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Theoretical Contributions

Contributions of functional Magnetic Resonance Imaging (fMRI) to the Study of Numerical Cognition

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Abstract

Using neuroimaging as a lens through which to understand numerical and mathematical cognition has provided both a different and complementary level of analysis to the broader behavioural literature. In particular, functional magnetic resonance imaging (fMRI) has contributed to our understanding of numerical and mathematical processing by testing and expanding existing psychological theories, creating novel hypotheses, and providing converging evidence with behavioural findings. There now exist several examples where fMRI has provided unique insights into the cognitive underpinnings of basic number processing, arithmetic, and higher-level mathematics. In this review, we discuss how fMRI has contributed to five critical questions in the field including: 1) the relationship between symbolic and nonsymbolic processing; 2) whether arithmetic skills are rooted in an understanding of basic numerical concepts; 3) the role of arithmetic strategies in the development of arithmetic skills; 4) whether basic numerical concepts scaffold higher-level mathematical skills; and 5) the neurobiological origins of developmental dyscalculia. In each of these areas, we review how the fMRI literature has both complemented and pushed the boundaries of our knowledge on these central theoretical issues. Finally, we discuss limitations of current approaches and future directions that will hopefully lead to even greater contributions of neuroimaging to our understanding of numerical cognition.

Keywords: fMRI, neuroimaging, numerical cognition, mathematics, dyscalculia, development, brain

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The use of neuroscientific methods has enriched many fields including that of numerical and mathematical cognition. Early work with neuropsychological patients first informed theories of numerical and mathematical processing (e.g. Triple Code Model, Dehaene, 1992; Dehaene & Cohen, 1995), and provided the foundation for later neuroscience research (Cohen Kadosh & Dowker, 2015). The advent of functional brain imaging in the 1990’s not only helped confirm many of the findings obtained from the study of neuropsychological patients, but also expanded existing theories of how numerical and mathematical abilities are processed in the brain. There now exist several examples where functional magnetic resonance imaging (fMRI) has successfully guided psychological theories of numerical and mathematical processes, constrained our understanding of how individuals process numbers, and formed novel and testable hypotheses. In this review, we discuss how fMRI has informed our understanding of numerical and mathematical processing by supporting or expanding existing cognitive theories.

Much fMRI research is now reaching beyond simple localization and is furthering our understanding of the mechanisms underlying numerical and mathematical processes and their developmental trajectories. Functional brain imaging has also provided insights that were not possible, or more difficult, with behavioural measures (e.g. Lyons et al., 2015; Supekar et al., 2013). Furthermore, fMRI has afforded researchers the opportunity to probe questions at a different level of analysis, which complement and converge with theories derived from behavioural research and other neuroscientific methodologies (e.g. neuropsychology, electroencephalography, etc.) Without placing it on a superior level of analysis, using functional brain imaging as a lens through which to understand numerical and mathematical processing can elucidate their underlying processes and can help refine existing theories. Moreover, understanding the neural basis of numerical and mathematical thinking has broader implications for how culturally acquired abilities, such as symbolic number skills, are learned and organized in the human brain and how these skills may be supported by evolutionarily ancient systems (Ansari, 2008; Butterworth & Walsh, 2011).

In the present paper, we review several examples where fMRI has made a significant contribution to the field of numerical and mathematical cognition. In particular, we outline several major questions within numerical cognition and how functional brain imaging uniquely contributed to these questions. We focus our discussion on neuroimaging literature examining typically developing individuals (children and adults), as well as children with learning disabilities in mathematics. Finally, we provide an outlook towards potential future fMRI research in numerical and mathematical cognition.

1) How Are Symbolic and Nonsymbolic Representations of Number Related to one Another?

It is thought that humans possess an evolutionarily ancient system to process numerical magnitudes (i.e. the number of items in a set) (for reviews see: Brannon, 2006; Cantlon, 2012; Gebuis, Cohen Kadosh, & Gevers, 2016; Leibovich, Katzin, Harel, & Henik, 2017). This system is thought to develop early and, consistent with this prediction, it has been shown that young infants can discriminate between non-symbolic numerical magnitudes (dots) (Xu & Spelke, 2000; Xu, Spelke, & Goddard, 2005). This representational system is also thought to be evolutionarily ancient due to a large body of evidence that suggests humans share a basic system for numerical magnitude representation with animals and non-human primates (for a review see Cantlon, 2012).

Symbolic numbers (Arabic digits), however, are a culturally acquired skill and need to be learned. How children learn the meaning of symbolic numbers (Arabic digits), and whether they are associated with nonsymbolic representations of number, has been a subject of significant debate in the field (Gebuis et al., 2016; Leibovich & Ansari, 2016; Leibovich et al., 2017; Merkley, Matejko, & Ansari, 2017; Wang, Odic, Halberda, & Feigenson, 2017). On the one hand, it has been proposed that the symbolic number representations are scaffolded on the evolutionarily ancient nonsymbolic system and that the human brain automatically converts symbolic numbers to quantity-based nonsymbolic representation (Dehaene, Dehaene-Lambertz, & Cohen, 1998). This hypothesis rests, in part, on evidence that performance on numerical discrimination tasks is related to the ratio between the two numbers being compared (smaller number/larger number), and that individuals are slower and less accurate as the ratio between the numbers is larger (Libertus & Brannon, 2009; Piazza, 2010). Because both symbolic and nonsymbolic discrimination tasks demonstrate this ratio effect, it has been inferred that they share a common representation. This hypothesis also makes specific predictions about how symbolic and nonsymbolic magnitude representations are represented in the brain, namely, that they should share the same underlying neural circuitry. On the other hand, another possibility has been posited. Namely, it has been proposed that number symbols are not grounded in nonsymbolic quantities and may have very different underlying neural representations (Cohen Kadosh & Walsh, 2009a; Krajcsi, Lengyel, & Kojouharova, 2016; Leibovich & Ansari, 2016; Leibovich et al., 2017). Indeed, whether symbolic and nonsymbolic formats have abstract representations has been strongly questioned (Cohen Kadosh & Walsh, 2009a). Even though some evidence suggests that symbolic and nonsymbolic tasks activate similar regions within the parietal cortex, the formats may not be represented in the same way within these brain regions (Cohen Kadosh & Walsh, 2009a). Neuroimaging can be used to examine these two different hypotheses concerning the relationship between symbolic and non-symbolic representations of number.

To date, a large body of research has accumulated to suggest that the intraparietal sulcus (IPS) processes numerical magnitudes. This stems from multiple lines of evidence including cases of neuropsychological patients with brain injuries (for a review see: Butterworth, 1999), positron emission tomography (PET) studies, as well as functional magnetic resonance imaging (fMRI) research (for reviews see: Brannon, 2006; Dehaene et al., 2003). Much interest has therefore been focused on how the IPS processes symbolic and nonsymbolic quantities due to multiple lines of evidence suggesting it is a critical region for number processing across formats. The fMRI evidence has been somewhat mixed, with some evidence showing the IPS responds to numerical quantities regardless of the format of presentation, suggesting that symbolic and nonsymbolic quantities have a shared underlying representation (Piazza, Pinel, Le Bihan, & Dehaene, 2007). Other research has found that the IPS has a format-dependent response, providing evidence for multiple or distinct representations (Cohen Kadosh et al., 2011; Cohen Kadosh & Walsh, 2009a; Holloway, Price, & Ansari, 2010). Several studies have also demonstrated that there may be hemispheric differences in the processing of numerical magnitudes in different formats (Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Piazza et al., 2007). For instance, the left IPS may be encoding symbolic numbers with greater precision (Chassy & Grodd, 2012; Piazza et al., 2007), whereas the right IPS may have coarse representation for both symbolic and nonsymbolic notations (Holloway et al., 2010; Piazza et al., 2007). Convergent with these data, a recent meta-analysis also revealed evidence for format-independent activation within the bilateral frontal and parietal cortices for both symbolic and nonsymbolic formats. However, the meta-analysis also suggested that the left parietal cortex is more consistently activated during the processing of symbolic quantities (visually-presented Arabic digits), whereas activity in the right parietal cortex is more reliably correlated with the processing of nonsymbolic formats (Sokolowski, Fias, Mousa, & Ansari, 2017). Collectively, there seem to be both common and distinct regions that process symbolic and nonsymbolic quantities (Holloway et al., 2010; Sokolowski et al., 2017), with some evidence pointing to format-independent (or nonsymbolic) magnitude processing in the right IPS, and symbolic processing in the left IPS (Chassy & Grodd, 2012; Cohen Kadosh et al., 2007; Piazza et al., 2007; Sokolowski et al., 2017).

These findings may initially point to a shared neural representation of symbolic and nonsymbolic quantities, particularly within the IPS. However, these studies are limited in a significant way that curtails the inferences that can be made about format-dependent versus independent processing. In particular, simply demonstrating that two tasks co-activate the same brain region does not imply equivalent processing within that brain region and does not reveal anything about the nature of common activation. One instrumental neuroimaging tool that can begin to disambiguate the representations of symbolic and nonsymbolic processing within the same brain region is Multi-Voxel Pattern Analysis (MVPA). Standard GLM analyses often require that the data be spatially smoothed to increase the sensitivity to a particular task, resulting in brain activity that is averaged across data points (i.e. voxels – three dimensional pixels that are the unit of analysis in fMRI studies) within particular regions of interest (Mur, Bandettini, & Kriegeskorte, 2009). In contrast, MVPA techniques examine patterns of brain activity across multiple voxels and utilize the fine-grained spatial information to investigate representational similarity at the neural level (Norman, Polyn, Detre, & Haxby, 2006). Therefore, these kinds of techniques can be especially useful when examining the nature of symbolic and nonsymbolic representations; rather than inferring similar processes based on common brain activation, MVPA methods can help determine whether symbolic and nonsymbolic formats have similar or dissimilar representations based on multi-voxel patterns of activation.

Several studies have now employed MVPA techniques to determine whether symbolic and nonsymbolic formats have the same or different underlying representations. In the first study to examine whether machine-learning algorithms can successfully predict quantities within and across-formats, Eger et al. (2009) found that symbolic and nonsymbolic quantities could be decoded within a parietal region of interest when the algorithm was trained in the same format. Cross-format decoding was only successful when predicting nonsymbolic quantities from symbolic brain activation, but symbolic quantities could not be predicted from nonsymbolic activity (Eger et al., 2009). However, the authors found no evidence for cross-format decoding using a searchlight analysis, suggesting that these findings did not hold across multiple spatial scales (for a greater discussion of these results see Cohen Kadosh & Walsh, 2009b). Successful within-format decoding and a failure of cross-format decoding has also been reported in two other more recent MVPA studies (Bulthé, De Smedt, & Op de Beeck, 2014; Damarla & Just, 2013). Damarla and Just (2013) found that quantities of objects (nonsymbolic) and digits (symbols) were decodable in the parietal cortex when the algorithm was trained in the same format, however, they found no evidence for cross-format decoding. If symbolic and nonsymbolic quantities had the same underlying representation, it should not matter which format the algorithm is trained or tested on. Therefore, these findings suggest that the representations for numerical quantities are format-specific. Converging evidence from Bulthé et al. (2014) also supports the notion that symbolic and nonsymbolic formats do not share an abstract representation of quantity. Using multiple spatial scales (whole-brain searchlight, lobules, and smaller regions of interest), Bulthé et al. (2014) found that symbolic and nonsymbolic formats were decodable in many regions of the cortex, however, they found no evidence of cross-format decoding. Therefore, by using MVPA as a tool to decode brain activity, the majority of studies have provided evidence that symbolic and nonsymbolic formats have different neural representations.

Other kinds of MVPA analyses, such as representational similarity analysis (RSA), can also be used to examine the underlying neural representations. RSA determines the degree of similarity (or dissimilarity) between patterns of brain activity; greater representational overlap should be indicated by stronger correlations between spatial patterns of brain activity. To determine the degree to which symbolic and nonsymbolic formats have similar underlying representations, Lyons et al. (2015) used RSA to examine whether the two formats showed correlated activity within the bilateral IPS. The authors found no correlations in the brain activity between quantities across formats (e.g. the digit “6” with six dots). Moreover, symbolic and nonsymbolic numbers had qualitatively different representations within each format. Voxelwise correlations between pairs of symbolic quantities showed modest correlations between numerals that did not vary as a function of the ratio between the two numbers. In contrast, the correlations between nonsymbolic quantities were predicted by the ratio between the numbers. Together, this evidence demonstrates that even though symbolic and nonsymbolic formats recruit the parietal cortex (specifically the IPS), the formats appear to be processed by the IPS in fundamentally different ways.

The studies discussed above illustrate how fMRI has furthered our understanding of how symbolic and nonsymbolic numbers are represented. By examining how similar or dissimilar symbolic and nonsymbolic processing is at the neuronal level, inferences can be made about whether these two formats are rooted in the same representation. MVPA analyses have also revealed information beyond what we could glean from behavioural evidence alone; even though symbolic and nonsymbolic formats demonstrate similar behavioural ratio effects, analyses of spatial patterns of brain activation suggest that they may have different neural origins. This evidence indicates that the two number formats may have fundamentally different underlying neural representations, even though they activate some common brain regions. Therefore, neuroimaging has expanded our knowledge of how numbers are represented and has challenged existing theories that symbolic and nonsymbolic formats have the same underlying representation. This has led to new hypotheses about how symbols acquire their meaning (Leibovich & Ansari, 2016), which is a fruitful avenue for future research.

2) Are Arithmetic Skills Rooted in an Understanding of Basic Numerical Concepts?

Several key pieces of evidence from the behavioural and neuroimaging literature point to arithmetic skills being scaffolded on (i.e. built on) earlier basic numerical competencies, such as symbolic number knowledge. A large body of literature has shown that fluency with symbolic numbers and understanding quantity relations are correlated with adults' and children's math achievement (Bugden & Ansari, 2011; Chen & Li, 2014; De Smedt, Noël, Gilmore, & Ansari, 2013; Holloway & Ansari, 2009; Lyons, Price, Vaessen, Blomert, & Ansari, 2014; Sasanguie, De Smedt, Defever, & Reynvoet, 2012; Schneider et al., 2016). Brain imaging can further constrain questions regarding the relationship between symbolic number processing and arithmetic by examining their relationships in the brain. For instance, if arithmetic is based on an understanding of symbolic number knowledge, one might predict that some of the same brain regions may be recruited for both symbolic number processing and arithmetic. Indeed, the neuroimaging literature has provided some evidence to suggest that arithmetic abilities are scaffolded on earlier basic number processing skills. In an fMRI meta-analysis that included studies on both number processing and arithmetic tasks, number processing skills and arithmetic had overlapping activity in the superior and inferior parietal lobules (in addition to a number of other regions) (Arsalidou & Taylor, 2011). Even though overlapping activation does not necessarily indicate similarity of representation (see discussion in Section 1 above), regions that are activated for both basic number processing (such as magnitude comparison) and calculation could serve as a neuroanatomical scaffold, where basic number processing skills form the basis from which arithmetic skills are learned.

The link between basic number processing and arithmetic has also been demonstrated with brain-behaviour correlations. For example, Matejko and Ansari (2017) found that children with stronger symbolic comparison and ordering skills (but not nonsymbolic skills) recruited the IPS more during single-digit arithmetic. Other studies have also demonstrated relationships between standardized tests of arithmetic and brain activity during symbolic (Bugden, Price, McLean, & Ansari, 2012) and nonsymbolic comparison tasks (Haist, Wazny, Toomarian, & Adamo, 2015). These findings suggest that individual differences in children's arithmetic skills are related to the processing of numerical quantities, and that the IPS may play an important role in mediating this relationship. The association between basic number knowledge and arithmetic skills has also been demonstrated in more naturalistic settings. For instance, brain activity measured while children were viewing number-related content on Sesame Street was found to be correlated with children's mathematical skills (Cantlon & Li, 2013; Emerson & Cantlon, 2012). In particular, greater fronto-parietal connectivity (more adult-like brain connectivity) was related to higher math scores (Emerson & Cantlon, 2012). Together, this work indicates that neuroimaging can be used to demonstrate relationships between neural representations of basic numerical concepts and individual differences in mathematical proficiency. Of course, brain-behaviour correlations cannot indicate the direction of the relationship between basic number processing and arithmetic, therefore, it is possible that the acquisition of arithmetic skills may also influence basic numerical representations.

Even though basic number processing skills and arithmetic have been related to one another using brain-behaviour correlations, it is necessary to examine these processes within the same participants in order to determine whether arithmetic and basic number processing skills have the same underlying neural basis. To date, only a handful of studies have carried out within-subjects investigations into the shared activation for basic numerical tasks and arithmetic. Some evidence has pointed to the idea that basic number processing skills and arithmetic may converge or diverge in the brain depending on participants' problem solving strategies. For example, Knops and Willmes (2014) investigated the neural representational similarity between symbolic ordering skills (determining whether a sequence of numbers are in the correct ascending order) and different arithmetic operations. They observed neural similarity in the IPS between symbolic ordering and both subtraction and addition, however, subtraction was more similar to symbolic ordering than addition. The authors posit that subtraction may show greater similarity with basic numerical processing skills such as ordering because subtraction problems are more often calculated and require a greater manipulation of quantities (Campbell & Xue, 2001). The notion that basic number processing skills are critical in procedural arithmetic is also supported by evidence that has shown no overlap within the parietal cortex between multiplication and number comparison tasks (Dehaene et al., 1996; Rickard et al., 2000). This lack of overlap in the parietal cortex, particularly in the IPS, could be due to the kinds of strategies that are used to solve multiplication problems. More specifically, single digit multiplication problems are predominantly solved by retrieval and are therefore not highly demanding of strategies that rely on the manipulation of quantities.

In concert with behavioural evidence, these neuroimaging findings suggest that arithmetic is closely associated with basic number processing skills (e.g. symbol-quantity and symbol-symbol relationships), and the relationship between these skills may be dependent on the cognitive operation being performed. Future research will need to examine the degree to which the four arithmetic operations relate to basic number processing tasks at the neural level and whether the degree of overlap is greater for operations that are more demanding of magnitude processing skills. It is also important to acknowledge that most of the conclusions on the relationship between arithmetic and basic number processing skills are based on brain-behaviour correlations or co-activation of two tasks (with a few exceptions, e.g. Knops & Willmes, 2014). These methods do not necessarily indicate that these skills involve the same mechanisms. It is possible that the recruitment of the parietal cortex for both tasks may be an epiphenomenon of a third, unknown cognitive process such as attention or cognitive control. The relationship between number processing and arithmetic could also be due to a number of domain general or domain specific factors (e.g. working memory, symbol processing, etc.). Future research will need to determine whether basic number processing and arithmetic rely on similar neural mechanisms using methods such as MVPA, and will also need to control for other related cognitive skills to more definitively determine whether

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arithmetic is scaffolded on basic numerical processes in the parietal cortex. Nevertheless, the work summarized above provides a neurobiologically plausible explanation for the relationship between basic number processing skills and arithmetic and parallels a large body of behavioural research demonstrating associations between individual differences in numerical magnitude processing and arithmetic (Schneider et al., 2016). fMRI evidence demonstrating shared neural substrates and brain-behaviour correlations between arithmetic and number processing within the IPS more narrowly (though not exclusively) points to the explanation that stronger representations of numerical magnitudes in the IPS are critical for arithmetic.

3) What Is the Role of Arithmetic Strategies in the Acquisition of Arithmetic Skills?

Different cognitive strategies are implemented depending on the type of arithmetic problem presented (ie. addition vs subtraction) and the difficulty of the problem. In particular, some problems will be solved by retrieving the solution from memory, whereas other problems will be solved by using a more procedural and time intensive strategy such as counting or decomposing the problem into smaller parts. In adults, problems such as simple multiplication and addition tend to be retrieved from memory whereas subtraction and division problems are more likely to be solved through more effortful procedural strategies (Campbell & Xue, 2001). Problem size can also influence strategy use, where problems with smaller operands are more likely to be retrieved (sums < 10), whereas problems with larger operands (sums > 10) are more likely to be solved by calculation (Campbell & Xue, 2001; LeFevre et al., 1996).

Research from neuropsychological patients provided some of the first evidence that there may be cortical distinctions for arithmetic problems that are typically retrieved (e.g. multiplication) versus those that tend to be calculated (e.g. subtraction). Patients with lesions to the left temporo-parietal cortex showed impaired performance on multiplication but intact performance on subtraction (Cohen, Dehaene, Chochon, Lehéricy, & Naccache, 2000; Lee, 2000), suggesting distinct neural underpinnings for the two operations. Functional brain imaging was later used to confirm differences between arithmetic problems that are typically retrieved versus those that are typically calculated (Chochon, Cohen, van de Moortele, & Dehaene, 1999; Rosenberg-Lee, Chang, Young, Wu, & Menon, 2011).

Verbal strategy reports and manipulations of problem size have also been used to investigate the functional and neurophysiological correlates of arithmetic strategies. Small problems, or problems that are typically solved using retrieval, have been shown to activate perisylvian language regions in the left hemisphere, particularly the left angular and supramarginal gyri (De Smedt, Holloway, & Ansari, 2011; Grabner et al., 2009; Kong et al., 2005). In contrast, large problems, or problems that are solved using procedural strategies, activate a fronto-parietal network of regions (De Smedt et al., 2013; Grabner et al., 2009). The distinct neural circuits for retrieval and calculation were highlighted by Grabner et al. (2009) who sorted imaging trials on the basis of post-scan strategy reports. They found that problems for which participants indicated that they had used retrieval-based strategies were associated with activation in the left angular gyrus, whereas problems on which participants used procedural strategies relied on frontal brain regions (see Seghier, 2013 for other theories of angular gyrus function). Similar functional distinctions between retrieval and calculation have also recently been replicated in children (Polspoel, Peters, & De Smedt, 2017). Together with behavioural studies (e.g. Siegler, 1987), such evidence provides convergent validity for the use of self-reports to distinguish between different strategies.

Training studies have also been instrumental in examining the causal mechanisms underlying experience-dependent changes in strategy use, and the corresponding changes to the neural correlates of arithmetic (for a review see Zamarian, Ischebeck, & Delazer, 2009). This literature has pointed to a shift in activation from the IPS to the angular gyrus following training of multi-digit multiplication problems (Delazer et al., 2003, 2005; Ischebeck et al., 2006). Multi-digit multiplication problems are likely relying on calculation strategies, and with repeated practice, they shift to more procedural fact-retrieval strategies. Therefore, a shift in the brain regions following training is thought to reflect a shift in strategies. It is also important to acknowledge several caveats when interpreting these studies. First, training-related changes in the brain could reflect other processes such as familiarity with the task or changes in task difficulty. Second, these training studies elucidate how changes in strategy use occur at the neurobiological level in adults and cannot generalize to how these processes occur in children. Recent research with children suggests similar neural dissociations between retrieval and procedural problems, indicating that children may have to undergo similar shifts in brain activation from the IPS to the temporo-parietal cortex as they learn to retrieve problems from memory (Polspoel et al., 2017). However, it will be important to conduct longitudinal studies with children to confirm how the neural correlates of arithmetic change with experience.

Accounting for strategy use has also been also been instrumental in determining whether operation effects (e.g. faster reaction times and higher accuracy on multiplication compared to subtraction) are due to fundamental differences in how different operations are solved, or whether they are a consequence of different frequencies of retrieval and procedural strategies. This distinction is particularly important because some studies have interpreted activation differences between arithmetic operations as fundamental differences in the representations and processes of these operations. To address this question, two studies have compared different arithmetic operations after accounting for the types of strategies being performed in adults (Tschentscher & Hauk, 2014) and children (Polspoel et al., 2017). Both studies found that there were no neural differences between operations after accounting for strategy, indicating that the frequency of retrieval and procedural strategies used during arithmetic operations can account for differences in their neural networks. These studies also found that brain activation during retrieval and procedural problem solving was similar across different arithmetic operations (Polspoel et al., 2017; Tschentscher & Hauk, 2014). Therefore, using behavioural assessments of strategy use in combination with neuroimaging has helped clarify the similarities between different arithmetic operations and the origins of operation effects.

Examining the neural distinctions between calculation and retrieval has also provided an important validation of behavioural methods that have uncovered distinct cognitive processes for different strategies. For example, it is possible that distinct verbal reports could have had similar underlying processes and neural substrates. Therefore, neuroimaging can strengthen existing hypotheses on the cognitive processes of arithmetic strategy use and can also provide insights into the kinds of cognitive operations being performed. For example, retrieval has been found to rely on brain regions that have traditionally been associated with language and phonological decoding (Taylor, Rastle, & Davis, 2013), which may indicate that retrieval is reliant on verbally-mediated systems. Indeed, children with dyslexia, who are thought to have impaired circuits within left perisylvian regions, have also been shown to have reduced activation within the left inferior parietal cortex during arithmetic compared to typically developing controls (Evans et al., 2014). Another investigation of white matter connectivity in typically developing children found that a left perisylvian white matter tract (the arcuate fasciculus) was correlated with individual differences in addition and multiplication but not subtraction or division, suggesting that this white matter tract is specifically related to arithmetic problems typically solved using fact retrieval (Van Beek, Ghesquière, Lagae, & De Smedt, 2014). This correlation disappeared once the authors controlled for measures that relied on phonological processing, further indicating that retrieval is likely reliant on verbally-mediated systems. These studies provide converging evidence that retrieval likely draws on language-based circuitry, which stands in contrast to strategies that require effortful calculation. While some of these conclusions could have been shown through behavioural methods alone (e.g. Lee & Kang, 2002; McKenzie, Bull, & Gray, 2003), these studies illustrate also how fMRI can provide converging and parallel evidence on the cognitive processes underlying arithmetic strategies.

4) Do Basic Numerical Concepts Scaffold Higher-Level Mathematical Skills?

Are sophisticated mathematical skills (e.g. calculus, algebra, complex geometry) grounded in more basic mathematical concepts such as an understanding of numerical magnitudes and single-digit arithmetic? Neuroimaging is an attractive method for investigating this question because it can be used to determine whether higher-level mathematical skills rely on brain regions that subserve more basic numerical skills, or whether these more sophisticated mathematical processes rely on an entirely different network of regions due to differing cognitive demands.

Some evidence has accumulated to support the hypothesis that higher-level mathematics are grounded in more basic numerical skills. For instance, Price, Mazzocco, and Ansari (2013) demonstrated that brain activity during single-digit arithmetic was related to proficiency on the preliminary scholastic aptitude test (PSAT), a test of high-school mathematics. Individuals with lower high-school math scores on the PSAT exhibited greater activity in the right IPS during an arithmetic task, potentially indicating the use of more procedural calculation strategies. In contrast, higher performers on the PSAT recruited regions that are more commonly associated with retrieval-based strategies including the left supramarginal gyrus and anterior cingulate cortex. It is also notable that the authors found no significant relationship between behavioural performance on the in-scanner arithmetic task and PSAT math performance. Information about the recruitment of different brain regions during single-digit arithmetic explained variance in high-school math achievement, but behavioural performance did not, indicating that neuroimaging potentially has additional predictive power above behavioural evidence alone. These data indicate that the types of cognitive operations performed on single-digit arithmetic problems (reflected in the brain regions recruited) are predictive of higher-level math achievement. A parallel study on the same participants also revealed similar findings in white matter, where individual differences in left parietal white matter tracts were associated with PSAT performance (Matejko, Price, Mazzocco, & Ansari, 2013). Importantly, these tracts have also been implicated in more basic arithmetic skills (Matejko & Ansari, 2015), suggesting that both higher-level mathematics and more basics arithmetic may also rely on similar white matter microstructures.

Another study involving mathematicians has found parallel conclusions (Amalric & Dehaene, 2016). Not only did higher-level mathematics (e.g. semantic judgments of mathematical statements in the fields of algebra, topology, analysis, or geometry) have overlapping brain activity with number recognition and simple arithmetic in the bilateral IPS and inferior temporal regions, but multivariate analyses also revealed that the patterns of brain activity were similar between higher-level mathematics and more basic numerical processing. Specifically, a representational similarity analysis (described in Section 1) revealed that brain activity during higher-level mathematical reasoning was correlated with simple arithmetic, algebra, number and formula recognition in the bilateral IPS and inferior temporal cortex.

Together, these findings suggest that regions within the parietal cortex may serve as a neuroanatomical scaffold for the acquisition of higher-level mathematical skills, and that higher-level mathematical concepts are rooted in more basic arithmetical skills and numerical concepts. Presently, the evidence linking basic numerical concepts and higher-level mathematical skills is largely correlational in nature. Future research will need to examine how these processes unfold longitudinally to determine whether more basic numerical concepts precede and provide a scaffold for more complex mathematical problem solving, or whether the acquisition of such higher-level skills changes the neural correlates of basic number processing, or both. It will also be important to determine whether other cognitive skills that commonly rely on parietal circuits (e.g. attention, working memory, processing speed) mediate the relationship between basic mathematical concepts and higher-level mathematical skills (as discussed in previous sections). Yet, the fMRI literature to date offers a unique insight into the relationship between basic and higher-level mathematical processes by elucidating the possible neurobiological mechanisms for the development and relationship between these skills.

5) Is Developmental Dyscalculia Underpinned by a Defective Number Module or Do Children Have Trouble Connecting Symbolic With Non-Symbolic Representations of Number?

Developmental dyscalculia (DD) is a learning disorder that refers to children who have an impairment in learning arithmetic facts, have poor calculation and math reasoning abilities, and have problems processing numerical information (American Psychiatric Association, 2013). These impairments are below what would be expected for the individual's age, intelligence, and level of educational instruction (American Psychiatric Association, 2013) Though the precise etiology of DD is still unknown, several different accounts have been put forward to explain the behavioural profiles of children with DD. The *defective number module hypothesis* proposes a core deficit in the innate capacity to represent and process numerical magnitudes (Butterworth, 2005). This account has been supported by evidence that shows that children with DD have general deficits with number processing including accessing verbal and semantic information, counting dots, reciting number sequences, and writing numbers (Landerl, Bevan, & Butterworth, 2004). Because children with DD perform poorly on both symbolic and nonsymbolic formats (and not just symbolic formats), it has been suggested that children have a core number deficit (Mussolin, Mejias, & Noël, 2010). In contrast, the *access deficit hypothesis* provides an alternative account and proposes that children with DD have intact numerical magnitude representations, however, they cannot access the semantic meaning (numerical magnitude) of symbolic numbers (Rousselle & Noël, 2007). Evidence that children with DD are impaired on comparing symbolic digits, but not nonsymbolic arrays, has been cited as support for the access deficit hypothesis (Rousselle & Noël, 2007). Together, there is mixed evidence on the origins of DD with supporting evidence for both the defective number module and access deficit hypotheses. In combination with behavioural methods, neuroimaging can help test fundamental hypotheses that DD is a disorder of the brain (Kosc, 1974) and can inform these theories on the origins of DD. By using brain imaging and electrophysiological methods to characterize the structural and functional impairments, neuroscientific methods have the capability to better understand the cognitive phenotype of this developmental disability.

Determining how symbolic and nonsymbolic magnitudes are processed at the neural level can provide further evidence towards the core number or access deficit hypotheses. For instance, if children with DD show atypical activation during both nonsymbolic and symbolic magnitude processing, this would support a core number deficit account of DD. In contrast, if differences were only observed for symbolic magnitude processing then the most parsimonious explanation would be an access deficit account. Few studies have systematically contrasted these theories by comparing symbolic and nonsymbolic activation in a sample of children. To date, most studies have separately investigated the neural correlates of symbolic or nonsymbolic processing in children with DD. This research has hinted at some candidate regions that differ between typically developing children and children with DD, and has also provided some insights into the underlying deficits in DD. For example, Price et al. (2007) found that typically developing children demonstrated a canonical neural distance effect in the right IPS during a nonsymbolic comparison task (greater activity for smaller distances than larger distances between dot arrays), but children with DD did not. Other research has also demonstrated atypical activation patterns in the IPS during nonsymbolic magnitude processing (Kaufmann et al., 2009; Kucian, Loenneker, Martin, & von Aster, 2011), however, the lateralization and direction of the atypical activation is not always consistent. For instance, Kaufmann et al. (2009) found that children with DD had greater activation in the bilateral IPS compared to controls. These relative increases in activity might be indicative of compensatory mechanisms in children with DD. Despite some inconsistencies with the findings from Price et al. (2007), both findings point to atypical activation in the IPS for nonsymbolic magnitude processing (however see Kovas et al., 2009 and Kucian et al., 2006 for conflicting data). Additional research has suggested that children with DD may have atypical neural signatures during symbolic number processing. Similar to nonsymbolic processing (Price et al., 2007), children with DD do not show typical modulation of the bilateral IPS when comparing symbolic numbers (Mussolin, De Volder, et al., 2010). However, this body of literature is still small and more research will likely clarify whether magnitude processing is impaired in symbolic, nonsymbolic, or both formats.

Beyond symbolic and non-symbolic number processing, it has also been shown that children with DD exhibit atypical activation of the right IPS during a visuo-spatial working memory task (Rotzer et al., 2009). This finding suggests that atypical processing of the IPS in DD may not be restricted to numerical processing but may also be related to impairments in visuo-spatial working memory, which have been reported in children with DD (Szucs, Devine, Soltesz, Nobes, & Gabriel, 2013). These findings support the notion that the underlying cause of DD cannot be characterized as a deficit in some kind of modular structure in the brain that supports numerical magnitude processing, but rather that DD is associated with both numerical and non-numerical deficits both at the level of brain and behavior (Fias, Menon, & Szucs, 2013).

The small number of studies and conflicting findings currently preclude our ability to determine whether the available literature points to a core defective number module or access deficit account of DD. However, these studies highlight how neuroimaging can help determine the etiology of DD and revise existing theories. Future research will need to examine both symbolic and nonsymbolic processing within the same sample of children with DD to disentangle which theory is best supported. Other more sensitive analytic techniques, such as

MVPA, will also be fundamental in investigating how symbolic and nonsymbolic processing is qualitatively different in children with DD (Bugden & Ansari, 2015). Unfortunately, to date, most neuroimaging studies of DD have relied on very small sample sizes and widely different criteria to define groups of children with DD. It is well established that the use of small sample sizes can lead to an overestimation of observed effect sizes and therefore some of these findings may not be replicable, which could explain some of the differences between the studies reviewed above (Button et al., 2013). Going forward, it will be critical for studies investigating the neural correlates of DD to move towards more strongly powered studies to allow for more precise inferences on the origins of DD. Alternatively, given that the criteria used to define DD are somewhat arbitrary and rely on standardized tests of math ability rather than some external criterion (such as a specific genetic and/or neurobiological marker), researchers may be better advised to study large samples with significant variability in math performance to capture how individual differences in mathematical competence relate to brain activity and structure.

Summary and Future Directions for fMRI Research in Numerical Cognition

Functional brain imaging provides an additional level of analysis that complements behavioural methods and also provides additional tools with which to address several outstanding questions in the field of numerical cognition. In this review, we have outlined several instances in which fMRI has supported and furthered our understanding of the cognitive underpinning of numerical and mathematical skills including: 1) whether symbolic and nonsymbolic magnitudes have the same underlying representation; 2) whether basic number processing skills provide the basis on which arithmetic is learned; 3) the role of strategies in the development of arithmetic skills; 4) how arithmetic and basic number processing skills scaffold higher-level mathematics; and 5) the neurobiological correlates of developmental dyscalculia. In some cases, fMRI research has supported and converged with behavioural investigations of numerical and mathematical processing, but there are some instances in which it has significantly extended our knowledge. For instance, fMRI has begun to disentangle whether symbolic and nonsymbolic magnitudes have the same underlying representation (Bulthé et al., 2014; Lyons et al., 2015), which was not clear from behavioural evidence alone. This provides evidence that fMRI can be used to tease apart theories in numerical cognition to form a more complete understanding of how numbers are processed.

There have also been instances in which neural indices have had greater predictive power than behavioural measures alone (e.g. Price et al., 2013). Recent evidence has also found that brain connectivity, but not a battery of behavioural measures, predicted developmental changes in math performance (Evans et al., 2015) as well as arithmetic gains following intensive math tutoring (Supekar et al., 2013). The number of data points in neuroimaging far exceeds what is possible with behavioural data, which could subsequently result in neuroimaging having greater predictive power. It is therefore possible that neuroimaging could become very useful in neuroprognosis in typically and atypically developing children (Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015). In the field of reading, neuroimaging measures have been found to be more predictive of long-term reading gains in dyslexia than behavioural measures of reading and phonological awareness (Hoeft et al., 2011). Though no studies have yet applied such methods to math learning disabilities, future research will need to determine whether neuroimaging will be a useful tool in identifying and predicting learning outcomes of children with developmental dyscalculia (Bugden & Ansari, 2015).

Examining the neurocognitive underpinnings of numerical and mathematical thinking can also have broader implications for how multiple cognitive systems interact within the brain. For instance, learning mathematics may not only change brain circuitry underlying math, but may also shape the circuitry underlying other functions (Amalric & Dehaene, 2016). Other studies have also explored how learning mathematics interacts with other brain circuits such as hippocampal systems for learning and memory. Qin et al. (2014) demonstrated that the hippocampus plays an important role in the development of children's arithmetic skills and may help promote the transition from using procedural to retrieval strategies on arithmetic problems. This suggests that the development of arithmetic is likely a product of multiple interacting cognitive systems. Together, such studies indicate that investigating the development and acquisition of mathematical thinking has broader implications for how multiple neurocognitive systems interact and develop in concert, which may be more difficult to disentangle with behavioural methods alone.

Even though fMRI has significantly added to our understanding of how numbers are represented, it is important to acknowledge some of its limitations. For example, it is often difficult to control for performance differences between groups (e.g. adults versus children, or dyscalculic children versus controls), and it can be difficult to determine whether neural differences between groups are a result of performance differences or fundamental differences on the dimension of interest (e.g. development or math impairment). One way to overcome this limitation is to use passive paradigms that do not rely on behavioural performance (e.g. fMR-adaptation paradigms). Such techniques can be particularly useful when there are performance differences because no overt response is necessary (for a greater discussion of this issue see Vogel, Matejko, & Ansari, 2016). Another significant concern when interpreting fMRI data is that it is often tempting to make reverse inferences about the engagement of a cognitive process from brain activation in a particular region (Poldrack, 2015). For example, the recruitment of the frontal cortex during arithmetic is often attributed to executive functioning skills, yet, this assumption is a reverse inference without directly measuring cognitive control or manipulating problem difficulty (for a notable exception see Menon, Rivera, White, Glover, & Reiss, 2000). Finally, not all theoretical questions in numerical cognition necessitate the use of fMRI, and behavioural methods alone or other cognitive neuroscience methods may be more suitable. For instance, fMRI can indicate which brain regions are active during a task, but cannot determine whether those brain regions are necessary to perform the task. Brain imaging has both practical and interpretive limitations, therefore, it is important to use neuroimaging where it may be most useful and can supplement and extend other behavioural and cognitive neuroscience research.

Conclusions

Using functional brain imaging as a lens through which to understand numerical and mathematical cognition has proved to be fruitful in complementing and expanding our existing knowledge on core theoretical issues such as how numbers are represented and how individuals learn to calculate. It has pushed the boundaries of our knowledge on the development of numerical and mathematical skills in both typically and atypically developing individuals. Importantly, fMRI can help examine how relatively recent cultural inventions, such as number symbols, become represented in the brain, and how evolutionarily ancient systems in the brain may or may not provide restrictions and shape the acquisition of mathematical thinking. Going forward, the use of fMRI to study questions within the field of numerical and mathematical cognition must follow recent recommendations for improved practices, including adequately powered studies and best practices for data analysis (Nichols et al., 2016).

It is important to clearly state that the use of any neuroimaging methodology (e.g. near infrared spectroscopy (NIRS), electroencephalography (EEG), etc.) to constrain our understanding of numerical cognition should not be viewed as a superior level of analysis, but rather a complementary one. Neuroimaging findings that confirm what has already been established using behavioural methods are of equal utility as are those that challenge and expand our understanding of a given phenomenon. Applying neuroimaging methods to better understand numerical and mathematical cognition is one of many tools available to researchers in the field and should be viewed as being on the same level playing field as other approaches.

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Competing Interests

The authors have declared that they have no competing interests.

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