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Empirical validation of the triple-code model of numerical processing for complex math operations using functional MRI and group Independent Component Analysis of the mental addition and subtraction of fractions

Vincent J. Schmithorst[a,*] and Rhonda Douglas Brown[b]

[a] *Imaging Research Center, Children's Hospital Medical Center, Cincinnati, OH 45229, USA*
[b] *Division of Educational Studies and Department of Psychology, University of Cincinnati, Cincinnati, OH 45221, USA*

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The suitability of a previously hypothesized triple-code model of numerical processing, involving analog magnitude, auditory verbal, and visual Arabic codes of representation, was investigated for the complex mathematical task of the mental addition and subtraction of fractions. Functional magnetic resonance imaging (fMRI) data from 15 normal adult subjects were processed using exploratory group Independent Component Analysis (ICA). Separate task-related components were found with activation in bilateral inferior parietal, left perisylvian, and ventral occipitotemporal areas. These results support the hypothesized triple-code model corresponding to the activated regions found in the individual components and indicate that the triple-code model may be a suitable framework for analyzing the neuropsychological bases of the performance of complex mathematical tasks.

Keywords: MRI; Triple-code model; Independent Component Analysis

Introduction

The precise neuropsychological model and neural substrates associated with math cognition continue to be a subject of investigation. The triple-code model of numerical processing by Dehaene (1992) and Dehaene and Cohen (1995, 1997) proposes that numbers are represented in three codes that serve different functions, have distinct functional neuroarchitectures, and are related to performance on specific tasks (see review in (van Harskamp and Cipolotti, 2001)). The analog magnitude code represents numerical quantities on a mental number line (Dehaene, 1989; Dehaene et al., 1990; Restle, 1970), includes semantic knowledge regarding proximity (e.g., 5 is close to 6) and relative size (e.g., 5 is smaller than 6), is used in magnitude comparison (Dehaene, 1989; Dehaene et al., 1990; Moyer and Landauer, 1967) and approximation tasks, among others, and is predicted to engage the bilateral inferior parietal regions (Chochon et al., 1999; Dehaene et al., 1999; Stanescu-Cosson et al., 2000). The auditory verbal code (or word frame) manipulates sequences of number words, is used for retrieving well-learned, rote, arithmetic facts such as addition and multiplication tables (Gonzalez and Kolers, 1982), and is predicted to engage general-purpose language modules, including the left perisylvian network and the left basal ganglia and thalamic nuclei, which have been associated with memory and sequence execution (Dehaene, 1997; Houk and Wise, 1995). The visual Arabic code (or number form) represents and spatially manipulates numbers in Arabic format (Ashcraft and Stazyk, 1981; Cohen and Dehaene, 1991; Dahmen et al., 1982; Weddell and Davidoff, 1991), is used for multidigit calculation and parity judgments (Dehaene and Cohen, 1991), and is predicted to engage bilateral inferior ventral occipitotemporal regions belonging to the ventral visual pathway (Dehaene, 1992), with the left used for visual identification of words and digits, and the right used only for simple Arabic numbers (Dehaene, 1997).

The triple-code model proposes various transcoding paths between the three representational codes. Overall, two major coordinated routes are proposed by Dehaene and Cohen (1995, 1997): a direct asemantic route that transcodes written numerals to auditory verbal representations in the left perisylvian language areas to guide retrieval of rote knowledge of arithmetic facts (e.g., presented with 2×3, processed as "two times three, six") without semantic mediation, and an indirect semantic route specialized for quantitative processing that manipulates analog magnitude representations in bilateral parietal areas to compare operands and uses back-up strategies by manipulating visual Arabic representations when rote knowledge is not available in verbal memory, such as decomposing complex problems into new problems for which facts can be retrieved (e.g., $13 + 5 = 10 + 5 + 3 = 15 + 3 = 18$) (LeFevre et al., 1996), and monitors the plausibility of the direct route using approximate means (Ashcraft and Stazyk, 1981; Dehaene and

* Corresponding author. Imaging Research Center, Children's Hospital Medical Center, 3333 Burnet Avenue ML 5031, Cincinnati, OH 45229. Fax: +1-513-636-3754.
E-mail address: Vince.Schmithorst@cchmc.org (V.J. Schmithorst).
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Cohen, 1991). Furthermore, prefrontal areas and the anterior cingulate associated with a global workspace are proposed to coordinate the sequencing of processing through the modules in the appropriate order, holding intermediate results in working memory, and detecting errors (Dehaene, 1997; Dehaene and Naccache, 2001; Dehaene et al., 1996; Kopera-Frye et al., 1996; Shallice and Evans, 1978).

Other theorists have proposed differing models. For example, McCloskey (Dagenbach and McCloskey, 1992; McCloskey, 1992; McCloskey et al., 1986) proposes modules for comprehension, calculation, and number production. Specifically, the comprehension module translates word and Arabic numbers into abstract internal representations of numbers, calculations are performed on these representations, and then the abstract representations are converted to verbal or Arabic numbers using specific number production modules. Thus, in McCloskey's model, amodal abstract internal representations of numbers are operated on, rather than numbers represented in specific codes (i.e., quantity, verbal, or Arabic) as in Dehaene's model. Furthermore, McCloskey's model assumes impairment affects individual representations of stored arithmetic facts, segregated by type of operations (e.g., addition vs. division), and thus predicts arbitrary rather than systematic dissociation between operations; whereas Dehaene's (Dehaene and Cohen, 1995, 1997) model predicts specific impairments to operations associated with distinct functional neuroarchitectures (e.g., impairment to indirect semantic route associated with complex addition, subtraction, and division) (van Harskamp and Cipolotti, 2001). Dehaene's model is conceptually similar to the encoding complex model by Campbell and Clark (1988), which also assumes that numbers are operated on using specific codes, rather than abstract representations, which is also consistent with the preferred entry code hypothesis by Noel and Seron (1992).

Previous lesion and neuroimaging studies have provided some support for Dehaene's distinction between the asemantic language- and culture-dependent system used for exact math and the semantic language-independent system used for approximate math (Ansari and Karmiloff-Smith, 2002). Neuropsychological evidence indicates a double dissociation between the two major routes. Patients with left perisylvian lesions, but spared inferior parietal regions, demonstrate impairment in tasks involving verbal representations of number, but can perform tasks involving nonverbal representations of number (i.e., quantity and Arabic) (Cipolotti and Butterworth, 1995; Cohen et al., 2000; Dagenbach and McCloskey, 1992; Dehaene and Cohen, 1997; Lampl et al., 1994; Pesenti et al., 2000a); whereas patients with parietal lesions show acalculia or deficits in understanding quantity meaning (Cipolotti et al., 1991; Dehaene and Cohen, 1997; Delazer and Benke, 1997). Neuroimaging studies indicate that parietal regions are activated during number processing and calculation (Gruber et al., 2001; Naccache and Dehaene, 2001; Pinel et al., 2001), such as digit comparison (Chochon et al., 1999), single digit multiplication (Dehaene et al., 1996), and approximation (Dehaene et al., 1999; Stanescu-Cosson et al., 2000), to a greater extent than for rote math and are not activated in phonological or lexical tasks (Dehaene et al., 1999; Pesenti et al., 2000b; Stanescu-Cosson et al., 2000). More specifically, Chochon et al. (1999) implicated a parieto-fronto-cingular network (intraparietal sulcus, postcentral gyrus, inferior frontal-BA 44/45, dorsolateral frontal-BA 46/9, superior frontal-BA 6/8, SMA, and premotor cortex) related to the performance of digit naming and comparison and multiplication and subtraction tasks. However, unexpected results were found for multiplication, including the absence of activation in the predicted language areas and the presence of activation in left intraparietal regions, which is consistent with other studies (Dehaene et al., 1996) and was discussed as possibly reflecting the combinatorial use of direct retrieval and quantity-based strategies. Stanescu-Cosson et al. (2000) found that left prefrontal and bilateral angular regions showed greater activation during rote addition tasks, especially for small numbers, while the bilateral intraparietal, precentral, dorsolateral, and superior prefrontal regions showed greater activation during approximate addition tasks. Larger single digit exact math problems were associated with increased activation in the same bilateral intraparietal regions as approximate math as well as left inferior and superior frontal gyri activation.

To explore the applicability of the triple-code model to complex mathematical operations, we designed a functional magnetic resonance imaging (fMRI) paradigm involving the mental addition and subtraction of fractions (e.g., $2/3 - 1/4$). The task is expected to recruit all three elements of the triple-code model: the analog magnitude code for information regarding relative size and for the proportional math techniques used to change denominators (e.g., transforming 2/3 into 8/12 and 1/4 into 3/12), the auditory verbal code for retrieval of rote facts (e.g., subtraction of the numerators $8 - 3 = 5$), and the visual Arabic code for the representation and mental manipulation of numerals in Arabic format (e.g., recognizing numerators vs. denominators and performing addition and subtraction when rote facts are unknown).

Because the hemodynamic response functions (HRFs) of the three components are not known precisely a priori, and may in fact have considerable variance across subjects (due to differences in speed of performing the problems, as well as possible differences in processing strategies), we selected group Independent Component Analysis (ICA) for analysis of the data. ICA has been previously proposed as a data-driven approach for analysis of fMRI data (McKeown et al., 1998). ICA operates by linearly unmixing the fMRI data into spatially independent component maps (details given in McKeown et al., 1998). The method has been extended for multisubject analyses (Calhoun et al., 2001b) and the generation of across-subjects random-effects statistical inferences. ICA offers the advantage of not requiring accurate modeling of the HRF for each subject and cognitive component. The group ICA technique has been shown to provide similar results to standard model-based approaches (Calhoun et al., 2001a) and has been used recently in studies investigating simulated driving (Calhoun et al., 2002), visual perception (Calhoun et al., 2001a), and language processing (Schmithorst and Holland, 2003).

Materials and methods

Fifteen college-educated adults (4 F, 11 M, mean age = 37.8 ± 15.2 years) were recruited to participate in the study. Institutional review board approval and written informed consent were obtained for all subjects, and each subject was prescreened for any history of neurological or psychiatric abnormalities, head trauma, or any other conditions that would prevent an MRI scan from being performed.

Stimuli were presented by an Apple Macintosh G3 (Apple Computer, Cupertino, CA) using MacStim through an MRI-compatible video system (Magnetic Resonance Technologies, Van Nuys, CA). A block-periodic fMRI paradigm was used. During the active condition, the subjects were presented with three fraction problems (either addition or subtraction) to perform mentally. The fractions all contained single-digit numbers in both the numerator and denominator. The denominators of the fractions were restricted to 5 or less; however, improper fractions were used, and the answers were sometimes negative. No specific instructions were given to the subjects on how to perform the task except the visual reminder on a board before the scanning session that a/b + c/d = (ad + bc) / bd. All subjects participated in a practice session outside of the magnet before the scanning session to ensure they understood and could perform the task. They were given 10 s to complete each problem and were instructed to move on to the next one if they did not finish in time. During the control condition, the subjects were presented with three sets of four numbers at 10-s intervals at the same positions on the screen as the fractions, but without any divisor bars or plus or minus signs. The subjects were given a 3-s visual cue of either ''Perform Math'' or ''Rest'' before the active and control task, respectively. Fifteen seconds of scans were acquired before the beginning of the paradigm to allow for T1 relaxation, followed by 10 alternating active and control conditions of 33 s each (including the 3-s cue), for a total scan time of 5 min 45 s. No performance data were collected due to the impossibility of the subjects' speaking aloud without introducing uncorrectable motion artifacts. However, the likelihood of any differences in task performance was greatly minimized due to the task being chosen to have a difficulty level well below the subjects' level of educational attainment, and the ''dry run'' performed before the scanning session.

MRI images were obtained using a 3-T Bruker Medspec system (Bruker Medical Instruments, Karlsruhe, Germany). For the functional imaging scans, a 24-slice blipped echo-planar imaging (EPI) sequence was used with the following parameters: matrix = 64 × 64, BW = 125 kHz, FOV = 25.6 × 25.6 cm, TE = 38 ms, TR = 3 s, slice thickness = 5 mm. In addition, a whole-brain T1-weighted scan was acquired for anatomical co-registration.

fMRI post-processing was performed with routines written in IDL (Research Systems Inc., Boulder, CO). During reconstruction, the EPI data were corrected for geometric distortion and Nyquist ghost artifacts via the multiecho reference method (Schmithorst et al., 2001). The images were corrected for motion via a pyramid iterative algorithm (Thevenaz and Unser, 1998) and linearly transformed into stereotaxic coordinates using landmarks (anterior commissure, posterior commissure, and cerebral bounding box) found from the whole-brain anatomical images. The fMRI data were smoothed with a Gaussian filter of width 4 mm.

A previously published method for generating group random-effects statistical inferences using ICA (Calhoun et al., 2001b), demonstrated to provide superior performance to other proposed methods (Schmithorst and Holland, 2004), was used. Each data set was preprocessed by normalizing the voxel time courses to a percent change from the mean, and the dimensionality was reduced via Principal Component Analysis (PCA) to 40 points in the time dimension, empirically shown to be a sufficient number of retained components (Beckmann et al., 2001). After concatenation across subjects in the time dimension, the dimensionality was again reduced to 50 points in the time dimension via PCA, and the FastICA (Hyvarinen, 1999) method was used to find independent components. A greater number of components was kept after the second data reduction stage because not all components are expected to be present in all subjects (each subject is expected to have unique artifactual components related to motion and cardiac and respiratory effects). Allowing a greater number of components minimizes the likelihood of these artifactual components mixing in to the task-related ones. The four components selected for display were the ones with the greatest correlations of the associated time courses with the on–off task reference function (shifted by 6 s to account for the hemodynamic delay). The displayed components were thresholded to $Z > 5.0$ ($P < 0.01$, random-effects analysis, Bonferroni-corrected for the approximately 10,000 voxels in the brain). In addition, for comparison, the data were processed using a standard General Linear Model (GLM) and also thresholded to $Z >$ 5.0 (random effects).

Results and discussion

Components were found with functional activation in the brain regions hypothesized to be associated with the analog magnitude code (Fig. 1a), auditory verbal code (Fig. 1b), and visual Arabic code (Fig. 1c). An additional component was found with activation in BA 19 (Fig. 1d). The associated time courses are also displayed (Fig. 2), along with the intersubject variability, as the method of Calhoun et al. allows the time course to vary across subjects. All displayed time courses had $R > 0.7$ with the task reference function (shifted by 6 s to account for the hemodynamic delay). No other components had an associated time course with $R > 0.7$ except the ones displayed.

A standard General Linear Model (GLM) analysis was also performed (Fig. 3) and revealed activation in many of the same regions as detected by ICA. There was not complete overlap between the areas detected via the GLM and the ICA analyses. This is due to the flexibility of the ICA technique in varying the time courses across subjects, which offers the prospect of overall greater sensitivity for detecting activation (such as seen in the fusiform gyrus and parietal lobe) but which comes at the possible price of reduced sensitivity in certain regions (such as anterior insula and medial frontal gyrus, only seen on the GLM analysis). Anterior insula and medial frontal activations were, however, detected with ICA on the component displayed in Fig. 1b, when the threshold was reduced to $Z > 3.0$. Significant overlap between the ICA and GLM results was seen in inferior parietal, prefrontal, and inferior occipital areas, and this overlap is expected due to the high degree of correlation of the associated time courses with the on–off task reference function. Using ICA, however, these activated regions may be separated into different maps due to small but relevant differences in hemodynamics between those regions. For instance, the time courses in Figs. 2c and 2d are highly correlated ($R = 0.85$). Subsequent exploratory Fourier power spectrum analysis, however, revealed that while both time courses had a highly significant component at the on–off task frequency ($\approx$0.015 Hz), a significant component at the rate of presentation of the problems ($\approx$0.09 Hz) was present only in the time course displayed in Fig. 2c (corresponding to the component map displayed in Fig. 1c).

The complex task of adding and subtracting fractions used in the current study was expected to involve a variety of numerical processes due to the number of component processes involved in solving the problems and differences in problem difficulty and subjects' knowledge. ICA is a useful technique for determining independent brain regions contributing to the performance on this type of task. Our ICA results confirmed that the brain regions hypothesized to correspond to particular functions within Dehaene's (Dehaene, 1992; Dehaene and Cohen, 1995, 1997) triple-code model of numerical processing were engaged by subjects performing complex mathematical operations. In performing

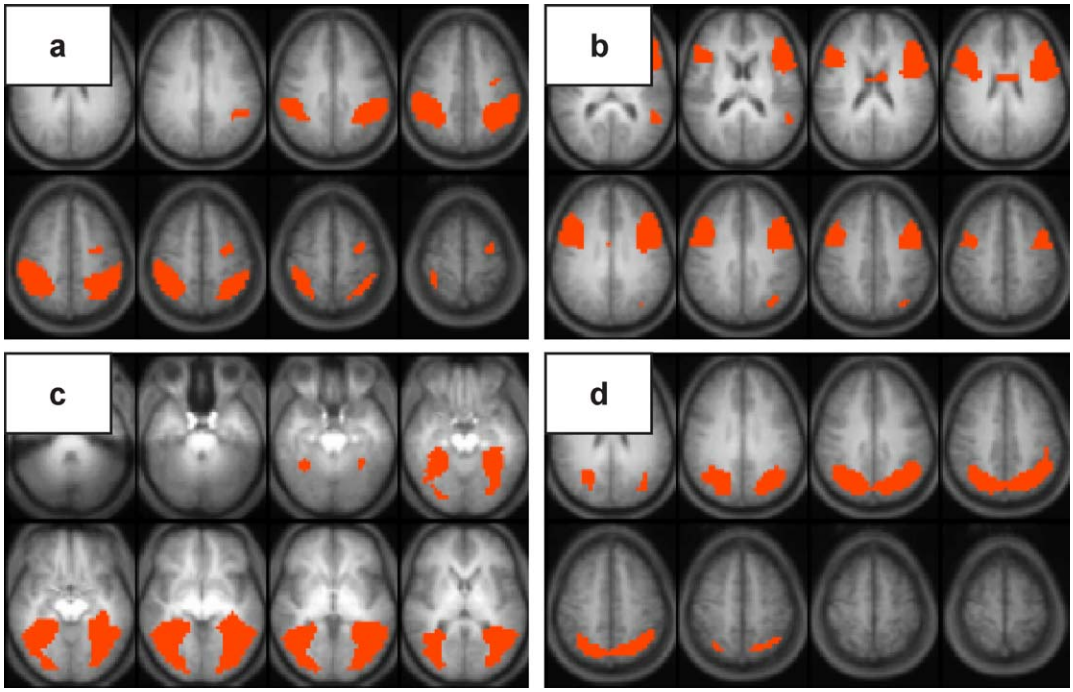

Fig. 1. Four group independent component maps obtained from group ICA analysis of 15 normal adults performing the mental addition and subtraction of fractions. Colored voxels have nominal $Z > 5.0$ ($P < 0.01$, corrected for multiple comparisons). Eight representative axial slices selected for display (radiologic orientation). Slice ranges (Talairach coordinates): Z = +25 to +60 mm (a); Z = +10 to +45 mm (b); −30 to +5 mm (c); +25 to +60 mm (d).

the addition and subtraction of fractions, components were demonstrated for the bilateral inferior parietal, left perisylvian, and ventral occipitotemporal areas (although not necessarily at the same time), all of the major networks predicted by the model, which are hypothesized to reflect the use of the analog magnitude, auditory verbal, and visual Arabic codes, respectively (Dehaene, 1992; Dehaene and Cohen, 1995, 1997). Although ICA cannot reveal the functional roles of its components, it can provide convergent evidence that, when combined with results from previous neuroimaging studies examining the functional roles of specific regions, can help support models of numerical processing and math cognition.

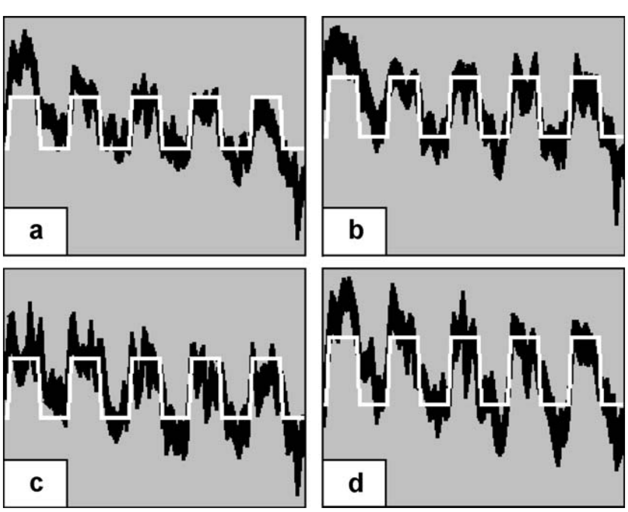

Fig. 2. Associated time courses (bands ± 1σ) corresponding to the group ICA maps displayed in Fig. 1. The on–off task reference function (delayed by 6 s) is overlaid; R = 0.71 (a), R = 0.76 (b), R = 0.70 (c), R = 0.80 (d).

Similar to previous neuroimaging studies examining calculation (Chochon et al., 1999; Dehaene et al., 1999; Gruber et al., 2001; Naccache and Dehaene, 2001; Pinel et al., 2001; Stanescu-Cosson et al., 2000), a clear bilateral inferior parietal component emerged (see Fig. 1a). Although brain regions may serve a variety of functions, this component may reflect use of abstract representations of numerical quantity of the proposed analog magnitude code to access semantic knowledge about the relative positions of fractions on a mental number line and relations between the sizes of fractions involved in proportional reasoning (Dehaene, 1989; Dehaene et al., 1990; Restle, 1970). Our results are also consistent with those of Simon et al. (2002) who compared functional activation for six tasks, including grasping, pointing, saccades, attention, calculation, and phoneme detection, and found that bilateral anterior intraparietal sulci activation was unique to calculation, while parietal activation for saccades was in more superior regions.

Another component (Fig. 1b) indicated activation of the left perisylvian network, including Broca's and Wernicke's areas, typically associated with language functions (as well as right prefrontal areas and left putamen), and basal ganglia, that may reflect use of the proposed auditory verbal code for retrieving rote arithmetic facts, such as addition and multiplication tables for adding and subtracting fractions and conversions to common denominators, respectively (Gonzalez and Kolers, 1982). Other results from our lab have also revealed similar activation for verbal memory on language tasks (Chiu et al., in press). These results are also consistent with those of Simon et al. (2002), who found a cluster of left activation including superior frontal gyrus, precentral sulcus, dorsolateral prefrontal areas, inferior prefrontal gyrus (BA

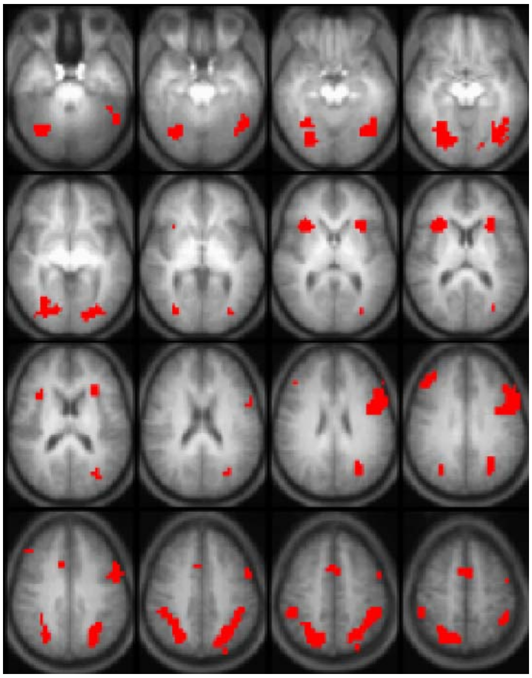

Fig. 3. Map obtained from GLM analysis of 15 normal adults performing the mental addition and subtraction of fractions. Colored voxels have nominal $Z > 5.0$ ($P < 0.01$, corrected for multiple comparisons). Sixteen representative axial slices selected for display (radiologic orientation). Slice range (Talairach coordinates): $Z = -25$ to +50 mm.

44/45), putamen, insula, and thalamus, as well as lesser activation in the right superior and inferior frontal gyri and bilateral activation in the anterior putamen and cingulate gyrus for calculation.

The remaining components that emerged from the analysis involve bilateral inferior ventral occipitotemporal regions belonging to the ventral visual pathway (Dehaene, 1992), including inferior temporal gyrus and fusiform gyrus (Fig. 1c), as well as secondary visual areas (Fig. 1d). The areas shown in Fig. 1c are consistent with those proposed by Dehaene to be associated with the visual Arabic code, which may have been used by participants in the current study to spatially manipulate the fractions in Arabic format and to calculate solutions that could not be retrieved via rote verbal memory (Ashcraft and Stazyk, 1981; Cohen and Dehaene, 1991; Dahmen et al., 1982; Dehaene and Cohen, 1991; Weddell and Davidoff, 1991). The significance of the medial–superior occipital gyrus (BA 19) activation seen in Fig. 1d is unknown; further research may investigate the possibility that the neural correlates of the visual Arabic code extend beyond the ventral visual pathway and into other secondary visual areas.

Theories of numerical processing continue to debate transcoding routes between various representations of number (Dagenbach and McCloskey, 1992; Dehaene, 1992; McCloskey, 1992; McCloskey et al., 1986). Dehaene and Cohen's proposal (Dehaene and Cohen, 1995, 1997) of a direct asemantic route that transcodes written numerals to auditory verbal representations in the left perisylvian language areas to guide retrieval of rote knowledge of arithmetic facts without semantic mediation, and an indirect semantic route that manipulates analog magnitude representations in bilateral parietal areas to compare operands and uses back-up strategies by manipulating visual Arabic representations when rote knowledge is not available in verbal memory, such as transforming complex problems into components for which facts can be retrieved (LeFevre et al., 1996), seems to be supported by our results. Although ICA cannot establish relationships between components, the presence of multiple components for brain regions corresponding to the hypothesized functional roles of the three codes for the complex task used in the current study suggests some relations between components, albeit speculative. Previous neuroimaging studies have indicated that as number sizes increase and problems become more difficult, bilateral activation of the intraparietal sulci increases due to the greater difficulty in retrieving facts from rote memory and increasing reliance on strategies (Molko et al., 2003; Stanescu-Cosson et al., 2000). Additionally, the prefrontal activation found in the current study may support Dehaene's proposal that these areas are involved with coordinating the sequencing of processing through the modules in the appropriate order, holding intermediate results in working memory, and detecting errors (Dehaene, 1997; Dehaene and Naccache, 2001; Dehaene et al., 1996; Kopera-Frye et al., 1996; Shallice and Evans, 1978). Future studies should be designed to specifically investigate relations between the components of the model.

The current study provides important information regarding brain areas associated with performing complex math operations that can be used to inform theories of math cognition. Furthermore, the identification of independent components of numerical processing can help psychologists develop a better understanding of genetic disorders involving visuospatial and number processing deficits, such as Turner, Williams, and Fragile X syndromes (Molko et al., 2003; Ross et al., 2000), and subtypes of math disabilities (Badian, 1983; Geary, 1990, 1993; Geary and Hoard, 2001; Geary et al., 1999, 2000; Strang and Rourke, 1985), which can be used to improve intervention strategies. Future studies should include longitudinal examinations of the development of various components of numerical processing and how they interact in children with and without disabilities, as well as the effects of particular intervention strategies on these developing brain systems for children with disabilities.

Conclusion

Group ICA analysis techniques were used on fMRI data obtained from normal adult subjects mentally adding and subtracting fractions. The results support the previously hypothesized triple-code model of analog magnitude, auditory verbal, and visual Arabic frames of number representation and processing, and indicate that the triple-code model may be a suitable neurocognitive framework for analyzing the performance of complex mathematical tasks.

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