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Neural underpinnings of numerical and spatial cognition: An fMRI meta-analysis of brain regions associated with symbolic number, arithmetic, and mental rotation

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ABSTRACT

Where and under what conditions do spatial and numerical skills converge and diverge in the brain? To address this question, we conducted a meta-analysis of brain regions associated with basic symbolic number processing, arithmetic, and mental rotation. We used Activation Likelihood Estimation (ALE) to construct quantitative meta-analytic maps synthesizing results from 83 neuroimaging papers (24–31 studies/cognitive process). All three cognitive processes were found to activate bilateral parietal regions in and around the intraparietal sulcus (IPS); a finding consistent with shared processing accounts. Numerical and arithmetic processing were associated with overlap in the left IPS, whereas mental rotation and arithmetic both showed activity in the middle frontal gyri. These patterns suggest regions of cortex potentially more specialized for symbolic number representation and domain-general mental manipulation, respectively. Additionally, arithmetic was associated with unique activity throughout the fronto-parietal network and mental rotation was associated with unique activity in the right superior parietal lobe. Overall, these results provide new insights into the intersection of numerical and spatial thought in the human brain.

1. Introduction

Mathematics is frequently conceived of and expressed in terms of spatial relations. Historically, many mathematical discoveries have made use of the human capacity to think and reason about space (Davis and Spatial Reasoning Study Group, 2015; Dehaene, 2011; Hubbard et al., 2005). For example, famous mathematical discoveries, such as Pythagoras's Theorem, the Real Number Line, Cavalieri's principle, and the Cartesian coordinate system all speak to the intricate and intimate connections between space and mathematics. Moreover, ancient tools such as the abacus and knotted arithmetic rope, and more recently the number line, are but a few examples of cultural inventions that directly map numbers and their relations onto space.

Critically, the link between numbers and space is not limited to inherently spatial aspects of mathematics, such as geometry and measurement, but appears to extend down to the most fundamental of mathematical entities and operations: numbers and arithmetic. Although there is extensive behavioral evidence for strong relations between spatial and numerical thinking (e.g., see Mix and Cheng, 2012; Hawes et al., 2019), questions remain regarding the underlying neural relations between these two cognitive constructs. To date, research on the neural correlates of spatial skills, such as mental rotation, and numerical reasoning have been studied in complete isolation from one another (e.g., see Zacks, 2008). While it has been well established that *basic* spatial processes (e.g., comparing line lengths) are related to basic numerical processes (e.g., comparing Arabic digits; e.g., see Sokolowski et al., 2017a, b), it is not yet known whether higher-level spatial skills (e.g., mental rotation) relate to numerical and mathematical processing in the brain. Thus far, investigations into the neural correlates of spatial and numerical processes has been limited to studies examining Spatial-Numerical Associations (SNAs; e.g., see Toomarian and Hubbard, 2018). This body of research is based largely on experimental paradigms that do not require intentional and effortful spatial processing, such as mental rotation. Instead, this body of research is interested in uncovering the unconscious links between space and number. Crucially, in this paper, we aim to do the opposite. We address the conscious and intentional processing of numbers, space, and the operations that link them.

The decision to focus on high-level spatial skills (of which mental rotation is but one of many), rather than lower-level spatial skills, was

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informed by the literature on individual differences. While consistent and robust relations exist between spatial visualization abilities[1], including mental rotation skills, and numerical and arithmetical reasoning, relations between low-level spatial and numerical processing (e.g., automatic SNAs) has failed to reveal reliable associations with higher level mathematics, including arithmetic (Cipora et al., 2015; Hawes et al., 2019; Mix and Cheng, 2012). Thus, by revealing the neural relations between mental rotation and numerical and arithmetical reasoning, we may be afforded new insights into the relations between high-level spatial skills (mental rotation) with both basic and more advanced numerical reasoning processes (i.e., basic symbolic number processes and arithmetic, respectively). To summarize, we have a good understanding of where, and to a lesser extent, how low-level spatial and numerical processes are associated in the brain (Dehaene et al., 2003; Sokolowski et al., 2017a, b). We do not, however, have a good understanding of where or how spatial visualization abilities are related to numerical and arithmetical processes in the brain.

To address this gap in the literature, we report the results of a meta-analysis of brain regions associated with neural activity in three key aspects of mathematical thinking: basic symbolic number processing, mental arithmetic, and mental rotation (a widely used measure of spatial ability). We targeted these three cognitive processes because they provided opportunities to test theoretically informed predictions as to when, why, and where we should expect to see common and distinct neural activity. As outlined in Fig. 1 – and described in detail in the following literature review – these three cognitive processes are hypothesized to be related to the extent that task performance involves common and distinct operations. For example, common to mental arithmetic and symbolic number, but not mental rotation, is the need for symbolic number processing. Accordingly, we hypothesized that we should see overlap in brain regions that are associated with symbolic number processing, shared by both arithmetic and symbolic number processes, but not mental rotation. Using this same logic, we should expect to see overlap between mental rotation and mental arithmetic, but not symbolic number, in regions that are more closely associated with mental manipulation. While mental arithmetic and mental rotation involve domain-general mental manipulation, symbolic number processing presumably does not (or at least to a much lesser degree)[2] . Lastly, we should expect to see overlap between all three processes based on the common need to represent and reason about magnitudes (e.g., see Walsh, 2003). Additionally, we hypothesize that these processes may also be linked through the role that spatial visualization (measured here with mental rotation) plays in mapping numbers onto space. By examining the representation versus manipulation of numerical information and the associated overlap with mental rotation, we aimed to better pinpoint the specific relationships between spatial and numerical processing. Taken together, the goals of this study were 1) to provide a meta-analysis of brain regions associated with three key aspects of mathematical thinking, and 2) provide a more nuanced and theoretically driven approach to understanding when and why spatial and numerical thinking may or may not recruit common neural mechanisms.

2. Behavioral evidence of connections between spatial and numerical cognition

The scientific study of relations between numbers and space has a lengthy history, beginning with studies by Sir Francis Galton in the late 1800’s and continuing to the present day (Galton, 1880; Toomarian and Hubbard, 2018). The majority of research in this area posits the ‘mental number line’ as the source of various empirical accounts of ‘numerical-spatial associations.’ According to this theory, humans conceptualize numbers and their various relations along a mental number line in which numbers are ordered in ascending magnitude from left-to-right. Empirical support for the theory comes from a number of behavioral findings, including the SNARC effect, (spatial-numerical association of response codes; Dehaene et al., 1993), line bisection effects (Calabria and Rossetti, 2005), and the operation momentum effect (Knops et al., 2009). In brief, the SNARC effect refers to the automatic association of small numbers (e.g., 1, 2, 3) to the left side of space and larger numbers (e.g., 7, 8, 9) to the right side of space. For example, people are faster to make parity judgments (i.e., determine whether or not a number is even or odd) when the left hand is used to make judgments about small numbers and the right hand is used to make judgments about larger numbers. This effect is said to be automatic because the task itself does not actually involve intentional judgments about the magnitude of the numbers. The line bisection effect is much less studied than the SNARC effect but similarly demonstrates automatic biases of associating small numbers with the left side of space and large numbers to the right side of space. For example, in one version of the line bisection task, individuals are asked to use a pencil to mark the midpoint of a string of numerals of small sing-digit numerals (e.g., 2222222) compared large single-digit numerals (e.g., 9999999). Results of these studies indicate that adult participants bias their estimates to the left when bisecting small single-digit numerals and bias their estimates to the right when bisecting large single-digit numbers (Calabria and Rossetti, 2005). Finally, operation momentum effects refer to the oft-reported finding that left-right response biases are associated with addition and subtraction, and even the operators themselves (i.e., + and −). For example, individuals tend to overestimate answers to addition problems and underestimate answers to subtraction problems (McCrink et al., 2007). Importantly, these associations appear to be culturally mediated and indicate the roles of learning, development, and cultural influences (left-to-right written notation) in forming these spatial-numerical associations. For example, the SNARC effect is reversed in cultures that read from right-to-left (Shaki et al., 2009). Taken together, a large body of research supports the presence of spatial-numerical associations and the tendency to map numbers and their various relations to space.

2.1. Contributions of spatial skills in mapping numbers to space

What are the cognitive bases for the ability to map numbers and mathematical objects onto space? Recent research suggests that spatial abilities play a key role in this process. For example, individual differences in the ability to map numbers to space (e.g., estimating where a number belongs on an empty number line) has been found to mediate relations between spatial ability and mathematics performance (Gunderson et al., 2012; Tam et al., 2019). One explanation for these findings is that stronger spatial abilities, such as being able to mentally rotate objects and visualize various visual-spatial relations, underlies a greater ease and fluency in which one can move up and down and

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[1] Note that mental rotation is but one example of what we refer to more generally as spatial visualization, which is defined here as the ability to generate, maintain, and transform visual-spatial images in mind (Lohman, 1996). In addition to mental rotation, other measures of spatial visualization include mental paper folding, composition/decomposition of 2D/3D shapes, and block design (Carroll, 1993; Hawes et al., 2019; Hegarty & Waller, 2005). We targeted mental rotation as our construct of interest to constrain our search criteria, but also because it is a well-established measure of spatial ability, has been found to correlate strongly with a variety of mathematical tasks, and has been subject to numerous fMRI investigations (Mix and Cheng, 2012; Zacks, 2008).

[2] We acknowledge that not all types of arithmetic require mental manipulation (e.g., memorized arithmetic facts). However, as revealed in the Methods section, many of the fMRI studies on mental arithmetic were explicitly designed to elicit effortful calculation and mental manipulation processes. We deliberately made no distinction between low-effort (recall-based) vs. high-effort (calculation-based) problems in creating our mental arithmetic ALE map. As discussed later, this decision was based on our intent to reveal brain regions associated with both basic symbol processing but also higher-level spatial reasoning (i.e., mental rotation). Note that domain-general manipulation refers to the manipulation of unspecified and amodal stimuli and forms of information (e.g., cube structures or numbers; verbally or visually coded information).

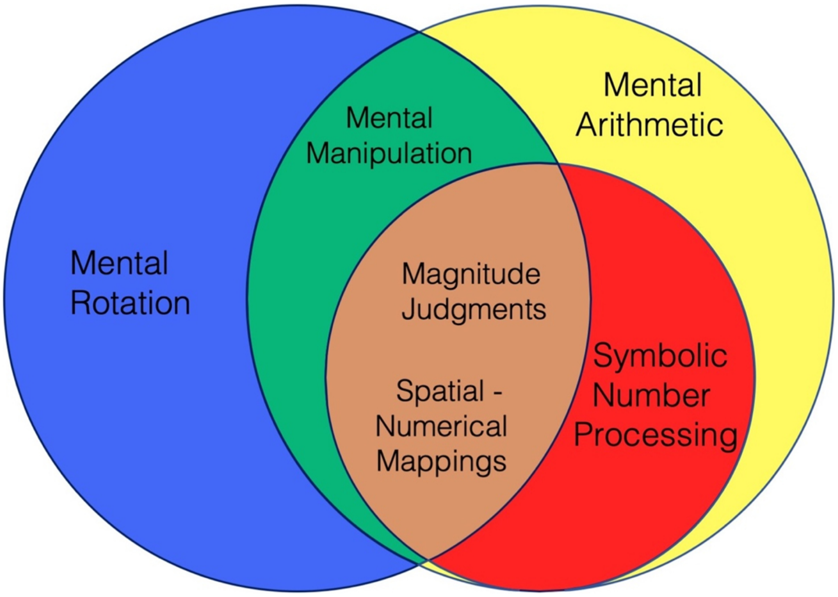

Fig. 1. Process-based account of common and distinct operations associated with symbolic number, mental arithmetic, and mental rotation.

carryout various operations along the ‘mental number line’ (Viarouge et al., 2014). Thus, spatial ability represents one potential cognitive mechanism that underlies numerical-spatial mappings.

Critically, the mapping of numbers to space might represent but *one* instantiation of the role spatial skills play in conceptualizing mathematical relations. Individual differences in spatial skills, such as mental rotation, have been linked to performance across a variety of mathematical tasks, including geometry (Delgado and Prieto, 2004), algebra (Tolar et al., 2009), word problems (Hegarty and Kozhevnikov, 1999), mental arithmetic (Kyttälä and Lehto, 2008), and advanced mathematics (e.g., function theory, mathematical logic, computational mathematics; Wei et al., 2012). According to a recent review, “*the connection between space and math may be one of the most robust and well-established findings in cognitive psychology*” (Mix and Cheng, 2012, p. 198). Taken together, an emerging body of research suggests that spatial skills, such as mental rotation, may play an important role in forming spatial-numerical associations, specifically, and spatial-mathematical associations, more generally (Marghetis et al., 2014; Hubbard et al., 2009).

3. Neural evidence for links between spatial and numerical cognition

3.1. Neuropsychological studies and the role of the left angular gyrus

Given the close coupling of number and space in behavioral studies, might we also see a close coupling of underlying neural mechanisms? Evidence to date suggests that this indeed may be the case. Some of the earliest studies that indicate that there is a link between numerical and spatial processing at the neural level came from neuropsychological case studies. It has long been recognized that lesions to the parietal lobe result in joint impairments in numerical and spatial processing (Gerstmann, 1940; Holmes, 1918; Stengel, 1944). For example, Gerstmann’s Syndrome, a rare condition associated with lesions to the left angular gyrus, is marked by deficits in numerical and spatial thinking and more specifically by a tetrad of symptoms that include deficits in carrying out basic calculations, left-right confusion, finger agnosia (trouble identifying one’s fingers), and dysgraphia (difficulty with writing) (Gerstmann, 1940). There is some evidence to suggest that the core deficit associated with Gerstmann’s Syndrome is due to difficulties in the mental manipulation of images, including impaired mental rotation skills (Mayer et al., 1999). These case studies suggest a potential interaction of number and space in the left angular gyrus. Recent support for this possibility has been demonstrated across several studies using transcranial magnetic stimulation (TMS); a methodology used to temporarily induce ‘lesion-like’ effects through altering electrical current in targeted areas of the brain. Studies have shown that disruptions to the left angular gyrus appear to impair one’s spatial representation of number, also referred to as the ‘mental number line’ (Cattaneo et al., 2009; Göbel et al., 2006, 2001).

Another line of neuropsychological research that supports the interaction of space and number in the parietal lobes comes from studies on patients with hemi-spatial neglect; a condition marked by the inability to attend to the contralesional portion of space (e.g., ignoring left side of space when the lesion is in the right parietal lobe). This results in a skewed ability to indicate the mid-point of both imagined and actual objects, including the mid-point of a physical line, but also the mid-point of numerical intervals (Bisiach and Luzatti, 1978; Zorzi et al., 2002). For example, Zorzi and colleagues (2002) found evidence to suggest that right-lateralized neglect patients tended to overestimate the mid-points of two spoken numbers, such as “two” and “six”; that is, rather than state that “four” falls in between “two” and “six,” patients were more likely to bias their estimates to the right and erroneously state “five” as the mid-point.

In sum, lesion studies as well as temporarily altered brain activity via TMS, suggests that the parietal lobe and specifically the left angular gyrus subserve both numerical and spatial processing. However, more recent research findings challenge these claims. For example, accumulating evidence suggests that the left angular gyrus may be the source of verbally stored symbolic number understanding and associated number facts, including arithmetic facts (Polspoel et al., 2017). This shift away from the left angular gyrus as a neural region associated with both numerical and spatial processes is perhaps best represented in Dehaene’s (1992; 2003) ‘Triple Code Model’ of numerical cognition. This model posits that the left angular gyrus is specific to verbally mediated symbolic number processes and the bilateral intraparietal sulci (IPS) supports the processing of abstract numerical magnitudes, including the spatial and semantic representation and manipulation of numbers (Dehaene and Cohen, 1997; Dehaene et al., 2003). A recent fMRI meta-analysis further suggests that the left angular gyrus might play a role in verbally mediated symbolic number knowledge (Sokolowski et al., 2017a). More specifically, while both symbolic and non-symbolic numbers (e.g., dot arrays) were processed by shared frontal and parietal regions, only symbolic number uniquely activated the left angular gyrus. Additionally, a meta-analysis of functional brain activity related to mental rotation failed to reveal regions specific to the left angular gyrus and instead pointed to activity in bilateral frontal and parietal regions (Zacks, 2008).

Taken together, while there is some evidence that the left angular gyrus might be implicated in both numerical and spatial processing, there is a growing body of evidence to suggest that the left angular gyrus is more specifically related to verbally mediated numerical knowledge. By directly contrasting brain regions associated with activity in basic symbolic number processing, arithmetic, and mental rotation, we aim to further shed light on the specificity of this region as one potentially more attuned to numerical and/or spatial processing. Furthermore, by contrasting regions specific to basic symbolic number processes and more complex symbolic number processes, i.e., arithmetic, we may be able to offer additional insight into whether this region is more active for basic vs. higher-level numerical tasks.

3.2. fMRI studies and the role of the intraparietal sulcus

The intraparietal sulcus (IPS) has been targeted as a central region of interest to researchers of numerical and spatial cognition alike. However, the conclusions and claims about the importance of the IPS for numerical and spatial cognition differ according to each field. Research on numerical cognition has described the IPS as the locus of the putative “number module,” “core quantity system,” and the “number-essential” region (Butterworth, 1999; Dehaene et al., 2003). Research on spatial cognition has described the IPS as a region underlying visual-spatial transformations (Jordan et al., 2001; Zacks, 2008). Presumably, these differences are because studies on the role of the IPS for numerical and spatial processes have been carried out in isolation from one another. Moreover, this lack of ‘cross-talk’ between fields may underlie differences in the ways in which domain-specific functions are ascribed to the IPS. These differences are especially apparent within the domain of numerical cognition.

For over two decades, the IPS has been theorized to house domain-specific processes related to number. Indeed, there is a large body of evidence showing that the IPS – the horizontal segment of the IPS in particular – is consistently activated during both symbolic (“3” or “three”) and non-symbolic (∴) number tasks. The fact that the meaning of number is processed and retained across formats (e.g., hearing the number “three” and seeing three objects) has been taken as evidence that the IPS represents number in the abstract. According to Dehaene’s influential ‘Triple Code Model,’ the IPS plays a critical role in the semantic manipulation of numbers and is the most plausible candidate for domain-specificity.

Critically, other perspectives on the role of the IPS in number processing espouse far less ‘domain-specific’ views. Instead, the IPS may represent an area that underlies a far more general magnitude system; one that is sensitive to a variety of magnitudes, including space, luminance, and even time (e.g., see Kadosh et al., 2008; Sokolowski et al., 2017a). For example, the IPS and other parietal regions are similarly activated when participants make number comparisons but also when comparing various line lengths (Pinel et al., 2004). There is strong evidence that basic spatial properties of objects are processed in the parietal cortex, including the IPS. In fact, a central challenge in the attempt to isolate number-specific regions of cortex is controlling for confounds related to basic spatial properties of objects. As is the case in natural world, continuous quantity and numerosity appear to be highly correlated in the brain (Newcombe et al., 2015; Walsh, 2003). The most influential model in this regard is Vincent Walsh’s (2003), ‘A Theory of Magnitude’, aka, ATOM. Walsh posits evolutionary reasons for widespread overlap for between the magnitudes of time, space, and quantity.

Given that the processing of basic spatial properties, such as size and shape, have been implicated in a general magnitude system, might higher-level spatial skills, such as mental rotation, also recruit some of the same neural resources? Although the neural foundations of mental rotation have been studied in isolation from studies of numerical reasoning, a review of the literature suggest highly overlapping areas of activation in the parietal lobes, including the IPS. In fact, a meta-analysis by Zacks (2008) demonstrated that the IPS was the most consistent and robust brain region associated with mental rotation performance. This finding has led to speculation that this brain region is responsible for visual-spatial transformations, including mental rotation but other visual-spatial transformations as well, such as geometric translations (Jordan et al., 2001; Seydell-Greenwald et al., 2017; Zacks, 2008). According to this view, the IPS is representative of a more general network that is involved in a variety of visual-spatial transformations.

Taken together, current evidence suggests that the IPS and closely surrounding parietal regions play a foundational role in numerical and spatial processes. However, the functions ascribed to the IPS vary and represent a range of possibilities, including number-specific processes, more general magnitude processes, and visual-spatial transformations. One of the aims of this study is examine the common and distinct regions in and around the IPS as they relate to numerical and spatial processes. If it is found that a high degree of overlap exists between symbolic number processing, arithmetic, and mental rotation, there may be reason to revisit current theories related to the functions of the IPS. The presence of distinct regions associated with each task might further provide guidance for future studies, as these regions might be particularly suited to specific processes related to each task.

3.3. Mathematical cognition and the general role of the fronto-parietal network

In addition to the parietal lobes, the frontal lobes are also consistently active during numerical, mathematical, and visual-spatial reasoning tasks (Desco et al., 2011; Matejko and Ansari, 2015; O’Boyle et al., 2005). However, in comparison to the parietal lobes, the frontal cortex has received less attention as a region of targeted interest. This may be due in part to more general functions ascribed to the frontal regions compared to the parietal lobes. It is well-recognized that the prefrontal cortex is commonly associated with top-down attentional and executive control processes (Fincham et al., 2002; Owen et al., 2005; Smith and Jonides, 1999). Thus, task-related activity in frontal regions is often taken as evidence of increased top-down control requirements. For example, increases in task difficulty are associated with increased activation of the dorsolateral prefrontal cortex (e.g., Kroger et al., 2002).

Neuroimaging studies of numerical reasoning demonstrate consistent activation in frontal regions (e.g., see Sokolowski et al., 2017a, b). However, the amount of frontal activity appears to be somewhat dependent on development and task difficulty. Early in development children tend to rely heavily on frontal regions but over time a general shift occurs and parietal regions become more actively engaged (Ansari et al., 2005; Cantlon et al., 2006; Zamarian et al., 2009). Relatedly, rote number processing, including memorized arithmetic facts, appears to rely less on frontal regions and more on parietal regions; calculation-based numerical reasoning, however, appears to more broadly recruit the fronto-parietal network. In short, fluency with number symbols and arithmetic facts is associated with less frontal activity and more parietal activity. Mental rotation also appears to rely on frontal regions, including regions thought to reflect general cognitive effort, but also regions thought to underlie motor planning and control (e.g., premotor cortex; Zacks, 2008).

Overall, the fronto-parietal network is implicated in both numerical and spatial reasoning and collectively represents the neural underpinnings of mathematical cognition (Desco et al., 2011; Matejko and Ansari, 2015). However, activity in the frontal regions appears to vary somewhat depending on task difficulty. In the current study, we expected to find more diffuse frontal activity for mental rotation and arithmetic compared to basic symbolic number processes.

4. The present study

The purpose of the current study was to identify underlying neuroanatomical structures that converge across multiple empirical neuroimaging studies to support numerical, arithmetical, and spatial reasoning at the meta-analytic level. We targeted these three cognitive functions because they represent some of the most well-established building blocks of mathematics (e.g., see Mix and Cheng, 2012; LeFevre et al., 2010). Relatedly, a better understanding of the neural correlates of these skills might provide additional evidence and insights into the historically tight relationship between spatial and mathematical thinking (Smith, 1964; Mix and Cheng, 2012). Another motivating factor behind this study was the intent to merge two traditionally separate bodies of neuroimaging research; one devoted to numerical processes and the other devoted to mental rotation. Critically, each body of literature suggests that numerical reasoning and mental rotation are sub-served by a highly overlapping fronto-parietal network; the IPS being of particular interest within each distinct body of literature. Thus, one of the aims of this study was examine the common and distinct regions in and around the IPS as they relate to numerical and spatial processes. Identifying brain regions that converge and diverge across the targeted constructs is an important step in working towards a better operational understanding of the brain (e.g., see Price and Friston, 2005). That is, rather than assign disciplinary specific terminology to different brain structures based on the findings from independent studies (e.g., the “number module”), a more fruitful approach may be to evaluate and define functional brain regions across studies and according to the operations that different areas perform (Price and Friston, 2005). Quantitative fMRI meta-analytic techniques, such as coordinate based Activation Likelihood Estimation (ALE), are ideally suited for this purpose (Eickhoff et al., 2009). By pooling data from different studies, which examine the same construct (e.g., mental arithmetic) but may employ variations of the experimental approach, one is better able to identify consistent responses across experiments (Laird et al., 2009a, b). In addition, this approach may help combat common problems associated with individual fMRI studies, including small sample sizes (low power), low reliability, and the problems inherent to the subtraction logic used to differentiate between two conditions (Price et al., 2005).

Against the background of the literature reviewed above, we entered this study with several predictions (see Fig. 1 and Table 1). Broadly speaking, we predicted the fronto-parietal network would be implicated in all three cognitive tasks. However, we predicted more frontal activation for arithmetic and mental rotation compared to basic symbolic number processing due to the higher cognitive demands of the former tasks. That is, from an operational perspective, we expected to see overlap between mental arithmetic and mental rotation due to the shared need to mental manipulate information (be they objects or numbers). We also reasoned that there may be regions of overlap specific to symbolic number and arithmetic processes, but not mental rotation. The presence of these regions, potentially in and around the left angular gyrus, might suggest areas that deal more exclusively with the representation of symbolic number compared to magnitudes more generally (e.g., angles of rotation). Finally, we predicted that we might identify regions that are specific to mental rotation that correspond to mental imagery and motor control.

In sum, by revealing the neural correlates of all three cognitive processes we aimed to systematically test the ways in which spatial and numerical cognition may converge and diverge in the brain. Specifically, we sought out to tease apart regions of activation subserving mental manipulation versus symbolic number representation.

5. Methods

5.1. Literature search and article selection

Three separate literature searches were conducted; one for each cognitive construct of interest. Each literature search involved the same two-step process: (1) a search of the PUBMED and PsychInfo databases, and (2) a review of the reference sections for any other relevant papers that may not have shown up in the initial search. Although the inclusion/exclusion criteria differed somewhat across constructs (detailed below), we adhered to the following general guidelines when deciding whether or not a study was relevant for inclusion: (1) Studies had to use and report whole-brain group analyses with stereotactic coordinates in Talairach/Tournoux or Montreal Neurological Institute (MNI) space. Contrasts that used region of interest (ROI) or multivariate statistical approaches were excluded; (2) Studies had to include a sample of healthy adults; (3) Only fMRI or PET imaging methods were accepted as these methods have comparable spatial uncertainty; (4) Studies had to have contrasts with active control conditions; studies that included contrasts against baseline, rest, or fixation were excluded. Note that all studies involved button/computer responses; (5) Studies had to be published in English. Our literature search includes papers published prior to August 9th 2018.

5.2. Mental rotation

Combinations of the key terms “mental rotation,” “mental imagery,” “spatial,” “visual-spatial,” “visuospatial,” “object rotation,” “mental transformation,” “PET,” “positron emission topography,” “fMRI,” “functional magnetic resonance imaging,” “neuroimaging,” and “imaging” were entered into the search databases. Studies that included the mental rotation of 2D or 3D task stimuli, including depictions of real world objects or abstract shapes, were included. As a result, the mental rotation ALE map is largely made up of studies that involved the mental rotation of 2D or 3D task stimuli contrasted against an active control condition. As is typical in mental rotation tasks, the control condition involved presenting participants with the same stimulus type and required the same response as the other mental rotation trials (e.g., ‘same’ or ‘different’ response) but the angle of disparity between the objects being compared was categorically smaller (e.g., < 30°) or 0. Studies were excluded if they, 1) involved the mental rotation of body parts (e.g., hands), 2) included contrasts that included mental rotation of number symbols, and 3) were designed to isolate stimulus-dependent mental rotation neural activation (e.g., contrasts mentally rotate tools > non-tools). We excluded studies that included mental rotation of body parts because prior research has found that mental rotation of body parts is distinguishable from mental rotation of objects (e.g., see Tomasino and Gremese, 2016). Moreover, research on relations

Table 1
Names of contrasts carried out in the meta-analysis and main mental process remaining after the contrast has been performed.

Name of contrasts	Predicted remaining mental process	Potential corresponding brain region(s)
Arithmetic > mental rotation	Symbolic number processing	Left angular gyrus
Symbolic number > mental rotation	Symbolic number processing	Left angular gyrus
Mental rotation > symbolic number	Mental manipulation	Frontal regions/prefrontal cortex
Arithmetic > symbolic number	Mental manipulation	Frontal regions/prefrontal cortex
Symbolic number > arithmetic	None	None
Mental rotation > arithmetic	Motor/object simulation	Motor cortex

Table 2
Summary of studies included in the mental rotation meta-analysis.

1 st Author	Year	Journal	N	Imaging method	Mean age	Gender	Tasks	Contrast name	Location
Barnes J	2000	Neuropsychologia	6	fMRI	34	4M 2F	Rotation of 3D objects	Rotational transformation > Rotational reference	6
Ecker C	2006	NeuroImage	10	fMRI	25	10 F	Rotation of 3D objects	100 degree angular disparity > 20 degree angular disparity	1
								60 degree angular disparity > 0 degree angular disparity	2
Gauthier I	2002	Neuron	15	fMRI		8M 7F	Rotation of 3D objects	Large > Small rotations	3
Halari R	2006	Experimental Brain Research	19	fMRI	25.8	9M 10 F	Rotation of 3D objects	Rotation > Control (men)	6
								Rotation > Control (women)	6
Hugdahl K	2006	Neuropsychologia	11	fMRI	31	5M 7F	Rotation of 3D objects	3D experimental > 2D control	4
Johnston S	2004	Neuroscience Letters	9	fMRI	25.8	5M 4F	Rotation of 2D abstract shapes	Rotation > Control	3
Jordan K	2001	NeuroImage	9	fMRI	21	1M 8F	Rotation of 2D shapes and 3D objects	3D > Control	2
								Abstract > Control	4
								Letter > Control	2
								Mental rotation > Control	2
Jordan K	2002	Neuropsychologia	24	fMRI	23.55	10 M 14F	Rotation of 2D shapes and 3D objects	Women (rotation > control)	13
								Men (rotation > control)	6
Kawamichi H	2007	Brain Research	12	fMRI	25.5	12M	Rotation of 3D objects in 2D and 3D space	3D Large > Small rotations	5
								2D Large > Small rotations	9
Keehner M	2006	NeuroImage	14	fMRI		7M 7F	Rotation of 3D objects	Mental rotation > 0	6
Kosslyn S M	1998	Psychophysiology	12	PET	20.1	12F	Rotation of 3D objects	Cubes > Cubes baseline	8
Kosslyn S M	2001	NeuroReport	8	PET	20	8F	Rotation of 3D objects	External action > Baseline	7
								Internal action > Baseline	9
Lamm C	2007	NeuroImage	13	fMRI	23-31	13M	Rotation of 2D shapes	Orientation > Location	11
Levin SL	2005	Evolutionary Psychology	12	fMRI	20.67	6M 6F	Rotation of 3D objects	Spatial > Same (collapsing across sex)	4
								Spatial > Different (collapsed across sex)	2
Ng V W K	2001	Journal of Cognitive Neuroscience	12	fMRI	20.25	12F	Rotation of letters	Activation > Baseline	9
Podzebenko K	2005	Journal of Cognitive Neuroscience	16	fMRI	31.5	8M 8F	Rotation of 2D abstract shapes	Rotation > Control	5
Schendan H E	2007	NeuroImage	13	fMRI	21.6	6M 7F	Rotation of 3D objects	Rotation > Control	26
Seurinck R	2005	NeuroImage	24	fMRI	23	24M	Rotation of 3D tool images	Rotation > Control (fixed-paced)	10
								Rotation > Control (self-paced)	6
Suchan B	2002	Behavioural Brain Research	10	PET	28.9	4M 6F	Rotation of 2D matrices	Main effect rotation	14
								Simultaneous matrix rotation > Simultaneous matrix comparison	8
								Successive matrix rotation > Successive matrix comparison	5
Thomsen T	2000	Medical Science Monitor	11	fMRI	30	5M 6F	Rotation of 3D objects	Main effect of stimulus	4
								3D drawings > 2D control (males)	2
								3D drawings > 2D control (females)	4
Logie R	2011	Neuropsychologia	21	fMRI	20-35	7M 14F	Rotation of 3D objects	Mental rotation > Control	2
Vanrie J	2002	Neuropsychologia	6	fMRI	25.5	3M 3F	Rotation of 3D objects	Invariance > Control	6
								Rotation > Control	8
Vingerhoets G	2001	NeuroImage	10	PET	26	5M 5F	Rotation of 2D abstract shapes	Figures rotation > Figures control	2
Vingerhoets G	2002	NeuroImage	12	fMRI	29	12M	Rotation of 3D tool images	Rotated tools > Non-rotated tools	9
Weiss E M	2003	Neuroscience Letters	20	fMRI		10 M 10 F	Rotation of 3D objects	Rotated images > Control	7
Wilson K D	2006	Perception	7	fMRI	18-23	3M 4F	Rotation of 3D objects and 2D letters	Rotation letters > Control	4
								Rotation objects > Control	7
Wraga M	2003	Brain and Cognition	16	PET	18-39	16M	Rotation of 3D objects	Rotation > Control	6
								Rotation > Control	4
Wraga M	2005	Neuropsychologia	11	fMRI	25	7M 4F	Rotation of 3D objects	Rotation > Control	7

between mental rotation and mathematics is almost exclusively based on paradigms that involve the mental rotation of objects (and not body parts). Thus, in an attempt to better reveal neural correlates of the well-established behavioral relations between mental rotation and mathematics (Mix and Cheng, 2012), we deliberately excluded studies that included rotation of body parts.

Table 2 provides a detailed summary of each study included in the mental rotation meta-analysis, including details on the number of participants per study, type of contrasts run, and the number of foci reported. In total, 28 studies (papers) met the inclusion criteria, providing data on 363 healthy adult participants. These studies included 276 activation foci obtained from 45 contrasts.

5.3. *Symbolic number*

The symbolic number map was initially created in a prior study by Sokolowski et al. (2017a, b). Using the two-step literature search process as outlined above, the authors conducted a meta search for studies on numerical and non-numerical magnitude processing. The key terms used in this search included: “number,” “numeral,” “symbol” “non-symbolic,” “magnitude,” “fMRI,” “PET,” “functional magnetic resonance imaging,” “positron emission topography,” “neuroimage,” “imaging,” “congruent,” “incongruent,” “stroop,” “quantity,” “amount,” “physical size,” “numerical size,” “object size,” “size,” “size interference,” “length,” “duration,” “distance,” and “area”. For the purpose of the current study, we only included studies from the meta-analysis by Sokolowski et al. (2017a,b) that included active and intentional symbolic number processing. Additionally, only studies that included whole numbers were included. As shown in Table 3, the majority of symbolic number studies used a number comparison paradigm where participants were asked to make within category comparisons (large vs. small numbers) or between category comparisons (number vs. size comparison). Studies were excluded if they contained 1) only nonsymbolic number processing or non-numerical magnitude processing, 2) only passive viewing or automatic processing. Notably, the current study (unlike previous basic number processing meta-analyses; Sokolowski et al. (2017a, b) excluded passive viewing tasks in an attempt to more closely align the symbolic number processing map to the novel arithmetic and mental rotation maps (Table 4).

Table 3 provides a detailed summary of each study included in the symbolic number meta-analysis, including details on the number of participants per study, type of contrasts run, and the number of foci reported. In total, 24 studies (papers) met the inclusion criteria, providing data on 396 healthy adult participants. These studies included 229 activation foci obtained from 42 contrasts.

5.4. *Arithmetic*

Combinations of the key terms “arithmetic”, “mental arithmetic”, “problem-solving”, “math”, “arithmetic operations,” “addition”, “subtraction”, “multiplication”, “division,” “mental math” “PET,” “positron emission topography,” “fMRI,” “functional magnetic resonance imaging,” “neuroimaging,” and “imaging” were entered into the search databases. Studies were included if they involved arithmetic with integers and visually presented problem stimuli requiring active responses done on a computer/button press. In effort to create a general map of mental arithmetic all problem types were included (e.g., easy/automatically recalled facts vs. difficult problems involving overt calculation). Moreover, because prior research has revealed distinct brain regions dependent on the operation being performed (e.g., multiplication vs. addition; see Table 3), we included contrasts between operation types. Studies were excluded if they 1) involved arithmetic with fractions and decimals 2) reported only effects relating to arithmetic training. We excluded studies that involved arithmetic with fractions or decimals in an effort to best align the arithmetic and symbolic number maps.

Table 3 provides a detailed summary of each study included in the mental arithmetic meta-analysis, including details on the number of participants per study, type of contrasts run, and the number of foci reported. In total, 31 studies (papers) met the inclusion criteria, providing data on 527 healthy adult participants. These studies included 710 activation foci obtained from 80 contrasts.

5.5. *Analysis procedure*

All analyses were done using GingerALE version 2.3.6, a freely available application by BrainMap (http://www.brainmap.org; Eickoff et al., 2017, 2012, 2009; Turkeltaub et al., 2012).

Preparation of the data to be analyzed in GingerALE was conducted with two programs developed by BrainMap: Scribe (version 3.3) and Sleuth (version 2.4). Scribe was used to code specific study details and input the coordinates (i.e. foci) from all relevant papers that were not already available in BrainMap database. Sleuth was used to select relevant experimental contrasts from papers in the BrainMap database, as well as those we entered into scribe, and create a text-file with foci included in the meta-analyses. Foci were grouped by subject group. Prior to analyses, all foci (coordinates) were converted into a common Talairach space; a process that involved transforming MNI coordinates into Talairach space. This was computed in Sleuth using the Lancaster transformation *icbm2tal* (Laird et al., 2010; Lancaster et al., 2007). Finally, GingerALE used to carry out single dataset meta-analyses for each construct. That is, a 3D map was created for each construct. These single dataset analyses were then used to carry out conjunction and contrast (subtraction) analyses.

5.6. *Single dataset analyses*

The present meta-analysis used activation likelihood estimation (ALE) to examine patterns of brain activity related to basic symbolic number processes, arithmetic, and mental rotation. ALE is used to quantitatively synthesize peak activation locations across many empirical neuroimaging studies in stereotactic coordinates (x, y, z) on normalized and ‘standard’ brain templates (Talairach or MNI). The input for ALE meta-analyses is 3D coordinates of peak activation within an empirical study that are referred to as foci. An ALE analysis involves modeling the foci from contrasts within each study as centers of 3D Gaussian probability distributions (Eickoff et al., 2009). This is done to model the spatial uncertainty associated with coordinate-based point estimates. The ALE algorithm then generates 3D activation maps by finding the maximum of each foci group’s Gaussian (Research Imagining Institute UTHSCSA [RII], 2013). This approach of using the maximum is a non-additive method and was created to deal with problems of within-experiment effects (e.g., see Turkeltaub et al., 2012). More specifically, the ALE algorithm was modified in an effort to prevent the influence of between study differences in the number of within study contrasts; a limitation of earlier ALE meta-analyses (Eickhoff et al., 2009; Turkeltaub et al., 2012). On a related note, ALE accounts for differences in sample sizes between studies by adjusting shape of the Gaussian distribution; larger sample sizes are weighted to have a tighter and taller Gaussian. The 3D activation maps are referred to as pre-ALE Modeled Activation (MA) maps and are generated for each contrast coded for and entered into GingerALE. It is through combining each MA map that a single dataset ALE map is created (RII, 2013). More specifically, the ALE maps are computed as the voxel-wise union of the MA maps across all studies.

GingerALE then creates a null-distribution by randomly redistributing the ALE scores and probability statistics from the activation maps. This procedure results in an analog brain space that shares the same properties as the original data, such as number of foci and sample sizes, but assumes no preferences for the spatial arrangement of the data. The null-distribution is then used to calculate the probability of obtaining statistically meaningful clusters present in the actual data.

Table 3
Summary of studies included in the symbolic number meta-analysis.

1 st Author	Year	Journal	N	Imaging Method	Mean Age	Gender	Tasks (s)	Contrast Name	Location
Ansari D	2005	NeuroReport	12	fMRI	19.8		Comparison	Distance effect (small > large) adults	12
Ansari D	2006	NeuroImage	14	fMRI	21	8F 6M	Comparison Size Congruity	Main effect of distance (small > large)	10
								Main effect of distance in the neutral condition (small > large)	7
Ansari D	2007	Journal of Cognitive Neuroscience	13	fMRI	21.5		Comparison	Conjunction of small and large symbolic number	8
Attout L	2014	PLoS ONE	26	fMRI	21	15 F 11M	Order Judgment	Distance effect of numerical order judgment	7
Chen C	2007	NeuroReport	20	fMRI	22.7	10 F 10M	Delayed-number-matching	Unmatched numbers > Matched numbers	8
Chochon F	1999	Journal of Cognitive Neuroscience	8	fMRI	22.3	4F 4M	Naming Comparison	Digit naming > Control	2
								Comparison > Control	13
								Comparison > Digit naming	1
Fias W	2003	Journal of Cognitive Neuroscience	18	PET	23	18M	Comparison	Number comparison vs Nonsymbolic stimuli comparison	13
Fias W	2007	Journal of Neuroscience	17	fMRI	20-37	9 F 8M	Comparison	(Number comparison-number dimming) – (letter comparison-letter dimming)	3
Franklin M S	2009	Journal of Cognitive Neuroscience	17	fMRI	21.8	10 F 7M	Ordering Task	Magnitude near > Far (common regions with order near > far)	1
								Order far > Near (common regions with magnitude near > far)	1
								Magnitude near > Far (unique regions)	3
								Order far > near (unique regions)	1
Fulbright R K	2003	American Journal of Neuroradiology	19	fMRI	24	8F 11M	Order Identification	Number > Shapes	0
								Far order number vs. Near order number	0
He L	2013	Cerebral Cortex	20	fMRI	21	8F 12M	Comparison	Symbolic > Nonsymbolic	2
								Digit-digit > Cross notation trials	1
								Overlap between (symbolic > nonsymbolic) and (small > large)	2
Holloway I D	2010	NeuroImage	19	fMRI	23.5	10 F 9M	Comparison	(symbolic – control) – (non-symbolic – control)	2
Kadosh R C	2005	Neuropsychologia	15	fMRI	28	7F 8M	Comparison	Numerical vs. Size	7
								Numerical vs. Luminance	8
								Numerical distance	3
Kadosh R C	2007	Journal of Cognitive Neuroscience	14	fMRI	25.6	9 F 5M	Comparison	Numerical comparison task: Incongruent vs. Congruent	2
Kaufmann L	2005	NeuroImage	17	fMRI	31	7F 10M	Stroop	Numerical comparison > physical comparison	5
								Numerical comparison (Distance 1 > Distance 4, only neutral trials)	5
								Physical comparison (incongruent trials > congruent trials)	0
Le Clec'H G	2000	NeuroImage	5	fMRI	37	5M	Compare to 12	Numbers > Body parts (Block)	4
			6	fMRI	27	3F 3M	Compare to 12	Numbers > Body parts (ER)	3
Liu X	2006	Journal of Cognitive Neuroscience	12	fMRI	18-45	7F 5M	Stroop	Distance of 18 vs. Distance of 27	6
Lyons IM	2013	Journal of Neuroscience	33	fMRI	18-22	16 F 17M	Comparison	Symbolic: Number ordinal > Luminance symbolic ordinal	3
								Symbolic ordinal > Luminance ordinal (symbolic) and Symbolic cardinal > Luminance cardinal (symbolic)	10
Park J	2012	Journal of Cognitive Neuroscience	20	fMRI	23.4	11 F 9M	Visual matching task	Number > Letter	1
Pesenti M	2000	Journal of Cognitive Neuroscience	8	PET	21-29	8M	Comparison	Number comparison > Number control (orientation judgement)	7
Pinel P	2004	Neuron	15	fMRI	24	18 F 6M	Stroop	Number comparison vs. Size comparison	5
								Number comparison small distance vs. Number Comparison large distance	3
Robertson B D	2015	NeuroImage	16	fMRI	23	8F 8M	Comparison	Incongruent – Congruent contrast	34
Tang J	2006	Journal of Cognitive Neuroscience	18	fMRI	25	7F 11M	Comparison	Numerical > Physical	10
								Physical task conflict trials > Physical task non-conflict trials	1
Vogel S E	2013	Neuropsychologia	14	fMRI	25	7F 7M	Number estimation	Number > Control	10
								Number specific activation	5

Table 4
Summary of studies included in the mental arithmetic meta-analysis.

Author	Year	Journal	N	Imaging Method	Mean Age	Gender	Tasks	Contrast Name	Location
Andres M	2011	NeuroImage	10	fMRI	21	10M	Subtraction and multiplication of Hindu-Arabic digits	Multiply and subtract	8
								Multiply > Subtract	7
Andres M	2012	NeuroImage	18	fMRI	21.3	18M	Subtraction and multiplication of Hindu-Arabic digits	Arithmetic > Letter reading	5
								Multiplication > Subtraction	2
Chochon F	1999	Journal of Cognitive Neuroscience	8	fMRI	20-30	4M 4F	Subtraction and multiplication of Hindu-Arabic digits	Multiplication > Control	12
								Subtraction > Control	14
								Multiplication > Digit naming	4
								Multiplication > Comparison	1
								Subtraction > Digit naming	11
								Subtraction > Comparison	13
								Subtraction > Multiplication	4
De Visscher A	2015	NeuroImage	20	fMRI	29	10 M 10 F	Multiplication of Hindu-Arabic digits	Retrieval > Non-retrieval	7
								Non-retrieval > Retrieval	7
Delazer M	2003	Cognitive Brain Research	13	fMRI	30.5	7M 6F	Complex multiplication (2 digit times 1 digit) and fact retrieval multiplication (1 digit times 1 digit)	Retrieval > Number matching	14
								Untrained complex multiplication > Number matching	13
Fehr T	2007	Brain Research	11	fMRI	26.8	5M 6F	1 and 2-digit addition, subtraction and multiplication	Addition complex > Addition simple (A)	17
								Subtraction complex > Subtraction simple (B)	18
								Multiplication complex > Multiplication simple (C)	9
								Division complex > Division simple (D)	15
								Conjunction (A + B + C + D)	8
Fehr T	2010	Neuropsychologia	11	fMRI	26.8	5M 6F	1 and 2-digit addition, subtraction and multiplication	Control Group: Complex > Simple (B)	18
Grabner R H	2007	NeuroImage	25	fMRI	25.7	25 M	1 and 2 digit multiplication	Multi-Digit > Single-Digit	15
								Single-Digit > Multi-Digit	1
Grabner R H	2009	Human Brain Mapping	28	fMRI	26.9	28M	Multiplication of Hindu-Arabic digits	Multiplication > Figural-spatial, untrained	2
Grabner R H	2009	Neuropsychologia	28	fMRI	26.9	28M	Addition, subtraction, multiplication and division of Hindu-Arabic digits	Retrieval > Procedural	1
								Procedural > Retrieval	9
Gruber O	2001	Cerebral Cortex	6	fMRI	25.8	6M	Multiplication of Hindu-Arabic digits	Compound number calculation > Result matching	7
								Simple number calculation > Result matching	8
Gullick M M	2014	Human Brain Mapping	24	fMRI	19	12 M 12F	Addition and subtraction of positive and negative integers	Positive operand problems > Negative-operand problems	7
								Negative operand problems > Positive operand problems	8
								Addition problems > Subtraction problems	1
								Subtraction problems > Addition problems	11
Hayashi N	2000	Journal of the Neurological Sciences	10	PET	26.2	10M	Serial number subtraction and multiplication	Subtra-task > Count-task	5
								Multi-task > Count-task	4
Hugdahl K	2004	American Journal of Psychiatry	12	fMRI	31	5M 7F	Addition of Hindu-Arabic digits	Mental Arithmetic – Vigilance, healthy subjects	4
Ischebeck A	2006	NeuroImage	12	fMRI	26.8	4M 8F	Subtraction and multiplication of Arabic digits	Multiplication untrained > Number matching	13
								Subtraction untrained > Number matching	21
Jost K	2009	NeuroImage	16	fMRI	24.5	6M 10 F	Single digit multiplication	Small multiplication > Storage	16
								Large multiplication > Small multiplication	8
								Small multiplication > Large multiplication	1
								Small multiplication > Zero multiplication	1
								Small multiplication > storage, Large multiplication > storage, Zero multiplication > storage	12

(continued on next page)

Table 4 (*continued*)

Author	Year	Journal	N	Imaging Method	Mean Age	Gender	Tasks	Contrast Name	Location
Keller K	2009	NeuroImage	49	fMRI	23.99	24 M 25F	Addition and subtraction in 3 operand equations	Conjunction (males and females) (Calculation – identification)	9
Knops A	2017	NeuroImage	17	fMRI	24.9	8M 9 F	Addition and subtraction of Hindu-Arabic digits	Subtraction > Addition	10
Kong J	2005	Cognitive Brain Research	16	fMRI	28	7M 9 F	Addition and subtraction of double digits	Main effect of arithmetic type (subtraction > addition)	5
								Main effect of procedure complexity (with carrying > without carrying)	4
Kuo B C	2008	Brain Research	11	fMRI	21-29	6M 6F	Single or dual addition and subtraction	Single addition > Baseline	13
								Single subtraction > Baseline	17
								Dual addition > Baseline	15
								Dual subtraction > Baseline	21
								Dual operation > Baseline	26
Lee K M	2000	Annals of Neurology	11	fMRI	25-35	6M 5F	Subtraction and multiplication of Hindu-Arabic digits	Multiplication > Subtraction	6
								Subtraction > Multiplication	8
Menon V	2000	Neuroimaging	16	fMRI	20.28	8M 8F	2 and 3 operand equations	3s 3-operand equations > Control equations	16
								3s 2-operand > Control equations	6
								6s 3-operand equations > Control equations	5
								6s 2-operand equations > Control equations	0
								Main effect, operands	3
Pesenti M	2000	Journal of Cognitive Neuroscience	8	PET	21-29	8M	Single digit addition	Addition > Comparison	2
								Addition > Orientation, characters (masked with addition > rest)	5
Rosenberg Lee M	2011	Neuropsychologia	20	fMRI	23.9	11 M 9 F	Addition, subtraction, multiplication and division of Hindu-Arabic digits	Subtraction: Calculation > Identification	5
								Multiplication: Calculation > Identification	6
								Division: Calculation > Identification	6
Soylu F	2017	Cognitive Processing	13	fMRI	24.67	7M 6F	1 and 2-digit addition	Main effect of addition difficulty (two digit > single digit)	4
								Main effect of addition difficulty (One digit > Two digit)	6
Stanescu-Cosson R	2000	Brain	7	fMRI	22-26	3M 4F	Single digit addition and approximation	All calculation > Letter matching	16
								Small numbers > Letter matching	7
Tschentscher N	2014	NeuroImage	26	fMRI		13 M 13F	1 and 2-digit addition and multiplication	Arithmetic fact retrieval > Procedural strategies	6
								Procedural strategies > Arithmetic fact retrieval	7
van der Ven F	2016	Brain Research	23	fMRI	21.04	8M 15F	Addition and subtraction of Hindu-Arabic digits	[(Arabic addition > Arabic memory) > (Dot addition > Dot memory)]	24
Venkatraman V	2005	Neuropsychologia	10	fMRI	20-25	7M 3F	Single digit addition and approximation	Symbolic exact addition > Control	5
								Symbolic approximate addition > Control	7
								Conjunction (symbolic and nonsymbolic addition, exact and approximate)	5
Zago L	2001	NeuroImage	6	PET	21	6M	1 and 2-digit multiplication	Retrieve > Read	7
								Compute > Read	14
								Compute and retrieve > Read conjunction	14
								Compute > Retrieve masked by compute > Read	15
Zarnhofer S	2012	Behavioral and Brain Functions	42	fMRI	23	20 M 21F	Subtraction and multiplication of Hindu-Arabic digits	Retrieve > Compute masked by retrieve > Read	2
								Subtraction > Multiplication	13
								Multiplication > Subtraction	8

Table 5
Mental rotation single dataset analyses.

	Anatomical Labels							
Cluster #	Talairach Daemon	Anatomy Toolbox	BA	X	Y	Z	ALE	Vol/mm3
1	R. Precuneus	hIP3 (IPS)	7	24	−60	48	0.029	12528
	R. Inferior Parietal Lobule	hIP2 (IPS)	40	36	−42	40	0.026	
	R. Precuneus	Area 7 (SPL)	7	20	−66	44	0.026	
	R. Superior Parietal Lobule	Area 5l (SPL)	7	16	−60	58	0.021	
	R. Precuneus	R. Middle Occipital	19	28	−74	30	0.020	
	R. Superior Occipital Gyrus	R. Middle Occipital	19	32	−70	22	0.016	
	R. Superior Parietal Lobule	Area 7PC (SPL)	7	24	−56	60	0.016	
	R. Inferior Parietal Lobule	hIP3 (IPS)	40	36	−48	50	0.016	
2	L. Superior Parietal Lobule	Area 7PC (SPL)	7	−28	−60	54	0.025	6568
	L. Precuneus	Area 7A (SPL)	7	−18	−64	46	0.020	
	L. Precuneus	L. Inferior Parietal	19	−28	−72	38	0.019	
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−14	−62	56	0.018	
	L. Precuneus	L. Superior Parietal	7	−18	−76	42	0.014	
	L. Precuneus	L. Middle Occipital	31	−24	−76	26	0.013	
3	L. Inferior Parietal Lobule	Area 2	40	−40	−40	50	0.027	2408
4	L. Middle Frontal Gyrus	L. Middle Frontal	6	−26	−2	60	0.024	2216
	L. Sub-Gyral	L. Middle Frontal	6	−24	−2	54	0.021	
	L. Middle Frontal Gyrus	L. Middle Frontal	6	−34	2	50	0.013	
5	R. Middle Frontal Gyrus	R. Middle Frontal	6	26	−8	52	0.024	2064
	R. Middle Frontal Gyrus	R. Superior Frontal	6	26	0	62	0.016	
6	L. Middle Frontal Gyrus	L. IFG	46	−42	18	22	0.016	928
	L. Middle Frontal Gyrus	Area 44	9	−52	4	32	0.014	

More specifically, the ALE algorithm performs a random-effects significance test and determines whether the clustering of converging areas of activity across contrasts is greater than chance. This process results in a parametric 3D map of the data along with the associated p-values.

Once the p-value image has been obtained, it is then used to set a significance threshold on the ALE scores (RII, 2013). In the present study, we used the recommended cluster-forming uncorrected threshold of $p < .001$ and the cluster-level corrected threshold of $p < .05$, obtained from running 1000 threshold permutations (Eickhoff et al., 2012; RII, 2013). This approach addresses the issue of multiple-comparisons through family-wise error (FEW) correction and has been found to provide optimal compromise between sensitivity and specificity (Eickoff et al., 2017).

Lastly, GingerALE generates a list of anatomical regions (clusters) that have passed the selected thresholds. GingerALE also provides the following statistics for each cluster identified: volume (mm^3), bounds, weighted center, and the locations and values at peaks within the region. Anatomical labels are also provided for each cluster using Talairach Daemon (talairach.org). In order to visualize the results (i.e., each cluster), we used a combination of Mango (RII, 2013) and the BrainNet toolbox for MATLAB (Xia et al., 2013). To supplement the anatomical labels provided by Talairach Daemon, we also report on the MNI labels provided in Anatomy Toolbox v2.2c (Eickhoff et al., 2017). This allowed us to more narrowly define certain anatomical regions, such as gyri, sulci, and even sulci subdivisions.

5.7. Conjunction and contrast analyses

Conjunction and contrast analyses were conducted in GingerALE and used to identify overlapping and distinct brain regions associated with symbolic number, arithmetic, and mental rotation. The single dataset ALE maps described above provided the bases for these analyses. We used an uncorrected threshold of $p < .01$ with 5000 threshold permutations and a minimum cluster volume of 50 mm^3. Note that the cluster-level correction used to produce the single dataset ALE maps (reported above), is not available for conjunction and contrast analyses. The choice to use a threshold of $p < .01$ was based on its use in prior meta-analyses (e.g., see Pollack and Ashby, 2018; Sokolowski et al. (2017a, b). Moreover, the use of $p < .01$ is appropriate given that the clusters used for conjunction and contrast analyses have already passed the strict cluster thresholds used to make the single data ALE maps.

Conjunction analyses were conducted in a pairwise fashion to compare regions of overlap amongst all three cognitive constructs. For each conjunction analysis, ALE uses the single dataset ALE maps for each construct of interest (e.g., symbolic number and mental rotation) and looks for voxels that are significantly active across both datasets. A conjunction or overlapping region is identified if it passes the statistical thresholds noted above and reaches a minimum size of 50 mm^3. The following three conjunctions were performed: symbolic $\cap$ mental rotation; symbolic $\cap$ arithmetic; mental rotation $\cap$ arithmetic.

Contrast analyses were conducted in order to determine regions of distinct activation between the three constructs. These analyses involved subtracting one single dataset ALE map from another. To conduct the subtraction analyses, ALE first pools the data from across the two studies and then randomly distributes the data into two groupings that are equal in size to the original datasets. One null dataset is then subtracted from the other. The remaining image is then compared to the true data. After a set number of permutations have been performed, a p-value image is created indicating where the true data's values sit on the distribution of values for any given voxel. In the current study, we ran 5000 permutations with an uncorrected threshold of $p < .01$. The following six contrasts were performed: symbolic > mental rotation; symbolic > arithmetic; mental rotation > symbolic; mental rotation > arithmetic; arithmetic > symbolic; arithmetic > mental rotation. To simply the interpretation of ALE contrast images, they are converted into z-scores.

6. Results

6.1. Single dataset meta-analyses

6.1.1. Mental rotation ALE map

The ALE map for mental rotation included 28 individual studies (Table 5) and revealed a six clusters of convergent brain regions associated with mental rotation performance. From largest to smallest, these regions included the right precuneus (hIP3), left superior parietal lobe, left inferior parietal lobe, left middle frontal gyrus, right middle frontal gyrus, and left middle frontal gyrus (Fig. 2; see Table 5 for

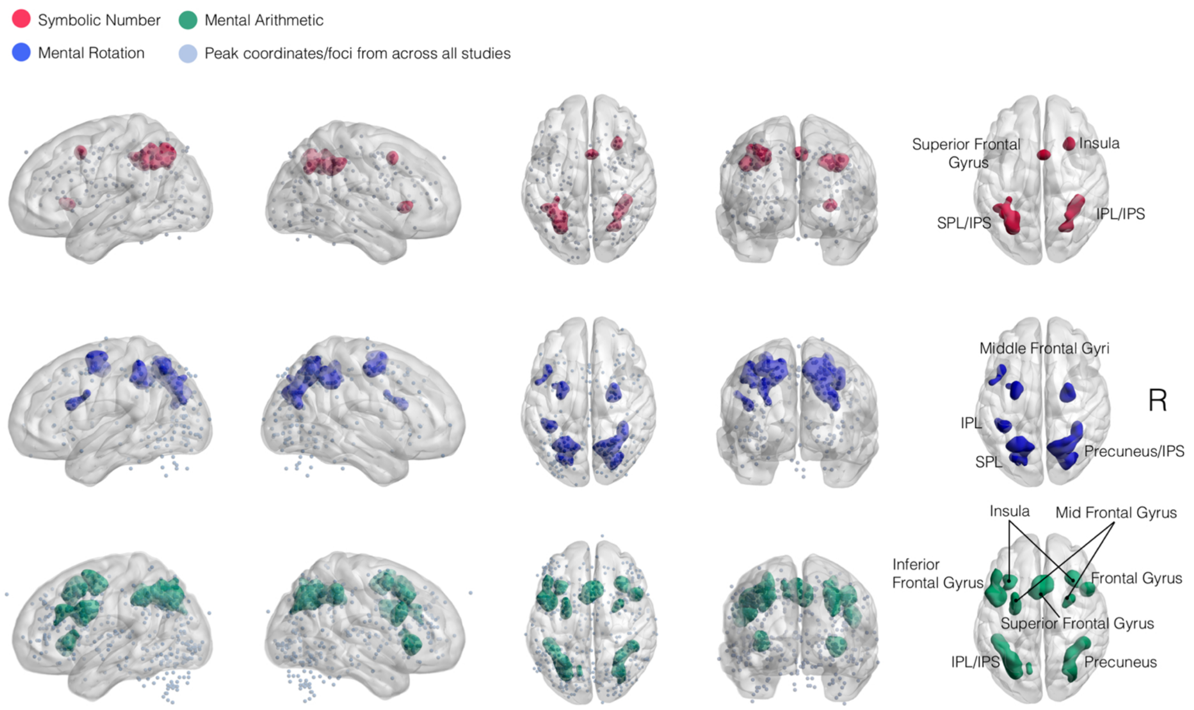

Fig. 2. Single dataset ALE maps for each cognitive construct of interest.

details). In sum, mental rotation was associated with neural activity in the bilateral parietal and frontal regions, with the largest regions of convergence in the right IPS.

6.1.2. *Symbolic number ALE map*

The ALE map for basic symbolic number skills included 24 individual studies (Table 6) and revealed four clusters of convergent brain regions associated with symbolic number processing. From largest to smallest, these regions included the left superior parietal lobule, right inferior parietal lobe (IPS), right superior frontal gyrus, and right insula (Fig. 2; see Table 6 for details). In sum, symbolic number processing was associated bilateral parietal activity and right frontal activity.

6.1.3. *Mental arithmetic ALE map*

The ALE map for mental arithmetic included 31 individual studies (Table 7) and revealed nine clusters of convergent brain regions associated with mental arithmetic. From largest to smallest, these regions included the left inferior parietal lobule (hIP3), right precuneus, left inferior frontal gyrus, left superior frontal gyrus, left insula, right insula, right middle frontal gyrus, left middle frontal gyrus, and right subgyral. (Fig. 2; see Table 7 for details). In sum, mental arithmetic was associated with neural activity in the left IPS and a host of bilateral parietal and frontal regions.

6.1.4. *Summary of single dataset meta-analyses*

All three cognitive tasks were associated with brain activity in fronto-parietal cortex (see Fig. 3). More specifically, for all three tasks the largest region of convergence was found in the IPS as well as neighboring regions including the inferior and superior parietal lobes. Additionally, all three tasks were associated with frontal activity.

6.1.5. *Conjunction and contrast analyses*

Conjunction and contrast analyses were computed to identify regions of brain activation that were overlapping and distinct for mental rotation, arithmetic, and symbolic number processing. Each conjunction and contrast analysis was carried out through a series of pairwise comparisons. All reported results were statistically significant at an uncorrected threshold of $p < .01$.

6.1.6. *Conjunction and Contrast ALE maps: Mental rotation and symbolic number*

The conjunction analysis for mental rotation and symbolic number

Table 6
Symbolic number single dataset analyses.

	Anatomical Labels							
Cluster #	Talairach Daemon	Anatomy Toolbox	BA	X	Y	Z	ALE	Vol/mm3
1	L. Superior Parietal Lobule	L. Superior Parietal	7	−26	−54	42	0.022	6248
	L. Superior Parietal Lobule	hIP3 (IPS)	7	−28	−58	42	0.022	
	L. Supramarginal Gyrus	hIP2 (IPS)	40	−42	−44	36	0.018	
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−28	−66	46	0.018	
	L. Inferior Parietal Lobule	Area 7PC (SPL)	40	−38	−50	50	0.017	
	L. Inferior Parietal Lobule	hIP1 (IPS)	40	−34	−52	36	0.016	
	L. Inferior Parietal Lobule	Area 2	40	−32	−38	44	0.014	
2	R. Inferior Parietal Lobule	hIP1 (IPS)	40	34	−44	38	0.031	4768
	R. Precuneus	R. Angular Gyrus	7	28	−64	38	0.024	
3	R. Superior Frontal Gyrus	R. Posterior-Medial	6	2	10	48	0.021	968
4	R. Insula	R. Insula		30	20	2	0.021	904

Table 7
Mental arithmetic single dataset analyses.

	Anatomical Labels							
Cluster #	Talairach Daemon	Anatomy Toolbox	BA	X	Y	Z	ALE	Vol/mm3
1	L. Inferior Parietal Lobule	hIP3 (IPS)	7	−30	−56	42	0.051	12144
	L. Superior Parietal Lobule	hIP3 (IPS)	7	−28	−62	44	0.048	
	L. Inferior Parietal Lobule	Area PFt (IPL)	40	−44	−38	40	0.038	
	L. Inferior Parietal Lobule	L. Inferior Parietal	40	−40	−44	42	0.031	
	L. Precuneus	Area 7A (SPL)	7	−12	−64	50	0.023	
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−12	−70	54	0.022	
2	R. Precuneus	R. Angular Gyrus	19	30	−66	40	0.046	9680
	R. Inferior Parietal Lobule	hIP2 (IPS)	40	42	−42	44	0.041	
	R. Inferior Parietal Lobule	hIP3 (IPS)	40	34	−50	42	0.036	
3	L. Inferior Frontal Gyrus	L. IFG	9	−44	6	28	0.069	7024
	L. Middle Frontal Gyrus	L. IFG	9	−46	26	30	0.027	
4	L. Superior Frontal Gyrus	L. Posterior-Medial	6	−2	14	50	0.033	5952
	L. Superior Frontal Gyrus	R. Superior Medial	8	0	18	48	0.032	
5	L. Insula	L. IFG	47	−32	24	2	0.036	2440
6	R. Insula	R. IFG	47	32	24	0	0.038	2328
7	R. Middle Frontal Gyrus	Area 45	9	48	14	26	0.032	2232
8	L. Middle Frontal Gyrus	L. Middle Frontal	6	−26	−6	52	0.025	1936
	L. Middle Frontal Gyrus	L. Middle Frontal	6	−26	6	60	0.023	
9	R. Sub-Gyral	R. Middle Frontal	6	28	2	52	0.021	912

revealed five brain regions that were activated by both cognitive processes, including the right inferior parietal lobule (IPS), the left superior parietal lobule, the left inferior parietal lobule (IPS), and two separate regions of the precuneus (Fig. 4; Table 8).

Contrast analyses revealed several brain regions that were specific to mental rotation (i.e., mental rotation > number), including the right precuneus, left middle frontal gyrus, left precuneus, right precuneus, right superior frontal gyrus, and the left cuneus (Fig. 4; Table 8). Regions that were specific to number (i.e., number > mental rotation) included the left inferior parietal lobule (hIP3) and right claustrum/insula (Fig. 4; Table 8).

These analyses highlight that both mental rotation and symbolic number processing were associated with overlapping brain activity in around the parietal lobe. However, each construct was also sub-served by specific distinct regions within the parietal lobe. Additionally, mental rotation was associated with frontal activation in the superior and middle frontal gyri.

6.1.7. Conjunction and Contrast ALE maps: Mental rotation and mental arithmetic

The conjunction analysis for mental rotation and mental arithmetic revealed six brain regions that were activated by both cognitive processes. From largest to smallest, these regions included the right precuneus (hIP3), left superior parietal lobule, left inferior parietal lobule, left sub-gyral, left middle frontal gyrus, and right sub-gyral (Fig. 4; Table 9).

Contrast analyses identified brain regions that were specifically related to mental rotation (i.e., mental rotation > mental arithmetic) including, the right superior parietal lobule, two separated regions of the right precuneus, and the left postcentral gyrus (Fig. 4; Table 9). Contrast analyses also identified brain regions that were specifically related to mental arithmetic (i.e., mental arithmetic > mental rotation) including the left inferior frontal gyrus, left precuneus/angular gyrus, right precuneus, right inferior parietal lobule, right insula, left claustrum, right medial frontal gyrus, left medial frontal gyrus, right middle frontal gyrus, left inferior parietal lobe (hIP2), left inferior frontal gyrus, and left middle frontal gyrus (Fig. 4; Table 9).

Together, these conjunction and contrast analyses revealed that mental rotation and mental arithmetic were associated with overlapping brain activity in regions associated with the fronto-parietal network. However, each task was also associated with distinct activity in the parietal lobe and in the case of mental arithmetic, regions in the frontal lobe as well.

6.1.8. Conjunction and Contrast ALE maps: Mental arithmetic and symbolic number

Results of the conjunction analysis for mental arithmetic and symbolic number revealed five brain regions that were activated by both tasks. These regions included large bilateral regions of the superior and inferior parietal lobes, including the IPS, right insula, and the left superior frontal gyrus (Fig. 4; Table 10).

Contrast analyses identified brain regions specifically related to mental arithmetic ((i.e., mental arithmetic > symbolic number), including the left inferior frontal gyrus, left medial frontal gyrus, right precuneus, right inferior parietal lobule, left sub-gyral regions, left precuneus, left claustrum, left inferior parietal lobule, right inferior frontal gyrus, right middle frontal gyrus, left middle frontal gyrus, left

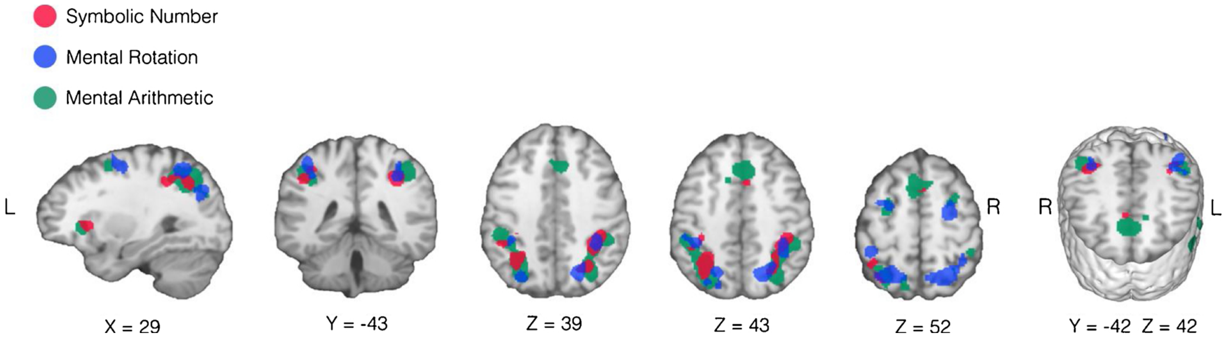

Fig. 3. Qualitative map of overlapping ALE maps for each cognitive process.

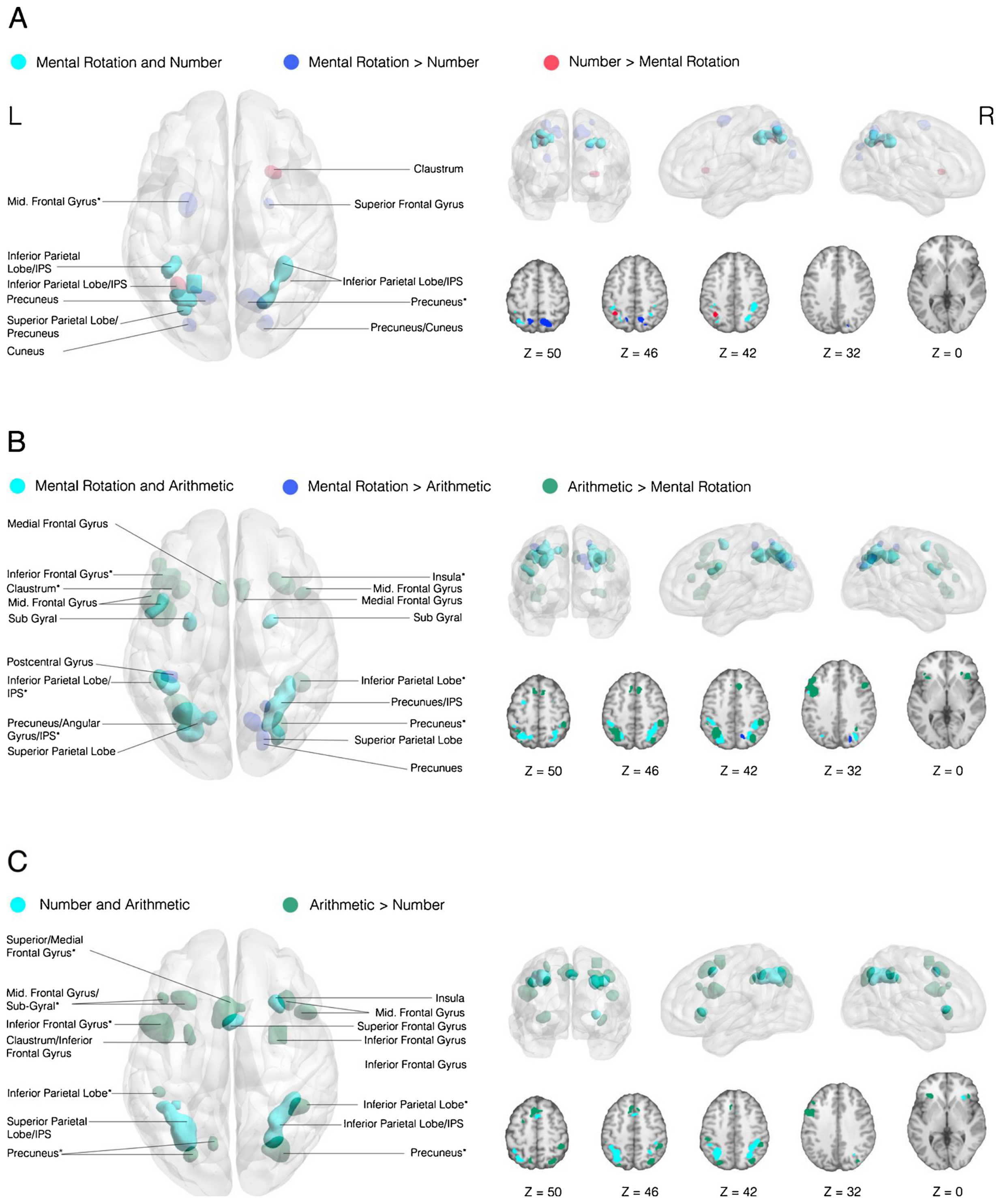

Fig. 4. Brain regions associated with the conjunction and contrast analyses. Note: * indicates regions that passed the uncorrected threshold of $p < .001$.

precuneus, and another region of the right middle frontal gyrus. No brain regions were specifically activated during symbolic number processing that were not also activated during arithmetic (i.e., number > mental arithmetic).

Therefore, mental arithmetic and symbolic number were associated with large overlapping regions in the bilateral parietal lobes, including all embankments of the IPS (i.e., hIP1-3). Mental arithmetic was also associated with distinct brain activity in a number of regions in the fronto-parietal network. There was no distinct brain associated with symbolic number.

7. Discussion

This study was designed to achieve two goals. First, we aimed to reveal the locations of brain regions associated with neural activity across three key aspects of mathematical thinking: Basic symbolic number processing, mental arithmetic, and spatial reasoning (mental rotation). Second, we aimed to go beyond identifying the locations of these processes, by also testing theoretically-informed predictions as to when, why, and where we should expect to see cognitively-defined associations and dissociations between numerical and spatial

Table 8
Conjunction and contrast analyses (mental rotation, number).

	Anatomical Labels							
Cluster #	Talairach Daemon	Anatomy Toolbox	BA	X	Y	Z	ALE	Vol/mm3
Mental rotation and Number								
1	R. Inferior Parietal Lobule	hIP2 (IPS)	40	36	−42	40	0.026	2264
	R. Superior Parietal Lobule	hIP3 (IPS)	7	26	−62	42	0.019	
	R. Superior Parietal Lobule	hIP3 (IPS)	7	30	−54	44	0.013	
2	L. Superior Parietal Lobule	Area 7A (SPL)	7	−32	−62	50	0.014	736
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−22	−66	46	0.014	
	L. Superior Parietal Lobule	L. Superior Parietal	7	−24	−58	46	0.013	
3	L. Inferior Parietal Lobule	Area 2	40	−36	−44	46	0.014	568
	L. Inferior Parietal Lobule	hIP3 (IPS)	40	−38	−44	40	0.013	
4	L. Precuneus	L. Superior Parietal	19	−28	−68	42	0.013	88
5	L. Precuneus	Area 5 L (SPL)	7	−22	−54	46	0.011	16
Mental rotation > Number								
1	R. Precuneus	Area 7A (SPL)	7	14.5	−64.1	52	3.54	1984
	R. Precuneus	R. Precuneus	7	8	−60.8	53.2	3.35	
	R. Precuneus	Area 7A (SPL)	7	20	−72	48	2.85	
2	L. Middle Frontal Gyrus	L. Middle Frontal	6	−28.2	2.3	63	2.95	1160
	L. Middle Frontal Gyrus	L. Superior Frontal	6	−22	−6	61	2.62	
3	L. Precuneus	L. Precuneus	7	−14	−61	52	3.35	1152
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−10	−64	58	3.04	
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−14	−62	58	2.91	
4	R. Precuneus	R. Superior Occipital	19	24	−78	38	2.91	288
	R. Cuneus	R. Superior Occipital	7	26	−82	36	2.77	
	R. Precuneus	R. Superior Occipital	6	18	−78	34	2.62	
5	R. Superior Frontal Gyrus	R. Superior Frontal	19	26	−2	64	2.67	88
6	L. Cuneus	L. Superior Occipital		−26	−80	24	3.09	64
Number > Mental Rotation								
1	L. Inferior Parietal Lobule	hIP3 (IPS)	40	−32	−54	44	2.88	376
2	R. Claustrum	unknown area		30	16	6	2.47	56
	R. Claustrum	unknown area		26.7	19.3	6	2.37	

Note: Bolded numbers represent clusters that passed the uncorrected threshold of $p < .001$ whereas un-bolded number indicate cluster regions significant at $p < .01$.

processing (see Fig. 1 and Table 1). Specifically, given the common need to engage in mental manipulation, we predicted overlap in brain regions subserving this shared process between mental arithmetic and mental rotation. Using similar logic, we aimed to reveal regions more sensitive to symbolic number processing by comparing neural activity common to symbolic number and arithmetic processes, but not mental rotation. Examining these three processes provided a means to examine the representation versus manipulation of numerical information in the brain. Moreover, by also studying the neural correlates of mental rotation, we were able to better pinpoint specific points of convergence and divergence between spatial and numerical processing.

Overall, results of the current quantitative meta-analyses revealed considerable overlap across mental rotation, arithmetic, and symbolic number processing in bilateral regions along the parietal lobe. This was apparent through a qualitative comparison of the meta-analytic ALE maps for each cognitive task (i.e., single dataset meta-analyses), but critically, further revealed through quantitative conjunction analyses. More specifically, the IPS was found to be the largest and most consistent region of overlap across all three cognitive tasks. Whereas the left IPS was the largest region of activation for symbolic number and arithmetic, the right IPS was the largest region of activation for mental rotation. The neighboring regions of the inferior and superior parietal lobules were also common to all three tasks. In addition, mental rotation and mental arithmetic were also associated with overlapping frontal regions, namely the middle frontal gyrus.

The results of the contrast analyses revealed several distinct regions of activity associated with each task. Despite widespread regions of overlap in the bilateral parietal lobes, all three tasks were also found to activate distinct activity in nearby parietal regions. Bilateral regions of the inferior parietal lobes, including the left IPS, were more active for symbolic number processing, including arithmetic, compared to mental rotation. Compared to symbolic number and arithmetic processes, mental rotation was associated with greater activity in the right precuneus. Regions common to both mental manipulation tasks (i.e., mental arithmetic and mental rotation), but not basic symbolic number processes, included the middle frontal gyrus. Lastly, compared to basic numerical processes and mental rotation, mental arithmetic was associated with a host of unique regions in both frontal and parietal regions.

In summary, our findings indicate that the performance of symbolic number processing, mental arithmetic, and mental rotation are all associated with widespread activity in the bilateral parietal lobes. Mental rotation and mental arithmetic were also associated with common frontal activity in the left middle frontal gyrus. Mental arithmetic and symbolic number were associated with common frontal activity in the right insula/claustrum. These findings provide important insight into the neural regions that support mathematical thinking more generally and the neural underpinnings of numerical and spatial reasoning more specifically. In the following sections, we discuss these key findings and offer several theoretical accounts for why spatial and numerical cognition recruit a common bilateral parietal network. We then turn our attention to brains regions found to be more uniquely active for some cognitive operations (e.g., mental manipulation) compared to others (symbolic processing).

8. Brain regions common to all three cognitive tasks

In line with prior research and theory, our findings suggest the parietal lobe is actively engaged during various mathematical tasks (Desco et al., 2011; Matejko and Ansari, 2015). More specifically, the neural activity associated with all three mathematical reasoning domains – symbolic number processing, arithmetic, and mental rotation – were all found to recruit the bilateral IPS and the closely neighboring regions of the inferior and superior parietal lobes. These results challenge domain-specific accounts of the IPS, suggesting instead that the

Table 9
Conjunction and contrast analyses (mental rotation, mental arithmetic).

	Anatomical Labels							
Cluster #	Talairach Daemon	Anatomy Toolbox	BA	X	Y	Z	ALE	Vol/mm3
Mental rotation and Arithmetic								
1	R. Precuneus	hIP3 (IPS)	7	28	−56	48	0.025	3936
	R. Inferior Parietal Lobule	hIP2 (IPS)	40	36	−44	42	0.024	
	R. Superior Parietal Lobule	hIP3 (IPS)	7	26	−62	44	0.022	
	R. Cuneus	R. Middle Occipital	19	30	−76	30	0.019	
2	L. Superior Parietal Lobule	Area 7PC (SPL)	7	−28	−60	52	0.024	2968
	L. Precuneus	L. Inferior Parietal	19	−28	−72	38	0.019	
	L. Precuneus	Area 7A (SPL)	7	−14	−62	50	0.017	
	L. Precuneus	Area 7A (SPL)	7	−18	−74	42	0.013	
3	R. Inferior Parietal Lobule	Area 2	40	−42	−42	48	0.021	1056
4	L. Sub-Gyral	L. Middle Frontal	6	−24	−2	54	0.021	920
	L. Middle Frontal Gyrus	L. Middle Frontal	6	−26	0	58	0.020	
5	L. Middle Frontal Gyrus	L. IFG	9	−42	14	24	0.014	464
	L. Inferior Frontal Gyrus	Area 44	9	−52	4	32	0.014	
6	R. Sub-Gyral	R. Superior Frontal	6	24	−4	54	0.017	248
	R. Sub-Gyral	R. Middle Frontal	6	28	−2	52	0.016	
Mental rotation > Arithmetic								
1	R. Superior Parietal Lobule	Area 7PC (SPL)	7	22	−54	58	2.748	240
2	R. Precuneus	R. Precuneus	7	14	−64	41	2.706	176
3	R. Precuneus	R. Superior Occipital	19	22	−74	34	2.447	112
	R. Cuneus	R. Superior Occipital	19	20	−80	32	2.374	
4	L. Postcentral Gyrus	L. Postcentral Gyrus	40	−36	−36	54	2.536	112
Arithmetic > Mental Rotation								
1	L. Inferior Frontal Gyrus	L. Precentral Gyrus	9	−42.6	6.1	31	3.719	4688
	L. Inferior Frontal Gyrus	Area 44	9	−47.2	1.2	26.8	3.540	
	L. Precentral Gyrus	L. Middle Frontal	9	−44	22	34	3.090	
	L. Middle Frontal Gyrus	L. Middle Frontal	9	−48	22	34	3.036	
	L. Inferior Frontal Gyrus	Area 44	44	−52	8	16	2.989	
	L. Middle Frontal Gyrus	L. Middle Frontal	9	−43	28	34	2.878	
2	L. Precuneus/Angular Gyrus	hIP3 (IPS)	39	−33	−57.5	42.3	3.719	3080
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−30	−68	46	3.156	
3	R. Precuneus	R. Angular Gyrus	19	33.3	−67.1	41	3.719	1528
4	R. Inferior Parietal Lobule	R. Area PF (IPL)	40	47.1	−39.5	43.8	3.719	1400
5	R. Insula	R. Insula	13	33.9	20.9	5.4	3.719	1216
	R. Insula	unknown area	13	28	26	8	3.353	
6	L. Claustrum	L. Insula		−30.7	17.3	6	3.719	1208
	L. Insula	L. Insula	13	−30	20	4	3.540	
7	R. Medial Frontal Gyrus	R. Superior Medial	8	8	20	44	3.036	1040
	R. Cingulate Gyrus	R. MCC	32	10	24	38	2.911	
8	L. Medial Frontal Gyrus	L. Posterior Medial	8	−8	17	50	3.156	744
	L. Medial Frontal Gyrus	L. Superior Medial	8	−8	22	48	3.036	
9	R. Middle Frontal Gyrus	Area 44	9	46.7	18.7	31.3	3.239	680
10	L. Inferior Parietal Lobe	hIP2 (IPS)	40	−44	−42	38	3.353	680
	L. Supramarginal Gyrus	hIP2 (IPS)	40	−48	−40	34	3.239	
	L. Supramarginal Gyrus	hIP2 (IPS)	40	−44	−38	34	3.090	
11	L. Inferior Frontal Gyrus	L. IFG	47	−38	26	0	2.489	64
12	L. Middle Frontal Gyrus	L. IFG	46	−44	36	16	2.948	64

Note: Bolded numbers represent clusters that passed the uncorrected threshold of $p < .001$ whereas un-bolded number indicate cluster regions significant at $p < .01$.

IPS may play a more general role in mathematical cognition.

What explains the observed neural overlap between number, arithmetic, and mental rotation? One explanation is that all three processes are part of a general magnitude system (Walsh, 2003; Leibovich et al., 2017). That is, all three tasks involve making comparisons and judgments about magnitudes. In the case of number and arithmetic, participants are required to reason about discrete and symbolic quantities (numerals 0–9). Mental rotation, however, involves reasoning about continuous relations and degrees of magnitude between objects (e.g., angles of rotation). The common need to reason about quantitative relations between objects (be they symbolic numbers or meaningless objects) may indeed be one reason for the observed overlap. That time and luminance judgments have also been found to consistently activate bilateral parietal regions (e.g., see Walsh, 2003), provides further evidence that a general magnitude system might be at work.

Another way in which number, arithmetic, and mental rotation might be linked is through a common action-based neural network dedicated to perceiving and acting on objects. Critically, this view is not at odds with the general magnitude theory, but aims to extend it through incorporating goal-directed behavior into the account (Walsh, 2003). For example, according to Walsh's 'a theory of magnitude,' space, quantity, and time are all linked through a common metric for action (Walsh, 2003). In this view, numbers and mental rotation stimuli (e.g., 3D cube figures) are alike in that they both represent objects to be acted on. Indeed, there is both theoretical as well as empirical support for the embodied perspective that numbers – although abstract – rely on neural resources specialized for interacting with the physical world (e.g., see Anderson, 2010, 2014; Lakoff and Núñez, 2000; Marghetis et al., 2014). According to the 'neuronal re-cycling hypothesis' (Dehaene and Cohen, 2007), numbers as well as other mathematical symbols, may co-opt or re-use the brain's more ancient and evolutionarily adaptive spatial and sensorimotor systems; systems that originally served the purpose of interacting with tools, objects, and locations in space (Johnson-Frey, 2004; Lakoff and Núñez, 2000; Dehaene et al., 2003). In short, "*we may recycle the brain's spatial prowess to navigate the*

Table 10
Conjunction and contrast analyses (mental arithmetic, number).

	Anatomical Labels							
Cluster #	Talairach Daemon	Anatomy Toolbox	BA	X	Y	Z	ALE	Vol/mm3
Arithmetic and Number								
1	L. Superior Parietal Lobule	L. Superior Parietal	7	−26	−54	42	0.022	4664
	L. Superior Parietal Lobule	hIP3 (IPS)	7	−28	−58	42	0.022	
	L. Supramarginal Gyrus	hIP2 (IPS)	40	−42	−44	36	0.018	
	L. Superior Parietal Lobule	Area 7A (SPL)	7	−28	−66	46	0.018	
	L. Inferior Parietal Lobe	Area 7PC (SPL)	40	−38	−50	50	0.017	
	L. Inferior Parietal Lobe	hIP1 (IPS)	40	−34	−54	36	0.015	
2	R. Inferior Parietal Lobule	hIP2 (IPS)	40	38	−40	40	0.026	3120
	R. Inferior Parietal Lobule	hIP3 (IPS)	40	34	−46	40	0.025	
	R. Precuneus	R. Angular Gyrus	7	28	−64	38	0.024	
3	R. Insula	R. Insula		30	22	2	0.021	520
4	L. Superior Frontal Gyrus	R. Posterior-Medial	6	0	10	48	0.020	520
5	L. Inferior Parietal Lobule	L. Inferior Parietal	40	−34	−42	42	0.011	8
Arithmetic > Number								
1	L. Inferior Frontal Gyrus	Area 44 (IFG)	44	−46.3	8.9	26.6	3.72	3168
2	L. Medial Frontal Gyrus	L. Superior Medial	8	−6.7	22	51.7	3.72	1880
	L. Superior Frontal Gyrus	L. Superior Medial	8	−6.5	18	53	3.54	
	L. Superior Frontal Gyrus	L. Superior Medial	6	−2	18	58	3.35	
	R. Medial Frontal Gyrus	R. Superior Medial	8	6	22	48	2.99	
	L. Cingulate Gyrus	L. Superior Medial	32	−6	24	40	2.60	
3	R. Precuneus	Area PGp (IPL)	19	30.3	−75.3	42.7	3.35	1408
	R. Precuneus	Area PGp (IPL)	19	34	−76	36	3.16	
	R. Precuneus	Area 7A (SPL)	7	24	−71	51	3.04	
4	R. Inferior Parietal Lobule	Area PFm (IPL)	40	42	−46	49	3.54	1000
	R. Inferior Parietal Lobule	Area PFm (IPL)	40	47.8	−44.6	47	3.35	
5	L. Sub-Gyral	L. Middle Frontal	6	−22.5	2.5	55.5	3.54	880
	L. Superior Frontal Gyrus	L. Middle Frontal	6	−24	8	62	3.24	
	L. Middle Frontal Gyrus	L. Middle Frontal	6	−26	0	61	3.09	
6	L. Precuneus	L. Superior Parietal	19	−24	−78	42	3.35	616
	L. Precuneus	L. Superior Parietal	19	−26	−74	36	3.09	
7	L. Claustrum	unknown area		−24	26	2	3.09	472
	L. Claustrum	L. IFG		−24	24	−2	2.99	
	L. Inferior Frontal Gyrus	L. IFG	47	−32	28	−2	2.91	
8	L. Inferior Parietal Lobe	Area 2	40	−46	−34	44	2.67	448
	L. Inferior Parietal Lobe	Area 2	40	−46	−30	38	2.59	
	L. Inferior Parietal Lobe	Area PFt (IPL)	40	−44	−33	34	2.47	
9	R. Inferior Frontal Gyrus	R. IFG	47	39	26	−5	2.91	432
10	R. Middle Frontal Gyrus	Area 45	46	50	20	24	2.88	384
	R. Middle Frontal Gyrus	Area 45	46	46	20	26	2.82	
	R. Middle Frontal Gyrus	R. IFG	46	46	18	22	2.73	
11	L. Middle Frontal Gyrus	L. Middle Frontal	9	−42	25.3	32.7	2.73	248
12	L. Precuneus	Area 7A (SPL)	7	−10	−66	48	2.79	208
	L. Precuneus	Area 7A (SPL)	7	−8	−70	50	2.65	
13	R. Middle Frontal Gyrus	R. Middle Frontal	6	30	2	62	2.73	56
Number > Arithmetic								

Note: Bolded numbers represent clusters that passed the uncorrected threshold of $p < .001$ whereas un-bolded number indicate cluster regions significant at $p < .01$.

abstract mathematical world" (Marghetis et al., 2014, p. 1580).

Taken together, both the 'general magnitude theory' and 'neuronal re-cycling hypothesis' present plausible explanations for the common neural activity observed between all three processes. More specifically, the 'neuronal re-cycling hypothesis' offers a more pointed explanation of why spatial and numerical thinking may recruit common neural substrate.

8.1. Spatial visualization as a key contributor to spatial-numerical relations

The present findings offer an extended possibility for the involvement of spatial processing in performing numerical and mathematical tasks. Although prior research efforts have examined neural relations between lower-level spatial processes, such as making simple comparative judgments involving a variety of spatial magnitudes (e.g., line lengths), the relations between more cognitively demanding visual-spatial reasoning tasks, such as mental rotation, and numerical cognition has yet to be examined. Our findings demonstrate that brain regions associated with mental rotation – a widely accepted proxy for higher-level visual-spatial reasoning – are also activated during numerical and arithmetical reasoning. This finding suggests that the relation between space and number is not limited to lower-level spatial processes, namely magnitude judgements. Instead, our findings hint at the possibility that higher-level spatial skills may be implicated in the formation of numerical-spatial associations. Consistent with prior behavioral findings, including the 'mental number line' hypothesis, spatial visualization skills may play a critical role in mapping number as well as other mathematical entities to space. In other words, one of the ways humans might conceptualize the meaning of numbers and various other mathematical concepts is by visualizing and, through practice, internalizing their inherent visual-spatial relations and structure. Further research is needed to more fully examine this possibility.

9. Distinct brain regions associated with each task

9.1. Brain regions more attuned to symbolic number processing

To gain insight into brain regions potentially underlying symbolic number processing, we carried out conjunction analyses between the symbolic number and arithmetic maps and then contrasted each individual map with the mental rotation map. Based on this logic, we hypothesized that if a symbolic number region exists it should be present in both the symbolic number and arithmetic maps and either absent or present to a much lesser extent in the mental rotation map. This approach yielded evidence that compared to mental rotation, symbolic numerical reasoning, including arithmetic, may be associated with larger regions of activity in the inferior parietal lobes, including the left IPS and regions that appear to overlap with the left angular gyrus. One explanation for this finding might have to do with the relatively ease and automaticity in which individuals are able to access the meaning of numerical symbols and basic operations (e.g., 2 + 1). Prior research indicates that fluency and automatic processing of numbers and arithmetic facts is associated with activity in left lateralized 'language based' regions, namely the left angular gyrus and supramarginal gyrus (Dehaene et al., 2003; Polspoel et al., 2017). The current findings might reflect the neural consequences of learning the symbolic number system and associated arithmetic facts. Compared to mental rotation, symbolic number and arithmetic facts are more likely to be stored as verbally mediated knowledge. This view is in general agreement with Dehaene's triple code model (2003), in which the left angular gyrus is posited as the location where number names and arithmetical facts are stored.

It is worth mentioning that the above findings are based on an uncorrected p-value of 0.01. When the more stringent cut-off is used ($p < .001$), a different pattern of findings emerges. Instead, the data fail to support the presence of regions unique to symbolic number compared to mental rotation. Thus, the above finding of regions more attuned to symbolic number compared to mental rotation should be interpreted with caution. A more parsimonious interpretation of the current meta-analysis is that both numerical and spatial reasoning engage highly similar bilateral regions of the parietal lobe. Evidently, more research is needed to further disentangle whether, when, and how symbolic number processes and visual-spatial reasoning engage distinct neural regions. The findings from these studies may prove useful in advancing theories of symbolic specific regions (triple code model) versus more general multi-purpose theories of cognitive processing (e.g., neuronal recycling and redeployment).

9.2. Brain regions more attuned to mental manipulation

Using the same logic as above, we also aimed to reveal brain regions potentially underlying mental manipulation. That is, we carried out conjunction analyses between the mental arithmetic and mental rotation maps and then contrasted each individual map with the symbolic number map. We reasoned that regions common to mental arithmetic and mental rotation but not symbolic number processing might be indicative of regions related to the general ability to engage in mental manipulation. Results revealed the left middle frontal gyrus as a potential site for mental manipulation. Note that this region survived the stricter threshold of $p < .001$. As outlined earlier, the dorsolateral prefrontal cortex, which is situated in the middle of the middle frontal gyri, is an important region for carrying out top-down executive tasks, such a planning, working memory, inhibition, and abstract reasoning (Owen et al., 2005; Miller and Cummings, 2017; Smith and Jonides, 1999). The current findings provide further evidence that the left middle frontal gyrus may indeed play a role in mental manipulation of information. However, some caution is warranted, as this region has also been associated with a variety of other cognitive tasks including the identification of sound sources (Giordano et al., 2014), imagined grasping (Grafton et al., 1996), and emotional prosody in speech (Mitchell et al., 2003). Thus, as is the case with the IPS, more research is needed to further operationalize the functions associated with this region.

The parietal lobes may also play an important role in the mental manipulation of information. Mental rotation has been found to consistently activate bilateral regions in and around the IPS (Zacks, 2008); a finding that has led some to conclude the IPS plays a critical role in performing visual-spatial transformations (e.g., see Jordan et al., 2001; Seydell-Greenwald et al., 2017; Zacks, 2008). The current study shows that mental arithmetic is associated with activation in some of these same regions. These findings provide preliminary support for the hypothesis put forward by Hubbard et al.: "*parietal mechanisms that are thought to support spatial transformation might be ideally suited to support arithmetic transformations as well*" (2009, pp. 238). An important question moving forward is the extent to which the common overlap in the parietal regions for spatial and arithmetical transformations (as well as other mathematical computations) are due to shared reliance on visual-spatial representations. Is it a coincidence that arithmetic relies on cerebral cortex most strongly associated with visual-spatial reasoning and not the traditional language regions, namely structures in and around the left sylvan fissure (e.g., inferior frontal lobe and temporal regions; Monti et al., 2009)? On the one hand, evidence to date suggests not. There is emerging consensus that arithmetical and mathematical thinking do not appear to be rooted in the neural mechanisms of natural language (Amalric and Dehaene, 2016; Monti et al., 2009). However, the extent to which arithmetic operations are dependent on visual-spatial representations and not some other form of mental representation remains an important research question (e.g., see Marghetis et al., 2014). For example, it is possible that arithmetic is carried out through purely symbolic or propositional processes independent from visual-spatial representations and also distinct from natural language mechanisms. Future research efforts are needed to test the extent to which the parietal regions that subserve visual-spatial transformations also subserve mental operations devoid of visual-spatial referents.

9.3. Brain regions associated with mental arithmetic

Mental arithmetic was associated with widespread frontal activity. Compared to mental rotation and symbolic number, mental arithmetic was associated with significantly more activation in the following frontal regions: left inferior frontal gyrus, left medial frontal gyrus, and right middle frontal gyrus. Based on prior research and as noted above, these regions are likely representative of activity associated with executive control processes (e.g., see Miller and Cummings, 2017). Given that mental rotation is commonly thought to be a highly cognitively demanding task, it is somewhat surprising that mental arithmetic was associated with more widespread frontal activity. In fact, mental rotation was not associated with any frontal activity that was not also engaged by mental arithmetic. This finding is deserving of more attention and perhaps points to differentiated frontal activity more attuned to the manipulation of symbols compared to less culturally defined visual-spatial objects (e.g., 3D cube figures).

The findings of widespread frontal and parietal activity associated with mental arithmetic may be due in part to the decision to include all types of arithmetic problem solving. That is, the arithmetic map includes arithmetical reasoning associated with relatively easy problem types (e.g., 2 + 1) but also difficult problem types (37 + 68 or 3 + 8 – 4). Thus, the arithmetic map includes questions requiring little cognitive effort as well as questions requiring concerted cognitive effort. These differences in the need to recall arithmetic facts compared to need to carryout novel calculations have been found to be associated with common and distinct neural networks (Zamarian et al., 2009). The decision to include all types of arithmetic problems was motivated by our aim to reveal regions associated with both basic symbol processing but also higher-level spatial reasoning (i.e., mental rotation). Although not directly tested, we reasoned that recall-based arithmetic would have more in common with basic symbolic processing and calculation-based arithmetic would have more in common with mental rotation. Thus, in an attempt to avoid such biases, we decided to include all studies on arithmetic processing. A logical next step is to formally test the hypothesis that low-effort arithmetic (recall-based) will share more neural regions associated with basic symbolic processes, while high-effort arithmetic (calculation-based) will share more neural regions associated with higher-level spatial reasoning, such as mental rotation. Such relations would provide additional evidence in favour of the grounded or embodied theories of the space-math link (as mentioned above; also see Mix et al., 2016 for further details). An absence of such relations would require reconsideration of such theories.

9.4. Brain regions associated with mental rotation

In comparison to both numerical reasoning tasks, mental rotation was more associated with activity in the right precuneus/superior parietal lobe. One interpretation of this finding is that the precuneus may play a role in visual-spatial imagery. Indeed, one of the primary functions ascribed to the precuneus is visual-spatial imagery (Cavanna and Trimble, 2006; Fletcher et al., 1995; Oshio et al., 2010). More specifically, the precuneus has been suggested to play a role in directing attention in space and planning and imagining goal-directed movements (Cavanna and Trimble, 2006; Kawashima et al., 1995). However, as evidenced in the present study, the precuneus has been found to be involved in a variety of cognitive tasks, including a pivotal role in the default mode network (Fransson and Marrelec, 2008). Thus, it appears that the precuneus serves a variety of functions, with visual-spatial (motor) imagery potentially being one of them.

Based on prior research, we had expected that we might see the activation of canonical motor regions (e.g., premotor cortex). Instead, we found very little evidence for activation of primary motor cortices. Like symbolic number and mental arithmetic, convergent activation of mental rotation was largely confined to activation in the bilateral parietal lobes. Although prior research has reported that mental rotation is associated with brain activation in motor regions (e.g., see Zacks, 2008), more recent research paints a more complicated picture. A recent meta-analysis suggest that the activation of motor cortex is dependent on experimental stimuli (Tomasino and Gremese, 2016). Mental rotation was found to be correlated with motor activity when the task involved imagining the rotation of body parts but not when it involved the rotation of objects. Thus, our decision to focus on the rotation of objects and to exclude studies that included rotation of body parts is the most probable reason for the absence of observed motor activity.

9.5. Limitations and future directions

Both a strength and a limitation of fMRI meta-analyses is that they provide a broad overview of the neural correlates of cognitive functions. However, by using this technique to ‘see the forest through the trees’ one runs the risks of obscuring important methodological details and findings. The very nature of the meta-analytic method employed – an averaging of peak activation across multiple studies – limits the ability to make specific claims about the findings. Indeed, this process may overestimate the amount of overlap between tasks by averaging across studies and minimizes potentially small, but important, differences across paradigms. For example, our decision to include all types of arithmetic problems, ranging from easy to difficult, may have resulted an arithmetic map that is in fact an average of two relatively distinct maps – one associated with solving simple problems and the other for solving complex problems. While this was a desirable outcome for the current study, it stands as an example of what might be happening more generally across and within fMRI studies. One approach to reduce problems associated with averaging across individuals and studies is the use of within-subject designs. By having the same individual perform multiple tasks (e.g., mental rotation and number comparison), it is possible to examine whether the same voxels are co-activated for different tasks.

At the same time, it is important to recognize that co-activation does not necessarily indicate functional equivalence. To this point, the shared neuronal account has been used as evidence and a potential causal explanation for the widely observed behavioural links between spatial and numerical cognition (e.g., see Cheng and Mix, 2014; Hawes et al., 2015). For example, even though mental rotation, basic numerical competencies, and arithmetic appear to recruit common parietal regions, this does not mean that these regions perform the same functions across all three tasks. Moreover, neither does it indicate that the same region is used for all three tasks within individuals. Thus, going back to the point above, the present study is only able to provide a general overview of common and distinct regions associated with the three targeted cognitive tasks. Whether or not the overlap observed is functionally meaningful remains an open question; ALE meta-analyses do not permit one to evaluate patterns of activation within overlapping regions. Moving forward, more sensitive methods of analyzing fMRI data, including multivariate pattern analyses (MVPA), are needed to better understand ways in which the same brain region(s) performs multiple cognitive functions. To this aim, we see the present meta-analyses as an important first step in demonstrating the engagement of a common parietal network underlying numerical and spatial cognition. We hope the present findings prove a source of motivation to carry out more sensitive studies and analyses in an effort to better understand the complex neural underpinnings of spatial and numerical cognition.

In interpreting the present findings it is worth considering how our decision to include within-category contrasts (e.g., two-digit addition > single-digit addition) may have influenced the results. On the one hand, within-category contrasts provide a stringent control condition, allowing one to optimally control for perceptual features (e.g., visual processing of numerals). On the other hand, our decision to include within-category contrasts may have resulted in the removal of regions more typically associated with other processes, including visual and language processing. For example, with respect to our symbolic number and arithmetic maps, the inclusion of within-category contrasts may have resulted in the removal of lower-level numerical processes (e.g., numeral identification); processes which have recently been shown to correlate with neural activity in the ventral visual pathway, namely the inferior temporal gyrus (ITG; Baek et al., 2018; Grotheer et al., 2018; Pinheiro-Chagas et al., 2018; Yeo et al., 2017). However, the presence of this region has not been consistently detected across studies to date (e.g., see Sokolowski et al., 2017a, b) and appears highly sensitive to task demands and the specificity of the contrasts employed (e.g., see Yeo et al., 2017). Together, these reasons may help explain why we did not see evidence of a “number form area” in the ITG or more wide spread activity in regions typically associated with language processing for arithmetic.

Lastly, we acknowledge that the current study represents but one of many ways in which spatial and mathematical thinking may converge/diverge in the brain. Both spatial and mathematical abilities are not unitary constructs, but skills made up of many different sub-skills (Mix and Cheng, 2012). Thus, in moving forward, it will be of value to study the neural correlations of spatial-mathematical relations beyond the one studied here. For example, an emerging body of research indicates strong relations between spatial scaling abilities (i.e., the ability to relate distances in one space to distances in another space) and mathematical performance across a variety of tasks, including proportional reasoning, number line estimation, and comprehensive tests of school-based mathematics (Frick, 2018; Gilligan et al., 2018; Jirout et al., 2018; Möhring et al., 2018). In short, we have only just begun to scratch the surface of the neural underpinnings of the space-math link. Opportunities to further probe the space-math link are many and varied and represent a promising area for future research.

9.6. Conclusion

Decades of behavioral, neuropsychological, and neuroimaging studies have demonstrated consistent and reliable associations between spatial and numerical processing (Hubbard et al., 2005; Mix and Cheng, 2012; Toomarian and Hubbard, 2018). However, much less is known about why and under what conditions spatial and numerical processes converge and/or diverge from one another (Mix and Cheng, 2012). The present study aimed to narrow this gap in understanding by carrying out the first systematic ALE meta-analysis on brain regions associated with spatial and numerical cognition. Consistent with a shared processing account, we revealed that symbolic number, arithmetic, and mental rotation processes were all associated with bilateral parietal activity. We also found evidence that numerical and arithmetic processing were associated with overlap in the left IPS, whereas mental rotation and arithmetic both showed activity in the left middle frontal gyrus. These patterns suggest regions of cortex potentially more specialized for symbolic number representation and domain-general mental manipulation, respectively. Additionally, arithmetic was associated with unique activity throughout the fronto-parietal network and mental rotation was associated with unique activity in the superior parietal lobe. Taken together, these findings contribute new insights into the neurocognitive mechanisms supporting spatial and numerical thought specifically, and mathematical thought more generally.

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