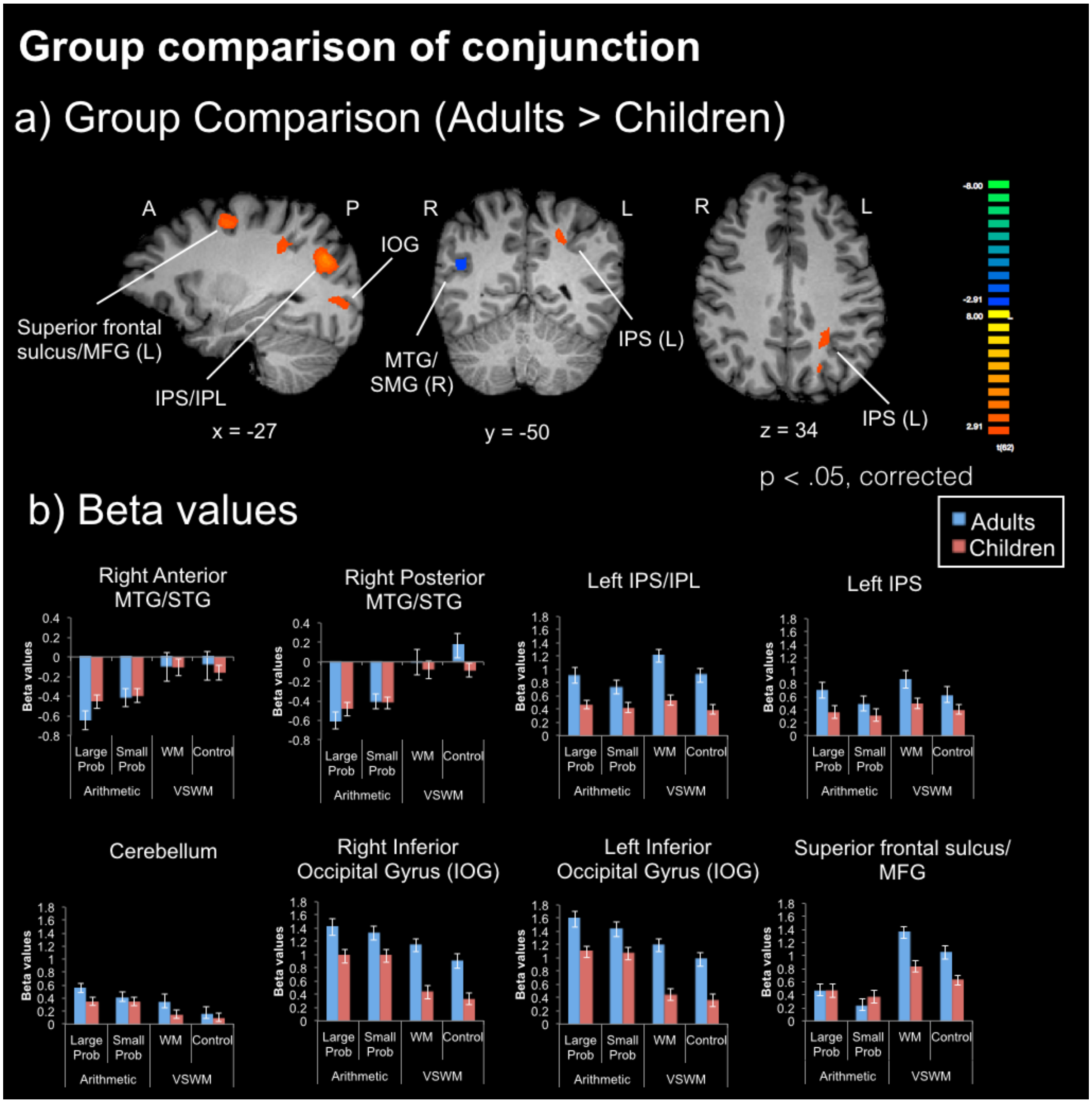

Figure 2.5 Statistical map showing age-related changes in regions associated with both arithmetic and VSWM (a). Regions that are more active in children than adults for the conjunction of VSWM and arithmetic are displayed in blue. Regions that are more active in adults than children are displayed in orange. Beta values from each statistically significant cluster are also shown (b), where adults are displayed in blue, and children are displayed in red.

Table 2.1 Anatomical regions, Talairach coordinates, mean t-scores, and number of voxels for each cluster in comparisons of interest.

Anatomical Region	TAL coordinates (x,y,z)			Mean t-score	Number of Voxels
Adults: Large Problems > Small Problems					
R IPS/ Postcentral sulcus	36.83	-37.52	38.14	3.69	1419
R Insula	28.54	21.59	6.52	4.11	2081
R Middle frontal gyrus	23.81	-2.82	42.02	3.40	1430
Bilateral superior frontal gyri	-4.58	14.04	44.12	3.82	3630
Cerebellum	1.18	-68.29	-24.51	3.49	1432
L Lingual gyrus	-8.54	-80.11	0.50	3.44	1449
L IPS	-31.06	-48.11	37.16	3.87	7844
L Lingual gyrus/Cerebellum	-31.28	-58.94	-26.42	3.78	2219
L Middle frontal gyrus/inferior frontal gyrus	-30.19	-3.19	42.65	3.65	4413
L Inferior frontal gyrus	-40.45	34.49	20.77	3.56	2781
Adults: VSWM > Control					
Bilateral IPS/SPL/IPL/inferior, superior, middle occipital gyri	0.06	-60.76	21.97	4.21	109562
R Inferior frontal gyrus	38.99	1.22	25.76	3.31	1485
R middle frontal gyrus/precentral gyrus	26.52	-7.78	54.14	3.92	6536
R Insula	29.48	18.08	7.39	3.95	2074
L middle frontal gyrus/precentral gyrus/superior frontal gyrus	-29.57	-6.48	46.74	3.95	11469
Adults: Conjunction [(Large problems > Small problems) ∩ (VSWM > Control)					
R IPS/superior parietal lobule	36.91	-37.32	38.31	3.62	1292
R Insula	30.00	19.64	6.28	3.77	1115
L IPS	-30.47	-45.83	37.93	3.54	4592
L superior frontal sulcus/ Middle frontal gyrus	-26.98	-6.10	50.42	3.53	1307
Children: Large Problems > Small Problems					
R IPS	32.36	-47.17	41.38	3.20	3104
R Insula	27.67	19.84	8.58	3.36	1232
Bilateral superior frontal gyrus	-1.91	19.93	44.11	3.27	1885
L IPS	-39.43	-47.05	41.85	3.28	4252
Children: VSWM > Control					
R IPS/SPL/IPL/ superior, middle, inferior occipital gyri	27.85	-60.82	30.94	3.83	35343
R Precentral gyrus/ inferior frontal gyrus	45.73	4.22	30.09	3.42	2920
R superior frontal sulcus/ Middle frontal gyrus	26.05	-5.50	54.04	3.58	3964
Bilateral lingual gyrus	4.40	-67.06	-17.72	3.21	1880
R thalamus	12.73	-18.06	11.00	3.47	1797
L MFG/precentral gyrus/superior frontal gyrus/superior frontal sulcus	-18.27	-4.71	48.15	3.74	5405
L IPS/SPL/IPL	-22.00	-58.12	43.60	3.75	15454
L thalamus	-18.38	-27.22	9.42	3.62	1217
L middle occipital gyrus	-32.34	-77.54	3.91	3.18	2039
L Precentral sulcus/precentral gyrus	-44.96	-3.15	33.42	3.42	2165
L inferior occipital gyrus	-43.92	-62.15	-3.67	3.30	2152
Children: Conjunction [(Large problems > Small problems) ∩ (VSWM > Control)					
R IPS	31.5	-47.47	41.09	3.20	2722
Age-related changes in the conjunction of Arithmetic and VSWM: Adults – Children					
R anterior middle temporal gyrus/supramarginal gyrus	62.54	-31.99	13.31	-3.20	673
R posterior middle temporal gyrus/supramarginal gyrus	49.35	-54.45	18.04	-3.10	602
R inferior occipital gyrus	35.69	-75.86	-5.78	3.27	1666
Cerebellum	0.22	-65.21	-30.23	3.24	914
L anterior IPS	-23.55	-46.30	35.18	3.16	580
L posterior IPS/IPL	-24.83	-69.36	24.01	3.48	1846
L inferior occipital gyrus	-36.70	-76.36	-9.44	3.10	1255
L superior frontal sulcus/middle frontal gyrus	-26.71	-8.02	47.61	3.28	584

2.3.2.4 Control analyses

To determine whether findings were related to performance differences between the groups we conducted several control analyses. To determine whether performance differences were driving any of the effects we examined, we selected 26 children who had the highest accuracy on the arithmetic task (large and small problem conditions). Performance was matched on the arithmetic task because children generally had poorer performance on this task compared to the VSWM task. We conducted the same conjunction analyses and group comparisons as described above using this sample of 26 children. Though adults still performed better (in accuracy and reaction time) on both tasks than children, there was no longer a task x group x condition interaction (3-way interaction for RT: $F(1,50) = .001$, $p = .97$), suggesting that relative differences in task difficulty for the two tasks were the same across groups. The conjunction analysis between VSWM and the problem size effect remained identical in the group of 26 children, with the right IPS remaining significantly active for both tasks ($p < .05$ corrected). We also examined whether the group comparison of the conjunction was affected when we compared adults to this higher performing sample of children. Similar to the analysis with the full sample, the left IPS/IPL and right inferior occipital gyrus were more active in adults than in children for both VSWM and arithmetic ($p < .05$ corrected). At uncorrected levels ($p < .005$ uncorrected) the other clusters also emerged including the two regions in the right MTG that were more active for children than adults, as well as the cluster in the left MFG/superior frontal sulcus that was more active for adults than children. Though these children still differed in their performance on these tasks, these control analyses indicate that the results remained very similar even with a sample of higher performing children, indicating that the findings are likely not entirely driven by group differences in performance. Moreover, because we did not observe a 3-way interaction (condition x task x group) in this sample of 26 children and 26 adults, we can be more certain that relative difference in task difficulty between the groups likely did not affect the fMRI findings in the full sample.

2.4 Discussion

Despite numerous studies showing correlations between VSWM and arithmetic at both the behavioral and brain-imaging levels of analyses, the literature to date has largely investigated the VSWM and arithmetic networks in isolation of one another. Research has also independently examined how these networks change with age (Klingberg et al., 2002; Rivera et al., 2005). However, the literature is limited in two major ways. First, no research to date has studied how VSWM and arithmetic networks overlap in children. Investigating this relationship in children is particularly critical because VSWM could be particularly important while children are learning arithmetic skills and are using time-intensive procedural strategies (Raghubar et al., 2010). Second, research has not yet examined whether there are age-related changes in these overlapping networks. The present study aimed to address these outstanding questions by examining the VSWM and arithmetic networks in both children and adults. We provide evidence that VSWM and arithmetic have common underlying neural substrates. Importantly, we also revealed that there are age-related changes in these shared circuits.

We demonstrated that adults recruit a bilateral fronto-parietal network for both VSWM and arithmetic that included the bilateral IPS, right SPL, left middle frontal gyrus/superior frontal sulcus, and right insula. This is consistent with previous literature that has shown significant overlap in the IPS, as well as superior parietal and frontal regions for visuo-spatial tasks and arithmetic problem solving (Zago & Tzourio-Mazoyer, 2002; Zago et al., 2008). As opposed to simply superimposing the VSWM and arithmetic networks, which was the case in the previous studies with adults, our analyses provide a more stringent test of the common underlying circuits by using conjunction analyses to identify regions that show significant activation for both VSWM and arithmetic. These findings also suggest that VSWM and arithmetic networks overlap in adults, even though they were solving single-digit addition problems that are likely less demanding of VSWM resources. Despite the fact that adults were given simple arithmetic and VSWM tasks, these findings are consistent with those from Zago et al. (2008) who used significantly more difficult tasks.

We also provide novel evidence that demonstrates how the VSWM and arithmetic networks overlap in children. Though arithmetic and working memory have been found to be correlated in children and adults, working memory may be particularly critical while children are using cognitively demanding strategies to solve arithmetic problems (Raghubar et al., 2010). Consequently, it is important to investigate how these networks relate to one-another in children. Our findings indicate that the only region to demonstrate overlapping activation for the two tasks was the right IPS. This is consistent with other developmental literature that shows individual differences in VSWM performance are correlated with greater activation in the right IPS during the solution of arithmetic problems (Demir et al., 2014; Metcalfe et al., 2013). However, these data go beyond such correlational evidence by showing that children recruit the same brain region for both VSWM and arithmetic. Adults also demonstrated overlap between VSWM and arithmetic in the right IPS, suggesting that the right IPS may exhibit age-invariant activity for both VSWM and arithmetic. The findings in the present study are also noteworthy because some of the previous research examining the relationship between VSWM and arithmetic has used a task with symbolic numbers to identify brain regions involved in VSWM (Dumontheil & Klingberg, 2012). It was therefore unclear from this work whether VSWM processes or symbolic number processing within the IPS were related to individual differences in arithmetic. Our results suggest an association between VSWM and arithmetic within the IPS, even though our VSWM task did not include any numerical processing.

2.4.1 Age-related Changes in the Parietal Cortex for VSWM and Arithmetic

Our findings also demonstrate that there are age-related changes in the networks subserving VSWM and arithmetic. We found that a number of regions were more active in adults than in children for the conjunction of VSWM and arithmetic. This included the left IPS, IPL, MFG/precentral sulcus, bilateral inferior occipital gyrus, and cerebellum. Furthermore, children showed greater activation than adults in the right middle temporal and supramarginal gyri for the conjunction between VSWM and arithmetic. These findings indicate that the VSWM and arithmetic undergo developmental changes together and become relatively more left-lateralized in adults.

A particularly notable finding is that the left IPS showed age-related increases in activation for VSWM and arithmetic whereas the right IPS was related to both tasks in adults in children. The left IPS may thus be undergoing more protracted developmental changes compared to the right IPS. Other literature examining longitudinal changes in the IPS in response to numbers is consistent with this finding; the right IPS has been shown to have greater continuity, whereas the left IPS shows greater developmental changes (Emerson & Cantlon, 2014). Other research has also suggested that activity in left IPS during a VSWM task may be an important predictor of arithmetic abilities 2 years later (Dumontheil & Klingberg, 2012). Indeed, the relationship between activation in the left IPS during VSWM processing and math achievement may be due to the fact that children who are higher math achievers are displaying more “adult-like” activity in this region. Our findings converge to suggest that the left IPS plays an important role in the developing relationship between VSWM and arithmetic.

Several studies have previously shown that arithmetic and the processing of numbers becomes left lateralized over development and that the left parietal cortex becomes increasingly specialized to process symbolic numbers (Emerson & Cantlon, 2014; Rivera et al., 2005; Vogel et al., 2015). Moreover, a large body of literature has also demonstrated that the VSWM network undergoes age-related changes, including in the left parietal cortex (Klingberg et al., 2002; Kwon et al., 2002). The data presented in this study demonstrate, for the first time, that the specialization of the left-parietal cortex for symbolic number processing may not necessarily reflect domain specific change, but rather may reflect other more domain general constraints on the way information is processed. It is possible that a common underlying mechanism is driving the processing of VSWM and arithmetic in the parietal cortex. For instance, the cortex undergoes developmental changes where some aspects of brain structure and function become more asymmetrical and lateralized (for a review see Duboc, Dufourcq, Blader, & Roussigné, 2015; Toga & Thompson, 2003). Functions such as face or word processing become more lateralized with development, and individuals with more lateralized processing of one function tend to have more lateralized processing of the other function in the opposite hemisphere (Pinel et al., 2015). Lateralization of function may have cognitive advantages by allowing the brain to process information in parallel (Duboc et al., 2015). Asymmetrical development of brain architecture is also shown in structural brain networks, where the left hemisphere shows greater developmental increases in network efficiencies, while the right hemisphere remains relatively stable from adolescence to adulthood (Zhong, He, Shu, & Gong, 2016). Together, this literature indicates that the brain undergoes large-scale changes in structure and function, with increasing lateralization of function over developmental time. Therefore, the shared developmental specialization of the left IPS for both VSWM and arithmetic may reflect maturational changes in processing within this region that constrain the development of both domains. In this way, the present findings raise doubts over domain specific accounts of the increasing left lateralization for arithmetic and symbolic number processing over developmental time.

It is also possible that the development of language and reading skills could impose constraints on the processing of visuo-spatial information as well as arithmetic. For example, literacy has been shown to impact other networks beyond those directly involved in reading (Dehaene et al., 2010). Moreover, there is indirect evidence to suggest that as children get older they increasingly use verbal rehearsal, or verbal recoding for visuo-spatial information (Hitch, Halliday, Schaafstal, & Schraagen, 1988; Pickering et al., 2001). Though speculative, it is possible that both VSWM and arithmetic are relying on more verbally mediated strategies and that language systems may be shaping these networks over development.

When investigating age-related changes in the VSWM and arithmetic networks we also found that children are recruiting the right middle temporal and supramarginal gyri more than adults. Other research has also found overlap between VSWM and arithmetic in adults in the right supramarginal gyrus (Zago & Tzourio-Mazoyer, 2002). The supramarginal gyrus (typically in the left hemisphere) is thought to be involved in verbally mediated strategies such as fact retrieval during the solution of arithmetic problems (Price, Mazzocco, & Ansari, 2013; Rivera et al., 2005) and becomes increasingly recruited with age (Rivera et al., 2005). However, the right supamarginal gyrus has been found to be active during VSWM tasks (Smith, Jonides, & Koeppe, 1996), and the engagement of this region is positively correlated with age (Kwon et al., 2002; Scherf, Sweeney, & Luna, 2006). An examination of the beta values from these regions indicated that the age-related differences were related to less deactivation in the middle temporal gyrus and supramarginal gyrus. Therefore, it is also possible that group differences could be related to developmental changes in the default mode network, which the middle temporal and supramarginal gyri are part of (Laird et al., 2009). Future research will need to examine the role of the right middle temporal gyrus and supramaginal gyrus to further clarify its role in the development of arithmetic skills.

2.4.2 Relationships Between Visuo-spatial Processing and Arithmetic

The numerical cognition literature has traditionally focused on the role of the IPS in the processing of quantities (Ansari, 2008; Dehaene, Piazza, Pinel, & Cohen, 2003). Arithmetic is thought to recruit the IPS because individuals need to manipulate and combine quantities in order to find a solution. This is particularly true of problems that are solved with more effortful calculation-based strategies (De Smedt et al., 2010; Delazer et al., 2005; Ischebeck et al., 2006; Zamarian, Ischebeck, & Delazer, 2009). Because these types of problems are also more demanding of VSWM it is possible that IPS activity during calculation is also somewhat attributed to the VSWM demands of the task. In other words, IPS activity during calculation could be a result of manipulating quantities, VSWM demands, or a combination of the two. Indeed, others have argued that activation in the IPS is likely not solely related to processing quantities and that there needs to be a new framework to account for how arithmetic and working memory networks interact (Fias et al., 2013). At the very least, the present findings significantly question the extent to which any developmental changes in IPS activity during arithmetic tasks are domain specific and instead suggest that these reflect changing neuronal mechanisms that underpin both calculation and visuo-spatial working memory.

The overlap of VSWM and arithmetic in the IPS in the present study and in others (Zago et al., 2008) also highlights that the close relationship between visuo-spatial processing and numerical processing. Compelling neuropsychological and neuroimaging evidence has been provided to suggest that number and space are closely related to one another (Hubbard, Piazza, Pinel, & Dehaene, 2005) and, more importantly, that visuo-spatial processing is important for calculation (de Hevia, Vallar, & Girelli, 2008). Memory for visuo-spatial information has been shown to have retinotopic organization in the IPS (Konen & Kastner, 2008; Silver & Kastner, 2009). Similar brain regions have been hypothesized to be involved in the spatial organization of number in the form of a mental number line (Dehaene & Changeux, 1993; Dehaene et al., 2003). Indeed, it has been proposed that number and space share a fronto-parietal network (Hubbard et al., 2005). Spatial maps localized in the intraparietal cortex could be utilized for spatial representations of number which could play a significant role in the relationship between VSWM in arithmetic (Dumontheil & Klingberg, 2012). Our findings provide converging evidence that visuo-spatial processing and arithmetic likely show a strong relationship due to common underlying networks.

The common underlying neural substrates for VSWM and arithmetic in the right IPS in children also have implications for children with developmental dyscalculia. These children often have poor performance on measures of arithmetic fluency as well as VSWM (Szucs et al., 2013). Neuroimaging studies have demonstrated that children with dyscalculia have impaired processing in right IPS for both magnitude comparison tasks and VSWM tasks (Price, Holloway, Räsänen, Vesterinen, & Ansari, 2007; Rotzer et al., 2009). Here we demonstrate, for the first time, that there is co-localization of activity in the right IPS for both VSWM and arithmetic in children. It is therefore possible that impairments in right parietal circuits could be the cause of both VSWM and arithmetic impairments. This challenges the notion that dyscalculia is caused solely by a domain specific impairment in the processing of numerical magnitude (Butterworth, Varma, & Laurillard, 2011; Butterworth, 2005, 2010) and instead might suggest that neuronal processes recruited during both mental arithmetic and VSWM are impaired in this learning disorder. It may be that a vulnerability to the shared neural circuitry leads to deficits in both domains. Future research will need to further investigate whether VSWM, numerical magnitude processing, and arithmetic impairments in dyscalculia stem from common neurobiological origins in the right IPS.

2.4.3 Limitations

It is possible that the age-related changes we observed in this study could be attributed to differences in overall performance between the two groups. In order to ensure that the same task was used across groups, the tasks needed to be child-friendly. This also resulted in performance differences between the groups where adults had higher accuracy than children on both tasks, and the tasks could consequently be less demanding of arithmetic and VSWM systems in adults. However, in our control analyses we determined that the findings were relatively consistent even when comparing the adults to a sample of the highest performing children. Furthermore, our adult findings closely resemble those of Zago et al. (2008) who used much more difficult tasks to examine VSWM and arithmetic abilities. This suggests that even though the tasks used in the present study are easier, they are still engaging networks typically associated with arithmetic and VSWM in adults.

A second limitation is that our arithmetic task consisted of only single-digit addition problems. It is possible that operation-specific (or strategy specific) differences exist in the overlap between VSWM and arithmetic. For instance, subtraction may rely more on working memory resources than addition due to a greater reliance on calculation-based strategies, which could subsequently reveal different overlapping circuits. Future research will need to examine how arithmetic strategies (calculation vs fact retrieval) and arithmetic operations affect the relationship with different components of working memory.

Finally, this study aimed to examine the overlapping rather than the distinct neural circuits involved in VSWM and arithmetic. This focus was motivated by the overwhelming behavioural literature that has demonstrated strong relationships between these two abilities (Peng et al., 2015; Raghubar et al., 2010). How VSWM and arithmetic are inter-related at the neural level has been poorly documented, particularly in children. Therefore, an investigation into which regions are shared among these networks provides additional evidence into their behavioural association. It is evident from the basic contrasts that VSWM and arithmetic also have distinct and non-overlapping regions of activation that are likely related to different cognitive demands of each task. However, a discussion of these regions and how they develop fell beyond the scope of the present study. It will also be important for future research examining the similarities between VSWM and arithmetic to use analyses such as representational similarity analyses (Kriegeskorte, Mur, & Bandettini, 2008). Demonstrating overlap between VSWM and arithmetic does not necessarily indicate that the tasks are relying on the same underlying processes. Other multivariate methods are needed help determine whether VSWM and arithmetic have similar representations at the neuronal level.

2.4.4 Conclusions

Previous neuroimaging research has largely used brain-behaviour correlations to examine how VSWM and arithmetic are related to one another, and no studies have examined whether VSWM and arithmetic have the same neural basis in children. The findings presented within this study expand on this literature by empirically examining whether VSWM and arithmetic recruit the same brain regions within the same sample of children and adults. In this study we provided novel evidence that VSWM and arithmetic have common underlying neural substrates in both children and adults. We also found that the overlap between VSWM and arithmetic is localized in the right IPS in children, but becomes increasingly left-lateralized in adults. These findings provide evidence for the possible neurocognitive mechanisms underlying the strong relationship between VSWM and arithmetic that has been documented in the behavioural literature.

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Chapter 3

3 Investigating the shared neural circuits for arithmetic and basic number processing in children and adults

3.1 Introduction

Before children can learn arithmetic they first need to have knowledge of basic numerical concepts. In particular, children need to understand that symbolic numbers refer to a specific quantity (i.e., that the digit 3 can refer to three dots or three apples). A large body of research has investigated how basic numerical competencies relate to arithmetic skills. This research has demonstrated that individual differences in symbolic number processing skills are predictive of arithmetic abilities in children and adults (Bartelet, Vaessen, Blomert, & Ansari, 2014; Bugden & Ansari, 2011; De Smedt, Noël, Gilmore, & Ansari, 2013; Goffin & Ansari, 2016; Holloway & Ansari, 2009; Lyons, Price, Vaessen, Blomert, & Ansari, 2014; Mundy & Gilmore, 2009; Sasanguie, De Smedt, Defever, & Reynvoet, 2012; Schneider et al., 2016). In particular, children's abilities to link symbolic (Arabic digits) and nonsymbolic quantities (e.g., dots) are related to individual differences on tests of arithmetic and mathematics (Bartelet et al., 2014; Brankaer, Ghesquière, & De Smedt, 2014; Kolkman, Kroesbergen, & Leseman, 2013; Mundy & Gilmore, 2009). Recently, it has been suggested that the ability to map between symbolic and nonsymbolic quantities predicts children's arithmetic performance even after other basic number processing tasks are taken into account (such as number comparison tasks) (Brankaer et al., 2014). This provides additional evidence in support of the notion that the mapping between symbolic and nonsymbolic representations of number is particularly important for the development of arithmetic skills. Other evidence has also shown that numeral knowledge, such as the ability to identify Arabic digits and associate then with nonsymbolic quantities, mediates the relationship between informal and formal mathematics (Göbel, Watson, Lervåg, & Hulme, 2014; Purpura, Baroody, & Lonigan, 2013). Together, these findings indicate that a fluent understanding of symbolic numbers and symbol-quantity relationships may be particularly important for arithmetic skills.

3.1.1 Shared Networks for Number Processing and Arithmetic

Even though studies have consistently demonstrated relationships between basic number processing skills and arithmetic at the behavioural level, limited research has examined how these abilities may be interrelated at the neural level. There are many reasons to predict that the brain circuits involved in arithmetic may overlap with those involved in basic number processing. For example, arithmetic problems that require effortful calculation involve the mental manipulation quantities. Therefore, arithmetic may rely on brain regions that are associated with basic number processing. Indeed, it has often been assumed that the recruitment of intraparietal sulcus (IPS) during the solution of arithmetic problems can be attributed to the activation of quantity representations within the IPS (Arsalidou & Taylor, 2011; Dehaene, Piazza, Pinel, & Cohen, 2003). However, surprisingly few studies have examined whether basic number processing tasks and arithmetic have overlapping brain activation in the same sample of participants.

Among the small body of studies that have investigated this question, there exists some indirect evidence that arithmetic and number processing may share common underlying circuitry. In particular, a large body of research has shown that magnitude processing skills and arithmetic both rely on the IPS (Ansari, 2008; Arsalidou & Taylor, 2011). However, this conclusion is derived from studies that have independently investigated either the neural correlates of magnitude processing or arithmetic. Indeed, in a fMRI meta-analysis that included studies on both number processing and arithmetic, number processing skills and arithmetic exhibited overlapping activity in the superior and inferior parietal lobules (in addition to a number of other regions) (Arsalidou & Taylor, 2011). Though this provides some evidence for shared neural substrates, meta-analytic methods can only provide indirect evidence because they combine data across multiple studies and are therefore comparing activation profiles for different tasks between-subjects; true overlap of activation patterns can only be established by taking a within-subjects approach.

The link between basic number processing and arithmetic in the IPS has also been indirectly demonstrated using brain-behaviour correlations. Bugden et al. (2012) found that children who had greater brain activation in the left IPS during a symbolic number comparison task had higher scores on a standardized test of arithmetic. A similar study identified regions involved in number-processing by having children map between symbolic and nonsymbolic quantities (Emerson & Cantlon, 2012). Specifically, children had to identify whether a digit and a set of dots showed the same quantity. Functional connectivity within the network activated by this matching task was found to be related to children's math performance (Emerson & Cantlon, 2012). These findings suggest that individual differences in children's arithmetic and math proficiency are related to neural networks involved in basic number processing skills, and that the IPS may be a particular critical region for this relationship.

The literature discussed above has resulted in claims for common underlying circuitry for arithmetic and basic number processing in light of similar patterns of brain activity across different studies. Few studies have directly examined whether these networks overlap in the same sample of participants. Though no research has examined whether basic number processing and arithmetic have overlapping networks in children, two studies have examined this relationship in the same sample of adults. This research demonstrated that multiplication and number processing tasks (i.e., number comparison tasks) were associated with overlapping activity in the bilateral occipital cortices, left precentral gyrus, and supplementary motor area, but not in the parietal cortex (Dehaene et al., 1996; Rickard et al., 2000). The lack of overlap in the parietal cortex, particularly the IPS, may largely be due to the kinds of strategies used to solve multiplication problems in adults. Different strategies are used to solve arithmetic problems and they have been shown to modulate brain activity. Networks involved in effortful calculation differ from those that are solved by retrieving the solution from memory (Zamarian, Ischebeck, & Delazer, 2009). Both of the studies that have examined the relationship between basic number processing and arithmetic used single digit multiplication problems, which are predominantly solved using retrieval rather than more effortful calculation strategies (Imbo & Vandierendonck, 2008). Therefore, these findings could be inconsistent with other literature because the neural association between number processing and arithmetic may be dependent on the kind of strategy that is used to solve the problem.

3.1.2 How Strategies Influence the Relationship Between Arithmetic and Number Processing

Different cognitive strategies are implemented depending on the type of arithmetic problem presented (i.e., addition versus subtraction) and the difficulty of the problem. Some problems are solved using by retrieving the solution from memory (i.e., retrieval), whereas other problems are solved using more time-intensive strategies such as counting or decomposing the problem into smaller parts (i.e., calculation). Problems with smaller operands are more likely to be retrieved (sums < 10), whereas problems with larger operands (sums > 10) are more likely to be solved by calculation (Campbell & Xue, 2001; LeFevre et al., 1996). Manipulations of problem size have been used to investigate the different neural networks that underlie calculation and retrieval. Smaller problems, which are often solved using retrieval, tend to activate perisylvian language regions in the left hemisphere such as the left angular and supramarginal gyri (Grabner et al., 2009; Kong et al., 2005). In contrast, problems solved using effortful calculation show more widespread fronto-parietal activation (Grabner et al., 2009). Arithmetic training studies have also demonstrated a similar pattern of findings that show a shift in activation from the IPS to the angular gyrus after participants become more fluent with arithmetic problems following training (Delazer et al., 2003, 2005; Ischebeck et al., 2006). This is likely indicative of a shift from procedural to retrieval strategies as individuals gain experience with the arithmetic problems. A similar pattern of findings also emerges as children become more experienced with arithmetic. Children increasingly use fewer procedural strategies (Ashcraft, 1982), and there are shifts in brain activation towards greater engagement of the inferior parietal cortex (Rivera, Reiss, Eckert, & Menon, 2005).

Problems that are solved using procedural strategies require more quantity manipulations. These problems may have greater overlap with brain regions involved in number processing compared to problems solved using retrieval, which do not rely on quantity manipulations. Therefore, it is not only important to determine how basic number processing and arithmetic networks overlap, but also how the overlap is affected by the kind of strategy used to solve the problem. Though it is often assumed that regions in the parietal cortex subserve both number processing and arithmetic due to the role of quantity manipulations in calculation, this still needs to be empirically examined using a within-subjects approach. Investigating the neural networks for arithmetic and basic number processing in the same sample of participants provides a unique opportunity to determine whether they have a shared neural basis in adults and children, and how this relationship changes as a function of the strategy used to solve the problem.

3.1.3 The Present Study

In view of the literature discussed above, the aim of the present study is to examine whether arithmetic and number processing recruit common brain regions and how problem size and age influence this relationship. Systematically investigating whether there is overlap in the neural circuitry for basic number processing skills and arithmetic may provide unique insights into how these skills are related to one another. It can also help to determine whether this neural overlap persists into adulthood, or whether it changes as arithmetic and basic number processing skills develop. Exploring the relationship between basic number processing and arithmetic in the context of the cognitive operation being performed can also provide a better understanding of age-related differences and similarities. For instance, it is possible that both adults and children will show overlapping activation in the IPS for arithmetic and number processing skills, but only for problems that are solved using calculation and require the manipulation of quantities. Therefore, the relationship between arithmetic and number processing may be more closely tied to the cognitive operation than to age. The present study therefore has the following aims: (a) to determine whether arithmetic and symbol-quantity processing have common underlying neural substrates in adults and children; (b) to examine whether the relationship between number processing and arithmetic is influenced by how demanding the problems are on procedural strategies; and (c) to explore how the relationship between arithmetic and number processing skills is related to the cognitive operation being performed rather than age.

3.2 Method

3.2.1 Participants

Twenty-six adults and 59 children were recruited to participate in this study. Two of the children did not complete the MRI session and one child was removed due to atypical neurological signs. Eight additional children were removed due to poor accuracy on the fMRI tasks (less than 50% accuracy on either the arithmetic or number matching task), and another 6 children were removed from analyses due to head motion that exceeded of 1.5 mm between volumes or more than 3 mm across the whole run. All adults were included in the analyses. The final sample of participants included 26 adults (12 females, all right-handed) and 42 children (20 females, 2 left-handed). Adults were undergraduate and graduate students between 19.5-26.3 years of age (M = 22.2), and children were between 7.5- and 10.4-years of age (M = 9.2). Participants had normal or corrected to normal vision and were fluent English speakers. The Health Sciences Research Ethics Board at the University of Western Ontario approved all methods and procedures in this study. All participants (or children's caregivers) gave informed consent and were reimbursed for their participation in the study.

3.2.2 Procedure

Participants completed two testing sessions. In the first session, adults and children were given a battery of cognitive tests that included measures of basic number processing skills, math achievement, working memory, and intelligence. In this session children also completed a mock scanning session to familiarize them with the MRI procedures and environment. Children practiced keeping their head still while completing a short arithmetic verification task in the mock scanner. Approximately 1-66 days following the first behavioural session, participants returned for the second MRI session, where they completed an arithmetic verification task and a symbolic-to-nonsymbolic number matching task. Children also completed an additional 2-3 tasks in the scanner and adults completed an additional 4 tasks that are not discussed here. The task order was counterbalanced using a Latin square design.

3.2.3 Experimental Tasks & Design

3.2.3.1 Arithmetic task

To investigate neural processing associated with arithmetic problem solving, participants completed two runs of a single-digit arithmetic verification task that consisted of three conditions: (1) Small Problems; (2) Large Problems; and (3) Plus 1 Problems. For all conditions, an addition problem with two addends was presented along with a solution. Participants were asked to identify if the solution was correct or incorrect. Small Problems had had a solution less than or equal to 10, Large Problems had a solution of greater than 10, and Plus 1 Problems were always a single digit plus 1 (Figure 3.1a). Tie problems (ie. 3 + 3) and problems containing a 0 were excluded from the problem list. In half of the trials the solution was incorrect and in the other half of trials the solution was correct. If the solution was incorrect, the presented solution was the correct solution +1 or +2. Each run consisted of 36 unique problems (12 problems per condition), resulting in 72 trials across both runs (see Appendix B for a problem list). For the Small and Large problem conditions, half the trials had the larger number presented on the left (4 + 2) and in the other half of the trials the larger number was presented on the right (3 + 5). If the larger number was presented on the left for a specific problem in run 1, it was presented on the right in the second run (e.g., Run 1 [4 + 2]; Run 2 [2 + 4]). All adults and most children had above chance performance and good motion on the two arithmetic runs (32/42 children had 2 usable arithmetic runs). If a child did not pass our selection criteria for either motion or accuracy on one of the runs it was excluded from the analysis and the other run was included.

3.2.3.2 Arithmetic problem solving strategy assessment

Large arithmetic problems are more often solved using procedural strategies (e.g., counting up, decomposition, etc.) whereas smaller problems tend solved by retrieving the solution from memory (Campbell & Xue, 2001). To verify this in the present sample of participants, we obtained strategy reports immediately after the MRI. Participants were first given three practice trials and were instructed to verbally provide an answer and to explain how they solved the problem. Participants were provided some examples of how they might solve the problem (e.g., Memory: “You might know the answer from memory”; Counting: “You can count to get the answer”; Decomposition: “9 and 1 make 10, and then there are 3 left over so the answer is 13”). Following the three practice trials, participants were asked to verbally provide a solution and explain how they solved the problem for every trial shown in the scanner (i.e., all 56 unique trials). Problems were presented in a pseudo-random order. If participants used a strategy that involved counting or decomposing the problem into smaller parts, we classified this problem as a *procedural* problem. If the participant said they knew the item from memory or just knew the answer we classified this as a *retrieval* problem. We were then able to use these strategy reports to determine the proportion of problems solved using procedural or retrieval strategies in each condition.

3.2.3.3 Matching Task.

We used a number matching task closely adapted from Emerson and Cantlon (2012, 2014) to assess neural networks associated with basic number processing. This task was selected due to the behavioural literature that has found correlations between arithmetic and the ability relate symbolic numbers to their respective quantities (Bartelet et al., 2014; Brankaer et al., 2014; Kolkman et al., 2013; Mundy & Gilmore, 2009). Two conditions were presented in this task: a number matching condition and a shape matching condition. In the number matching condition participants were presented with a number symbol and a set of dots, and were asked to identify whether they had the same quantity (Figure 3.1b). In half the trials the quantities were the same and in the other half of trials the quantities differed. When the trials did not match, the difference between the two number formats was ± 2, 3 or 4. In the shape matching condition (a control condition), two shapes were presented and the participant was asked to determine if they were the same or different shapes. In half the trials the shapes matched and in the other half they did not. One run of the matching task was presented which had a total of 18 trials in the number matching condition and 18 trials in the shape matching trials (36 trials across the entire run).

3.2.3.4 Task Design.

The arithmetic and number matching tasks were presented using a block design (see Figure 3.1c for an illustration of the timing and design of the tasks). Both tasks had an initial fixation of 6500 ms and end fixation of 12000 ms. Each block consisted of 6 trials, with an average inter-trial interval (ITI) of 1500 ms (1000,1500, and 2000 ms). In the arithmetic task, each trial was presented for 4500 ms and participants could respond during while the stimulus was presented or during the ITI screen. In the number matching task the trials were presented for 2000 ms and participants could also respond while the stimulus was presented or during the ITI. Each trial was randomly selected, and the conditions were randomly presented across the run. The inter-block interval (IBI) was an average of 9 seconds across the runs in both tasks. Due to the nature of the task design, all trials (correct and incorrect) were included in the analysis.

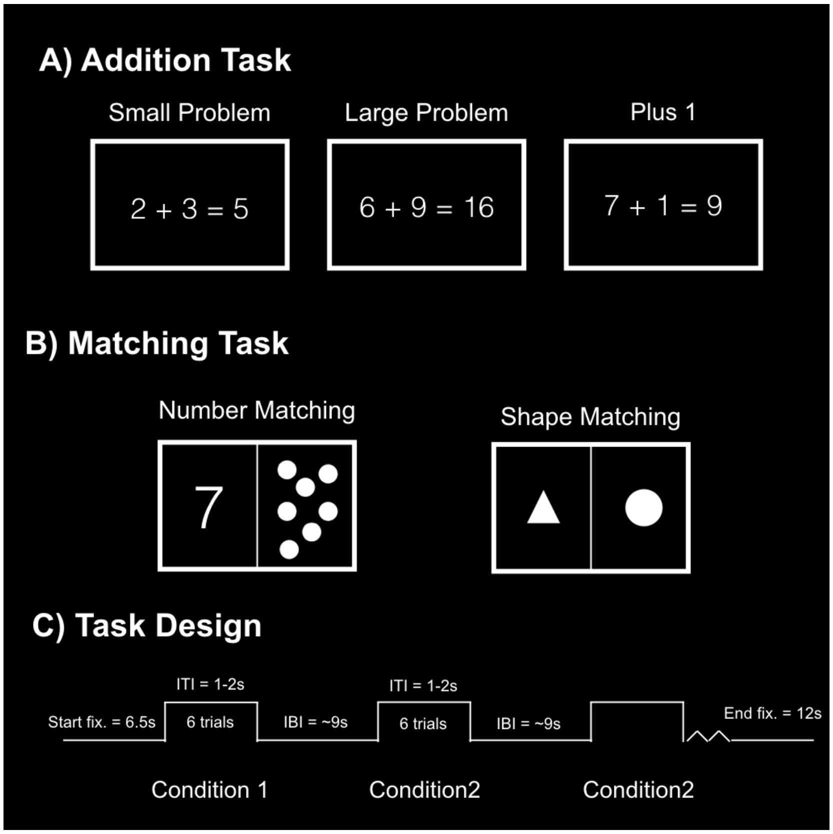

Figure 3.1 Tasks performed during the scanning sessions a) Examples of the three conditions in the arithmetic verification task b) Examples of the number matching and shape matching (control) conditions c) Schematic of the timing in the block design for both tasks

3.2.4 MRI Data Acquisition

MRI data were acquired on a 3T Siemens Prisma Fit whole-body scanner, using a 32-channel receive-only headcoil (Siemens, Erlangen, Germany). A whole-brain high resolution T1-weighted anatomical scan was collected using an MPRAGE sequence with 192 slices, a resolution of 1x1x1 mm voxels, and a scan duration of 5 minutes and 21 seconds (TR = 2300 ms; TE = 2.98 ms; TI = 900 ms; flip angle = 9°). The in-plane resolution was 256x256 pixels. Functional MRI data were acquired during the arithmetic and VSWM tasks using a T2* weighted single-shot gradient-echo planar sequence (TR = 2000 ms, TE = 30 ms, FOV 210 x 210 mm, matrix size =70 x 70, flip angle = 78°). Thirty-five slices were obtained in an interleaved ascending order with a slice thickness of 3 mm, an in-plane resolution of 3 x 3 mm, and a .75 mm gap. There were 2 runs of the arithmetic task with 144 volumes, and 1 run of the number matching task with 99 volumes. Padding was used around the head to reduce head motion. The total scan duration was approximately 40 minutes for children and 1.5 hours for adults (more tasks and runs were obtained for adults that are not discussed here).

3.2.5 Analyses

Brain imaging data were analyzed using Brain Voyager QX 2.8.4 (Brain Innovation, Maastricht, Netherlands). Functional data were corrected for differences in slice-time acquisition, head motion, linear trends, and low-frequency noise. Functional images were spatially smoothed with a 6mm FWHM Gaussian smoothing kernel. The functional images were then coregistered to the T1-weighted anatomical images and transformed into Talairach Space (Talairach & Tournoux, 1988). Using adult-templates to spatially normalize pediatric populations have been found to result in systematic differences in brain anatomy and anatomical variability in children (Burgund et al., 2002). However, such methods have not been found to cause spurious findings when comparing fMRI data across groups (Burgund et al., 2002). A 2-gamma hemodynamic response function was used to model the expected BOLD signal. A random-effects GLM was then performed on the data. Whole-brain contrasts were first thresholded at a voxelwise *p*-value of 0.005, uncorrected, then corrected for multiple-comparisons using

Monte-Carlo simulation procedure to determine a minimum cluster threshold (Goebel, Esposito, & Formisano, 2006), resulting in an overall $\alpha < .05$. This cluster thresholding method estimates and accounts for spatial smoothness and spatial correlations within the data (estimates of spatial smoothness are based on the formula discussed in Forman et al., 1995).

We first investigated the arithmetic and number processing networks in children and adults. To determine whether the relationship between the basic number processing and arithmetic was dependent on the problem size (i.e., the type of strategies used to solve arithmetic problems), we separately examined the regions activated for Small and Large problems by contrasting each condition with the Plus 1 control condition [(*Large > Plus 1*) and (*Small > Plus 1*)]. Independently examining Small and Large problems can help determine if the relative differences in the proportion of calculated problems influences whether or not arithmetic networks overlap with those for basic number processing.[2] To isolate regions involved in basic number processing, we contrasted the number matching condition with the shape matching condition (*Number Matching > Shape Matching*). In order to examine whether the overlap between basic number processing skills and arithmetic is dependent on problem size, we conducted independent conjunction analyses for Small and Large problems with the number matching task [(*Large problems > Plus1 problems*) ∩ (*Number Matching > Control*) & (*Small problems > Plus1 problems*) ∩ (*Number Matching > Control*)].

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[2] Note: Rather than using the neural problem size effect like in Chapter 2, we separately investigated Large and Small problems against the Plus 1 condition in this chapter. In Chapter 2 we used the neural problem size effect because we wanted to investigate how the cognitive demands of arithmetic are related to working memory networks. However, the questions being investigated in this chapter were not well suited to this contrast, because we were interested in the number processing demands within each condition rather than the differences in difficulty between them.

3.3 Results

3.3.1 Behavioural Performance

Reaction time (RT) and accuracy data on the arithmetic and matching tasks were separately examined in 2 pairs of mixed-design ANOVAs (see Figure 3.2 for RT and accuracy data). The two ANOVAs for RT and accuracy were identical except for the dependent variable. These analyses paralleled the functional neuroimaging analyses in order to better understand how the tasks and conditions compared to one another in each group. The first pair of analyses examined the effects of group (adults vs. children), task (arithmetic vs. matching) and condition (Large problems/Plus1 problems vs. number matching/shape matching). The second pair of analyses were identical except that they included performance on the Small problems rather than the Large problems. Therefore, the analyses examined the effects of group (adults vs. children), format (arithmetic vs. matching) and condition (Small problems/Plus1 problems vs. number matching/shape matching). All significant interactions were followed with post-hoc tests.

To determine whether adults and children differed in the proportion of calculation strategies used in the arithmetic task, we also conducted a mixed-design ANOVA with condition (Large, Small and Plus 1 problems) as a within subjects factor, and group as a between subjects factor. Any significant interactions were followed with post-hoc tests.

3.3.1.1 Effects of Group, task and condition on reaction time

3.3.1.1.1 Large problems and number matching task

Adults were significantly faster than children, $F(1,66) = 124.4, p < .001$ and all participants were significantly faster on the matching task than the arithmetic task $F(1, 66) = 236.4, p < .001$. We also found a main effect of condition where participants were slower on the experimental conditions (Large arithmetic problems/number matching problems) compared to the control conditions (Plus 1/shape matching), $F(1, 66) = 194.3$, $p < .001$. We found an interaction between task and group, $F(1, 66) = 81.4, p < .001$. Post-hoc tests revealed that children had greater differences in RT between the arithmetic task and matching task than adults (*t(*64.9) = 10.3, *p* < .001). The ANOVA also revealed an interaction between condition and group *F*(1, 66) = 6.0, *p* = .017, where the differences between conditions were greater in children than in adults (*t*(66) = 2.5, *p* = .017). There was also an interaction between task and condition *F*(1, 66) = 69.6, *p* < .001, where differences between conditions were greater in the arithmetic task than in the matching task (t(67)= 8.8, p < .001). Finally, we also observed a Task x Condition x Group interaction, *F*(1, 66) = 8.1, *p* = .006. Post-hoc tests indicated that the magnitude of the difference between conditions in the arithmetic task was greater in children than in adults (*t*(65.6) = 3.1, *p* = .003), but the difference between the conditions in the matching task was the same across groups (*t*(66) = -.19, *p* = .85).

3.3.1.1.2 Small problems and number matching task

The ANOVA from the analysis examining the relationship between Small problems and the number matching task closely resembled those from the above analysis. Adults had significantly faster reaction times than children, *F*(1,66) = 1166.6 *p* < .001, and there was a main effect of task where participants were faster on the matching task than the arithmetic task *F*(1, 66) = 127.4, *p* < .001. A main effect of condition indicated that the experimental conditions (Small arithmetic problems/number matching problems) were slower than the control conditions (Plus 1/shape matching), *F*(1, 66) = 120.9, *p* < .001. The ANOVA also revealed an interaction between task and group *F*(1, 66) = 71.0 , *p* < .001 where children showed greater differences between the tasks than adults (*t(*51.7) = 10.3, *p* < .001). There was also an interaction between condition and group *F*(1, 66) = 7.7, *p* = .007. Post-hoc tests indicated that differences between conditions were greater in children than in adults (*t*(62.6) = 3.2, *p* = .002). We also found an interaction between task and condition *F*(1, 66) = 8.5, *p* = .005, where the arithmetic task had greater differences between conditions than in the matching task (t(67)= 3.6, p = .001). There was also an interaction between Task x Condition x Group *F*(1, 66) = 13.6, *p* < .001. The difference between conditions in the arithmetic task was significantly greater in children than in adults (*t*(52.9) = 4.3, *p* < .001), however, the difference between conditions in the matching task was the same across groups (*t*(66) = -.19, *p* = .85).

3.3.1.2 Effects of group, task, and condition on accuracy

3.3.1.2.1 Large problems and number matching task

To examine the effects of group, task, and condition on accuracy, we conducted identical analyses to those on reaction time above. This mixed ANOVA revealed a main effect of group $F(1,66) = 44.8, p < .001$, where adults were more accurate than children. A main effect of condition also revealed that all participants were more accurate on the experimental conditions (Large problem/number matching) than the control conditions (Plus 1 problems/shape matching) $F(1, 66) = 70.9, p < .001$. However, there was no main effect of task $F(1,66) = 2.23, p = .08$, indicting that overall accuracy was equal on the two task. The ANOVA revealed an interaction between task and group $F(1, 66) = 10.0, p = .002$. Children had higher performance on the matching task than the arithmetic task ($t(41) = -3.27, p = .002$), but adults performed equally well on both tasks (t(25) = 2.01, $p = .06$). We also found an interaction between condition and group $F(1, 66) = 17.8, p = < .001$, where children had greater differences in accuracy between the conditions than adults (t(64.3) = -4.8, $p < .001$). There were no other significant interactions.

3.3.1.2.2 Small problems and number matching task.

Adults had higher accuracy than children on the arithmetic and matching tasks $F(1, 66) = 34.8$, $p < .001$. We also found a main effect of task $F(1, 66) = 4.14, p = .046$ where participants were more accurate on the arithmetic task than the matching task. The ANOVA also showed a main effect of condition $F(1, 66) = 194.3, p < .001$, indicating that participants were more accurate on the control conditions (Plus 1 problems/shape matching) than the experimental conditions (Small problems/number matching). We also found an interaction between condition and group $F(1, 66) = 4.35, p = .041$, where children had greater differences in accuracy between the conditions than adults (t(56.0) = -2.5, $p = .015$). There was also an interaction between task and condition $F(1, 66) = 7.8, p = .007$, where there was a greater difference between conditions in the matching task than the arithmetic task ($t(67) = 3.1, p = 002$). No other interactions were significant.

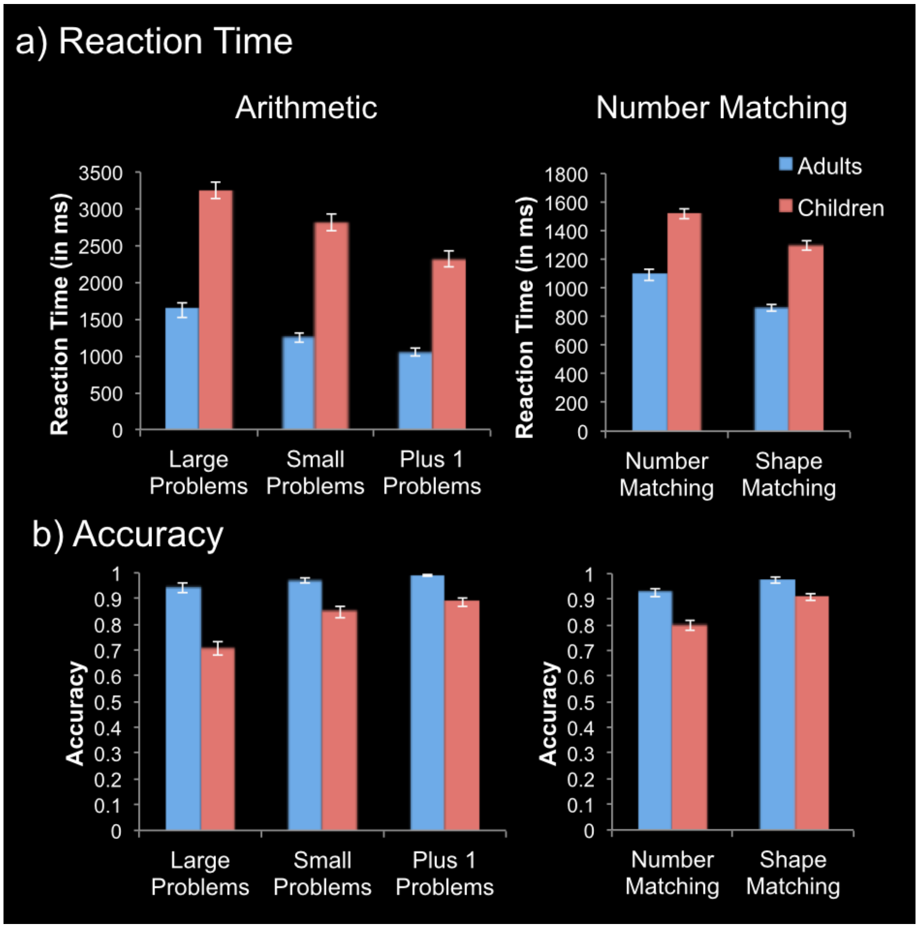

Figure 3.2 Reaction time (a) and accuracy (b) data on the arithmetic and number matching tasks in adults (in blue) and children (in red).

3.3.1.3 Post-scan strategy reports

To determine how children and adults solved the arithmetic problems, post-scan strategy reports were obtained on each problem in all children and 25/26 adults (Table 3.1). Because the assumption of sphericity was violated, a Greenhouse-Geisser correction was applied to all within-subjects effects. A main effect of group revealed that adults used calculation strategies less often than children, $F(1,64) = 14.2$, $p < .001$. There was also a main effect of condition, $F(1.6, 104.2) = 126.1$, $p < .001$, where Large problems were solved using calculation strategies more often than Small problems ($t(66) = 12.9$, $p < .001$) and Plus 1 problems ($t(66) = 13.1$, $p < .001$). Also, a greater proportion of Small problems were solved using calculation strategies compared to Plus 1 problems ($t(66) = 5.1$, $p < .001$). An interaction between condition and group, $F(1.6, 104.2) = 7.0$, $p = .003$, revealed that strategy use was only significantly different between the groups on the Large (t(65) = 2.9, *p* = .006) and Small problems (t(48.5) = 5.6, *p* < .001), but not the Plus 1 problems (t(65) = . 18, *p* = .89). Consequently, the Plus 1 condition was ideally suited as a control condition in the fMRI analyses because children and adults used similar strategies to solve the problems (see Table 3.1).

Table 3.1 Proportion of arithmetic problems solved using procedural strategies (counting up, decomposition, etc.) in adults and children (values reported in percentages).

	Large Problems	Small Problems	Plus 1 Problems
Adults (n = 25)	41.0	3.3	3.0
Children (n= 42)	59.2	25.1	3.7

3.3.2 Brain Imaging

3.3.2.1 Adults

3.3.2.1.1 Arithmetic and number processing networks

We identified regions involved in arithmetic by using two contrasts, *Large* > *Plus 1 problems* and *Small* > *Plus 1 problems*. Regions activated in the first contrast (*Large* > *Plus 1 problems*) are more likely to be involved in effortful calculation, whereas the second contrast (*Small* > *Plus 1*) allows for regions that are relatively less associated with calculation processes to be mapped. The *Large* > *Plus 1* contrast revealed a fronto-parietal network of regions that included the bilateral IPS, middle frontal gyri (MFG), insula, superior frontal gyri (SFG) and left inferior frontal gyrus (IFG) (see Table 3.2 for a full list of regions, and areas in blue in Figure 3.3a). The contrast *Small* > *Plus 1* revealed a different set of regions that included the right supramarginal gyrus (SMG), left IFG, left fusiform gyrus, and several regions in the occipital cortex (see orange regions in Figure 3.3). Finally, to isolate regions involved in number processing, we identified areas that were more active for number matching than shape matching (*number matching* > *shape matching)*. This contrast revealed a fronto-parietal network that included the bilateral IPS, left MFG, insula, thalamus, caudate, as well as regions in the occipital cortex (see regions in green in Figure 3.3a). All of these networks have been superimposed onto one another in Figure 3.3a to better observe regions that are common to each contrast.

3.3.2.1.2 Conjunction analyses

Two conjunction analyses were conducted to examine whether arithmetic and number processing networks have common underlying substrates, and to determine whether the overlap is related to the cognitive operation being performed on the arithmetic problem. In the first analysis we examined the conjunction between Large problems and number matching relative to their respective control conditions [(*Large problems > Plus1 problems*) ∩ (*Number Matching > Control*)]. This analysis revealed that the left IPS, left MFG, and bilateral superior occipital and lingual gyri were active for both large arithmetic problems and number matching (see Table 3.3 and regions in blue in Figure 3.4a). In contrast, the conjunction between Small problems and number matching [(*Small problems > Plus1 problems*) ∩ (*Number Matching > Control*)] only showed overlap within the bilateral lingual and superior occipital gyri (regions in orange in Figure 3.4a). Together, these findings may indicate that the overlap between arithmetic and basic number processing in the IPS may be dependent on task difficulty and the kind of strategies used to solve the arithmetic problems.

3.3.2.2 Children

3.3.2.2.1 Arithmetic and number processing networks

We identified networks involved in arithmetic and basic number processing skills in the same way described above for adults. We first identified regions that were more active for Large arithmetic problems than Plus 1 problems (*Large problems > Plus 1 problems*). Similar to adults, this analysis revealed a fronto-parietal network of regions that included the bilateral IPS, right superior parietal lobule (SPL), bilateral SFG, bilateral MFG, bilateral insula, left precentral gyrus, right middle and inferior temporal gyri, and several regions within the occipital cortex (see Table 3.2 and Figure 3.3b in blue). The contrast *Small problems > Plus 1 problems* revealed a similar set of regions including the bilateral IPS, left precentral sulcus and inferior frontal sulcus, the left postcentral sulcus, as well as bilateral regions of the occipital cortex and cerebellum (see

Figure 3.3b in orange). Finally, we also examined regions involved in basic number processing (*Number Matching* > *Shape Matching*). Regions that were more active for number matching than shape matching included the bilateral IPS, bilateral SFG, bilateral insula, and regions throughout the bilateral occipital cortex and cerebellum (see Figure 3.3b in green). All networks are superimposed onto each other in Figure 3.3b to visualize their overlap.

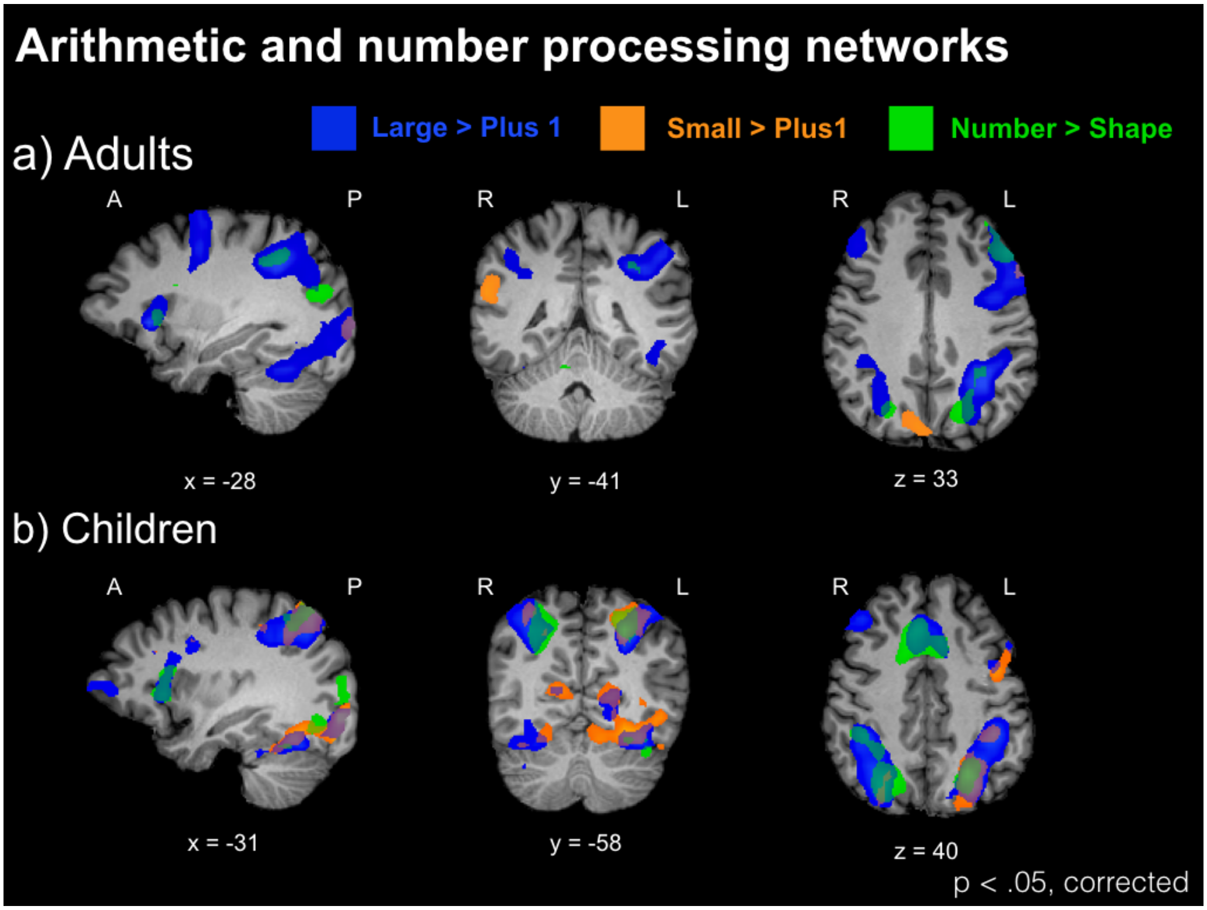

Figure 3.3 Statistical maps illustrating regions activated for Large problems, Small problems, and number matching relative to their control tasks in (a) adults and (b) children. Regions that are more active for Large problems than Plus 1 problems are displayed in blue, regions more active for Small problems than Plus 1 problems are shown in orange, and regions more active for number matching than shape matching are shown in green. Note: only significant positive activation (not deactivation) is shown in this figure.

3.3.2.2.2 Conjunction analyses

To statistically examine whether arithmetic and basic number processing activated the same brain regions, we conducted two conjunction analyses. Identical to the analyses shown above with the adults, the first conjunction analysis examined regions that were active for both Large problems and number matching relative to their controls [(*Large problems* > *Plus1 problems*) ∩ (*Number Matching* > *Control*)]. The bilateral IPS, right SPL, right insula, bilateral SFG, and bilateral lingual and superior occipital gyri were active for both Large problems and number matching (see Figure 3.4b in blue). The second conjunction analysis examined regions that were active for both Small problems and number matching relative to their control tasks [(*Small problems* > *Plus1 problems*) ∩ (*Number Matching* > *Control*)]. This analysis revealed several regions including the bilateral IPS and SPL, as well as the bilateral lingual and superior occipital gyri (see Figure 3.4b in orange).

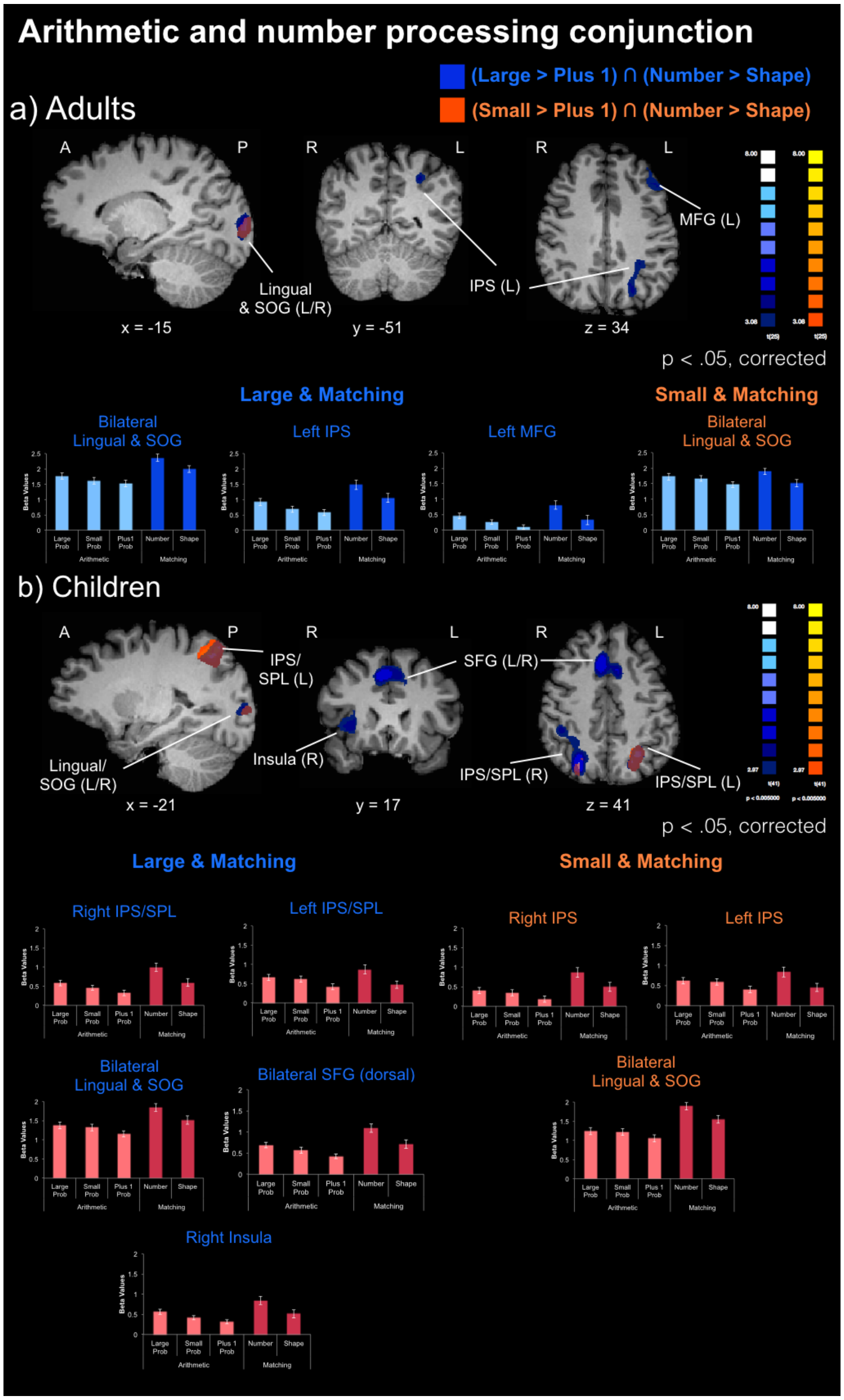

Figure 3.4 Statistical map illustrating the conjunction between the arithmetic and matching task in (a) adults and (b) children. Regions in blue show the conjunction (*Large problems > Plus1 problems*) ∩ (*Number Matching > Control*), whereas regions in orange show (*Small problems > Plus1 problems*) ∩ (*Number Matching > Control*). Mean beta values are shown for each significantly activated cluster from the conjunction. Note: Only regions that showed significant positive activation (not deactivation) for the conjunction are shown in this figure. Refer to Table 3.3 for a full list of regions.

3.3.2.3 Similarities of Activation Profiles in Children and Adults

The above conjunction analyses demonstrated some striking similarities between adults and children: the conjunction between Large problems and number matching in adults was similar to the conjunction between Small problems and number matching in children. Both of these conjunction analyses revealed significant activation in the left IPS for number matching and the respective arithmetic conditions in adults and children. This may suggest that adults process large arithmetic problems in a similar way that children process small arithmetic problems. Moreover, this could indicate that adults and children are reliant on basic number processing to the same degree for these conditions.

To test this prediction we conducted several post-hoc analyses to determine whether the conjunction between Small problems and number matching had similar patterns of activation to the conjunction between Large problems and number matching in adults. We first examined whether the RT differences between the Large and Plus 1 conditions in adults were similar to the Small and Plus 1 conditions in children. The independent-samples t-test suggested that the magnitude of the difference between these conditions was the same across groups ($t(66) = -1.21, p = .23$), suggesting that the relative difficulty of between these two conditions was the same in children and adults.

To determine whether adults and children recruited the left IPS to the same or differing degrees for these two conjunction analyses, we directly compared them. We first conducted fixed-effects GLM for each subject and subsequently calculated conjunction maps for each individual. The individual conjunction maps were combined into separate group-average maps for adults and children. We then used a random effects t-test to compare the conjunction between Large problems and number matching in adults [(*Large* > *Plus 1*) ∩ (*Number* > *Shape*)] to the conjunction between Small problems and number matching in children [(*Small* > *Plus 1*) ∩ (*Number* > *Shape*)]. This analysis revealed that there were no significant differences in the recruitment of the left IPS for these two conjunction analyses in adults and children. The only region that was found to be significantly different between the two groups was the left MFG which adults recruited more for Large problems and number matching than children did for Small problems and number matching (see Figure 3.5). This provides some additional evidence that the neural processing of Large problems in adults in the left IPS is similar to the way children process Small problems in the left IPS, and that they could be recruiting basic number skills to the same degree.

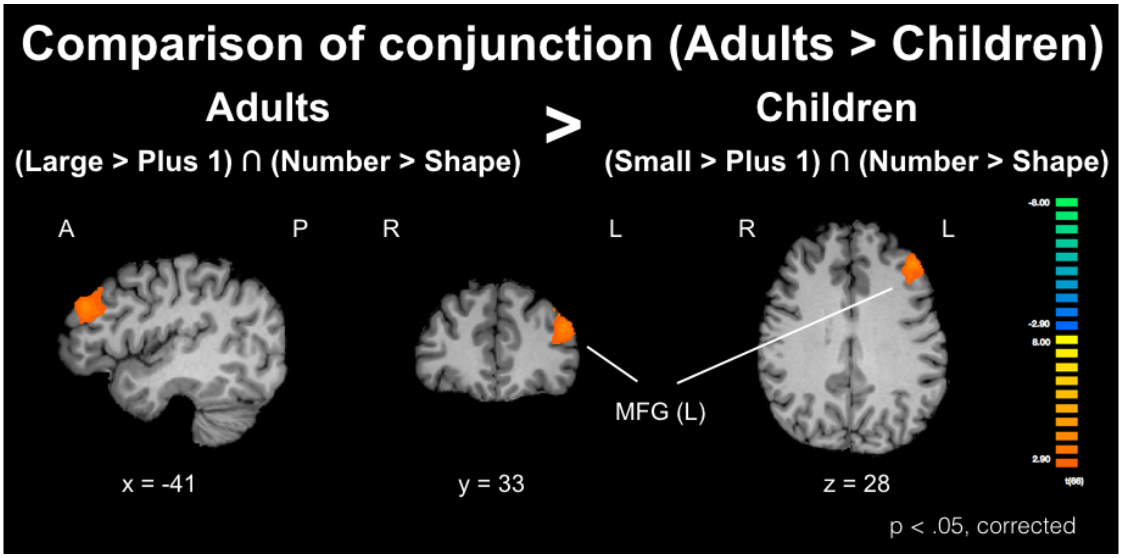

Figure 3.5 Statistical maps comparing Large problems and number matching in adults [(*Large* > *Plus 1*) ∩ (*Number* > *Shape*)] to the conjunction between Small problems and number matching in children [(*Small* > *Plus 1*) ∩ (*Number* > *Shape*)]. Regions in orange reflect significantly greater activation for adults.

Table 3.2 Anatomical regions, Talairach coordinates, mean t-scores, and number of voxels for each cluster in each simple contrast

Anatomical Region	TAL coordinates (x,y,z)			Mean t-score	Number of Voxels
Adults: Large Problems > Plus 1 Problems					
Right MFG	37.59	32.24	29.59	3.56	2651
Right insula	32.93	17.72	7.47	3.66	3104
Bilateral lingual gyri/middle and inferior occipital gyri/cerebellum	-7.13	-71.60	-7.32	3.73	50643
Right intraparietal sulcus	31.00	-51.55	34.88	3.47	3449
Bilateral thalamus	0.54	-15.54	13.71	3.44	1448
Bilateral superior frontal gyrus	-1.42	9.22	47.48	3.78	6059
Left MFG/IFG/insula/SFS/postcentral sulcus	-38.67	13.17	28.72	4.10	24107
Left intraparietal sulcus	-32.29	-51.64	37.41	4.15	14973
Adults: Small Problems > Plus 1 Problems					
Right supramarginal gyrus	52.56	-40.97	21.98	3.34	1118
Right inferior and middle occipital gyri	31.09	-82.24	-1.72	3.40	1712
Right fusiform gyrus	32.03	-59.94	-13.17	3.57	935
Right precuneus	8.28	-73.82	32.00	3.27	1050
Left inferior and middle occipital gyri	-21.74	-91.66	-2.01	3.71	2997
Left IFG	-51.46	11.30	26.96	3.65	1133
Adults: Number Matching > Shape Matching					
Right cerebellum	29.31	-53.63	-26.09	3.39	1874
Right IPS	26.51	-67.51	25.54	3.36	1585
Bilateral lingual gyrus/left superior occipital gyrus	-1.94	-81.04	-1.45	3.67	10555
Brainstem/Pons	-1.79	-23.82	-25.11	3.55	2103
Left IPS/SPL	-19.60	-63.58	36.65	3.49	7499
Left caudate/thalamus	-12.77	-5.05	14.05	3.41	1822
Left MFG/insula	-37.37	21.06	22.71	3.41	5278
Children: Large Problems > Plus 1					
Right middle and inferior temporal gyrus	51.40	-38.30	-8.10	3.70	1627
Right IPS/SPL	30.16	-55.07	43.28	3.95	17211
Right MFG/insula	33.36	21.17	29.72	3.69	11164
Bilateral lingual gyrus/inferior and middle occipital gyri/cerebellum/left inferior temporal gyrus	-4.08	-72.45	-9.93	3.73	39946
Bilateral superior frontal gyrus	-0.69	15.27	44.25	3.86	7404
Left IPS	-32.11	-53.28	42.42	4.15	16371
Left MFG/precentral gyrus/insula	-37.82	14.00	26.36	3.65	7929
Left inferior frontal gyrus	-35.81	50.56	7.45	3.24	1816
Children: Small Problems > Plus 1 Problems					
Bilateral lingual gyrus/inferior occipital gyrus/cerebellum	-7.62	-73.83	-9.46	3.70	39199
Right IPS	24.60	-66.86	47.58	3.32	2340
Right lingual gyrus	14.29	-58.74	4.71	3.34	1223
Left IPS	-24.63	-63.48	44.49	3.78	7525
Left IPS/postcentral sulcus	-40.01	-37.46	44.28	3.42	1232
Left precentral sulcus/inferior frontal sulcus	-42.05	8.13	35.56	3.39	4295
Children: Number Matching > Shape Matching					
Bilateral IPS/superior and middle occipital gyri/lingual gyrus	4.35	-71.76	26.11	3.58	29181
Right insula	30.38	18.22	7.42	3.47	2507
Bilateral superior frontal gyri	3.38	12.87	43.99	3.86	8586
Left cerebellum/inferior occipital gyrus/fusiform gyrus	-31.26	-66.53	-17.56	3.29	2966
Left insula	-32.38	16.92	9.11	3.51	1779

Table 3.3 Anatomical regions, Talairach coordinates, mean t-scores, and number of voxels for each cluster in the conjunction analyses.

Anatomical Region	TAL coordinates (x,y,z)			Mean t-score	Number of Voxels
Adults: Conjunction (Large > Plus 1) ∩ (Number > Shape)					
Bilateral lingual gyrus and superior occipital gyrus	-3.86	-82.88	-0.92	3.43	5137
Left IPS	-25.25	-57.73	34.55	3.34	2231
Left MFG	-40.67	27.56	30.28	3.42	2471
Adults: Conjunction (Small > Plus 1) ∩ (Number > Shape)					
Bilateral lingual gyrus and left superior occipital gyrus	-14.98	-93.67	-2.16	3.48	869
Children: Conjunction (Large > Plus 1) ∩ (Number > Shape)					
Right IPS/SPL	25.82	-58.86	42.70	3.54	6733
Right insula	29.87	19.72	6.18	3.52	1829
Bilateral lingual gyrus/superior occipital gyrus	-5.31	-85.96	-1.66	3.19	3231
Cingulate gyrus/superior frontal gyrus (ventral portion)	-1.29	41.26	3.19	-3.44	4201
Superior frontal gyrus (dorsal portion)	0.53	14.40	44.06	3.77	5432
Superior frontal gyrus	-8.92	52.01	31.02	-3.29	1618
Left IPS	-24.17	-63.44	43.86	3.50	3962
Children: Conjunction (Small > Plus 1) ∩ (Number > Shape)					
Right IPS/SPL	20.98	-69.64	47.66	3.30	1289
Bilateral lingual gyrus/superior occipital gyrus	-2.26	-87.78	0.79	3.21	4392
Left IPS/SPL	-23.60	-62.77	45.38	3.53	4274
Adults (Large > Plus 1) ∩ (Number > Shape) > Children (Small > Plus 1) ∩ (Number > Shape):					
Left MFG	-40.36	31.90	28.39	3.40	2492

3.3.2.4 Control analyses

It should be acknowledged that differences between adults and children could be attributed to performance differences between the groups. Therefore, we also conducted an analysis that included 26 children who had the highest accuracy on the Small and Large arithmetic problems. We aimed to match performance on the arithmetic task because performance was generally lower on this task than the matching task. Behavioural performance still significantly differed between the two groups, though the higher-performing children were more similar to the adults than the full sample of children. Using this sample of 26 children, we conducted the two conjunction analyses to determine whether task performance was related to the outcome of these analyses. The conjunction analysis between Large problems and number matching (relative to their controls) remained nearly identical in the highest performing children, with the bilateral IPS, SFG and right insula all remaining significant ($p < .05$ corrected). The conjunction between Small problems and number matching was also similar to the full sample and included the left IPS as well as the bilateral SFG ($p < .05$ corrected).

3.4 Discussion

The recruitment of the IPS during arithmetic has long been assumed to be due to the manipulation of quantities during calculation. However, arithmetic and number processing networks have largely been investigated in isolation of one another and any conclusions about the role of the IPS during calculation has been inferred from comparing across studies or by investigating brain-behaviour correlations. Previous research with adults has failed to find an association between magnitude processing and arithmetic in the parietal cortex (Dehaene et al., 1996; Rickard et al., 2000). However, these studies used multiplication problems to identify regions involved in calculation, which are typically solved using retrieval strategies in adults and therefore require little manipulation of quantities (Imbo & Vandierendonck, 2008). Consequently, the lack of neural overlap between multiplication and magnitude processing may have been related to the type of strategy being used to solve the arithmetic problems. The present study aimed to address these unresolved questions by using a within-subjects approach to determine whether arithmetic and basic numerical processes rely on the IPS in adults and children. We provide the first evidence to suggest that arithmetic and basic number processing have common neural substrates in the IPS in adults and children. Importantly, we found that this relationship differs depending on arithmetic problem size (i.e., proportion of problems that are calculated). Moreover, adults and children recruit the left IPS similarly for number processing and arithmetic when the cognitive demands of the arithmetic task are comparable.

In the present study we found that the IPS plays an important role in the relationship between arithmetic and the processing of the semantic referents of number symbols (i.e., symbol-quantity associations). Similar evidence has been shown using brain-behaviour correlations where children who recruited the left IPS more during a symbolic number comparison task also had higher math scores (Bugden et al., 2012). The present findings, therefore, extend those from Bugden et al (2012) by indicating that the IPS is particularly important for the relationship between symbol-quantity associations and arithmetic. Behavioural research has also provided compelling evidence that a fluent understanding of symbol-quantity relationships is important for the acquisition of arithmetic skills (Brankaer et al., 2014; Mundy & Gilmore, 2009). It is possible that individuals with more efficient access to the meanings of number symbols have greater ease in manipulating quantities in the context of calculation.

One particularly novel finding was that the recruitment of the IPS for arithmetic and number matching was also related to the proportion of problems that were calculated. The conjunction analyses revealed that adults exhibit significant overlap in the left IPS for basic number processing and arithmetic, but only for the large addition problems of which 41% of the problems were solved using procedural strategies. In contrast, adults only showed significant activation in the bilateral lingual and superior occipital gyri for the conjunction between small problems and basic number processing, suggesting that these problems do not rely on quantity-based systems in the IPS. Instead, the regions in the conjunction analysis between small problems and number matching are likely related to common visual processing demands for both tasks. The lack of overlap within the IPS is consistent with the post-scan strategy reports that showed adults used procedural strategies on only 3% of the small addition problems. Small problems are more often solved using fact-retrieval strategies (Campbell & Xue, 2001; LeFevre et al., 1996), therefore, these problems rely on different neural substrates, which are non-overlapping with those for basic number processing skills. Problems that are solved using retrieval have been found to be associated with activation in the angular and supramarginal gyri (Grabner et al., 2009; Grabner, Ansari, Koschutnig, Reishofer, & Ebner, 2013; Price, Mazzocco, & Ansari, 2013). The present data also reveal a similar pattern of findings even when contrasting Small problems with Plus 1 problems, where the right supramarginal gyrus was more active for Small problems than Plus 1 problems.

Related to the notion that the IPS is crucial for problems that require quantity-based strategies, we also found that children recruited the bilateral IPS for both arithmetic and basic number processing, and this was relatively consistent for small and large problems. The post-scan strategy reports revealed that this could have been related to children using procedural strategies for both small and large addition. Behavioural research has found that the strength of the relationship between symbolic number processing and arithmetic changes depending on the type of strategy that is implemented.

A fluent understanding of symbolic numbers has been shown to be more related to problems that rely on mental calculation versus those that are solved using algorithms (Linsen, Verschaffel, Reynvoet, & De Smedt, 2015a, 2015b). Together, these findings indicate a close association between basic number processing and arithmetic at the behavioural and neural levels, however, the relationship changes depending on the type of strategies that are used to solve the arithmetic problem.

The arithmetic training literature provides some additional context to the findings in this study, and shows that brain activity shifts away from the IPS to the angular and supramarginal gyri when individuals become more familiar with arithmetic problems (for a review see Zamarian, Ischebeck, & Delazer, 2009). Adults initially activate in the IPS for multi-digit arithmetic problems, but after being trained on these problems, there is a shift in activation to the angular gyrus for the same problems (Delazer et al., 2003, 2005; Ischebeck et al., 2006). This has been linked to changes in strategy use from more quantity-based strategies to fact-retrieval (Zamarian et al., 2009). These findings have been corroborated with post-scan strategy reports (Grabner et al., 2009), and in studies investigating individual differences in arithmetic proficiency (Grabner et al., 2007; Price et al., 2013). In the present data, we see a similar pattern of findings in both adults and children where the IPS is recruited for basic number processing and arithmetic when a significant portion of the problems are solved using calculation. However, arithmetic problems that are predominantly solved with retrieval (e.g., small problems in adults) show no overlap in the IPS.

One of the central findings in this study was that adults and children showed similarities of processing once the cognitive demands of the arithmetic task were similar. These similarities were evident when examining the conjunction between small problems and number matching in children and the conjunction between large problems and number matching in adults; in both of these analyses children and adults recruited the left IPS. By directly comparing these conjunction analyses, we found that the there were no statistically significant differences between groups in the left IPS. This provides evidence that adults process large problems in a similar way to the way children process small problems in the left IPS, and importantly, that the link between arithmetic and symbol-quantity relationships is similar for these conditions in each group. Even though there remained differences in the proportion of problems that reported to be calculated (adults: 41.0 % calculated on large problems; children: 25% calculated on small problems), the reaction time data indicated that the relative task difficulty of these two conditions was the same across groups. These findings suggest that basic number processing skills are recruited in a similar manner for problems that have similar levels of task difficulty. Therefore, once cognitive demands of the arithmetic problem are matched, adults and children show markedly similar patterns of brain activation within the IPS for number processing and arithmetic. It is possible that the association between number processing and arithmetic is not dependent on age, but rather on the cognitive operation being performed.

3.4.1 Limitations

In the present study we used a block design to assess brain activation for large problems and small problems. Therefore, we were not directly able to assess trials solved using calculation or retrieval and could only make inferences about cognitive procedures based on problem size. However, it is likely that the outcome would have been similar if even if we had divided the trials by strategy rather than problem size; though there might be some differences in the extent of brain activity, adults and children are likely to recruit similar brain regions when they are performing the same cognitive operations. Future research will need to empirically examine how the relationship between number processing and arithmetic is modulated by strategy on a trial-by-trial basis.

A second limitation of this study was that we only used addition problems to assess brain networks involved in arithmetic. We used addition because it is an age-appropriate task that most children can solve with a relatively high degree of accuracy. Moreover, a good proportion of addition problems are solved using procedural and retrieval strategies, particularly in children. Our findings could have differed had we selected an operation such as subtraction, but these differences likely would not have been operation-specific but related to the extent to which the operation demanded procedural or retrieval strategies. Recent research has found that neural differences between operations are related to the proportion of problems that are calculated or retrieved and are not operation-specific (Tschentscher & Hauk, 2014). For example, subtraction problems tend to be solved using more procedural strategies than in addition (Campbell & Xue, 2001). Therefore, subtraction may have shown greater overlap with number processing skills in the IPS compared to addition.

3.4.2 Conclusions

By using a within-subjects approach to examine arithmetic and number processing, we were able to investigate which brain regions underlie these two skills, and how these relationships change with age. Our findings provide evidence that the IPS is a particularly important region for arithmetic and symbol-quantity associations in both adults and children. However, problem size was found to influence the relationship between these two tasks, which may be related to the proportion of problems being solved by calculation or retrieval. We also provided novel evidence that the IPS was recruited to a similar degree for small problems in children and large problems in adults, indicating that these conditions may have similar cognitive demands. Therefore, the association between number processing and arithmetic is related to the cognitive operation being performed rather than age. These findings provide the first evidence to directly test the common underlying relationship between basic number processing and arithmetic and suggest the IPS is recruited during arithmetic due to the importance of manipulating quantities in calculation.

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Chapter 4

4 Individual differences in children's domain specific and domain general abilities relate to brain activity within the intraparietal sulcus during arithmetic

4.1 Introduction

Achieving fluency with arithmetic is important milestone in the development of mathematical skills. It is therefore important to investigate which competencies scaffold the development of arithmetic fluency in children. The cognitive foundations of arithmetic have been studied extensively using behavioural methods. Researchers differentiate between domain specific and domain general predictors of arithmetic abilities. Domain specific skills refer to abilities that are specifically related to mathematical competencies (e.g., understanding the meanings of number symbols), whereas domain general skills are abilities that are important for information processing across domains (e.g., working memory or attention) (Vanbinst & De Smedt, 2016). Much research has investigated how domain specific and domain general competencies predict concurrent and future arithmetic skills, but how these skills relate to the recruitment of different brain regions in the arithmetic network is still unclear. This study aims to better understand these relationships and elucidate the cognitive underpinnings of the neural basis of arithmetic.

Behavioural research has identified several domain specific competencies that predict concurrent or future arithmetic skills. This includes skills such as symbolic (e.g., Arabic numerals) and nonsymbolic (e.g., dot arrays) number processing skills, which are often assessed using number comparison tasks (Bartelet, Vaessen, Blomert, & Ansari, 2014; De Smedt, Verschaffel, & Ghesquière, 2009; Holloway & Ansari, 2009; Nosworthy, Bugden, Archibald, Evans, & Ansari, 2013; Schneider et al., 2016). More recently, symbolic ordering abilities (e.g., being able to identify that a series of numbers are in the correct ascending order) have also been found to be related to individual differences in arithmetic (Goffin & Ansari, 2016; Lyons & Ansari, 2015; Lyons & Beilock, 2011; Lyons, Price, Vaessen, Blomert, & Ansari, 2014).

In addition to research showing that a variety of domain specific skills relate to individual differences in arithmetic abilities, several studies have documented the importance of domain general skills in the solution of arithmetic problems (Alloway & Passolunghi, 2011; DeStefano & LeFevre, 2004; Passolunghi & Lanfranchi, 2012; Peng, Namkung, Barnes, & Sun, 2015; Raghubar, Barnes, & Hecht, 2010; Swanson & Kim, 2007). Visuo-spatial working memory (VSWM) may contribute to arithmetic by manipulating numbers and holding intermediate solutions in mind when calculating. Other skills such as verbal and phonological skills may also play a role in the acquisition of arithmetic skills (De Smedt, Taylor, Archibald, & Ansari, 2010; Durand, Hulme, Larkin, & Snowling, 2005; Passolunghi & Lanfranchi, 2012; Szucs, Devine, Soltesz, Nobes, & Gabriel, 2014; Vukovic & Lesaux, 2013).

Though some consensus has emerged on how individual differences in domain general and domain specific abilities predict future success in arithmetic, much less is known about how individual differences in these skills are related to the neural networks that underlie arithmetic problem solving. Many studies have mapped out the brain regions supporting arithmetic problem solving. This body of literature converges to suggest that a fronto-parietal network is engaged during arithmetic in both adults and children (Arsalidou & Taylor, 2011; Davis et al., 2009; De Smedt, Holloway, & Ansari, 2010; Kucian, Von Aster, Loenneker, Dietrich, & Martin, 2008; Rivera, Reiss, Eckert, & Menon, 2005). The frontal cortex is thought to be more involved in domain general demands of arithmetic, such as cognitive control and working memory. In contrast, the parietal cortex, particularly the intraparietal sulcus (IPS), is believed to be involved in domain specific processes such as magnitude representations (Dehaene, Piazza, Pinel, & Cohen, 2003; Menon, Rivera, White, Glover, & Reiss, 2000). However, brain activity in the IPS could be attributed to a number of factors because arithmetic shares common brain regions with other processes such as VSWM (Constantinidis & Klingberg, 2016; Klingberg, 2006; Zago et al., 2008) and basic magnitude processing (Ansari, 2008; Arsalidou & Taylor, 2011; Vogel, Goffin, & Ansari, 2015). Thus, the contributions to the recruitment of the IPS during arithmetic are likely multifaceted and could be a product of domain general or domain specific processes, or a combination of the two. Understanding how individual differences in domain general and domain specific abilities contribute to the recruitment of the parietal cortex during arithmetic can provide a better understanding of the neural basis of arithmetic. Moreover, it can provide convergent validity with studies that have examined the overlap between arithmetic, domain general and domain specific skills (e.g., Chapters 2 and 3). For instance, if the recruitment of the IPS during arithmetic not only overlaps with VSWM and number processing skills, but also correlates with individual differences on these abilities, then this provides additional evidence that brain activity IPS partially reflects the engagement of these cognitive processes.

Though some research has employed brain-behaviour correlations to better understand the relationship between arithmetic and domain general or domain specific skills, these studies have not simultaneously examined these abilities in the same sample of participants. Therefore it is still unclear whether some cognitive skills contribute to IPS activity more than others, or whether they contribute equally. Studies that have used brain-behaviour relationships to determine how domain general and domain specific abilities are related to arithmetic have provided evidence that the IPS is an important locus in all of these abilities. For instance, Dumontheil and Klingberg (2012) measured brain activity during a VSWM dot-matrix task and found that individual differences in the recruitment of the left IPS were related to arithmetic scores 2 years later, even after accounting for other behavioural measures. Other research has investigated how working memory abilities are related to individual differences in the recruitment of different brain regions during the solution of arithmetic problems (Metcalfe, Ashkenazi, Rosenberg-Lee, & Menon, 2013). Children who had higher VSWM scores also showed greater recruitment of the right IPS, left supramarginal gyrus, and several regions within the frontal cortex during arithmetic (Metcalfe et al., 2013). A similar study demonstrated that, among typically developing children, individual differences in VSWM were related to brain activity during arithmetic in fronto-parietal brain regions (Ashkenazi, Rosenberg-Lee, Metcalfe, Swigart, & Menon, 2013). However, children with math learning disabilities showed no such relationship between VSWM and individual differences in the recruitment of the arithmetic network (Ashkenazi et al., 2013). Together, these findings provide evidence that there is a relationship between VSWM and arithmetic and that the IPS seems to be consistently implicated in this association.

The studies discussed above have begun to examine the relationship between brain activation during arithmetic and well-known behavioural correlates of arithmetic competence. However, no study to date has explored how individual differences in domain specific or basic number processing skills modulate brain activity during arithmetic. Some existing literature has indicated that activity in the IPS during basic number processing is related to individual differences in arithmetic. One study demonstrated that children who exhibit greater modulation of the left IPS during a symbolic number comparison task also performed better on a standardized test of mathematical fluency (Bugden, Price, McLean, & Ansari, 2012). Similarly, greater modulation of the right parietal cortex (including the right IPS) during nonsymbolic number comparison has been associated with a standardized measure of math performance (Haist, Wazny, Toomarian, & Adamo, 2014). Based on this literature, it remains unclear whether individual differences in basic number processing skills are related to differences in the neural correlates of arithmetic. Put differently, while these studies related behavioural measures of arithmetic to neural correlates of symbolic and nonsymbolic number processing, there exists no research that has related domain specific basic number processing measures to brain activation associated with arithmetic.

The behavioural predictors of brain activity in the IPS may also depend on the neural indices that are being used. For example, a common way of isolating brain regions involved in calculation is to examine regions that are more active for large arithmetic problems (e.g., sums > 10) than small problems (e.g., sums < 10), which is also referred to as the neural problem size effect (PSE) (e.g., De Smedt, Holloway, et al., 2010). The PSE is marked by more accurate and faster reaction times on small compared to large problems (Campbell & Xue, 2001; LeFevre, Sadesky, & Bisanz, 1996). Different brain regions are activated as a function of problem size; large problems recruit the bilateral IPS and several frontal brain regions more than small problems, whereas small problems activate the supramarginal and angular gyri more than large problems (Stanescu-Cosson et al., 2000). The neural PSE is thought to reflect increasing demands on calculation (De

Smedt, Holloway, et al., 2010; LeFevre et al., 1996), therefore it is possible that this index of brain activity might be more tied to domain general processes such as working memory. In contrast, brain activation for relatively easy (Small problems) and more difficult problems (Large problems) might both be related to basic number processing skills because similar relationships have been demonstrated at the behavioural level (e.g., Linsen, Verschaffel, Reynvoet, & De Smedt, 2015b; Vanbinst, Ghesquiere, & De Smedt, 2012). By only using the PSE as a measure of brain activity underlying arithmetic, it is possible that processes that are common to both small and large problems cannot be assessed. Therefore, it is important to examine how domain general and domain specific competencies relate to multiple indices of arithmetic activity within the IPS as they may be related to different cognitive processes.

Behavioural research has demonstrated that there are multiple domain general and domain specific predictors of arithmetic skills, and the same may be true of the arithmetic network. It is likely that the brain activity during arithmetic originates from multiple cognitive sources, particularly in the IPS where arithmetic shares common neural substrates with domain general and domain specific skills (e.g., Arsalidou & Taylor, 2011; Zago et al., 2008). The literature to date has been fragmented, and the above-discussed studies examining the brain-behaviour relationships between arithmetic and domain general and domain specific skills have only examined one predictor at a time.

The present study aims to examine how children's domain general and domain specific skills are related to individual differences in the recruitment of the bilateral IPS during the solution of arithmetic problems. Previous literature has demonstrated that the IPS is a particularly critical region for arithmetic, and has been shown to be associated with VSWM and basic number processing skills (e.g., Bugden et al., 2012; Dumontheil & Klingberg, 2012). Therefore, it is unclear whether domain general skills, domain specific skills, or a combination of the two contribute to the recruitment of the IPS during arithmetic. To examine this question, we first isolated regions that were more active for large problems than small problems in children between 7-10 years of age. This is a particularly important developmental period because children are actively becoming more fluent with arithmetic during this time (Butterworth, 2005; Carr & Alexeev, 2011).

We examined how domain general and domain specific skills predicted the neural PSE and overall brain activity within the IPS, and selected measures that have consistently been associated with arithmetic proficiency in the behavioural literature such as: verbal skills, VSWM, nonsymbolic comparison, symbolic comparison, and symbolic ordering. Simultaneously examining multiple measures allows us to determine whether domain general or domain specific skills contribute more to brain activity in the IPS, or whether they each uniquely predict the recruitment of this brain region.

4.2 Method

4.2.1 Participants

Fifty-nine children between 7.5-10.4 years of age (M = 9.2) were recruited to participate in this study. Two children did not complete the MRI, and 9 children were removed from analyses because they had accuracy below chance on the arithmetic task in the scanner or on the non-standardized behavioural measures. Three additional children were excluded from analyses due to head motion that exceeded of 1.5 mm between volumes or more than 3 mm over the entire scan, and 1 child was removed due to atypical neurological signs. A total of 44 children were included in the final analysis (19 females, 2 left-handed). All children were fluent English speakers and had normal or corrected to normal vision. The Health Sciences Research Ethics Board at the University of Western Ontario approved the methods and procedures in this study. Children's caregivers gave informed consent, and children were reimbursed for their participation in the study.

4.2.2 Procedure

This study consisted of two testing sessions: a behavioural session and an fMRI session. In the behavioural session we assessed performance on three number processing tasks (nonsymbolic and symbolic number comparison, and symbolic ordering), intelligence, standardized measures of math achievement, and visuo-spatial working memory. Children also completed a mock scanning session to familiarize them with the MRI environment and procedures. Children practiced keeping their head still while completing a short arithmetic verification task in the mock scanner. Approximately 1-66 days following the behavioural session (M = 13 days), participants returned to complete the MRI component of the study. During the MRI session participants completed arithmetic verification task, as well as an additional 3-4 tasks in the scanner, which are not discussed here. The order of the tasks was counterbalanced using a Latin square design.

4.2.3 Experimental Tasks & Design

4.2.3.1 Behavioural Assessment

4.2.3.1.1 Domain specific measures

We included 3 measures of basic number processing skills: nonsymbolic and symbolic number comparison, and symbolic ordering. Previous research has identified each of these tasks as predictors of arithmetic skills (Bartelet et al., 2014; Goffin & Ansari, 2016; Lyons et al., 2014; Nosworthy et al., 2013; Schneider et al., 2016).

4.2.3.1.1.1 Nonsymbolic and symbolic number comparison

For the nonsymbolic comparison task, participants were presented with two arrays of dots (from 1-9 dots), and were instructed to select the array with more dots. On half of the trials the two dot arrays were equated on total surface area, and on the other half of trials the arrays were equated on total circumference. In the symbolic comparison task, participants were presented with two Arabic digits (from 1-9) and were instructed to select the larger number. On both symbolic and nonsymbolic tasks, the participant was asked to press a button with their right hand if the stimulus on the right side of the screen was bigger, and to press the button with their left hand if the stimulus on the left side of the screen was bigger. The side that had the greater quantity was counterbalanced; half of the trials had the larger quantity on the left side of the screen, and the other half of trials the larger quantity was presented on the right side of the screen. The stimuli were presented for 850 ms with an inter-trial fixation of 3000 ms. Participants could respond while the stimulus was presented or on the fixation screen. The task consisted of 2 blocks with 32 trials (64 trials in total), with a break separating each block. The number pairs were identical in the symbolic and nonsymbolic tasks, and had distances that ranged from 1-8 (see Appendix C for number pairs for each unique trial). Each task had a set of 6 practice problems, and participants were instructed to respond as quickly and accurately as possible.

4.2.3.1.1.2 Symbolic ordering

Participants were shown 3 Arabic digits that were presented horizontally. On half of the trials the digits were in a numerically increasing order (e.g., 1 2 3 or 4 6 8), and on the other half of trials the digits were not in order (e.g., 3 1 2 or 6 8 4). Participants were instructed to press a button with their right hand if the numbers were in increasing order and a button with their left hand if the numbers were mixed. The digits were separated by a distance of 1, 2, or 3 (e.g., Distance 1 = 2 3 4; Distance 2 = 3 5 7; Distance 3 = 2 5 8). There were 2 blocks of trials that were separated by a break, with 30 trials per block (60 trials in total across both blocks). Of the 15 trials that were in order in each block, 7 trials had a distance of 1, 5 trials had a distance of 2, and 3 trials had a distance of 3 (see Appendix D for a list of stimuli). There were an unequal number of trials per distance because we only used single digits trials, therefore, there are only a limited number of possible sequences. The out-of-order trials were identical to the in-order trials, except they were mixed. The mixed trials in Blocks 1 and 2 had different combinations. The ordering task had a set of 10 practice problems, and participants were asked to respond as quickly and accurately as possible.

4.2.3.1.2 Domain general measures

4.2.3.1.2.1 Verbal and nonverbal intelligence

Intelligence was assessed using the Kaufman Brief Intelligence Test- Second Edition (KBIT2) (Kaufman & Kaufman, 2004). The KBIT2 measures verbal abilities using two subtests: verbal knowledge and riddles. Verbal knowledge assesses receptive language skills, whereas the riddles subtest assesses verbal reasoning skills. We combined the two verbal subtests into one measure of verbal intelligence by averaging children’s scores on the verbal knowledge and riddles subtests. Nonverbal intelligence was assessed using the matrices subtest, which requires participants to understand the relationships among visually presented stimuli (both meaningful and abstract visual stimuli). In all analyses we report raw scores rather than standard scores because standard scores were negatively correlated with age $r(42) = -.39$, $p = .009$, suggesting that the test norms were not representative of the children in this sample.

4.2.3.1.2.2 Visuo-Spatial Working Memory

We assessed VSWM using the computerized Automated Working Memory Assessment (AWMA) (Alloway, Gathercole, Kirkwood, & Elliott, 2008). In the dot matrix task, the participant is presented with a four by four matrix and a dot moves positions through the matrix. The participant is then asked to recall the dot sequence by tapping it on the screen. Even though age was not correlated with the standard scores on the AWMA, we report raw scores to remain consistent with the other standardized measures.

4.2.3.1.3 Math Achievement

The Math Fluency subtest from the Woodcock Johnson III was administered to each participant. This is a timed measure of arithmetic fluency where children solve single-digit addition, subtraction, and multiplication problems as quickly possible in 3 minutes (Woodcock, McGrew, & Mather, 2001). We also administered Numerical Operations and Math Reasoning from the Wechsler Individual Achievement Test (Second Edition: Canadian) (Wechsler, 2005). However, our analyses and results only discuss the Math Fluency subtest from the Woodcock Johnson III due to the focus on single digit arithmetic skills. In all analyses we use raw scores because age was negatively correlated with standard scores on the Woodcock Johnson III $r(42) = -.35$, $p = .02$, indicating that the test norms were not representative of the children in this sample.

4.2.3.2 fMRI Arithmetic Task

To investigate neural processing associated with arithmetic problem solving, participants completed two runs of a single-digit arithmetic verification task that consisted of three conditions: (1) Small problems (2) Large problems and (3) Plus 1 problems. For all conditions, an addition problem with two addends was presented along with a solution. Participants were asked to identify if the solution was correct or incorrect. Small problems had a solution less than or equal to 10, Large problems had a solution greater than 10, and Plus 1 problems were always a single digit plus 1 (Figure 4.1a). Tie problems (ie. 3 + 3) and problems containing a 0 were excluded from the problem list. In half of the trials the solution was incorrect and on the other half of trials the solution was correct. If the solution was incorrect, the presented solution was +1 or +2 above the correct solution. Each run consisted of 36 unique problems (12 problems per condition), resulting in 72 trials across both runs (see Appendix B for problem list). For the Small and Large problem conditions, half the trials had the larger number presented on the left (4 + 2) and in the other half of the trials the larger number was presented on the right (3 + 5). If the larger number was presented on the left for a specific problem in run 1, it was presented on the right in the second run (e.g., Run 1 [4 + 2]; Run 2 [2 + 4]). Thirty-five out of the 44 children passed the motion and accuracy criteria on both arithmetic runs, and only 1 run was used for the other 9 children.

The arithmetic task was presented using a block design with an initial fixation of 6500 ms and end fixation of 12000 ms (see Figure 4.1b for a schematic of the timing and design). Each problem was presented for a total of 4500 ms, and the inter-trial interval (ITI) was 1500 ms on average (duration was 1000, 1500, and 2000 ms). Participants could respond during the presentation of the problem or on the ITI screen. The duration of the inter-block interval (IBI) averaged to 9 seconds in each run. The conditions and trials were randomly presented.

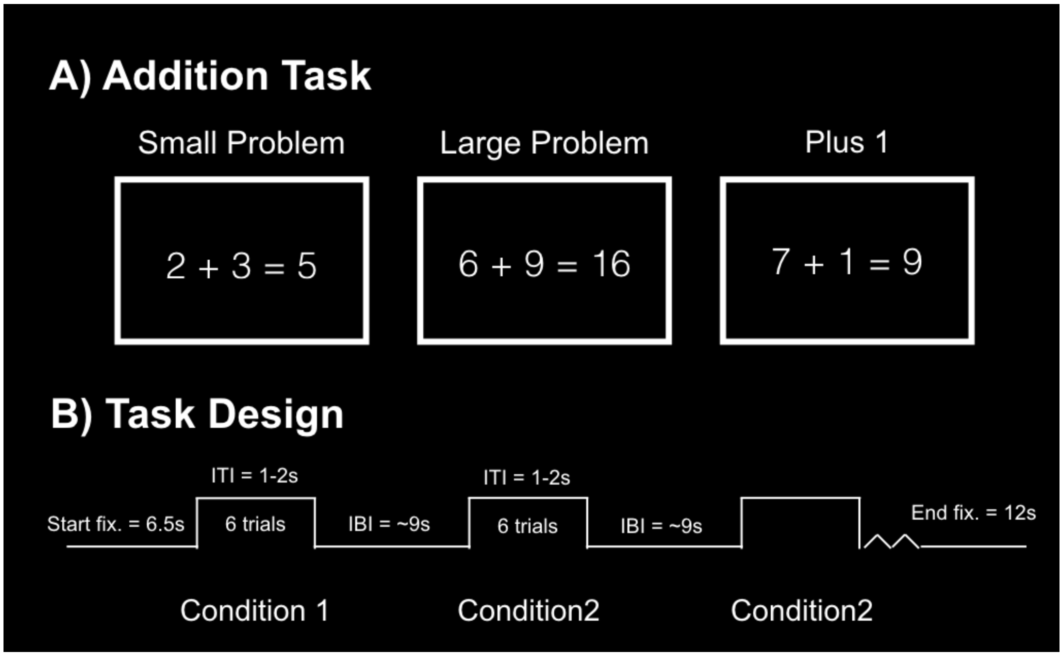

Figure 4.1 a) Examples of the three conditions in the arithmetic verification task. Participants were asked to identify if the solution was correct or incorrect. b) Schematic of the timing of the arithmetic task in the scanner

4.2.4 MRI Data Acquisition

MRI data were acquired on a 3T Siemens Prisma Fit whole-body scanner, using a 32-channel receive-only headcoil (Siemens, Erlangen Germany). A whole-brain high resolution T1-weighted anatomical scan was collected using an MPRAGE sequence with 192 slices, a resolution of 1x1x1 mm voxels, and a scan duration of 5 minutes and 21 seconds (TR = 2300 ms; TE = 2.98 ms; TI = 900 ms; flip angle = 9°). The in-plane resolution was 256x256 pixels. Functional MRI data were acquired during the arithmetic task using a T2* weighted single-shot gradient-echo planar sequence (TR = 2000 ms, TE = 30 ms, FOV 210 x 210 mm, matrix size =70 x 70, flip angle = 78°). Thirty-five slices were obtained in an interleaved ascending order with a slice thickness of 3 mm, an in-plane resolution of 3 x 3 mm, and a .75 mm gap. There were 2 runs of the arithmetic task with 144 volumes. Padding was used around the head to reduce head motion. The total scan duration was approximately 40 minutes.

4.2.5 Analyses

4.2.5.1 Behavioural analyses

In all analyses, raw scores on the standardized measures of intelligence and visuo-spatial memory were used due to the negative correlations between age and standard scores. For each of the domain specific measures we could have used task-specific dependent measures such as distance or reverse distance effects (e.g., Goffin & Ansari, 2016; Turconi, Campbell, & Seron, 2006). However, we used dependent measures of overall task performance to make the variables more comparable across tasks. Performance scores were calculated to combine reaction time and accuracy data on the domain specific measures (nonsymbolic and symbolic comparison, and symbolic ordering). Accuracy and reaction time (on correct trials only) were combined to form performance scores based on the formula described in Lyons et al. (2014): Performance = RT(1+2ER). ER refers to the error rate, or 1 – total accuracy (e.g., 70% accuracy = 0.3 ER). Using this formula, higher values indicate poorer performance.

To examine how domain general and domain specific factors contributed to arithmetic skills, we conducted correlations between Math Fluency scores from the Woodcock Johnson III and each domain general and domain specific measure. Any measures that were significantly correlated with Math Fluency were then entered into a linear regression to determine which measures predicted unique variance in arithmetic performance.

4.2.5.2 Brain imaging analyses

Brain imaging data were analyzed using Brain Voyager QX 2.8.4 (Brain Innovation, Maastricht, Netherlands). Functional data were corrected for differences in slice time acquisition, head motion, linear trends, and low frequency noise. Functional images were spatially smoothed with a 6mm FWHM Gaussian smoothing kernel. The functional images were then coregistered to the T1-weighted anatomical images and transformed into Talairach Space (Talairach & Tournoux, 1988). A 2-gamma hemodynamic response function was used to model the expected BOLD signal. A random-effects GLM was then performed on the data. Whole-brain contrasts were first thresholded at a voxelwise *p*-value of 0.005, uncorrected and then corrected for multiple-comparisons using Monte-Carlo simulation procedure to determine a minimum cluster threshold (Goebel, Esposito, & Formisano, 2006), resulting in an overall $\alpha < .05$. This cluster thresholding method estimates and accounts for spatial smoothness and spatial correlations within the data (estimates of spatial smoothness are based on the formula discussed in Forman et al., 1995).

We isolated regions involved in the neural PSE by contrasting Large problems with Small problems (*Large > Small*). We then extracted beta values from the bilateral IPS, which demonstrated a significant neural PSE (after a cluster correction). We separately calculated the neural PSE in the left and right IPS by subtracting the Large and Small beta estimates (Large – Small). We then correlated each of the behavioural measures neural PSE in each hemisphere. To examine whether these relationships were specific to the neural PSE, we also examined the average activation to Large and Small problems in the IPS. In order to directly compare the brain-behaviour correlations between the neural PSE and average arithmetic activation in the IPS, we used the same clusters from the analysis above. We averaged the beta estimates for the Large and Small conditions within the left and right IPS ([Large Problems + Small Problems] / 2), and subtracted the beta values from the Plus 1 condition from this average (average arithmetic activation – Plus 1 condition). If more than one of the domain general or domain specific skills was significantly correlated with the neural measures, we entered these variables into a linear regression to determine which of these measures explained unique variance in the neural effect.

To better understand the relative strength of the relationships between measures, we conducted both frequentist and Bayesian statistics on all of the behavioural analyses as well as any brain-behaviour analyses. Bayesian analyses provide information about the strength of the evidence, and Bayes Factors (BF) can indicate whether the evidence is in favor of the alternative hypothesis (BF_{10}) or the null hypothesis (BF_{01}) (Wagenmakers, Wetzels, Borsboom, & van der Maas, 2011). Bayes factors (BF_{10}) above 3 are considered moderate evidence for a relationship between the variables of interest, whereas Bayes factors above 10 are considered strong evidence (Jeffreys, 1961). A Bayes factor of 10 indicates that the relationship being investigated (ie. the alternative hypothesis) is 10 times more likely than the null hypothesis. Behavioural and neuroimaging analyses were completed on all 44 children except for analyses that included the Dot Matrix task (VSWM) from the Automated Working Memory Assessment. We did not obtain data from 1 child on this task, therefore any analyses that included the Dot Matrix task were conducted on 43 children. All frequentist and Bayesian analyses were conducted in JASP (JASP Team, 2016)

4.3 Results

4.3.1 Behavioural Assessment: Domain General and Domain Specific Predictors of Math Achievement

To determine which domain general and domain specific skills were related to math achievement, we first examined whether the measures were correlated with Math Fluency performance. Higher arithmetic performance on the Math Fluency test was related to better performance on four measures: (1) verbal IQ $r(42) = .45$, $p = .002$; (2) VSWM $r(41) = .32$, $p = .037$; (3) symbolic number comparison $r(42) = -.46$, $p = .002$; and (4) symbolic ordering $r(42) = -.54$, $p < .001$ (see Table 4.1). The negative correlations between Math Fluency and symbolic comparison and ordering are related to the way those measures were scored (see above), where higher scores indicate poorer performance. None of the other domain general or domain specific measures were significantly correlated with math achievement. As expected, Math Fluency scores were also correlated with age $r(42) = .33$, $p = .027$, indicating that older children performed better on the Math Fluency task (Table 4.1). In addition to significance testing, we also calculated Bayes Factors for each of the correlations. The results of this analysis indicated that the evidence was in favour of a relationship between arithmetic and verbal IQ (BF_{10}= 16.18), symbolic comparison (BF_{10}= 20.07) and symbolic ordering (BF_{10}=162.96). Whereas there was weaker evidence for a relationship with VSWM (BF_{10}= 1.55).

To further examine whether age, verbal IQ, VSWM, symbolic number comparison, and symbolic ordering predicted unique variance in children's math achievement, we entered each of these measures as predictors in a linear regression. The regression model was significant $F(5,37) = 7.95$, $p < .001$, and predicted 52% of the variance in children's arithmetic scores. However, only verbal IQ and symbolic ordering were found to uniquely predict individual differences in arithmetic performance (see Table 4.2). The Bayes factors of inclusion also indicated that there was strong evidence that verbal IQ and symbolic ordering were unique predictors of arithmetic fluency. Together, these findings suggest that verbal skills and symbolic ordering are unique predictors of a child's arithmetic abilities, independent of age, and other domain general and domain specific skills.

Table 4.1 Pearson correlation matrix with Bayes Factors (BF$_{10}$) shown below in brackets

	1	2	3	4	5	6	7	8	9	10	11	12
1. Neural PSE Right IPS	—											
2. Neural PSE Left IPS	.801*** (1.61x10^{8})	—										
3. Avg. arithmetic Right IPS	.162 (.32)	.276 (.92)	—									
4. Avg. arithmetic Left IPS	.112 (.24)	.264 (.80)	.696*** (1.28 x10^{5})	—								
5. Math Fluency	.352* (2.67)	.392** (5.39)	.384** (4.61)	.278 (.95)	—							
6. Verbal IQ	.269 (.85)	.136 (.27)	-.05 (.197)	.05 (.20)	.446** (16.18)	—						
7. Nonverbal IQ	.287 (1.05)	.172 (.34)	-.059 (.20)	.081 (.21)	.179 (.36)	.324* (1.75)	—					
8. VSWM	.34* (2.12)	.305* (1.29)	.036 (.20)	.023 (.19)	.319* (1.55)	.143 (.29)	.245 (.64)	—				
9. Nonsymbolic Comparison	.094 (.22)	.172 (.34)	-.062 (.20)	.008 (.12)	-.162 (.32)	-.17 (.34)	-.032 (.19)	-.222 (.51)	—			
10. Symbolic Comparison	-.104 (.23)	-.11 (.24)	-.441** (14.49)	-.302* (1.28)	-.455** (20.07)	-.078 (.21)	-.032 (.19)	-.549*** (211.77)	.626*** (6098.67)	—		
11. Ordering	-.254 (.72)	-.252 (.70)	-.419** (9.17)	-.221 (.51)	-.535*** (162.96)	.031 (.19)	-.218 (.50)	-.386* (4.51)	.257 (.74)	.616*** (2673.38)	—	
12. Age (in months)	.126 (.26)	.089 (.22)	.118 (.25)	.075 (.21)	.333* (2.01)	.357* (2.91)	.178 (.36)	.311* (1.40)	-.555*** (307.95)	-.436** (13.06)	-.29 (1.09)	—

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

Table 4.2 Regression analysis predicting Math Fluency scores

Predictor	**β**	***b***	***SE***	***t***	**BF** $_{\textbf{Inclusion}}$
Age (in months)	-.051	-*.07*	.19	-.037	.27
Verbal IQ	.458	1.71	.46	**3.70****	87.58
VSWM	-.001	-.003	.43	-.008	.28
Symbolic Comp	-.157	-.010	.01	-.94	.42
Ordering	-.476	-.0008	.003	**-3.256****	66.25

Note. * < .05 and ** < .01

4.3.2 Brain Imaging

4.3.2.1 Behavioural performance on the in-scanner arithmetic task

We used paired samples t-tests to examine mean reaction time (RT) and accuracy performance on the in-scanner arithmetic task. Children had longer reaction times on the Large problems (*M* = 3240 ms, *SD* = 672.7) than the Small problems (*M* = 2821 ms, *SD* = 749.2), *t*(43) = 5.87, *p* < .001. They were also less accurate on the Large problems (*M* = .71, *SD* = .17) than the Small problems (*M* = .84, *SD* = .14), *t*(43) = -5.81, *p* < .001. Performance on the Math Fluency test was also correlated with overall accuracy on the arithmetic task in the scanner (average performance on the Small and Large problems), *r*(42) = .65, *p* < .001.

4.3.2.2 Neural problem size effect

We first identified regions that were more active for Large problems than Small problems. The bilateral IPS were the only regions that were more active for Large problems than Small problems (Figure 4.2, Table 4.3). There were additional regions that were more active for Small problems than for Large problems, however, they are not discussed here because they were not the focus of the chapter.

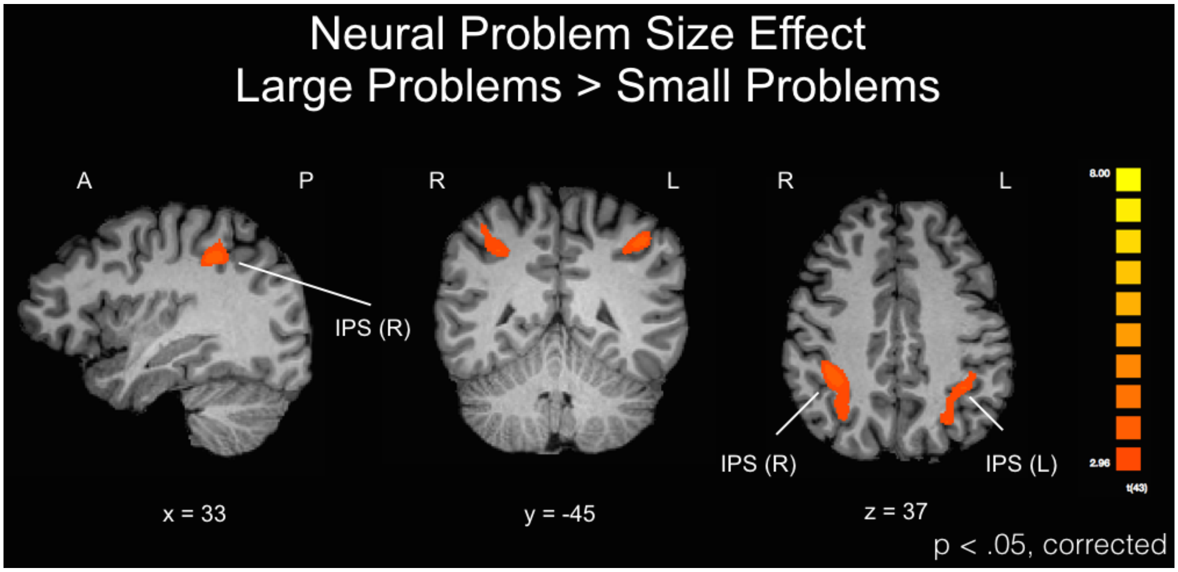

Figure 4.2 Regions showing a significant neural problem size effect (*Large problems* > *Small problems*). Regions that are more active for Large problems are shown in orange.

Table 4.3 Anatomical regions, Talairach coordinates, mean t-scores, and number of voxels for the neural problem size effect (*Large problems* > *Small problems*)

Anatomical Region	**TAL coordinates (x,y,z)**			**Mean t-score**	**Number of Voxels**
Large Problems > Small Problems					
R Intraparietal Sulcus (IPS)	34.27	-43.13	40.30	3.27	2803
L Intraparietal Sulcus (IPS)	-36.36	-49.79	39.81	3.23	1489

4.3.2.3 Brain-behaviour correlations with the neural PSE

To better understand how individual differences in domain general and domain specific skills related to the neural PSE within the IPS, we extracted the beta values from these regions and conducted zero-order correlations to examine these relationships (see Table 4.1). Individual differences in VSWM were correlated with the neural PSE in the right $r(41) = .34$, $p = .025$, and left IPS $r(41) = .31$, $p = .047$. These correlations indicate that children who recruit the bilateral IPS more for Large problems than Small problems tend to have higher performance on measures of VSWM. The Bayes factors demonstrated that evidence for the relationship between the neural PSE and VSWM was relatively weak ($BF_{10\,(R\,IPS)} = 2.12$, $BF_{10\,(L\,IPS)} = 1.29$). Because VSWM was the only domain general or domain specific measure to correlate with the neural PSE, we did not follow the correlation analyses with a regression.

4.3.2.4 Brain-behaviour correlations with average arithmetic activation

Because the neural PSE examines the relative differences between the Large and Small conditions, it is also a reflection of relative differences in task difficulty between the two conditions. Therefore, the neural PSE is an index of the demand on computational resources and it could be more closely related to domain general skills. Children still use calculation strategies for both Small and Large problems and it is possible they are using basic number processing skills in both conditions (see Chapter 3). Consequently, the neural PSE may be removing a large part of the variance associated with number processing skills.

To determine whether this may be the case, we examined average activation to Large and Small problems compared to the Plus 1 control condition. These analyses were conducted in the same IPS regions defined above to ensure the findings for the PSE and average arithmetic activation were comparable. We first used a one-sample t-test to determine whether both Small and Large conditions activated the IPS above zero, and both conditions significantly activated the left and right IPS above zero (all tests $p < .001$). Paired-samples t-tests revealed that both Small and Large conditions activated the left and right IPS significantly more than the Plus 1 condition in both regions (all tests $p < .05$). We therefore averaged the beta values from the left and right IPS (Large + Small / 2) and subtracted the Plus 1 control condition (Average arithmetic activation – Plus 1 condition).

Compared to the neural PSE, the average activation in the left and right IPS related differently to the domain general and domain specific variables (Table 4.1). In the right IPS, greater overall arithmetic activation was related to better performance on the symbolic comparison ($r(42)= -.44$, $p = .003$) and symbolic ordering tasks ($r(42)= -.42$, p

= .005). Greater activation for arithmetic in the left IPS was associated with better performance on the symbolic comparison task (*r*(42)= -.30, *p* = .046). Bayes factors revealed a similar pattern of findings, with evidence in favour of a relationship between activity in the right IPS and symbolic comparison (BF_{10}=14.49) and symbolic ordering (BF_{10}=9.17). In the left IPS, frequentist statistics suggested a correlation between average arithmetic activity and symbolic comparison (*r*(42)= -.302, *p* = .046). However the Bayes factor indicated that there was relatively weak evidence for this relationship (BF_{10}=1.28).

To further examine whether symbolic comparison and symbolic ordering predicted unique variance in arithmetic activity within the right IPS, we conducted a linear regression with average arithmetic activation in the right IPS (Average arithmetic activation – Plus 1 condition) as the dependent variable. The overall model was significant *F*(2,41) = 6.11, *p* = .005 and predicted 23% of the variance in children's brain activity (Table 4.4), however, neither symbolic comparison or symbolic ordering were significant unique predictors of brain activity within the right IPS. It is possible that neither domain specific ability was a unique predictor due to multicollinearity as the correlation between the two variables was high (*r*(42) = .62, *p* < .001).

Table 4.4 Regression analysis predicting average arithmetic activation in the right IPS.

Predictor	**β**	***b***	***SE***	***t***	**$BF_{\text{Inclusion}}$**
Symbolic Comp	-.294	$-2.86\text{x}10^{-4}$	$1.69\ \text{x}10^{-4}$	-1.69	2.30
Ordering	-.238	$-6.28\ \text{x}10^{-5}$	$4.6\ \text{x}10^{-5}$	-1.37	1.25

Note: No variables were significant unique predictors

It was notable that, unlike in some previous studies (Haist et al., 2014; Metcalfe et al., 2013), we did not find any association between VSWM or nonsymbolic performance with average arithmetic activity in the IPS. To determine whether the evidence supported the null hypothesis (i.e., no significant association between these measures), we conducted additional Bayesian analyses on the relationships between overall arithmetic activity in the IPS, VSWM, and nonsymbolic performance. Bayes factors indicated that there was no association between VSWM and average arithmetic activation in the left or right IPS, and that the null hypothesis was 5 times more likely than the alternative hypothesis (BF_{01_RIPS}= 5.13; BF_{01_LIPS}= 5.21). The same was also true for nonsymbolic performance and brain activity in the bilateral IPS, and Bayes factors suggested that the evidence was in favor of the null hypothesis rather than the alternative hypothesis (BF_{01_RIPS}= 4.92; BF_{01_LIPS}= 5.32).

4.4 Discussion

To date, the fMRI literature on the relationship between arithmetic and domain general and domain specific skills has been fragmented. Given that there is great overlap in the neural architecture supporting these abilities (Arsalidou & Taylor, 2011; Zago et al., 2008), particularly in the IPS, there is reason to believe that domain general and domain specific skills may both contribute to individual differences in brain activity within this region. The present study provides the first systematic examination into how individual differences in multiple domain general and domain specific abilities are related to the recruitment of the IPS during arithmetic problem solving. Importantly, we investigated this question in a group of children that are in the early elementary school years (Grades 2-4), and are still becoming fluent with arithmetic (Butterworth, 2005; Carr & Alexeev, 2011). Variability in skills such as VSWM or basic number processing is likely to play a critical role in children's arithmetic fluency during this developmental period.

The above-reported results replicated previous behavioural literature by demonstrating a relationship between behavioural measure of arithmetic and children's verbal and ordinal processing skills (LeFevre et al., 2010; Lyons & Ansari, 2015; Lyons et al., 2014; Vukovic & Lesaux, 2013). Though we found that VSWM and symbolic comparison abilities were correlated with arithmetic fluency, they did not uniquely predict variance once other abilities were accounted for. We also extended previous research by demonstrating that domain general and domain specific skills contribute to the recruitment of the IPS, however, the relationship is dependent on the neural index that is being assessed; the neural PSE is more related to VSWM abilities (albeit weakly so), whereas overall arithmetic activity is more closely associated with individual differences in basic numerical competencies.

These results demonstrated that the pattern of associations between IPS activity, domain general and domain specific abilities differs depending on the index of brain activity. The neural PSE likely reflects demands on computational resources because large problems are more computationally demanding than small problems (which is reflected in poorer accuracy and slower reaction times). Therefore, individual differences in domain general variables such as VSWM may modulate the neural PSE more than domain specific measures. The present findings confirmed this by showing that individuals with higher VSWM capacities had a greater neural PSE. Though little research has specifically investigated the neural PSE and its association with domain general abilities, there has been some evidence that the bilateral IPS are both recruited for VSWM and arithmetic in adults (Zago et al., 2008; and see Chapter 2). Moreover, other research using brain-behaviour correlations has provided evidence that children's VSWM abilities (measured behaviourally) are related to brain activity during arithmetic (Metcalfe et al., 2013). In this study, the authors contrasted complex (3 + 4 = 8) problems with simple arithmetic problems (3 + 1 = 4; identical in format to the Plus 1 condition in the present study). In a whole-brain regression, VSWM abilities were related to greater neural activity during complex problems relative to simple Plus 1 problems in the bilateral IPS (in addition to a number of other frontal and inferior parietal brain regions). The findings from Metcalfe et al (2013) converge with those from the present study to indicate that individual differences in the neural response to arithmetic complexity are related to VSWM in the bilateral IPS. Other research has also demonstrated that children who recruit the left IPS more for VSWM have higher arithmetic scores 2 years later (Dumontheil & Klingberg, 2012). Greater recruitment of the left IPS has also been related to larger VSWM capacities (Klingberg, Forssberg, & Westerberg, 2002), therefore, children with higher VSWM abilities show greater modulation of the IPS which may in turn, be related to arithmetic proficiency. The role of VSWM in the IPS during arithmetic problem solving may be to modulate brain activity according to cognitive and computational demands of the problem, and individuals with higher VSWM capacities can modulate these regions to a greater degree (Klingberg et al., 2002).

The IPS has also been consistently implicated in basic numerical processing (Ansari, 2008; Franklin & Jonides, 2009; Holloway, Price, & Ansari, 2010; Vogel et al., 2015). We found evidence for a relationship between individual differences basic number processing skills and overall arithmetic activity in the IPS. However, there was no such association between basic number processing skills and the neural PSE. It is possible that basic number processing skills are related to brain activity on both small and large problems, and any variance associated with basic number processing is therefore subtracted out when contrasting the two conditions in the neural PSE. This may especially be the case in children because they still rely on effortful calculation strategies for both small and large problems (see Chapter 3). This notion was supported by the present findings. Specifically, when overall brain activity for both small and large arithmetic problems was considered, we found significant relationships between individual differences in symbolic comparison in the bilateral IPS and symbolic ordering in the right IPS. Therefore, children with better performance on the symbolic number processing tasks recruited the IPS to a greater degree when solving both small and large arithmetic problems. It is also noteworthy that arithmetic activity for small and large problems was not related to VSWM skills, with Bayes factors suggesting that the null hypothesis is 5 times more likely than the alternative hypothesis ($BF_{01\_RIPS}= 5.13$; $BF_{01\_LIPS}= 5.21$). Together, these findings indicate that individual differences in VSWM are weakly related to the neural PSE, whereas basic number processing skills explain more variance in IPS activation across all arithmetic problems studied. They also indicate that the neural correlates of arithmetic are more strongly predicted by basic number processing than they are by VSWM.

Though no research has directly examined whether basic number processing skills and arithmetic have shared neural substrates in children (see Chapter 3), some adult literature has suggested that this is likely to be true. For example, one meta analysis found qualitative similarities between basic number processing and arithmetic networks (Arsalidou & Taylor, 2011) and other work has found similarities in ordinal processing and arithmetic within the right IPS (Knops & Willmes, 2014). The data presented in this chapter provide converging evidence to suggest that the IPS does not just show overlap between basic number processing skills and arithmetic, but the recruitment of this region during arithmetic is also related to individual differences in basic number processing skills. Critically, the relationship between neural activity during basic arithmetic and basic number processing was only true for symbolic comparison and ordering. There was no significant correlation between non-symbolic number comparison and arithmetic. Therefore, this provides further evidence that brain activity in the IPS during arithmetic is related to symbolic number representations.

For the first time we demonstrated that individual differences in children's basic numerical competencies are associated with the degree to which the IPS is activated during the solution of arithmetic problems. Greater activity in the bilateral IPS was related to higher symbolic comparison abilities, and the right IPS was additionally related to symbolic ordering abilities. Research with adults has found symbolic ordering and arithmetic have common neural substrates in the right IPS, and that spatial patterns of activation in this region are similar for the two tasks (Knops & Willmes, 2014). Our findings are consistent with the idea that the right IPS plays an important role in linking ordinal processing and arithmetic. They also extend this literature by demonstrating that individual differences in children's symbolic ordering abilities are associated with brain activity in the right IPS during arithmetic. Our results are also similar to those of Bugden and colleagues (2012) who found that higher Math Fluency scores were associated with more mature neural signatures of symbolic number processing in the left IPS. Together, these studies indicate that the IPS may play an important role in mediating the relationship between symbolic number processing (comparison and ordering) and arithmetic.

It may be surprising that we did not find any relationship between nonsymbolic abilities and activity in the IPS during arithmetic, given some literature has found associations between nonsymbolic comparison skills and arithmetic at both behavioural and neural levels of analysis (Chen & Li, 2014; Haist et al., 2014; Schneider et al., 2016). Indeed, Bayesian analyses indicated that the null hypothesis was 5 times more likely the alternative hypothesis (BF_{01_RIPS}= 4.92; BF_{01_LIPS}= 5.32). The relationship between arithmetic and symbolic comparison has been shown to be stronger and more consistent than with nonsymbolic comparison (De Smedt, Noël, Gilmore, & Ansari, 2013; Schneider et al., 2016). Neuroimaging studies have also found that symbolic and nonsymbolic processing have qualitatively different representations in the IPS by using multi-voxel pattern analyses (Bulthé, De Smedt, & Op de Beeck, 2014; Lyons, Ansari, & Beilock, 2015). It is therefore possible that we did find not a relationship between arithmetic and nonsymbolic skills at the neural level because they have fewer shared cognitive processes than arithmetic does with symbolic skills. This is particularly notable because even though nearly all of the performance measures on the basic number processing tasks were correlated with one another (Table 1), they did not all predict brain activity similarly, indicating that these measures are sensitive to different cognitive constructs.

It is worth noting that the behavioural and neuroimaging results reported above are marked by some converging as well as divergent findings. For instance, though VSWM and symbolic number processing skills were related to both behavioural and neural metrics, verbal abilities were not related to any of the neural indices within the IPS. This is likely related to the brain regions being investigated. The IPS has rarely been implicated in verbal fluency and other regions of the arithmetic network may be more tied to verbal processing. For example, developmental and training studies have provided evidence that as individuals become more familiar with arithmetic problems, they rely more on verbally mediated retrieval strategies (e.g., remembering the solution from memory), and this is associated with a shift in brain activity from the IPS to the angular or supramarginal gyri (Delazer, 2003; Ischebeck et al., 2006; Rivera et al., 2005; Zamarian, Ischebeck, & Delazer, 2009). Other work from structural brain imaging has demonstrated that a left inferior parietal white matter tract, the superior longitudinal fasciculus, was related to arithmetic operations that were more reliant on retrieval strategies (addition and multiplication) (Van Beek, Ghesquière, Lagae, & De Smedt, 2013). This relationship disappeared once the authors controlled for phonological processing abilities, suggesting a close association between left inferior parietal structures, language-related abilities, and arithmetic skills. Therefore, it is not surprising that individual differences in the IPS were unrelated to verbal skills, because the association between verbal abilities and arithmetic is likely mediated by other brain structures.

4.4.1 Limitations & Future Directions

The data in this study indicate that individual differences in VSWM and symbolic number processing skills relate to the recruitment of the IPS during arithmetic. However, it is important to acknowledge a few limitations. First, it was not possible to ascertain precisely which problems were solved using retrieval or calculation due to the nature of our fMRI design. The present study could not determine whether the relationship between arithmetic and domain general and domain specific abilities is dependent on the strategy that is being used. For instance, it is possible that basic number processing abilities may be more essential for trials that are calculated compared to those that are retrieved. Similarly, individual differences in VSWM capacity may be more related to brain activity on trials that required effortful calculation. Future research will need to examine strategies on a trial-by-trial basis to further disentangle these relationships.

Other research has also demonstrated that the domain specific and domain general predictors of arithmetic change over developmental time (Lyons et al., 2014; McKenzie, Bull, & Gray, 2003; Raghubar et al., 2010; Rasmussen, McAuley, & Andrew, 2007). It is likely that these relationships are highly dynamic, and increase or decrease in strength over time. For example, as children develop fluent arithmetic skills by relying more on retrieval-based strategies, working memory demands may decrease. Individual differences in VSWM and basic numerical competencies may then become less critical for arithmetic fluency and the neural response within the IPS. The same may also be true basic number processing skills; as children rely on fewer quantity-based strategies the relationship between basic number processing skills and the neural response in the IPS may decline. Future research will need to examine how these relationships with the IPS change and whether they strengthen or weaken over time.

4.4.2 Conclusions

Previous research has suggested that the IPS may have multiple functions during the solution of arithmetic problems related to both domain general and domain specific processes. This study provides the first evidence to systematically examine how individual differences in multiple domain general and domain specific abilities predict the recruitment of the IPS during arithmetic. These results from the present chapter indicate that children's VSWM and symbolic number processing skills are related to brain activity within the IPS, however, the relationships depend on the index of brain activity that is being measured; VSWM is more closely related to the neural PSE in the bilateral IPS, whereas symbolic number processing skills (comparison and ordering) are related to overall arithmetic activity regardless of problem size. This provides converging evidence that the role of the IPS is multifaceted and cannot be attributed to one particular cognitive ability. Together, these findings provide a better understanding of the neural basis of arithmetic in children by exploring the domain general and domain specific predictors of brain activity within the IPS.

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Chapter 5

5 General Discussion

5.1 Integration of Findings

An accumulating body of research has demonstrated the importance of particular domain general and domain specific abilities in the acquisition of arithmetic skills (Vanbinst & De Smedt, 2016). This literature has come to some consensus that both basic numerical competencies, such as symbolic number knowledge, and domain general skills, such as working memory, play an important role in arithmetic (De Smedt, Noël, Gilmore, & Ansari, 2013; Lyons, Price, Vaessen, Blomert, & Ansari, 2014; Peng, Namkung, Barnes, & Sun, 2015; Raghubar, Barnes, & Hecht, 2010; Schneider et al., 2016). This begs the question as to how arithmetic, basic number processing, and working memory might be interrelated at the neural level, and whether the same brain regions might support these skills. Neuroimaging can help shed light on how arithmetic is related to these competencies by providing evidence for similarity of processing at the neurobiological level. Even though behavioural research has established strong links between arithmetic, visuospatial working memory (VSWM), and basic number processing skills, most brain imaging research has studied how these factors relate to arithmetic in isolation of one another. Indeed, very few studies have simultaneously examined these abilities within the same individuals to determine if they have shared neural circuits, and no study to date has done so in children. This may be a particularly important period to investigate these relationships because children are using computationally demanding strategies that require VSWM resources (e.g., remembering intermediate steps) and a fluent understanding of symbol-quantity relationships in order to manipulate the quantities to come to a solution.

Much of our current understanding of the domain general and domain specific contributions to the brain networks associated with arithmetic is based on inferences from comparing across studies that have examined these processes in different groups of individuals, or through studies that have examined relationships between neural and behavioural measures. Such studies cannot establish whether these skills have the same underlying neuronal basis. Instead, a within-subjects approach is necessary to determine whether or not domain general and domain specific competencies share common brain circuits with arithmetic.

The present thesis used such an approach to investigate the common underlying neural substrates between arithmetic, VSWM, and basic number processing in both children and adults. By doing so, this thesis tests a number of commonly held assumptions about the role of the IPS in arithmetic, and begins to resolve some of the outstanding questions related to the development and neurocognitive underpinnings of arithmetic. First, previous research has not explored whether VSWM and arithmetic have common neural substrates in children and adults, and whether these shared regions undergo age-related changes. Second, it is often assumed that arithmetic recruits the IPS due to its role in processing quantities, however this has never explicitly been tested. Therefore, it remains to be determined how arithmetic and basic number processing skills overlap in the brain of adults and children, and how this relationship is related to the strategies being used to solve arithmetic problems. Finally, whether domain general and domain specific competencies both uniquely predict the recruitment of the parietal cortex during arithmetic has largely been unexplored. The present thesis aimed to address these outstanding questions by simultaneously examining domain general and domain specific processes and how they relate to arithmetic networks in adults and children.

5.1.1 Summary of Thesis and Common Themes

The previous literature has identified a fronto-parietal network of brain regions that are recruited for arithmetic (Arsalidou & Taylor, 2011). Typically, frontal brain regions have been associated with domain general functions such as working memory, whereas parietal regions are thought to be related to domain specific functions (Arsalidou & Taylor, 2011; Menon, Rivera, White, Glover, & Reiss, 2000). However, a survey of the literature shows that both domain general and domain specific processes recruit the parietal cortex. For instance, both symbolic number processing and VSWM tasks elicit brain activity within the IPS (Ansari, 2008; Arsalidou & Taylor, 2011; Constantinidis &

Klingberg, 2016). The role of the IPS during arithmetic is therefore likely to be multifaceted and could reflect both VSWM and basic number processes.

The three studies in this thesis aimed to better understand how VSWM and number processing are related to the fronto-parietal arithmetic network, and together they suggest that the role of the IPS in arithmetic cannot be attributed to one function. In Chapter 2, I provide the first evidence to demonstrate that VSWM and arithmetic both recruit the IPS in adults and in children. Moreover, the shared circuits for VSWM and arithmetic exhibit age-related changes where children show more focal activity in the right IPS, and adults recruit the IPS in both hemispheres. This indicates that there is common activation in the IPS for arithmetic and VSWM, and the left IPS undergoes age-related changes in the processing of both VSWM and arithmetic.

In Chapter 3, I provide empirical evidence that tests long-held assumptions about the domain specific role of the IPS in arithmetic. The findings in this chapter are consistent with the notion that there is a strong relationship between symbol-quantity associations and arithmetic within the IPS in both adults and children. This chapter also shows that the association between basic number processing and arithmetic in the IPS is moderated by the cognitive operations being performed. Specifically, the IPS emerges as a common neural locus for arithmetic and basic number processing when the arithmetic stimuli presented require more procedural problem solving strategies, which likely involve the manipulation of numerical quantities.

Finally, Chapter 4 integrates questions from the two preceding chapters (Chapters 2 & 3) by examining how individual differences in children's domain general and domain specific skills are related to the recruitment of the bilateral IPS during arithmetic. In this chapter, I provide evidence that individual differences in both VSWM and basic number processing skills are related activity in the IPS. However, I reveal that the relationships are dependent on the index of brain activity; individual differences in VSWM were correlated with the neural problem size effect whereas symbolic comparison and ordering skills were related to brain activity for both small and large problems. This converges with the previous two chapters by showing that the neural problem size effect is associated with VSWM in the IPS (Chapter 2), and that basic number processing skills are related to both small and large problems in children (Chapter 3). The data from Chapter 4 also suggest that it is important to consider what cognitive processes the index of arithmetic activity may reflect because measures of arithmetic complexity (i.e., problem size) may differ from arithmetic activity more generally. Together, these findings provide a better understanding of how the arithmetic network develops and how it interacts with both domain general and domain specific skills.

The data presented across the thesis revealed two common themes. First, the IPS is an important brain region for domain general and domain specific skills in arithmetic for both adults and children. Even though much research on the neural correlates of arithmetic has focused on the IPS as a domain specific region in calculation (Arsalidou & Taylor, 2011; Dehaene, Piazza, Pinel, & Cohen, 2003), the data presented in this thesis suggest that the role of the IPS is more complex. Even different measures of brain activity with the IPS during arithmetic are related to different domain general and domain specific competencies. Second, this thesis demonstrates that the overlap between arithmetic, domain general, and domain specific processes undergo developmental changes. Although the IPS was found to be associated with arithmetic, VSWM, and number processing, there were differences in the degree to which the left and right IPS were recruited in adults and children. These age-related differences may reflect maturational or experience-dependent changes in the brain. Below, I will provide a greater discussion on both of these themes, and how data from each of the chapters supports them.

5.2 Domain General and Domain Specific Contributions to the IPS During Arithmetic

5.2.1 Domain Specific Contributions

The previous literature has demonstrated consistent and reliable associations between number processing and the IPS (Ansari, 2008; Arsalidou & Taylor, 2011; Cohen Kadosh, Lammertyn, & Izard, 2008; Dehaene et al., 2003). This has been shown using multiple methods. For instance, the IPS is activated by symbolic and nonsymbolic comparison tasks (Cantlon, Brannon, Carter, & Pelphrey, 2006; Holloway & Ansari, 2010; Holloway, Price, & Ansari, 2010), and the relative distance between symbolic (e.g., Arabic digits) and nonsymbolic (e.g., dots) numbers has been shown to modulate IPS activity in a parametric fashion (Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Piazza, Pinel, Le Bihan, & Dehaene, 2007; Vogel, Goffin, & Ansari, 2015). The IPS (particularly the horizontal segment) has also been found to respond more to calculation than to a diverse assortment of other tasks (e.g., attention, language, saccades etc.) (Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002). Against this literature, it has been argued the IPS is a good candidate for a domain specific region that processes numerical quantities (Dehaene et al., 2003). For these reasons, it has been hypothesized the recruitment of the IPS during calculation is associated with numerical magnitude processing (Dehaene et al., 2003).

The data in this thesis provided empirical support for the notion that the IPS is a critical region for both number processing and arithmetic. The evidence from Chapter 3 demonstrated that arithmetic and basic number processing recruit the bilateral IPS in children and the left IPS in adults. I also found (Chapter 4) that children with better basic symbolic number processing skills (but not non-symbolic skills) also recruited the IPS more during arithmetic. These studies suggest that the IPS plays a key role in quantity manipulations and symbol-quantity associations during arithmetic. However, the evidence presented in this thesis goes beyond simply revealing an association between number processing and arithmetic in the IPS; it shows that the type of arithmetic problem moderates this relationship. Specifically, adults showed overlap between number processing and large problems in the left IPS, but there was no such overlap between number processing and small problems. Large problems were also more likely to be solved using calculation than small problems, which were almost always retrieved. Therefore, the IPS was recruited for both basic number processing and arithmetic when many of the problems were calculated. Children, on the other hand, were more likely than adults to calculate on both small and large problems, and this was reflected in the overlap between number processing and arithmetic; both small and large arithmetic problems showed significant overlap with basic number processing in the bilateral IPS. Chapter 4 also demonstrated a similar pattern of findings where the relationship between number processing and arithmetic held across small and large arithmetic problems in children. This is likely because children used calculation strategies on both types of problems (Chapter 3).

IPS activation during calculation has never been explicitly linked to symbol-quantity relationships. The findings from Chapters 3 and 4 provide the first evidence to suggest that the association between arithmetic and basic number processing is dependent on the processing demands of the arithmetic stimuli (i.e., the degree to which cognitively demanding calculation strategies are used). These data not only test-long held assumptions about the relationship between basic number processing in adults and children, but also provide novel evidence that the relationship depends on the cognitive operation being performed.

5.2.2 Domain General Contributions

Even though the data in Chapters 3 and 4 indicate that the IPS is an important locus for domain specific processes and arithmetic, the data in this thesis fail to support a domain specific account of the IPS. VSWM also demonstrated overlap with arithmetic in this region (Chapter 2), and individual differences in children's VSWM capacity were related to the recruitment of the bilateral IPS (Chapter 4). Activation within the IPS during arithmetic is likely related to a combination of VSWM processes as well as the processing of symbol-quantity associations, because both are required during calculation. These findings converge with other literature that has shown that VSWM and arithmetic are related within the IPS. Previous research has demonstrated that spatial working memory and arithmetic have overlapping activity in the bilateral IPS in adults (Zago et al., 2008), which was replicated in Chapter 2. Brain-behaviour correlations have also pointed to the IPS as a key region in the associations between VSWM and arithmetic (Ashkenazi, Rosenberg-Lee, Metcalfe, Swigart, & Menon, 2013; Dumontheil & Klingberg, 2012; Metcalfe, Ashkenazi, Rosenberg-Lee, & Menon, 2013). Critically, the data from this thesis go beyond some of the previous literature by demonstrating a relationship between VSWM and arithmetic in the IPS, even when the VSWM task did not include any symbolic numbers (e.g., Dumontheil & Klingberg, 2012). Therefore, the overlap between VSWM and arithmetic cannot be attributed the processing of symbolic numbers in the VSWM task.

It is important to note that domain general contributions to activation in the frontal cortex cannot be discounted simply because I provide evidence that the IPS is recruited for VSWM and arithmetic. For example, the superior frontal gyrus, middle frontal gyrus, and insula may be recruited for processes such as error monitoring, inhibitory control, attention, and other components of working memory (Aron, Robbins, & Poldrack, 2004; Cole & Schneider, 2007; Duncan & Owen, 2000; Smith & Jonides, 1998). These domain general processes were likely not common to the tasks that were used in in the present thesis, which resulted in little overlap within these regions. The present data and previous literature do not support a domain specific account of the IPS in arithmetic, but they cannot specifically determine the cognitive underpinnings of brain activation within other regions of the arithmetic network.

Neuropsychological and neuroimaging evidence suggests a close association between numerical and spatial representations (Hubbard, Piazza, Pinel, & Dehaene, 2005; Piazza, 2010; Walsh, 2003), which could be one possible account for the relationships between visuo-spatial memory, number processing, and arithmetic in the IPS. Indeed, the IPS has been shown to have retinotopic organization for visuo-spatial information (Konen & Kastner, 2008; Silver & Kastner, 2009), and the same region has been associated with the spatial organization of number (e.g., a mental number line) (Vogel, Grabner, Schneider, Siegler, & Ansari, 2013). Therefore, numbers could utilize or "recycle" already existing spatial maps within the IPS, which might play role in the relationship between VSWM in arithmetic (Dumontheil & Klingberg, 2012).

5.2.3 Implications for Developmental Dyscalculia

The findings in this thesis may also provide some insights into the possible neural mechanisms underlying deficits in developmental dyscalculia. Dyscalculia is a learning disorder where children have specific impairments in learning arithmetic facts, have poor calculation and math reasoning abilities, and have problems processing numerical information. These impairments lead to skill levels that are below what would be expected for the individual’s age, intelligence, and level of educational instruction (American Psychiatric Association, 2013). However, the impairments in dyscalculia are neither limited nor specific to number processing and arithmetic. Several studies have documented poorer visuo-spatial working memory and inhibition abilities in children with dyscalculia (De Weerdt, Desoete, & Roeyers, 2013; Fias, Menon, & Szucs, 2013; McLean & Hitch, 1999; Menon, 2016; Szucs, Devine, Soltesz, Nobes, & Gabriel, 2013). Similar evidence has been observed at the neural level. Children with dyscalculia have been shown to have atypical patterns of brain activity in the IPS in response to nonsymbolic number processing (Kaufmann et al., 2009; Kucian, Loenneker, Martin, & von Aster, 2011; Price, Holloway, Räsänen, Vesterinen, & Ansari, 2007). They also have reduced activation of the right IPS during a VSWM task (Rotzer et al., 2009), and fail to show any associations between individual differences in VSWM and brain activity in the arithmetic network in the way that typically developing children do (Ashkenazi et al., 2013). The data from Chapters 2 and 3 may also indicate that the reason for deficits across arithmetic, basic number processing, and VSWM is due to the common role of the IPS for each of these skills. Based on the findings of the current thesis, atypical organization of the right IPS (or an inability to shift processing towards left IPS) could lead to impairments in all three of these abilities, as it was found to be associated with VSWM (Chapter 2), number processing (Chapter 3) and arithmetic (Chapters 2, 3, and 4) in children. Though these data cannot point to the cognitive origins of dyscalculia, they do indicate that the cognitive profile of deficits in dyscalculia could be attributed to the impaired functioning of the right IPS.

5.3 Age-related Changes and Similarities

Brain systems are not static and undergo many changes though learning and development. Age-related changes have been demonstrated in the neural networks that underlie VSWM (Klingberg, Forssberg, & Westerberg, 2002; Kwon, Reiss, & Menon, 2002), number processing (Ansari & Dhital, 2006; Ansari, Garcia, Lucas, Hamon, & Dhital, 2005; Emerson & Cantlon, 2014;Vogel et al., 2015) and arithmetic (Kucian, Von Aster, Loenneker, Dietrich, & Martin, 2008; Rivera, Reiss, Eckert, & Menon, 2005; Rosenberg-Lee, Barth, & Menon, 2011). In the present thesis, I expand on this literature by demonstrating continuity and change in the brain regions that facilitate the relationship between these skills. In the sections below, I provide a discussion of the differences and similarities between adults and children, as well as the possible cognitive and maturational factors that may contribute to these age-related changes and similarities.

5.3.1 Lateralization of Function

Chapters 2 and 3 had some parallels in the way that adults and children recruited the IPS for VSWM, number processing, and arithmetic. Namely, adults tended to show more left-lateralized activation, whereas children tended recruit the bilateral or right IPS more often. In Chapter 2, the conjunction analysis revealed shared recruitment of the right IPS for VSWM and arithmetic in children, whereas adults recruited the bilateral IPS for these tasks. When directly comparing these analyses, adults recruited the left IPS more for VSWM and arithmetic than children, demonstrating age-related changes this region. Again in Chapter 3, children showed overlap between basic number processing and arithmetic in the bilateral IPS, whereas adults only recruited the left IPS for large problems and number matching. There are two possible accounts for left-lateralization over development in the parietal cortex: 1) the lateralization could be a product of domain specific changes in the processing of symbolic numbers; or 2) it could reflect other changes to the organization of the brain that constrain the way information is processed across domains.

There are precedents in the literature for increasing engagement of the left IPS for numerical processing over development. For example, Emerson and Cantlon, (2014) demonstrated that the neural response to a number processing task (similar to the one presented in this study) was relatively consistent in the right IPS across a 1-2 year period, whereas the left IPS exhibited greater changes. Others have also provided evidence for domain specific specialization of the left IPS by showing that the left IPS becomes more tuned to the relative distance between symbolic numbers as children get older (Vogel et al., 2015). Therefore, the increasing engagement of the left IPS during basic numerical tasks could reflect a relatively domain specific change related to the way symbolic numbers are processed. However, there are also alternative accounts of how lateralization over developmental might occur. In Chapter 2, I provided evidence that showed how the left IPS had age-related increases for the conjunction between VSWM and arithmetic. This suggests the greater engagement of the left IPS may not be specific to numbers or to arithmetic, because VSWM also exhibited these changes. The greater engagement of the left IPS over development may therefore reflect other maturational factors that affect the neural processes underlying many cognitive abilities. One factor that may exert influence the organization of the brain is the development of language and reading skills. Literacy has been shown to influence other brain networks outside of those directly involved in reading (Dehaene et al., 2010). Both VSWM and arithmetic can be solved using verbally-mediated strategies (De Smedt, Taylor, Archibald, & Ansari, 2010; Hitch, Halliday, Schaafstal, & Schraagen, 1988; Pica, Lemer, Izard, & Dehaene, 2004; Pickering et al., 2001; Vukovic & Lesaux, 2013), so the development of language could affect these systems. Other maturational changes also occur that affect the symmetry of brain structure and function (Duboc, Dufourcq, Blader, & Roussigné, 2015; Toga & Thompson, 2003). For example, there are developmental changes in network architecture where the left hemisphere has greater increases in network efficiencies over development, whereas the network efficiencies in the right hemisphere remain relatively stable from adolescence to adulthood (Zhong, He, Shu, & Gong, 2016). This may reflect maturational processes that reorganize brain structure and function that subsequently lead to lateralization. It has been suggested that functional lateralization may have cognitive advantages such as more efficient parallel processing of information (Duboc et al., 2015). Though the precise cause of age-related changes in the left IPS is unclear, it could be related to more global changes in brain structure and function.

5.3.2 Cognitive Similarities Across Age

Even though adults and children showed some differences in the recruitment of the IPS for VSWM, number processing, and arithmetic, there were also some notable similarities in the neural substrates underlying these abilities. For example, Chapter 2 showed similarities of processing in the right IPS for VSWM and arithmetic. Both adults and children recruited the right IPS for these tasks and there were no age-related changes in this region. Previous studies have also found that there may be more continuity in brain structure (Zhong et al., 2016) and function within (Emerson & Cantlon, 2014) the right hemisphere. Chapter 3 also showed that when adults and children calculated problems of relatively equal difficulty (large problems for adults versus small problems for children), they recruited the left IPS to the same degree. This provides evidence that when the cognitive demands of the arithmetic task are approximately matched, the underlying cognitive processes may be very similar across development. Similarly, there is also some evidence that the relationship between working memory and arithmetic is relatively consistent across age[3]. In a meta-analysis examining how different components of working memory are related to arithmetic, Peng et al. (2015) found some continuity in association between working memory and arithmetic across age. This finding contradicted their predictions because individual studies have found age-related differences in the associations between working memory and arithmetic (Alloway & Passolunghi, 2011; McKenzie, Bull, & Gray, 2003; Rasmussen & Bisanz, 2005). The authors suggest that studies included in the meta-analysis likely used harder and more age-appropriate arithmetic tasks as children got older. Therefore, working memory is likely important for arithmetic across development as long as the arithmetic task requires the manipulation of information and the maintenance of intermediate steps.

Together, these findings raise some often-neglected questions about the cognitive predictors of arithmetic skills over development. Many studies have demonstrated changes in the cognitive predictors of arithmetic skills, both cross-sectionally and longitudinally (Alloway & Passolunghi, 2011; Lyons et al., 2014; McKenzie et al., 2003; Rasmussen & Bisanz, 2005). Age-related changes in the cognitive predictors of arithmetic could be driven by a wide variety of factors, such as changing strategies or decreasing cognitive demands with increasing fluency. Though it is difficult to disentangle the roles of maturation and experience, one way for future research to examine this question might be to match the strategies being implemented and the difficulty of the arithmetic problems. It is possible that the same cognitive predictors are

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[3] The present thesis cannot speak to the cognitive similarities between VSWM and arithmetic between adults and children because Chapter 2 did not use the same contrasts as in Chapter 3. For a discussion why different contrasts were used, see Chapter 3 page 76.

related to arithmetic across development once the relative difficulty of the task is held constant.

5.4 Limitations and Future Directions

Several limitations of this thesis should be acknowledged. First, both Chapters 2 and 3 examine how arithmetic shares common neural circuits with domain general and domain specific processes. However, simply because the same brain region is recruited for different tasks does not imply a common cognitive process. For instance, VSWM and arithmetic may both recruit the IPS, however, the neural computations within this region may not be similar for these tasks. Other multivariate methods, such as representational similarity analyses, will need to be used to determine whether the patterns of brain activity are similar across tasks (Kriegeskorte, Mur, & Bandettini, 2008). This will be an important avenue for future exploration because it could help elucidate the precise relationship between VSWM and arithmetic. For example, it is often assumed that arithmetic relies on VSWM resources when the problem requires effortful calculation and the storage of intermediate steps (Raghubar et al., 2010). It would thus follow that neural response in the IPS could be more similar for VSWM and large arithmetic problems than small problems. Moreover, these relationships may decrease with age as the cognitive load decreases. Similar predictions could be made about the association between arithmetic and basic number processing in the IPS. Future research will need to employ multivariate methods to better understand the relationship between arithmetic, domain general, and domain specific skills to determine whether they have common neural representations that go beyond shared localization of function.

In many of the chapters in this thesis I have stressed that that it is important to examine the cognitive operations being performed during arithmetic in order to understand how arithmetic is associated with domain general and domain specific skills. For example, in Chapter 3 I discuss how basic number processing skills may play a greater role (and show greater neural overlap) for problems that are more reliant on effortful calculation strategies. This was largely inferred from problem size, which is not a precise way of examining the cognitive strategies being used on each problem. The strategy reports that were obtained after the scan did confirm that there was as a distinction between the number of calculated items in the large and small problem conditions and suggested differences in the cognitive processes underlying large and small problems. However, it will be important for future research to examine strategies on a trial-by-trial basis. It is likely that neural correlates of large and small problems will not show any distinction when they are solved using the same cognitive operation.

Related to the discussion above, the present thesis only examined how domain general and domain specific competencies were related to addition, and did not include any other arithmetic operations. However, it is likely that the findings would have been similar if I had used a different operation such as subtraction. It has been proposed that any differences in the neural networks for different arithmetic operations are likely related to the frequency with which procedural and retrieval strategies are used in each operation (Tschentscher & Hauk, 2014). For instance, single digit multiplication problems tend to be solved using retrieval, whereas addition and subtraction problems are usually solved using procedural strategies (Campbell & Xue, 2001). This distinction is demonstrated at the neural level where addition relies more on a fronto-parietal network, whereas multiplication elicits activity in the supramarginal and angular gyri (Tschentscher & Hauk, 2014). These differences, however, are not specific to the operation but are related to the kind of strategies these operations tend to employ. Addition was used in this thesis because it is an age-appropriate operation that most children can solve with a high degree of accuracy, and also has a good distribution of problems that are solved using procedural and retrieval strategies.

Another potential caveat relates to examining age-related changes by comparing adults to children. This is a coarse way of assessing developmental change, and group differences could be attributed to a number of factors that are unrelated to experience in mathematics or maturation (i.e., educational background or socioeconomic status). Even the sample of children included in this study ranged from 7-10 years, which is a developmental period when children are undergoing rapid cognitive changes and are becoming increasingly fluent within arithmetic (Butterworth, 2005). Even within a three year period, the domain specific predictors of arithmetic shift from cardinal to ordinal skills (Lyons et al., 2014). Therefore, longitudinal approaches will be important to examine how the cognitive predictors of arithmetic change over development at the behavioural and neural levels of analysis.

Finally, this thesis largely focused on the role of VSWM and symbol-quantity relationships with arithmetic, which was motivated by the prior behavioural literature and the commonly predicted associations between these skills. However, other abilities such as verbal working memory, language skills, and symbolic ordering are all important predictors of individual differences in arithmetic proficiency. Indeed, individual differences in verbal working memory have also been associated with the recruitment of the IPS during arithmetic in addition to a number of other regions (Metcalfe et al., 2013). Future research will need to explore how these other cognitive predictors are related to the arithmetic network, however this fell outside of the scope of the present thesis.

5.5 Final Remarks

To date, much of our understanding of the arithmetic network has been based on reverse inferences, brain-behaviour correlations, or comparisons across studies. None of these methods can definitively establish whether domain general and domain specific competencies have the same neural basis as arithmetic. By using a within-subjects approach I investigated how the neural networks for domain general and domain specific skills overlap with those for arithmetic, and how individual differences in these skills are simultaneously related to the recruitment of the IPS. The findings within this thesis revealed that the IPS plays a complex and multifaceted role in arithmetic and, contrary to some suggestions from previous literature, it is not exclusively related to domain specific processes. Moreover, the neural relationships between arithmetic, domain general, and domain specific skills change with age. Though much remains to be learned about the foundations of arithmetic skills, the present thesis provides unique insights into the neurocognitive underpinnings of arithmetic in children and adults.

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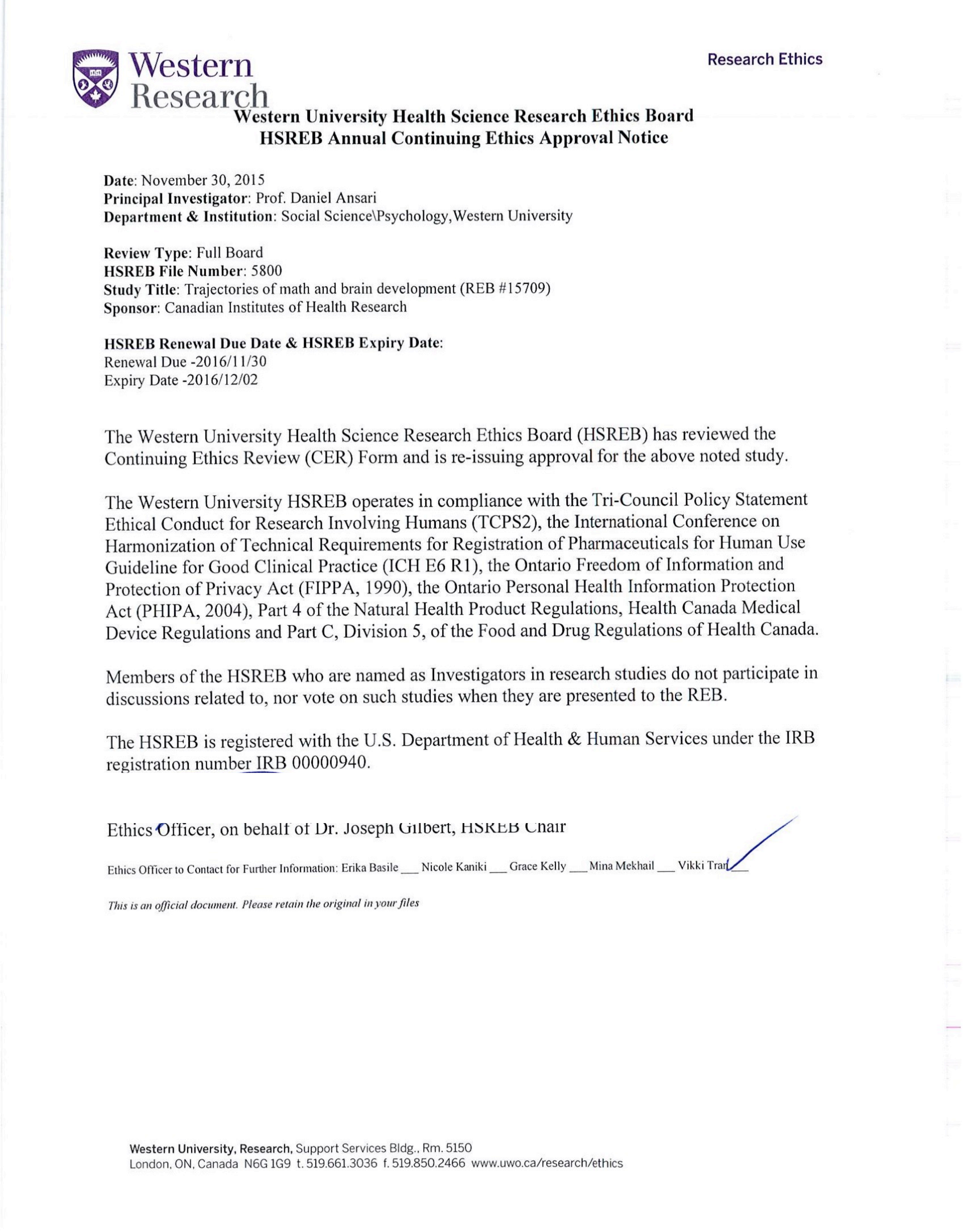
Appendices

Appendix A: Documentation of ethics approval



Western Research

Research Ethics

Western University Health Science Research Ethics Board
HSREB Annual Continuing Ethics Approval Notice

Date: November 30, 2015
Principal Investigator: Prof. Daniel Ansari
Department & Institution: Social Science\Psychology,Western University

Review Type: Full Board
HSREB File Number: 5800
Study Title: Trajectories of math and brain development (REB #15709)
Sponsor: Canadian Institutes of Health Research

HSREB Renewal Due Date & HSREB Expiry Date:
Renewal Due -2016/11/30
Expiry Date -2016/12/02

The Western University Health Science Research Ethics Board (HSREB) has reviewed the Continuing Ethics Review (CER) Form and is re-issuing approval for the above noted study.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice (ICH E6 R1), the Ontario Freedom of Information and Protection of Privacy Act (FIPPA, 1990), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Ethics Officer, on behalf of Dr. Joseph Gilbert, HSREB Chair

Ethics Officer to Contact for Further Information: Erika Basile ___ Nicole Kaniki ___ Grace Kelly ___ Mina Mekhail ___ [✓ Vikki Tran]___

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Appendix B: Trials on arithmetic task in fMRI

Note: C = correct solution; I = incorrect solution

Run 1

Problem					Response	Condition
2	+	1	=	3	C	Plus1
3	+	1	=	5	I	Plus1
4	+	1	=	5	C	Plus1
5	+	1	=	8	I	Plus1
6	+	1	=	7	C	Plus1
7	+	1	=	9	I	Plus1
8	+	1	=	9	C	Plus1
9	+	1	=	12	I	Plus1
3	+	1	=	4	C	Plus1
4	+	1	=	6	I	Plus1
7	+	1	=	8	C	Plus1
8	+	1	=	11	I	Plus1
2	+	3	=	5	C	Small
4	+	2	=	8	I	Small
2	+	5	=	8	I	Small
6	+	2	=	8	C	Small
2	+	7	=	9	C	Small
8	+	2	=	11	I	Small
3	+	4	=	9	I	Small
5	+	3	=	8	C	Small
3	+	6	=	9	C	Small
7	+	3	=	12	I	Small
4	+	5	=	10	I	Small
6	+	4	=	10	C	Small
2	+	9	=	11	C	Large
8	+	3	=	13	I	Large
3	+	9	=	13	I	Large
7	+	4	=	11	C	Large
4	+	8	=	12	C	Large
9	+	4	=	14	I	Large
5	+	6	=	13	I	Large
7	+	5	=	12	C	Large
5	+	8	=	13	C	Large
9	+	5	=	16	I	Large
6	+	7	=	14	I	Large
8	+	6	=	14	C	Large

Run 2

Problem	Response	Condition
2 + 1 = 4	I	Plus1
3 + 1 = 4	C	Plus1
4 + 1 = 7	I	Plus1
5 + 1 = 6	C	Plus1
6 + 1 = 8	I	Plus1
7 + 1 = 8	C	Plus1
8 + 1 = 11	I	Plus1
9 + 1 = 10	C	Plus1
2 + 1 = 3	C	Plus1
5 + 1 = 7	I	Plus1
6 + 1 = 7	C	Plus1
9 + 1 = 12	I	Plus1
3 + 2 = 7	I	Small
2 + 4 = 6	C	Small
5 + 2 = 7	C	Small
2 + 6 = 9	I	Small
7 + 2 = 10	I	Small
2 + 8 = 10	C	Small
4 + 3 = 7	C	Small
3 + 5 = 10	I	Small
6 + 3 = 11	I	Small
3 + 7 = 10	C	Small
5 + 4 = 9	C	Small
4 + 6 = 11	I	Small
9 + 2 = 13	I	Large
3 + 8 = 11	C	Large
9 + 3 = 12	C	Large
4 + 7 = 12	I	Large
8 + 4 = 13	I	Large
4 + 9 = 13	C	Large
6 + 5 = 11	C	Large
5 + 7 = 14	I	Large
8 + 5 = 15	I	Large
5 + 9 = 14	C	Large
7 + 6 = 13	C	Large
6 + 8 = 15	I	Large

Appendix C: Unique trials on behavioural symbolic and nonsymbolic comparison tasks

Note: L = number presented on the left is bigger; R = number presented on the right is bigger

Left Num	Right Num	Ratio	Distance	Response
1	9	0.11	8	R
1	7	0.143	6	R
2	9	0.222	7	R
2	8	0.25	6	R
2	6	0.333	4	R
3	8	0.375	5	R
3	7	0.429	4	R
4	8	0.5	4	R
4	7	0.571	3	R
3	5	0.6	2	R
4	6	0.667	2	R
5	7	0.714	2	R
3	4	0.75	1	R
4	5	0.8	1	R
6	7	0.857	1	R
8	9	0.889	1	R
9	1	0.11	8	L
7	1	0.143	6	L
9	2	0.222	7	L
8	2	0.25	6	L
6	2	0.333	4	L
8	3	0.375	5	L
7	3	0.429	4	L
8	4	0.5	4	L
7	4	0.571	3	L
5	3	0.6	2	L
6	4	0.667	2	L
7	5	0.714	2	L
4	3	0.75	1	L
5	4	0.8	1	L
7	6	0.857	1	L
9	8	0.889	1	L

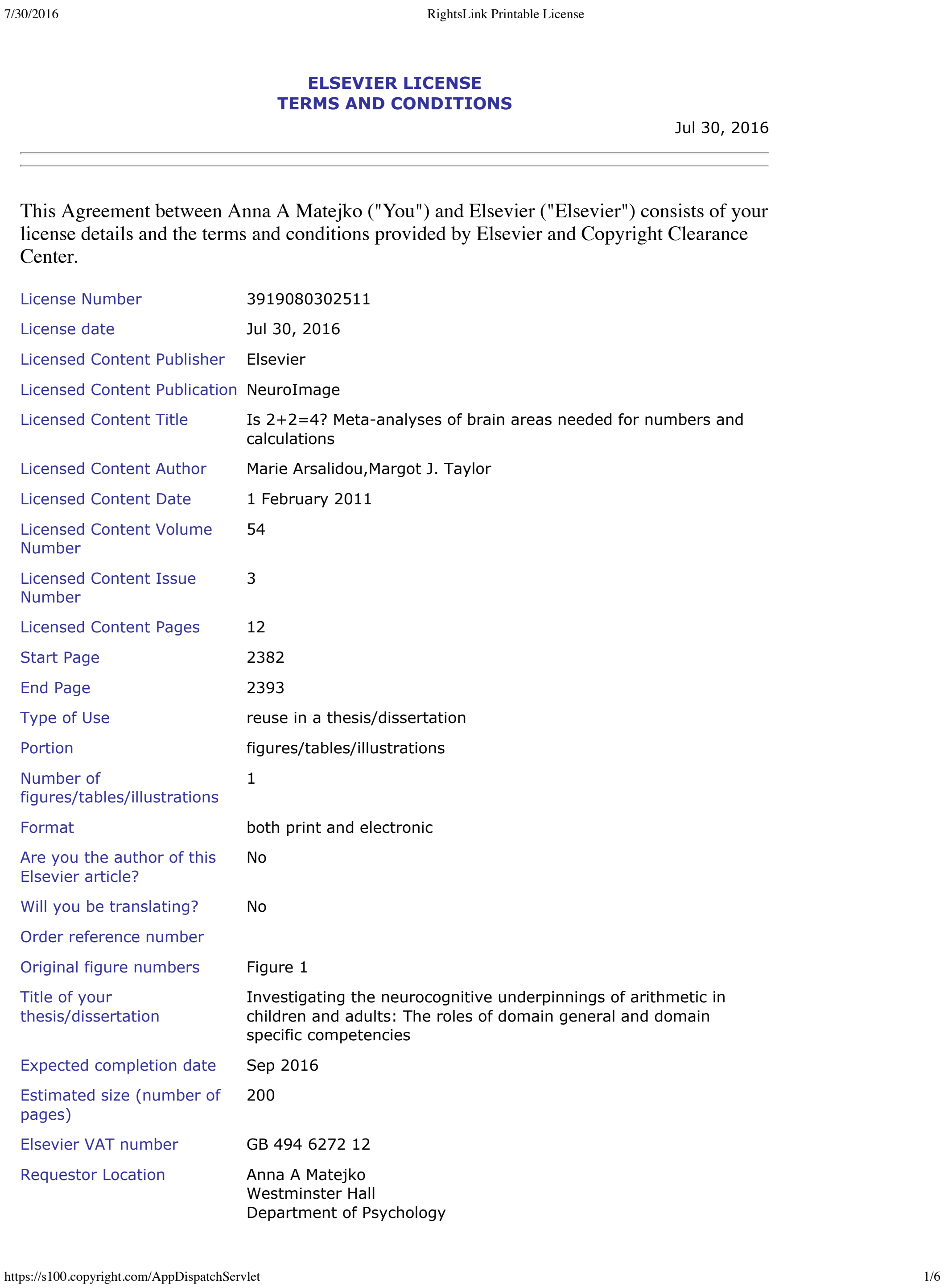
Appendix D: Unique trials on behavioural symbolic ordering task

Note: O = trials in order; M = trials mixed

Left Num	Middle Num	Right Num	Condition	Distance	Response
1	2	3	inc1	1	O
2	3	4	inc1	1	O
3	4	5	inc1	1	O
4	5	6	inc1	1	O
5	6	7	inc1	1	O
6	7	8	inc1	1	O
7	8	9	inc1	1	O
1	3	5	inc2	2	O
2	4	6	inc2	2	O
3	5	7	inc2	2	O
4	6	8	inc2	2	O
5	7	9	inc2	2	O
1	4	7	inc3	3	O
2	5	8	inc3	3	O
3	6	9	inc3	3	O
1	3	2	mix1	1	M
3	4	2	mix1	1	M
5	3	4	mix1	1	M
5	4	6	mix1	1	M
6	7	5	mix1	1	M
6	8	7	mix1	1	M
8	9	7	mix1	1	M
3	1	5	mix2	2	M
6	2	4	mix2	2	M
5	7	3	mix2	2	M
4	8	6	mix2	2	M
7	9	5	mix2	2	M
7	1	4	mix3	3	M
5	2	8	mix3	3	M
3	9	6	mix3	3	M

Appendix E: Figure permissions

Chapter 1- Figure 1



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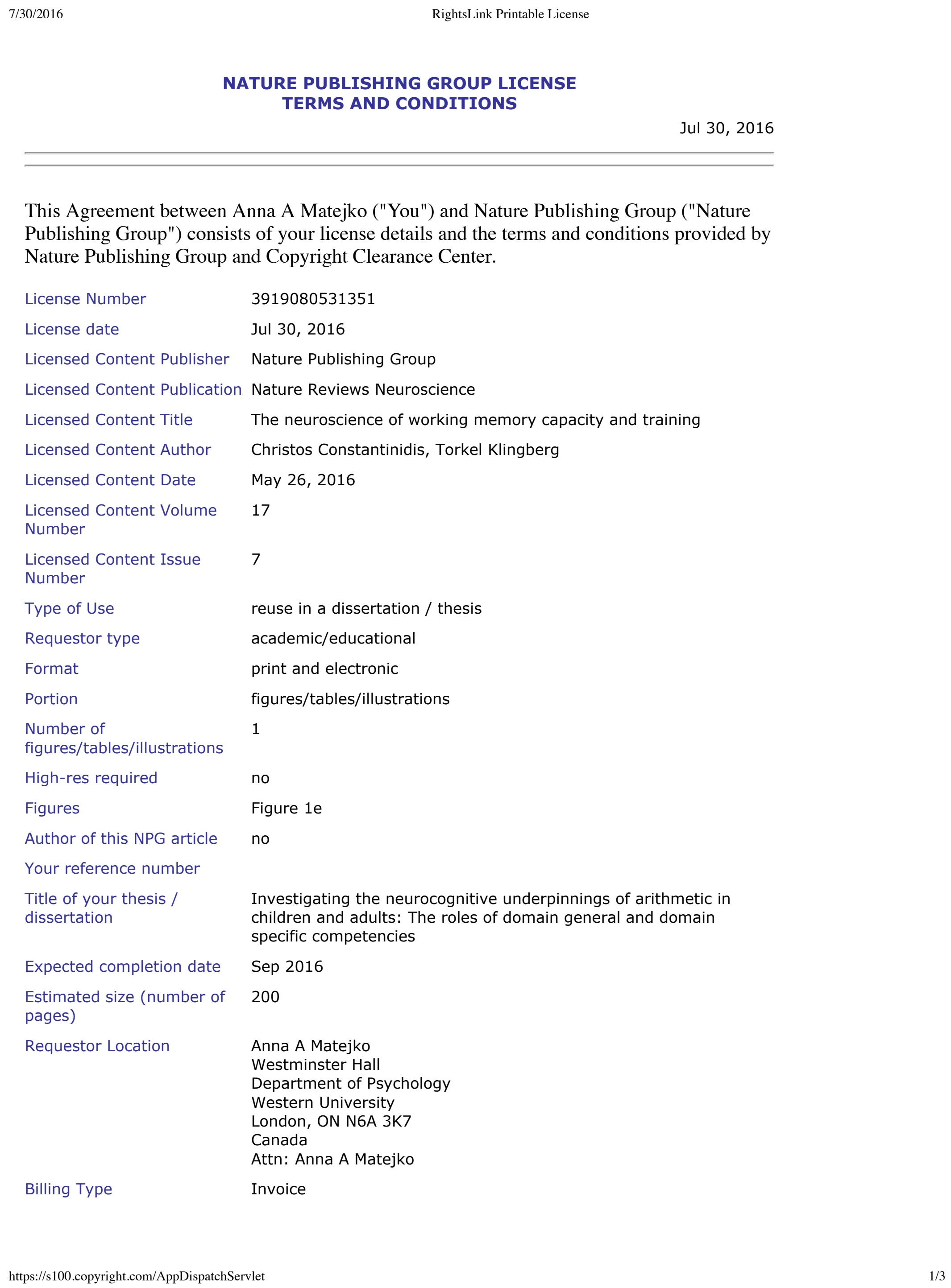

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BSc (Honors) in Psychology with First Class Honors at The University of Alberta Honors thesis: *Neurocognitive and microstructural profiles in twins with Fetal Alcohol Spectrum Disorder* Supervised by Carmen Rasmussen & Jeffrey Bisanz	2010

SCHOLARSHIPS, AWARDS & GRANTS

Marilyn (Pack) McClelland Award ($750)	2016
Ontario Graduate Scholarship ($15, 000)	2015 - 2016
Shirley Kniazky Award ($1000)	2015
Vanier Canada Graduate Scholarship ($150 000 over 36 months)	2012 - 2015
Ontario Graduate Scholarship (Declined)	2012 - 2013
Leola E. Neal Memorial Award ($450)	2012
Institute for Human Development Poster Award (September 2012) $100	2012
Children's Health Research Institute- Internal Research Grant Fund (P.I. Daniel Ansari) ($6692.50)	2012
Ontario Graduate Scholarship ($15, 000)	2011 - 2012
Western Graduate Research Scholarship ($2000)	2010 - 2011
NSERC Alexander Graham Bell Canada Graduate Scholarship (CGS-M) ($17,500)	2010 - 2011
University of Alberta First Class Standing (Average GPA above 3.5)	2007-2010

University of Alberta Dean's Silver Medal Award (non-monetary)	2010
University of Alberta Undergraduate Academic Scholarship ($750)	2009
Jason Lang Scholarship ($1000)	2009
Women and Children's Health Research Institute Summer Studentship Grant ($1000)	2009
Alberta Heritage Foundation for Medical Research Summer Studentship Award ($5,200)	2009
University of Alberta Undergraduate Academic Scholarship ($500)	2008
Jason Lang Scholarship ($1000)	2008
NSERC Undergraduate Student Research Award ($4,275.00)	2008
Jason Lang Scholarship ($1000)	2007
Rutherford Scholarship ($1000)	2006

PUBLICATIONS

Peer Reviewed:

Matejko A.A., & Ansari D. (2016) Trajectories of Symbolic and Nonsymbolic Magnitude Processing in the First Year of Formal Schooling. *PLoS One, 11,* e0149863.

Matejko, A. A., & Ansari, D. (2015). Drawing connections between white matter and numerical and mathematical cognition: A literature review. *Neuroscience and Biobehavioral Reviews, 48,* 35-52.

Pincham, H*., Matejko, A. A.*, Obersteiner, A.*, Killikelly, C.*, Abrahao, K. P., Benavides-Varela, S., Gabriel, F., Rato, J. R., & Vuillier, L. (2014). Forging a New Path for Educational Neuroscience: An international young-researcher perspective on combining neuroscience and educational practices. *Trends in Neuroscience and Education, 3*(1), 28-31.

Matejko, A. A., Price, G. R., Mazzocco, M. M. M., & Ansari, D. (2013). Individual differences in left parietal white matter predict math scores on the Preliminary Scholastic Aptitude Test. *NeuroImage*, *66*, 604–610. doi:10.1016/j.neuroimage.2012.10.045

Book Chapters and Other Publications:

Merkley, R., Matejko, A. A., & Ansari D. (in press) Strong causal claims require strong evidence: a commentary on Wang et al. (2016). Journal of Experimental Child Psychology.

Merkley R.*, Wilkey E. D.*, Matejko A. A.* (2016) Exploring the Origins and

Development of the Visual Number Form Area: A Functionally Specialized and Domain-Specific Region for the Processing of Number Symbols? *Journal of Neuroscience, 36*, 4659–4661.

Vogel, S.*, Matejko, A*, & Ansari, D. (2016) Imaging the developing human brain using functional and structural Magnetic Resonance Imaging: Methodological and practical guidelines. In J. Prior & J. Van Herwegen, (Ed.) *Practical Research with Children.* Psychology Press.

Matejko, A. White matter counts: Brain connections help us do 2+2 (2014). *Frontiers for Young Minds, 2 (19),* 1-4. doi: 10.3389/frym.2014.00019

Ansari, D., & Matejko, A. (2014). The development of the numerate brain. *Principal Connection, 18 (1),* 18-20.

Matejko, A. & Ansari, D. (2012) Developmental Cognitive Neuroscience and Learning. In N.M. Seel (Ed.) *Encyclopedia of the Sciences of Learning*. Springer.

* listed as co-first authors

TEACHING & ACADEMIC POSITIONS

Teaching Assistant for Psychology 3443G – Development of the Mathematical Brain	January-April 2016
Teaching Assistant for Psychology 2720B - Introduction to Social Psychology	January-April 2013
Teaching Assistant for Psychology 2410- Introduction to Developmental Psychology	September 2011-April 2012
Teaching Assistant for Psychology 2800- Research Methods in Psychology	January-April 2011
Teaching Assistant for online course Psychology 2060- The Psychology of People, Work, and Organizations	September-December 2010
Electroencephalography (EEG) research assistant with Dr. Mrazik (Educational Psychology) and Dr. Singhal (Psychology)	January-April 2010
U of A (Departments of Pediatrics and Biomedical Engineering) Research assistant for Dr. Rasmussen and Dr. Beaulieu	April-August 2009
U of A (Department of Pediatrics) Research Assistant for Dr. Rasmussen	April-August 2008

U of A (Department of Psychology) Research Assistant for 2007-2010
Dr. Bisanz

SUPERVISORY EXPERIENCE

Senior Honors Thesis 2015 – Jane Hutchison
"An investigation of the neural & behavioural mechanisms distinguishing numerical and non-numerical ordinal processing"

Senior Honors Thesis 2014 – Dana Smith
"Numerical Magnitude Processing and Math Achievement in Grade 1 Students"

Senior Honors Thesis 2013 – Moriah Sokolowski
"Training of Early Numeracy Skills in Preschool and Kindergarten: An iPad Training Study"

TALKS AND WORKSHOPS

Matejko, A. & Ansari, D. (2016, September). Individual differences in children's domain specific and domain general abilities relate to brain activity within the intraparietal sulcus during arithmetic. *Talk at the International Mind Brain and Education Society, Toronto, Canada*

Matejko, A. (2015, December). The role of working memory and basic number processing in the development of arithmetic skills: An investigation of common and distinct neural pathways. *Talk at the L'Université du Québec à Montréal (UQAM), Montreal, Canada.*

Matejko, A & Ansari, D. (2015, October) The role of working memory abilities in the development of arithmetic skills: An investigation of common and distinct neural pathways. *Invited talk at the International Symposium on Neuroeducation of Number Processing (Only one submission was selected for a talk). Hannover, Germany*

Matejko, A. (2014, June). Trajectories of math and number development in Grade 1: Evidence from brain and behavior. *Invited talk at the JURE Conference of EARLI, Nicosia, Cyprus, Greece.*

Matejko, A. (2014, June). Trajectories of math and number development in Grade 1: Evidence from brain and behavior. *Talk at the University of Leuven, Leuven, Belgium.*

Vogel, S. & Matejko, A. (2014, June). Workshop on Education and Neuroscience. *Workshop at the JURE Conference of EARLI, Nicosia, Cyprus, Greece.*

Matejko, A. (2014, June). An Introduction to Diffusion Tensor Imaging. *Invited workshop at Georg-August-University Göttingen, Göttingen, Germany.*

Matejko, A., Sokolowski, H.M., & Ansari, D. (2012, September). Early development of numeracy skills through technology. *Talk and workshop at the Thames Valley District School Board Professional Development Day, London, ON, Canada.*

Matejko, A., Rasmussen, C., Lebel, C., Beaulieu, C. (2010, February). Neurocognitive and microstructural profiles in twins with Fetal Alcohol Spectrum Disorder. *Talk at the Annual Alberta Fetal Alcohol Spectrum Disorder Conference, Calgary, AB, Canada.*

Matejko, A. (2009, April). Neurocognitive differences in twins with Fetal Alcohol Spectrum Disorder or Prenatal Alcohol Exposure. *Talk at Brian Harder Honors Day Annual Conference, Edmonton, AB, Canada.*

CONFERENCE PRESENTATIONS

Matejko, A., Ansari, D. (2015, February). The development of symbolic and nonsymbolic magnitude processing skills in the first year of formal schooling. *Poster at the Lake Ontario Visionary Establishment, Niagara Falls, ON, Canasa.*

Matejko, A., Ansari, D. (2014, June). How the first year of formal schooling shapes symbolic number development: Evidence from brain and behaviour. *Poster at the EARLI Sig 22 Education and Neuroscience Conference, Göttingen, Germany.*

Matejko, A., Ansari, D. (2014, May). Trajectories of math and number development in Grade 1: Evidence from brain and behavior. *Poster at Minds on Minds Symposium, London, ON, Canada.*

Matejko, A., Ansari, D. (2014, May). How the first year of formal schooling shapes symbolic number development: Evidence from brain and behaviour. *Poster presented at the NIH Math Cognition Meeting "Development of Mathematical Cognition: Neural Substrates and Genetic Influences", Washington DC, USA.*

Matejko, A., Ansari, D. (2014, May). Trajectories of math and number development in Grade 1: Evidence from brain and behavior. *Poster presented at the BASICS Conference, Banff, AB, Canada.*

Matejko, A., Price, G., Mazzocco, M., & Ansari, D. (2013, June). Individual differences in left parietal white matter predict scores on the preliminary scholastic aptitude test. *Poster presented at the Brain Plasticity, Learning, and Education Symposium, London, ON, 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.*

Matejko, A., Erdeg, B., Lefcoe, A., Sokolowski, H. M., & Ansari, D. (2012, September). Training early numeracy skills in Kindergarten children: An iPad pilot study. *Poster presented at the Connought Global Challenge Symposium, Institute for Human Development, Toronto, ON, Canada.* * Given award for best poster (see awards)

Matejko, A., Price, G., Mazzocco, M., & Ansari, D. (2012, May). Individual differences in left parietal white matter predict scores on the preliminary scholastic aptitude test. *Poster presented at the EARLI Sig 22 Education and Neuroscience Conference, London, UK.*

Matejko, A., Price, G., Mazzocco, M., & Ansari, D. (2012, February). Individual differences in white matter predict scores on the preliminary scholastic aptitude test. *Poster presented at the Lake Ontario Visionary Establishment, Niagara Falls, ON, Canada.*

Piatt, C., Matejko, A., Watchorn, R., & Bisanz, J. (2011, March). Limits on children's understanding of mathematical inversion. *Poster presented at the Society for Research in Child Development Biennial Meeting, Montreal, QC, Canada.*

Rasmussen, C., Carroll, A., Hodlevskyy, O., Lebel, C., Matejko, A., & Beaulieu, C. (2011, March). Executive functions in child psychiatry: Tourette Syndrome. *Presentation and workshop at the Annual General Meeting of the Alberta Psychiatric Association, Banff, AB, Canada.*

Matejko, A., Bisanz, J., C. Beaulieu, C., Rasmussen, C. (2010, April). Neurocognitive and microstructural profiles in twins with Fetal Alcohol Spectrum Disorder. *Poster presentation at the Brian Harder Honors Day Annual Conference, Edmonton, AB.*

Matejko, A., Lebel, C., Carroll, A., Hodlevskyy, O., Beaulieu, C., & Rasmussen, C. (2009, November). Neurocognitive and Microstructural Abnormalities in Children with Tourette Syndrome. *Poster Presented at the Women and Children's Foundation For Medical Research Annual Research Day, Edmonton, AB, Canada.*

Matejko, A., Lebel, C., Carroll, A., Hodlevskyy, O., Beaulieu, C., & Rasmussen, C. (2009, November). *Neurocognitive and Microstructural Abnormalities in Children with Tourette Syndrome. Poster Presented at the Glenrose Spotlight on Research Conference, Edmonton, AB, Canada.*

Matejko, A., Lebel, C., Carroll, A., Hodlevskyy, O., Beaulieu, C., & Rasmussen, C. (2009, October). Neurocognitive and Microstructural Abnormalities in Children with Tourette Syndrome. *Poster Presented at the Alberta Heritage Foundation for Medical Research Annual Research Day, Edmonton, AB, Canada.*

Piatt, C., Matejko, A., Watchorn, R., Bisanz, J. (2009, April). *The mathematical principle of inversion: How "alien" is it? Poster Presented at Society for Research in Child Development Biennial Meeting, Denver, CO, USA.*

ADVANCED COURSES/WORKSHOPS

2015 Visceral Mind: A hands-on course in the neuroanatomy of cognition (September 7-11). Bangor, Wales, UK.

2014 Mortimer D. Sackler, M.D. Summer Institute (July 14-18, 2014). Manhattan, New York, USA.

Latin American School for Education, Cognitive, and Neural Sciences (March 3-15, 2013). Comandatuba, Bahia, Brazil

FSL & FreeSurfer Course (June 20-24, 2011). Montreal, Quebec, Canada.
A course on FSL and FreeSurfer software

SERVICE

Committees:

Department of Psychology Colloquium Committee	2015-2016
Graduate Representative on Department of Psychology Appointments Committee	2014-2015
Coordinator of Department of Psychology, Developmental Brown Bag Presentations	2011-2012
Treasurer and Member of Executive Committee for The Psychology Graduate Student Association	2011-2012

Journal Reviews:

Journal of Experimental Child Psychology
Mind, Brain & Education
Learning and Individual Differences