Chapter 13

Neuroanatomical Approaches to the Study of Mathematical Ability and Disability

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Our goal in this chapter is to describe the cognitive neuroscience approach to the study of numerical and mathematical ability and disability and to demonstrate its potential value for informing both the diagnosis and remediation of impairments. To begin, we compare the cognitive neuroscience approach to others that have been used, emphasizing that as all methods have both strengths and weaknesses, their suitability for different kinds of studies depends on the objectives of the research. Our focus here is on studies that have attempted to identify the areas of the human brain involved with numerical thinking and how those brain regions relate to the processes used by a person carrying out a task.

Behavioral studies of children's math performance, such as those that describe children's use of everyday mathematics (see Pellegrini & Stanic, 1993), or their ability to perform arithmetic operations such as counting and calculating (e.g., Canobi, Reeve, & Pattison, 2002; Fuson, 1992), have provided a wealth of information about the typical and atypical development of math ability. This approach, however, is primarily descriptive in nature

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and does not significantly advance our understanding of the specific thinking processes underlying these abilities, or how and where they are implemented in terms of the neuroanatomy of the brain.

Standardized tests involve giving specific problems to a child to work through and then comparing his or her performance with that of a large, normative sample of children. Such tests are enormously useful for determining appropriate or inappropriate developmental progress and for assessing and reporting outcomes (e.g., in evaluating the effectiveness of various interventions). Also, standardized tests are frequently used very effectively as measurement tools in a range of clinical research studies (e.g., Murphy, Mazzocco, Gerner, & Henry, 2006). Much like behavioral studies, however, these tools typically provide us with little specificity about the precise cognitive processes a child is employing to achieve a given level of performance.

Cognitive experiments (e.g., Geary & Wiley, 1991; Siegler & Booth, 2004) are designed to assess very specific aspects of math ability in a given domain. As a result, they are much more able to explicitly delineate the cognitive processes that groups of children carry out; yet, they give only very broad and somewhat speculative ideas as to how these processes are actually related to specific brain regions or circuits. When used in conjunction with information about brain structure and function, however, such experiments provide a critical component of cognitive neuroscience research. The major goal of such investigations is the explication of structure–function relationships between the mental computations carried out in the mind and the neuroanatomical structures of the brain that support those computations. Of course, gaining information about brain structure and function has historically been the most challenging problem for researchers, and recent advances have been crucial to the development of cognitive neuroscientific methods.

Lesion studies provided many of the first important insights into how changes in the brain can alter specific functions of the mind. Individuals, usually adults, who have experienced damage, disease, or injury to the brain, have been studied in an attempt to understand the relationship between alterations to brain tissue and the resulting changes in behavior and/or abilities. This research method essentially began with the famous case of Phineas Gage, who suffered frontal lobe damage when a tamping iron pierced his skull in a railroad construction accident in 1848. The damage was assumed to be related to his resulting personality changes, which led Gage's acquaintances to the impression that "he was no longer Gage" (see Damasio, Grabowski, Frank, Galaburda, & Damasio, 1994). Since that time, the field of clinical brain research has become highly sophisticated and has produced many important insights (Roman et al., 2003; Semenza et al., 2006; Tohgi et al., 1995; Verstichel & Masson, 2003). However, although brain injury can now be accurately characterized using modern imaging methods, neural changes, even those resulting from specific surgical procedures, are rarely localized to specific anatomical structures or functional circuits. This makes it hard to draw the kind of precise structure–function inferences that are important to nonclinical, basic research questions.

Technological advances, including the development of brain imaging methods such as functional Magnetic Resonance Imaging (fMRI) and event-related potentials (ERP), have brought researchers closer than ever to the goal of localizing brain function for specific cognitive processes. These two methods detect two fundamentally different physiological phenomena associated with brain activity. ERPs are averages of the electrical activity arising from the firing of neurons that are time-locked to particular stimulus presentations. They rely on electroencephalography (EEG), the continuous recording of brain electrical activity measured by electrodes placed on the scalp surface (for more details, see Luck, 2005). The transmission of electrical potentials during ERP recording is virtually instantaneous, with measurable activity occurring within milliseconds from the presentation of a stimulus. Thus, the temporal resolution of the ERP is excellent. Nevertheless, the spatial resolution of scalp-recorded electrical potentials is notoriously imprecise, and it cannot be assumed that the neural generators of a given electrical signal are located directly under the scalp area of the electrode recording the signal.

In contrast to ERPs, the fMRI method measures a blood-oxygenation-level-dependent (BOLD) response and is based on the proposition that when brain areas become active, they increase their blood flow disproportionately to metabolic need, resulting in a net increase in tissue oxygenation (see Fox, Raichle, Mintun, & Dence, 1988). Highly oxygenated areas of the brain have a stronger MR signal than less oxygenated regions. It is this signal increase that is detected by a computer analysis of the image data and then represented as color-coded "activation maps" (for more details, see Buxton, 2002). This resultant signal increase, however, is not instantaneous, and its peak is thought to occur as late as 5 to 6 seconds after the actual neuronal activity that generated the blood flow changes. Thus, while fMRI provides excellent spatial localization in the millimeter range, its temporal resolution falls far short of that provided by the ERP method. In response to this tradeoff, some cutting-edge studies have been able to combine both techniques in the same scanning session to optimize spatiotemporal resolution. Of course, it should be noted that neither of these techniques creates a direct measure of neuronal activity. ERPs are a remote measurement of the electric potential generated by neuronal activity, whereas fMRI measures the changes in blood oxygenation that result from neuronal activity.

Both of these imaging methods have been shown to hold some promise for studies of mathematical thinking. Although attempts have been made to use ERPs for the purposes of localization of function (Montgomery,

Montgomery, & Guisado, 1992), more often the research goals have been geared toward parsing mathematical thinking into its constituent components (e.g., in delineating the differences in brain function between processing incongruous versus correct arithmetic results) or to ascertain what strategies subjects were using during arithmetic processing by looking for ERP signatures consistent with one type of thinking versus another (El Yagoubi, Lemaire, & Besson, 2005; Galfano, Mazza, Angrilli, & Umilta, 2004; Iguchi & Hashimoto, 2000; Pauli et al., 1994; Szucs & Csepe, 2005; Wang, Kong, Tang, Zhuang, & Li, 2000). Other studies have used fMRI to investigate the neuroanatomical bases of numerical processing, and many of those studies will be reviewed below.

Before we begin to examine the research using brain imaging techniques, it is useful to ask the following: In what specific ways do these techniques add to the findings from studies using the other methods? One is that, as mentioned above, the use of noninvasive imaging techniques has allowed for a much more precise localization of function in the brain than is possible with neuropsychological, behavioral, or lesion studies. Thus, these techniques allow questions about both precisely where and when maturational changes occur in the brain and how these changes relate to the development of cognitive abilities. Another advantage of using brain imaging techniques becomes clear when one considers that behavioral performance is an index of what might be referred to as an “output state.” For example, looking at an individual’s performance on a given arithmetic task as the sole determinant of his or her numerical ability might mean missing an important part of the cognitive processing as well as the developmental picture. Individuals can arrive at the same answer to a problem whether or not they are using the same underlying mental processing algorithms and brain circuitry to do so. Therefore, the methods that exemplify cognitive neuroscience allow a deeper understanding of precisely which mental processing and brain activity patterns, combine to produce an output state. In other words, when asking questions about the neural substrates for accomplishing a given skill in either typical or atypical development, there is a significant value added with the use of brain imaging techniques, especially when they are combined with cognitive processing experiments, as is typical of most cognitive neuroscience research programs. As we begin to describe studies in which neural activation in various brain regions has been detected, consult Figure 13.1 for information pertaining to the precise locations of these neuroanatomical subtrates.

STUDIES OF ACTUAL AND SIMULATED BRAIN INJURY

Much of the knowledge about how the brain processes numerical stimuli initially came from lesion studies. Most of the documented lesions were the

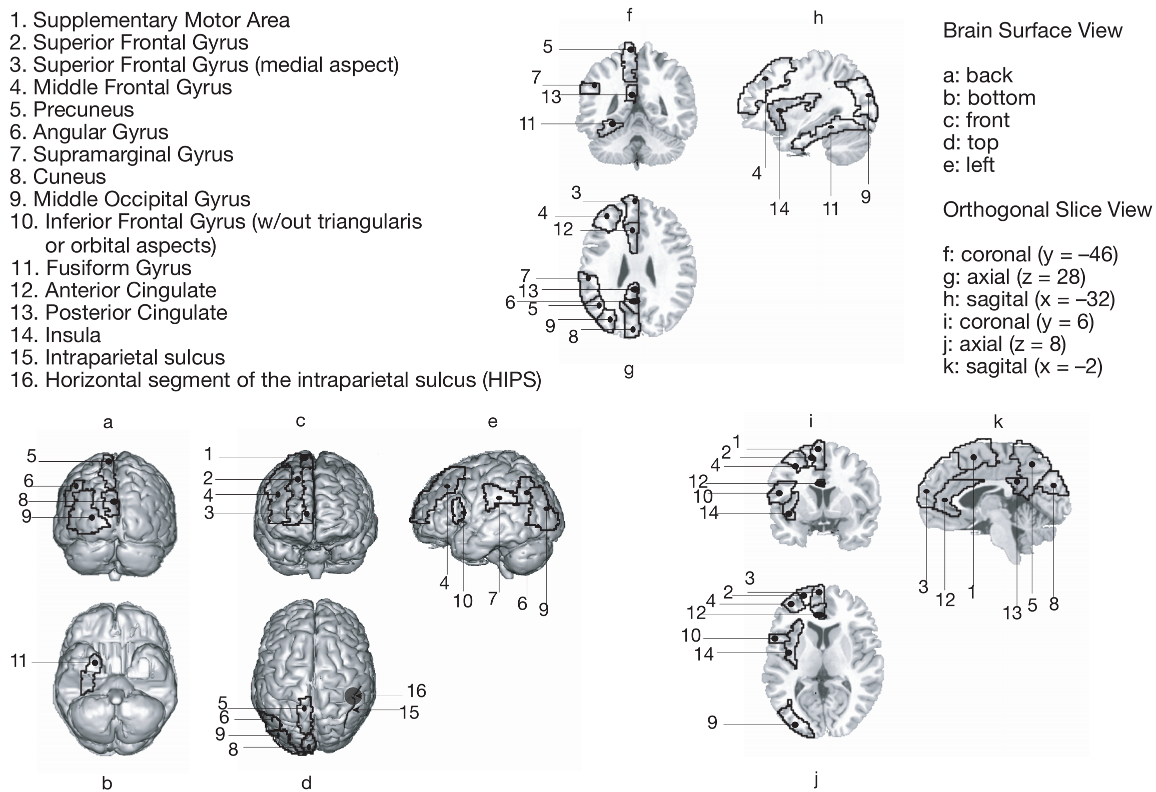

Figure 13.1. Identification of brain regions in which neural activation was detected in the studies reported in this chapter. (*Key:* (a) rendering of brain surface viewed from behind; (b) rendering of brain surface viewed from below; (c) rendering of brain surface viewed from the front; (d) rendering of brain surface viewed from above; (e) rendering of brain surface viewed from the left; (f) posterior region brain slice viewed from behind; (g) superior region brain slice viewed from above; (h) lateral region brain slice viewed from the left; (i) anterior region brain slice viewed from the front; (j) inferior region brain slice viewed from above; (k) medial region brain slice viewed from the left.)

result of stroke or some other brain insult or injury process and so occurred predominantly in middle-aged to older adults (see Chapter 12 for a detailed discussion of single case studies). Thus, the information gathered was largely restricted to impairments in numerical processing that emerged long after full acquisition of numerical and mathematical knowledge and procedures had taken place. A typical finding was that acalculia, the impaired ability to perform arithmetic calculations, resulted from damage to the parietal cortex, usually in the left hemisphere (Benson & Weir, 1972; Cohen, Dehaene, Chochon, Lehericy, & Naccache, 2000; Dehaene, 1997; Dehaene & Cohen, 1991; Grafman, Passafiume, Faglioni, & Boller, 1982; Henschen, 1920; Lampl, Eshel, Gilad, & Sarova-Pinhas, 1994; McCarthy & Warrington, 1988; Rosselli & Ardila, 1989; Takayama, Sugishita, Akiguchi, & Kimura, 1994; Tohgi et al., 1995; Warrington, 1982; Whalen, McCloskey, Lesser, & Gordon, 1997). In addition, lesions to prefrontal (Fasotti, Eling, & Bremer, 1992), frontoparietal (Cipolotti, Butterworth, & Denes, 1991), and subcortical structures, including the thalamus (Ojemann, 1974), showed associations with impaired calculation. In an early report, Cipolotti and colleagues (1991) described the case of a woman who demonstrated the Gerstmann syndrome after damage to her left parietal lobe. This syndrome is characterized by four primary symptoms: writing disability (agraphia or dysgraphia), disability for calculation or arithmetic (acalculia or dyscalculia), an inability to distinguish right from left, and an inability to identify one's own fingers (finger agnosia). In particular, her acalculia was so serious that she was unable to comprehend any number above 4. A less dramatic and much less typical example comes from the case of an 18-year-old male who showed some features of the Gerstmann syndrome, particularly a developmental acalculia. A magnetic resonance spectroscopy imaging study showed that he had reduced metabolism in the left temporal/parietal region, involving the angular gyrus (Levy, Reis, & Grafman, 1999). So, the early impression was that the inferior parietal lobe, especially involving the left angular gyrus, was an important neuroanatomical substrate for adult mathematical thinking. It was also recognized that this brain region was likely part of an extended functional circuit that includes prefrontal and subcortical areas.

A significant number of studies of individuals with spatial neglect have revealed further details about the relationship between numerical processing and the typically developing brain. Spatial neglect is defined as a "clinical syndrome in which patients are unaware of entire sectors of space on the side opposite to their lesion [. . . that] is produced by a lateralized disruption of spatial attention and representation" (Chatterjee, 2002). For example, Vuilleumier, Ortigue, and Brugger (2004) studied 14 adults with right hemisphere damage, half of whom showed left-sided spatial neglect and half of whom showed no spatial neglect, and 7 individuals considered healthy controls. To investigate numerical function, they used a standard numerical distance effect task, which generally involves the participant deciding whether a presented single-digit number (from 1 to 9) is greater or smaller than a remembered or visually presented standard. Difficulty in this task increases as the "numerical distance" between the target number and the standard decreases. In contrast to the comparison groups (individuals from nonneglect and healthy control groups), individuals with left neglect showed a unique handicap in responding to numbers that were smaller than the standard and immediately to the "left" of the standard (i.e., as represented along a mental number line). Interestingly, they showed this effect for the number 4 but not for 6 when the standard was 5; then, when the standard was changed to 7, they showed the same effect for the numbers 5 and 6. This result demonstrated the importance of spatial attention and cognitive processes to some noncomputational aspects of numerical cognition.

A similar study of four individuals with unilateral left spatial neglect resulting from right parietal lesions found that they systematically misstated the midpoint number (i.e., misidentified the spatial center point) between two aurally perceived numbers, with increasing inaccuracy as the distance between the two numbers increased (Zorzi, Priftis, & Umilta, 2002). Small intervals produced significant leftward shifts (e.g., the midpoint between 11 and 13 was given as 10), and large intervals produced rightward shifts (e.g., the midpoint between 11 and 19 was given as 17). This pattern of results was found despite the individuals' intact numerical and arithmetical abilities, whereas neither healthy participants nor individuals with injury to the right brain but without spatial neglect exhibited such errors. Clearly, damage to inferior parietal areas impairs the processing of spatial as well as numerical information and points to an important relationship between the two.

One concern about drawing strong inferences from studies of brain function following injury such as stroke is that the damage is unlikely to be precise in terms of localization to only a specific cortical structure or region or to its connections to other structures or regions that could potentially affect the functioning of the target region. Furthermore, adults with sufficiently serious health problems who have experienced a stroke may not be the ideal model from which to draw inferences about structure–function mappings in other populations. This is especially true when children constitute the group of interest. Thus, it is particularly interesting to consider the results of studies using transcranial magnetic stimulation (TMS), which is a method of temporarily and noninvasively "deactivating" fairly precise areas of cortex to examine the effects on resulting function. To date, this has typically been carried out with healthy young adult participants, so although differences are still likely to exist between these participants and children, these differences are likely to be less significant than is true for older individuals with stroke.

One such study by Göbel and colleagues (Göbel, Calabria, Farne, & Rossetti, 2006) actually showed that the effect reported by Vuilleumier and colleagues (2004) could be transiently induced in healthy adults by simulating left-sided neglect. Using repetitive transcranial magnetic stimulation (rTMS), researchers temporarily deactivated the left and right posterior parietal sites (angular gyrus and posterior supramarginal gyrus) and medial occipital cortex. Before stimulation, the participants' error in the numerical bisection task varied with interval size, just as with Zorzi and colleagues's (2002) participants. However, error was significantly increased by rTMS over right posterior parietal cortex and shifted in the rightward direction (consistent with Zorzi et al.'s findings, as the intervals were large and varied from 16 to 64). A nonsignificant effect was found in the same direction for left parietal stimulation, but no effect was found on bisection error.

To summarize, these results show that adults who have achieved typically developed levels of numerical and arithmetical ability experience significant impairments in that domain when areas of the posterior parietal lobes are damaged or deactivated by rTMS. The posterior parietal areas implicated by most of these reports are the angular and supramarginal gyri. Some studies have also indicated that impairments can occur when either the left or right parietal areas are affected, although the effects are not identical. Researchers naturally concluded that, at least in adults, the posterior parietal lobes are critical brain regions for numerically related processing, especially when the tasks involved retain some of the spatial characteristics associated with more approximate numerical reasoning (such as magnitude comparison). The neglect studies also implicate spatial attention processes as an important component of numerical cognition. The weakness of these studies, from the standpoint of researchers whose goal is to accurately localize numerical functioning in the brains of typically developing adults, is their low spatial resolution (but see Chapter 12 for a discussion of insights gained on a wide range of numerical processes from neuropsychological case studies). Brain injury is never restricted to specific anatomical structures or circuits. Furthermore, although rTMS can be applied accurately to specific areas of the scalp, its effect has far less than pinpoint accuracy. Thus, in the 1990s, many researchers turned to the emerging technology of fMRI to gain much more accuracy in their attempt to localize numerical and arithmetical functioning in typically developing adults.

THE NEUROIMAGING CORRELATES OF NUMERICAL PROCESSING IN ADULTS

Although space limitations prevent us from reviewing the now considerable number of functional neuroimaging studies of numerical processing, we will start by presenting perhaps the predominant view of the neural circuitry involved. Then we will summarize several studies that augment or complement that view in one way or another.

Dehaene, Piazza, Pinel, and Cohen (2003) presented evidence from neuroimaging and neuropsychological (i.e., primarily individuals with lesions) studies in support of what they described as a "tentative model" for three parietal circuits on which number processing depends in adults who are typically developing. Despite their use of the term *parietal circuits,* each of the three components mentioned is actually a rather distinct anatomical structure. We will address other brain areas that appear to form circuits in tandem with these regions later in this section. The horizontal segment of the intraparietal sulcus (or HIPS) is the landmark that separates the superior and inferior sections of the parietal lobe. The reference known as *Gray's Anatomy* (Lewis, 1924) states that

> From about the middle of the postcentral sulcus, or from the upper end of its inferior ramus, the horizontal portion of the intraparietal sulcus is carried backward and slightly upward on the parietal lobe, and is prolonged, under the name of the occipital ramus, on to the occipital lobe, where it divides into two parts, which form nearly a right angle with the main stem and constitute the transverse occipital sulcus. (pp. 828–829)

Dehaene and colleagues proposed that "a nonverbal representation of numerical quantity, perhaps analogous to a spatial map or 'number line' is present in the HIPS of both hemispheres" (2003, p. 489). They presented evidence that the HIPS is active when mental arithmetic requires a quantitative representation of numbers and when a comparative operation, such as is called upon by magnitude comparison or numerical distance effect tasks, is required. They also suggested that the HIPS is domain specific for numbers but indicated that it is not yet clear whether the HIPS "is strictly specific for numbers or whether it extends to other categories that have a strong spatial or serial component (e.g., the alphabet, days, months, spatial prepositions)" (p. 492).

The left angular gyrus (AG), located below and behind the HIPS in the posterior parietal lobe, is identified by Dehaene and colleagues (2003) as the locus of a very different kind of numerical processing. They stated that

> The left AG does not seem to be concerned with quantity processing, but shows increasingly greater activation as tasks put greater requirement on verbal processing. We therefore propose that this region is part of the language system, and contributes to number processing only inasmuch as some arithmetic operations, such as multiplication, make particularly strong demands on a verbal coding of numbers. (2003, p. 494)

Finally, Dehaene and colleagues (2003) suggested that an area of the posterior superior parietal lobe (PSPL) behind the HIPS and above and more medial than the left angular gyrus is involved in number comparison, approximation, subtraction, and counting. This area also appears to be more active when a participant carries out two operations during a calculation rather than a single one. The authors indicated that this area is not specific to the number domain. They explained that the PSPL is involved in these tasks because "it also plays a central role in a variety of visuospatial tasks including hand reaching, grasping, eye and/or attention orienting, mental rotation, and spatial working memory" (p. 498). It should be noted that Dehaene and colleagues (2003) were careful to limit their claims about the specificity of these regions for numerical processing to the HIPS only. Although their hypothesis appears to minimize the impact of development and experience by assuming "an initial prespecialization of the brain circuits that will ultimately support high-level arithmetic in adults" (p. 499), the authors indicated that "much of the human capacity for number processing [within the parietal lobe] relies on representations and processes that are not specific to the number domain" (p. 501). This at least leaves open the possibility implied by the lesion studies that spatial and attentional processes may not just be important components of fully developed numerical and mathematical cognition but may even be necessary precursor abilities. Such a view has been advanced by one of us (TJS) elsewhere (Simon, 1997, 1999).

Obviously, the three regions identified by Dehaene and colleagues (2003) are not the only brain areas that are consistently found to activate when typically developing adults engage in a range of numerical processing tasks. What follows is a very brief review of brain activations that show some degree of consistency for different kinds of tasks. Given the short history of neuroimaging studies in this domain, far too few studies have yet taken place for a definitive set of "typical adult numerical brain circuits" and their variants in special populations to have been identified. Except where specified, activations will refer to those found in young, healthy adults.

Perhaps the largest set of studies has employed magnitude comparison or numerical distance effect tasks, like those described earlier, to explore the neuroanatomy of numerical processing. Pinel and colleagues (Pinel, Dehaene, Riviere, & LeBihan, 2001; Pinel et al., 1999) not only reported parietal activations like those already described in response to such a task but they also found them to be part of a large, distributed network that "included visual and motor cortical areas as well as prefrontal and anterior cingulate cortices" (1999, p. 1477). Visual cortex is situated primarily in the occipital lobes, the most posterior lobe of the cerebral cortex, and is comprised of Brodmann's areas 17, 18, and 19. Motor cortex is the region of cerebral cortex that is situated in the most posterior part of the frontal lobe, just in front of the central sulcus, which divides frontal and parietal cortical areas. It is comprised of the primary motor cortex (Brodmann's area 4) and the lateral and medial premotor or supplementary motor cortex (Brodmann's area 6). These researchers took their studies a step further by carrying out fMRI and ERP experiments to enable a more precise examination of the location and timing of brain activity during different processing stages of a magnitude comparison task. Their main finding was that varying numerical distance produced most activation change "in the bilateral parietal lobes, in the banks of the intraparietal sulcus, and in the precuneus, with small additional effects in the posterior cingulate cortex and middle temporal region" (Pinel et al., 2001, p. 1022). The intraparietal and precuneus areas appear to map rather closely onto the aforementioned HIPS and PSPL regions, respectively.

Turconi and her collaborators (Turconi, Jemel, Rossion, & Seron, 2004) used ERPs to compare processing on a magnitude comparison task with two tasks in which order (i.e., before or after the target in a list rather than smaller or greater magnitude) was the dimension of interest. They found that all three tasks were associated with neural activity in electrodes sited in the temporal, occipital, and parietal regions, and they also found activity in medial frontal regions. The distance effect task produced bilateral parietal activations that were more left biased when judging *magnitude* using numbers and more right biased when judging *order* using numbers. The control task of judging order using letters inverted the polarity of the ERP signal but still showed a bilateral parietal effect that was more pronounced in the left hemisphere.

Fulbright and colleagues (Fulbright, Manson, Skudlarski, Lacadie, & Gore, 2003) carried out an fMRI task that also required order judgments, either in terms of alphabetic location, position in the number line, or relative physical size of shapes. They also created "near" and "far" trials as in most distance effect studies. All three order tasks produced intraparietal sulcus activations. These were bilateral in all cases except for the physical size task, in which the left IPS activations did not reach the statistical threshold. Comparing near to far trials showed that the more difficult near trials activated inferior frontal regions for all three tasks, with the left supramarginal gyrus being the only parietal activation for numbers. Interestingly, the intraparietal sulcus was activated for near trials more than far only for physical size judgments.

Several studies have combined fMRI investigations of numerical magnitude comparison tasks with judgments made on other physical characteristics of the stimuli. Cohen-Kadosh and collaborators (Cohen-Kadosh et al., 2005) compared activations for comparisons based on number, physical size, and luminance, showing

> Activation of a widespread cortical network that was highly similar for all the comparisons. Clusters of activation included the bilateral occipitotemporal and occipitoparietal pathways, IPS, FEF, SMA, IFG, insula and the sensorimotor areas. There was more activation in the right temporal lobe than the left, whereas the angular gyrus was more activated on the left than on the right. (pp. 1243–1244)

(IPS is the intraparietal sulcus; FEF, SMA, and IFG are the frontal lobe areas of the frontal eye fields, supplementary motor areas, and the inferior frontal gyrus, respectively). Much of this network is similar to the extended one described earlier from Pinel et al.'s 2001 study. Although the intraparietal sulcus was activated by all three kinds of comparisons, the authors concluded that there was a specific area of the left IPS (and right temporal lobe) that was associated with the numerical distance effect.

A very similar study by Pinel and colleagues (Pinel, Piazza, LeBihan, & Dehaene, 2004) also required participants to compare physical size (with numbers and letters) and luminance as well as numerals. Numerical comparisons activated the HIPS area bilaterally as well as the left precentral gyrus, whereas the other comparisons activated different networks, each involving some part of the intraparietal sulcus (though not usually the HIPS). There was little overlap with Cohen-Kadosh and colleagues' (2005) activations for these other tasks. Despite the similarity of the judgments involved, these findings may have been due to great differences in the stimuli and task demands.

Overall, these studies appear to support the evidence for posterior parietal involvement in numerical processing, although not exactly in the same way as specified by Dehaene and colleagues (2003). These activation studies also introduce evidence of some prefrontal and temporal region involvement, as was indicated by the lesion literature. Finally, they also suggest that the posterior parietal activations observed are not necessarily domain specific and limited only to numerical cognition.

Of course, the tasks of judging numerical order or relative magnitude are only two of the numerically relevant tasks that adults might undertake. Several studies have addressed other aspects of numerically relevant processing. Using positron emission tomography (PET), Sathian and colleagues (1999) examined counting as well as visual search. Though subitizing (the rapid and accurate detection and enumeration of one to three objects) was most strongly associated with the middle occipital gyrus, counting activated a large fronto-parieto-cerebellar network that included the cerebellar vermis (the central or wormlike structure that separates the two hemispheres of the cerebellum), middle occipital regions, the right inferior frontal gyrus, and bilateral intraparietal sulcus areas. Similar middle occipital and intraparietal activations were found by Piazza and colleagues (Piazza, Mechelli, Butterworth, & Price, 2002) using fMRI, especially when six to nine randomly placed dots were presented. These studies contribute a further link between space and number processing. This is because counting of visually presented objects, which usually requires the use of spatial search and working memory processes, appears to also involve prefrontal along with similar posterior parietal regions to those seen in the magnitude comparison tasks.

Some studies have looked directly at activations associated with arithmetic itself. Dehaene and colleagues (Dehaene, Spelke, Pinel, Stanescu, & Tsivkin, 1999) examined the differences in brain activations when individuals chose an exact answer to computations (such as 4 + 5 = either 9 or 7) compared with when they selected the best approximate, or most plausible, answer (such as 4 + 5 = either 8 or 3). The latter task, which resembles a magnitude comparison judgment, activated the left and right intraparietal sulcus in the region of the HIPS along with the right superior parietal cortex and left prefrontal areas among others. The authors ascribe this activation pattern to the spatial nature of this version of the numerical task. Conversely, the exact calculation task, which the authors claim is based on well-established linguistic representations and processes, mainly activated a left inferior frontal region associated with verbal association tasks. This latter task also produced some parietal activations, including the left (and right) angular gyri and precuneus along with the left cingulate and right middle temporal areas, just below the inferior parietal supramarginal area. An associated ERP study produced signals consistent with the fMRI activations.

There seems to be rather less consensus concerning the brain regions involved in mental arithmetic. In a study with addition problems using Arabic numerals or canonical (i.e., dice-like) dot patterns, Venkatraman and colleagues (Venkatraman, Ansari, & Chee, 2005) found no differences between exact and approximate versions of their addition task and no significant activation in left hemisphere language areas for the exact addition task. In all cases, activations were produced bilaterally in the anterior IPS (in the same region as the HIPS) as well as the left posterior IPS and left precentral gyrus when compared with a control task that presented single examples of stimuli identical to those in each addition task. Those stimuli were chosen to control for the assumed automatic activation of magnitude-related areas of the parietal lobes in response to the viewing of any numbers and thus to isolate areas associated with mental addition. In addition, most tasks activated medial frontal gyrus, dorsolateral prefrontal cortex, insula, and fusiform gyrus. So the specifics of task design appear to affect the activations that are observed quite strongly in studies of mental arithmetic. This is presumably because they directly affect the representations and processes required for each different set of conditions.

Kong and colleagues (2005) studied much more complex, exact computation by using large magnitude addition and subtraction tasks whose products would not be readily available for retrieval from memory. The left posterior IPS, close to the area reported by Venkatraman and colleagues (2005), was activated for all computations along with the left inferior frontal gyrus, left superior parietal and precuneus regions, and the right inferior parietal lobe in the area of the supramarginal gyrus. When the more complex problems (involving borrowing and carrying) were compared with the simpler (not involving borrowing and carrying) ones, the left posterior IPS and left inferior frontal gyrus activations were accompanied by activity in the bilateral medial frontal and anterior cingulate cortex. Similar to Venkatraman and colleagues's study, all tasks activated the left insula along with the left occipital gyrus and medial frontal gyrus/cingulate cortex, and most tasks activated the left fusiform and right insula.

Menon and colleagues (Menon, Rivera, White, Eliez, et al., 2000; Menon, Rivera, White, Glover, & Reiss, 2000) examined the relative contributions of prefrontal and parietal regions to components of arithmetical processing. In their studies, participants were asked to indicate whether the given result for an arithmetic equation was correct or incorrect. Researchers manipulated complexity in terms of the number of operands a problem contained; they also manipulated difficulty in terms of the solution time available. Two-operand tasks were of the form $1 + 2 = 3$; three-operand tasks were of the form $6 - 3 + 5 = 7$. Problems were presented either quickly (one every 3 seconds) or slowly (one every 6 seconds) during the fMRI scanning experiment. Because college-age adults solved the slow (6-second), easy (two-operand) problems fairly effortlessly, there were no significant activations during those trials. All of the other trial types activated a network rather similar to the other arithmetic studies: the inferior frontal gyrus, medial frontal gyrus, supramarginal and angular gyri in the inferior parietal lobe, and the presupplementary motor area. Because the task design involved one manipulation of difficulty that did not involve calculation (rate) and one that did (number of operands), it was possible to dissociate the relative neural contributions of these two factors. In response to an increase in rate (i.e., going from slow to fast presentation), frontal activity was observed—specifically in the left insula and the basal operculum of the orbitofrontal gyrus. The orbitofrontal cortex lies on the base of the frontal cortex in its most anterior segment, above the eyes or orbits. In response to an increase in the number of operands to be calculated (i.e., going from two to three), posterior parietal activity was observed, namely, the left and right angular gyrus. This dissociation served to pinpoint the areas responsible for arithmetic computation independent of other processing demands. Of note, in a follow-up experiment, the same authors showed that the only difference that discriminated a subset of the participants who produced 100% correct performance in the fast, difficult condition from those who made at least one error was significantly lower activation in the left angular gyrus. This is consistent with Dehaene and colleagues's (2003) claim that, in adults, this area typically activates for tasks such as mental arithmetic, and it suggests that the amount of activation may be positively correlated with the difficulty of the task for the participant.

A similar but much more intensive study of the effects of complexity on several types of numerical calculation tasks, and similarly structured but nonnumerical reasoning tasks, was carried out by Gruber and colleagues (Gruber, Indefrey, Steinmetz, & Kleinschmidt, 2001). Despite the much greater numerical magnitude of the values used in this study than those used in the Menon and colleagues's studies (Menon, Rivera, White, Eliez, et al., 2000; Menon, Rivera, White, Glover, et al., 2000), all tasks, including the nonnumerical ones, nonetheless activated a very similar network of areas. Gruber and colleagues reported that their "five conditions showed a similar left-dominant, bilateral prefrontal, premotor and parietal response pattern" (p. 353). The main areas included the inferior frontal sulcus and gyrus, premotor cortex (the medial part of which overlaps with the supplementary motor area), the posterior intraparietal sulcus and adjacent inferior and superior parietal cortex, and the presupplementary motor area extending into the anterior cingulate cortex. Like Menon and colleagues's findings, the authors reported a particular focus of activity in the left angular gyrus associated with numerical calculation. Gruber et al. found a strong association between activations in the medial posterior parietal region and the easier tasks, but the harder tasks tended to activate left inferior, prefrontal cortex adjacent to the anterior inferior frontal sulcus and the anterior cingulate cortex.

A study by Delazer and colleagues (Delazer et al., 2003) took calculation a step further and trained healthy adults to carry out complex multiplication problems. They also increased the complexity in a series of conditions. Compared with a control number-matching condition, problems that required just fact retrieval activated a network rather similar to the ones described above in response to arithmetical tasks. This network comprised the bilateral posterior intraparietal sulcus and adjoining left angular gyrus; left superior, bilateral middle, and inferior frontal gyri; left precentral sulcus; insular cortex; and anterior cingulate and bilateral cerebellum. Moving from relatively easy fact retrieval problems to hard, novel, or untrained multiplication problems also produced bilateral activations in the posterior intraparietal sulcus, inferior frontal gyrus, and cerebellum. Left hemisphere activations of the superior frontal gyrus and cuneus were seen, along with activations of the right hemisphere fusiform and medial frontal gyrus. The difference between the hardest task (the untrained multiplication problems) and the more familiar trained multiplication problems was seen only in the left hemisphere. The less difficult problems activated posterior IPS, inferior parietal and sylvian fissure regions, lingual gyrus, and the inferior frontal gyrus more than did the more difficult problems. Conversely, the main effect of maximum difficulty was seen in activations of the left angular gyrus, inferior frontal, and anterior cingulate gyrus, along with bilateral paracentral and cerebellar hemisphere.

So the circuits involved in typical adults' processing of exact and approximate arithmetic remain rather less clear than for magnitude comparison tasks. However, this is not necessarily cause for concern. Instead, it demonstrates a central tenet of cognitive neuroscience studies: that *subtle changes in task requirements will have specific effects on the representational and processing demands of the subject, and these will be directly observable in terms of distinct activation patterns.* Overall, however, the brain does seem to rely on a complex and extensive set of prefrontal, cingulate, insular, parietal, and temporal regions depending on the nature and complexity of the task and the processes required of the participant. Clearly, an extensive program of cognitive neuroscience investigation is needed in order to specify the different processes associated with the wide range of numerical processes in which most adults engage and the neuroanatomical substrates with which they are associated.

NEUROIMAGING STUDIES OF NUMERICAL PROCESSING IN CHILDREN

As with the lesion studies, most of what we know about the neuroanatomical correlates of numerical processing from neuroimaging studies has been garnered from investigations carried out with adult participants. This means that the pathways to typical and atypical development of numerical cognition and the necessary and sufficient building block competencies remain largely unstudied. It also means that the current consensus of the neurocognitive basis of function in this domain, as described previously, is likely to be skewed by the omission of developmental studies. However, brain imaging studies of mathematical reasoning have recently begun to be conducted with children only (Rivera, Reiss, Eckert, & Menon, 2005) and with both children and adults (Kawashima et al., 2004). Rivera and colleagues (2005) conducted fMRI with participants ranging in age from 9 to 18 years who performed a simple two-operand addition and subtraction task, for which accuracy was comparable across age. The study revealed both increases and decreases in activation with age, suggesting disparate levels and trajectories of functional maturation in particular brain regions. Although older children reached similar levels of accuracy on these simple problems to younger children, they presumably exhibited a more efficient recruitment of neural resources to do so. Accordingly, they demonstrated more activation in left parietal areas that have been consistently implicated in mental arithmetic processing, including the supramarginal gyrus and adjoining intraparietal sulcus. Older subjects also demonstrated more activation in the left lateral occipital-temporal cortex, an area thought to be important for visual word and symbol recognition (Cohen & Dehaene, 2004; Hart, Kraut, Kremen, Soher, & Gordon, 2000; Kronbichler et al., 2004; Price & Devlin, 2003, 2004). By contrast, younger subjects showed greater activation in the prefrontal cortex, including the dorsolateral and ventrolateral prefrontal cortex and anterior cingulate. Taken together, these findings suggest a process of increased functional specialization of the left posterior parietal cortex with age, with decreased dependence on working memory and attentional resources.

SUMMARY AND DISCUSSION

In this chapter, we have reviewed evidence from several sources that have been used to establish an understanding of the neuroanatomical correlates of numerical and mathematical thinking. Studies of adults who have experienced brain injury or who have had certain brain regions temporarily deactivated with transcranial magnetic stimulation indicate that posterior parietal areas are strongly associated with numerical competence. These studies also point to a relationship between spatial and numerical cognition, especially when magnitude comparison tasks are used. Various brain imaging methodologies (such as PET, fMRI, and ERP) have indicated that even those tasks tend to activate an extensive neural network involving the frontal and parietal lobes as well as some subcortical structures and the cerebellum. Studies of arithmetic show that different variants of this neural network become active depending on the precise details of the task requirements presented to the participant. This undoubtedly reflects the fact that different representations and processes are required by each task variant, and those differences involve different neural substrates for their implementation. The diversity of neural activity reported in response to the different tasks is clear evidence that the relationship between cognitive processes and neural substrates can be investigated and understood to a very high level of detail. Nonetheless, that encouraging interpretation does point to several shortcomings with the current state of this scientific enterprise.

One such weakness is that current understanding of how activity in the brain relates to mental processes associated with numerical and mathematical thinking does not provide a definitive picture of how domain specific that activity is. To an extent, this issue will be addressed when more developmental studies of the foundational competencies of mathematical cognition and studies of atypical development of numerical abilities are carried out. However, different views still remain and have yet to be reconciled. One position is that there are no initially domain-specific number areas in the brain and that neural circuits involved in the early development of object and spatial cognition, including spatial attention, form the foundation of the network that supports later mathematical ability (e.g., Simon, 1997). Another view suggests much more prespecification of a neuroanatomy for numerical processing. In this view, the horizontal section of the intraparietal sulcus (HIPS) has been advanced as a candidate for a domain-specific numerical processing region. Dehaene and colleagues stated "At least two of the three parietal circuits that we have described . . . are thought to be associated with broader functions than mere calculation" (2003, p. 501). The remaining HIPS area is, they claim, "a more plausible candidate for domain specificity," though they prefer the term "number-essential."

However, the HIPS region is also reliably activated in adults by many nonnumerical functions that might form the foundation for the construction of domain-specific numerical processing. In an fMRI experiment, Wojciulik and Kanwisher (1999) looked for overlap activation in multiple tasks (AOMT) involving spatial attention and object processing. None of the tasks was numerical in nature. The most reliable areas of AOMT were in the intraparietal sulcus, with most participants activating a region that Wojciulik and Kanwisher referred to as anterior intraparietal sulcus (AIPS). The location of this region and the volume of activated tissue indicate strong overlap with Dehaene and colleagues's HIPS region. Another, even more reliably activated part of the IPS was the one at the junction of the transverse occipital sulcus (IPTO), leading to Wojciulik and Kanwisher's conclusion that "IPTO and AIPS . . . may be part of a more extensive network of overlapping activations that span much of IPS and SPL" (1999, p. 750). This means that both the HIPS and superior parietal "numerical circuits" described by Dehaene and colleagues (2003) would be included in these regions. Shuman and Kanwisher (2004) even directly tested the numerical domain specificity claim for HIPS by using nonsymbolic stimuli to test for numerical versus nonnumerical judgments and for difficulty effects. They concluded that their experiments "failed to support the hypothesis that the human parietal lobe contains the neural instantiation of a domain specific mechanism for representing abstract numerical magnitude" (p. 7).

Another shortcoming of the current body of evidence is that almost all of the neuroanatomical studies of numerical cognition have been carried out on adults. This is perfectly understandable in a historical context. It is likely, however, that the impression left by these studies of a single "neuroanatomy of mathematical ability" is a false one. If subtle changes in representation and processing are related to significant changes in neural activations, then the neural activation seen in children who are typically developing (i.e., who are in the fluid state of still acquiring numerical and mathematical knowledge and skills) might be quite different from that reported in typically developed adults, who have crystallized that ability. The neural activity associated with those processes used by children who are not developing typically in the acquisition of numerical competence will likely be characteristically different from both of those groups. Thus, it is safest to assume for now that there will be different neuroanatomical correlates associated with the varieties of numerical abilities that individuals have at different points in the lifespan. Considerable research is clearly needed in order to specify those different patterns.

The activation of brain regions detected in adults in response to numerical tasks should not necessarily lead one to assume that those circuits are hardwired into the brain and prespecified as the basis of numerical processing. To adopt such a view would lead to the further inference that numerical and mathematical disability necessarily arises from lesions to or dysfunctions in those specific circuits. Indeed, as Johnson and colleagues (Johnson, Halit, Grice, & Karmiloff-Smith, 2002) suggested, those two assumptions are inappropriate for understanding typical and atypical neural development in any domain. The former, or "static," assumption is that brain–behavior relationships are fixed and that the age at which individuals are studied in order to determine that relationship is unimportant. The latter, or "deficit," assumption refers to the unidirectional inference that "damage to specific neural substrates both causes and explains the behavioral deficits observed in developmental disorders" (p. 525).

Despite this critique, the assumptions just described remain widespread and are implied by Landerl and colleagues's (Landerl, Bevan, & Butterworth, 2004) statement that "neuropsychological evidence indicates that numerical processing is localized to the parietal lobes bilaterally, in particular the intra-parietal sulcus (Dehaene et al., 2003), and is independent of other abilities. Developmental dyscalculia is likely to be the result of the failure of these brain areas to develop normally, whether because of injury or because of genetic factors" (p. 121). Obviously, a greater understanding of these issues is needed and will likely emerge only when extensive developmental studies of typical and atypical numerical and mathematical cognitive development have been carried out using experimental and neuroimaging methods. The results of such a program of research are likely to provide deep insights into the cognitive and neuroanatomical bases of numerical and mathematical disability that will help us to understand and ultimately remediate or even prevent such outcomes from occurring.

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