The Neurobiological Basis of Reading: A Special Case of Skill Acquisition

Peter E. Turkeltaub[1], Jill Weisberg[1], D. Lynn Flowers[1,2], Debi Basu[1], and Guinevere F. Eden[1]

[1] 4000 Reservoir Road, Building D Suite 150; Georgetown University Medical Center, Washington, District of Columbia 20057, USA

[2] Wake Forest University Medical Center at Bowman Gray, Winston-Salem, North Carolina. 27157, USA

Corresponding Author:
Guinevere F. Eden
edeng@georgetown.edu
Center for the Study of Learning
4000 Reservoir Road
Building D, Suite 150
Washington, DC 20057, USA
Phone: (202) 687-6893
Fax: (202) 784-2414

INTRODUCTION

Characterizing the neurobiological basis of cortical plasticity is critical to the understanding of normal learning and memory processes and to the investigation of developmental disorders of cognition. Beginning with the seminal work of Wiesel and Hubel demonstrating that monocular deprivation leads to a reorganization of ocular dominance columns in visual cortex (e.g. Wiesel & Hubel, 1963), a large body of literature has accumulated documenting the dynamic nature of the nervous system. In recent years our understanding of the genetic, molecular, and cellular mechanisms underlying long-lasting changes in the structure and function of the brain that occur with normal brain development, with learning and memory, and with recovery from, or adaptation to, injury has grown tremendously. At the same time, functional brain imaging techniques have evolved, enabling the observation of brain systems engaged in complex cognitive functions such as reading. While most functional brain imaging studies focus on mapping functional anatomy at a single point in time (i.e. "static" pictures of brain regions involved in a cognitive process), recently more studies are employing cross sectional and longitudinal approaches to explore how brain systems change over the course of learning.

The adaptability and plasticity of the brain is nowhere more apparent than in the fact that throughout our lives we continue to learn new information. Among the most important skills learned during childhood is reading. Written language is a recent invention relative to the course of human evolution. In that brief time, writing schemes have grown from collections of simple shapes representing objects encountered in daily life to sophisticated systems of symbols representing spoken sounds. Alphabetic systems have been passed on to various societies who have altered them to suit the phonetic structures of their oral languages, leading to the widespread use of written languages. Reading, and with it writing, is a fundamental skill for information exchange in today's society; the importance of good reading skills is enormous. Not being part of the human evolutionary heritage, it requires extensive effort and training to learn. Over several years of reading instruction and practice, the consolidation of orthographic and phonological skills, combined with automaticity and vocabulary gains, leads to the acquisition of a skill that is uniquely human and particularly important in today's literate society. From a neuroscientific perspective, this protracted time course of learning to read provides a unique opportunity to examine the mechanisms of neural plasticity associated with skill learning. From an educational perspective, considering reading in the context of biological plasticity, learning, and acquisition of expertise opens the potential for optimizing instructional approaches.

This chapter will examine the functional specialization of reading in the developing brain as an example of skill learning and neural plasticity. We will first present a brief discussion of neural plasticity associated with skill learning in humans. Recently, several neuroimaging studies have examined changes in brain anatomy and function that occur with acquisition of motor or perceptual skills. These studies elucidate general mechanisms of skill learning in tightly controlled experimental settings. Their findings may suggest potential biological adaptations associated with learning to read. In particular, we will discuss musical training, which shares some attributes with reading: it too is a distinctly human skill, requires integration and sequencing in multiple sensory modalities, and is learned through years of effortful training, usually initiated during childhood. Furthermore, musical training is somewhat easier to study than reading acquisition because musicality is less linked to confounding sociocultural factors than is literacy. Next we will review the implications of social and academic experiences on the neural wiring of the brain. Evidence suggesting experiential learning in two cortical areas will be discussed: (1) the right hemisphere "fusiform face area," which seems specialized for processing faces, and the homologous left hemisphere "visual word form area," which in literate adults seems specialized for processing text. Finally, we will discuss the neural plasticity associated with learning to read. We will first discuss behavioral models of learning to read, which consistently describe phases in the development of reading skill. Then we will examine evidence from neuroimaging studies suggesting neural mechanisms associated with these behavioral changes. In particular we will focus on two recent studies from our laboratory. The first addresses changes in the functional neuroanatomy of reading in a cross section of good readers ranging from kindergarten through the end of college. The second examines the neural mechanisms of reading in a 9-year-old hyperlexic boy who acquired extremely advanced reading skills at a young age despite severe expressive and receptive language delay.

THE EFFECT OF ENVIRONMENTAL EXPERIENCES ON THE BRAIN

Learning

Functional neuroplasticity following sensory deprivation has been extensively documented in studies of both animals and humans. Often, deprivation in one modality effects the development of the intact modalities both behaviorally and neurally (see Kujala, Alho, & Naatanen, 2000; J. P. Rauschecker, 2002 for reviews). The loci for these effects include multimodal, early sensory, and even primary sensory cortices, and theorized mechanisms include changes in local connectivity, stabilization of normally transient connections, and modification of cortical feedback loops (see Bavelier & Neville, 2002; J. Rauschecker, 1997 for reviews). While neural adaptation secondary to sensory deprivation is a classic example of brain plasticity, the learning of novel information or new skills also engenders plastic changes in brain structure and function.

One type of learning in which we continually engage is commonly referred to as procedural, or skill learning. Procedural learning occurs implicitly, and can be contrasted with declarative learning, which requires conscious awareness of that which is being learned. Functional neuroimaging studies of procedural learning, including motor and perceptual skill acquisition, have shown that learning-dependent changes in the brain may manifest as increases or decreases in extent or magnitude of activity, and as shifts in the locus or temporal relationships of neural responses (see Gilbert, Sigman, & Crist, 2001 for review).

In a typical perceptual or motor learning study, subjects are trained to perform a task (e.g. motor tapping sequence) until performance asymptotes, and then some parameter of the task is manipulated such that performance returns to a pre-skill acquisition baseline level. To study the cortical changes consequent to long term practice on a motor task, Karni and colleagues (1995) trained subjects to perform two different finger-thumb opposition sequences, which they were instructed to execute as quickly and accurately as possible, without looking at their hand. Subjects were scanned after measuring baseline performance on both sequences, then weekly as they practiced one of the sequences for 10-20 minutes each day for three weeks. Behaviorally, there were no differences between performance of the two sequences during baseline testing. After practice, however, subjects more than doubled their speed and accuracy of the practiced sequence, as compared to the untrained sequence. Interestingly, in addition to a lack of transfer to the untrained sequence, improvements were limited to the trained hand with little transfer of learning to the untrained hand. The specificity of practice effects to stimulus and task conditions is a common finding in procedural learning paradigms (see Gilbert et al., 2001 for further discussion, but see Green & Bavelier, 2003 for alternative findings). Functional magnetic resonance imaging (fMRI) data revealed that the experience-dependent changes in motor performance were reflected by an increase in the extent of motor cortex devoted to performing the trained sequence compared to the untrained sequence. Thus, the authors concluded that the effect of practice was the recruitment of additional neurons in motor cortex, resulting in an altered cortical topography, perhaps through new or stronger synaptic connections, effectively expanding the network of neurons dedicated to performing the trained sequence.

In addition to motor learning, practice can also bring about perceptual learning, reflected by an improved ability to detect differences in sensory stimuli. While cortical changes accompanying perceptual learning have been documented within each sensory domain (visual, auditory, tactile and olfactory), perhaps the visual modality has received the most attention. fMRI data have shown that after just a few minutes of practice on a coherent motion detection task, the extent of activation in area MT/V5, which mediates motion perception and is located at the occipito-temporal junction, was five times greater than when subjects initially performed the task (Vaina, Belliveau, des Roziers, & Zeffiro, 1998). This increased activity was highly correlated with behavioral performance, which was near chance for the first set of trials, and near perfect after several minutes. Furthermore, as subjects' performance improved and the extent of activity in area MT/V5 grew, activity was reduced in other extrastriate regions, creating a more focused representation, suggesting that perceptual processing had become more efficient. Additional learning-related changes were found in the cerebellum, where activity was inversely correlated with learning, decreasing by more than 90% as learning proceeded. When the visual stimulus was changed such that subjects had to detect motion in the opposite direction, performance returned to chance levels and cerebellar activity showed a marked increase. The specific region of the cerebellum modulated in this study has been implicated in visual attention (Allen, Buxton, Wong, & Courchesne, 1997), suggesting that fewer attentional resources are required as we become more proficient at visual perception tasks.

Studies of professional musician's brains offer further insight into the neuroanatomical substrates of skill learning. Like reading, performing music is a complex skill which, for most accomplished musicians, is learned from an early age, and lifelong practice leads to automatic processing with respect to the component skills (visual, auditory and tactile sensory skills, motor skills, and multimodal sensorimotor skills) (for review, see Munte, Altenmuller, & Jancke, 2002). In one study, musicians were found to have an extended hand area in right primary motor cortex compared to non-musicians, with reduced asymmetry (non-musicians show a pronounced asymmetry favoring the dominant hand) (Amunts et al., 1997). Similarly, in a study of string instrument players, Elbert et al. (1995) reported increased somatosensory cortex representation for the fingers of the left, but not the right hand, compared to control subjects. String players use the left hand for intricate finger movements on the strings, entailing finely skilled motor movements and intense somatosensory stimulation. In contrast, the right hand manipulates the bow, requiring considerably less skill and sensory stimulation. Moreover, in each of these studies, the size of the hand area was negatively correlated with the age at which musical training began, and in Amunts et al. (1997), with behavioral measurements of left (and therefore right hemisphere) index finger tapping rates. In a morphometric analysis comparing the brains of professional musicians, amateur musicians, and non-musicians, a positive correlation was found between musician status and increased gray matter volume in visual, auditory and motor regions (Gaser & Schlaug, 2003). While the relationship between length of musical training and neuroanatomy seems to reflect experience-dependent plasticity, it remains possible that the brain differences reviewed above were innate, resulting from a genetic propensity for musical ability in these individuals. However, a recent report by Draganski et al. (2004) provides compelling evidence in favor of learning-dependent structural changes in the human brain. They scanned subjects before and after training them to juggle, then again following three months without practice. Compared to a control group with no juggling experience, training induced an expansion in gray matter in the visual motion perception area MT/V5 and in left intraparietal sulcus, followed by a reduction after three months without practice. As in the studies mentioned above, structural changes mirrored behavioral performance measures. Clearly, further studies are required to tease apart the contributions of genetics versus experience to the functional and structural organization of the human brain.

BRAIN REGIONS TUNED TO SOCIAL AND ACADEMIC STIMULI

Identifying faces and reading printed words are an essential part of communication and socially meaningful interaction. For these reasons, social and academic pressures might play a role in optimizing these skills, leading to a fine tuning in the organization of the brain regions subserving face processing and reading. Although two apparently independent systems, it is useful to consider the mutual characteristics described in the literature that are relevant to the development of face and word recognition skills and their disorders.

While it is well documented that face and word processing each rely on a distributed cortical network, the right fusiform gyrus (RFG) is thought to be preferentially involved in processing facial identity and the left fusiform gyrus is thought to be preferentially involved in word processing, resulting in the respective terms “fusiform face area” and “visual word form area” (Cohen et al., 2000; Kanwisher, McDermott, & Chun, 1997). However, an active debate regarding the specificity of these extrastriate regions is ongoing (Kanwisher, 2000; Price & Devlin, 2003; Tarr & Gauthier, 2000) and will be discussed in turn.

The fusiform face area

A key component of meaningful human interactions is the ability to recognize individuals on subsequent occasions. The processing demands for face recognition require not only the skill to determine category membership (i.e., ‘this is a face’), but also to determine individuation (i.e., ‘this is Jack’). Correctly interpreting potentially threatening stimuli has enabled humans to survive from an evolutionary perspective (Zeki, 1999), and hence it seems plausible that specific regions of the brain are hard-wired in their devotion to face processing. In monkeys, single unit recordings from the inferior temporal cortex have revealed groups of cells that show a preference for faces (Perrett, Hietanen, Oram, & Benson, 1992). Initial evidence that an analogous region of human extrastriate cortex is devoted to face perception was derived from patient studies: stroke victims with selective impairment in face recognition, termed prosopagnosia, exhibited damage to the fusiform gyrus (Hier, Mondlock, & Caplan, 1983; Kumar, Verma, Maheshwari, & Kumar, 1986; Nardelli et al., 1982). Symptoms varied depending on the site of the lesion, suggesting that different parts of the fusiform gyrus are specialized for different aspects of face recognition (Sergent, Ohta, & MacDonald, 1992).

These patient data, bolstered by functional brain imaging data demonstrating that this region responds preferentially to pictures of faces compared to other objects, have led to the use of the term “fusiform face area” (FFA), implying a domain-specific area subserving face processing (Kanwisher, 2000). However, there is considerable debate as to whether this region is specialized for processing faces, or if in fact face recognition skills are the result of experience, in which case the FFA might mediate processing of other objects with which we have sufficient experience (Tarr & Gauthier, 2000). Gauthier and colleagues (Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999) addressed this question by training subjects to recognize novel objects called “greebles” until they reached a pre-determined level of expertise in identifying individual greebles as well as their family categories. The subjects underwent fMRI scanning before, during and after greeble expertise training. Since, compared to other objects, face recognition seems to be especially sensitive to stimulus orientation, Gauthier had subjects perform a matching task with upright or inverted faces and greebles in the scanner, hypothesizing that greeble expertise would be specific to viewing them in the trained, upright orientation. When comparing the activity for upright versus inverted greeble matching, Gauthier et al. found little activity in the FFA for greeble matching prior to training, but reported comparable activation for greeble and face matching following training. They interpreted these results as an indication that activation in the FFA is driven by expertise for novel objects. The authors concluded that “the face selective area in the middle fusiform gyrus may be most appropriately described as a general substrate for subordinate level discrimination that can be fine tuned by experience with any object category” (Gauthier et al., 1999), arguing against the notion of a module dedicated to the recognition of faces. In other words, contrary to the claim that this is a domain-specific region (Kanwisher, 2000), Gauthier and colleagues argue that the

FFA is specialized for processing any object in which the individual has visual expertise (Tarr & Gauthier, 2000).

The visual word form area

Numerous brain imaging studies have shown activity in a region of the left fusiform gyrus (LFG) when literate subjects read (Cohen et al., 2002). This "visual word form area" (VWFA) shows stronger activation in response to real letters and words as compared to letter strings or pseudo-fonts of equal visual complexity. Its activity during reading is invariant to the spatial location and the specific case or font used to present words (Cohen et al., 2002), and it has been suggested that this region contains orthographic representations of written words (Booth et al., 2002). The spatial location of the VWFA also may be a critical lesion site for pure alexia, a reading deficit which spares writing and auditory word comprehension (Takada, Sakurai, Takeuchil, & Sakuta, 1998). Furthermore, developmental dyslexics show reduced activity in this region of the LFG compared to control subjects when performing reading tasks (Brunswick, McCrory, Price, Frith, & Frith, 1999). Based on these findings it has been proposed that the LFG develops to process orthographic visual word forms in the course of learning to read.

However, the debate over the existence of a specialized cortical area for visual word form representation has many parallels with arguments that have emerged in support of and against the existence of the fusiform face area. As for face processing, it has been claimed that multiple brain regions are involved in word recognition, and that word recognition cannot be achieved by a single area in the LFG (Price & Devlin, 2003). Furthermore, evidence for engagement of the VWFA in tasks not involving visual word form processing, such as color and picture naming, support a more general role for this region (Moore & Price, 1999). Finally, brain imaging data from blind Braille readers suggests the VWFA performs complex linguistic processing of words in multiple modalities (Buchel, Price, Frackowiak, & Friston, 1998; Buchel, Price, & Friston, 1998), possibly linking abstract orthographic representations (containing information about the letter sequences composing words) with phonological representations (containing the sound structure of words). Thus, further investigation is required to determine whether or not the VFWA is (1) exclusively dedicated to word processing, (2) if it might serve several functions thereby making it a more general purpose processing region, or (3) if it serves a single function that can be recruited for different kinds of tasks (Price & Devlin, 2003). Evidence that the primary site for processing single letters lies anterior and lateral to the VWFA, make it unlikely that the VWFA alone can support word recognition (Flowers et al., 2004).

Finally, there is no direct evidence to date that word processing mechanisms within the VWFA develop over the course of learning to read.

Exploring and characterizing the neurobiological basis of skill acquisition and learning should prove valuable in resolving these debates. Reading, which is a complex multimodal skill learned only through explicit training, serves as an excellent model for cognitive skill learning in general.

READING

Reading Acquisition

The behavioral profile of reading acquisition of alphabetic languages has been well characterized (Chall, 1983; Ehri, 1999; Frith, 1985; Hoien & Lundberg, 1988; Stanovich, 1988; Wagner & Torgesen, 1987; Wagner et al., 1997; Wolf, 1999), as has its neural signature in adults (Fiez & Petersen, 1998; Friedman, Ween, & Albert, 1993; Petersen, Fox, Posner, Mintun, & Raichle, 1988; Price, 2000; Price, Wise, & Frackowiak, 1996; Pugh et al., 2001; Snyder, Abdullaev, Posner, & Raichle, 1995; Turkeltaub, Eden, Jones, & Zeffiro, 2002) allowing the generation of specific research questions regarding the neurobiological basis of childhood reading acquisition. A lifelong history of reading experience leaves its mark on the brain: it alters the behavioral performance and functional anatomy of linguistic tasks such as non-word repetition and object naming (Castro-Caldas, Petersson, Reis, Stone-Elander, & Ingvar, 1998). Therefore changes associated with reading experience necessarily have anatomical and physiological correlates that change throughout the period of acquisition. However, due to the radiation exposure associated with many neuroimaging techniques, in vivo neurophysiological measurements of healthy children have historically been limited. In the past decade, functional magnetic resonance imaging (fMRI) has emerged as a non-invasive functional imaging tool posing little or no risk to the subject, making it suitable for the study of children. Recently, fMRI studies of healthy children have examined cognitive processes as varied as executive control (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002), working memory (Kwon, Reiss, & Menon, 2002; Thomas et al., 1999) and language (Gaillard et al., 2001). Here, we will discuss the behavioral manifestations of reading acquisition and their neural correlates based on functional neuroimaging data.

Developmental Phases in Learning to Read

Behavioral neuropsychology research has revealed consistent developmental patterns of reading acquisition and identified variables critical to successful learning. Several models of childhood reading skill acquisition have been proposed describing similar sequences of behavioral development (Chall, 1983; Ehri, 1999; Frith, 1985; Hoien & Lundberg, 1988). Learning to read is typically described as a series of stages in which new decoding skills are acquired and applied. Skills learned in earlier stages are retained and can still be applied by advanced readers when need arises. Thus, learning to read is a process of adding decoding tools and strategies to one's repertoire and honing those skills with practice. The rate at which children move between stages varies depending on their ability, environment, and native language, but the developmental sequence remains fairly consistent (Hoien & Lundberg, 1988).

While the number of stages described differs depending on the depth and scope of the model, the overall developmental milestones described are strikingly similar. Children begin reading by recognizing words based on visual features or context. After gaining some knowledge of the alphabet and its associations with speech sounds, children begin using a few prominent letters in words as phonetic cues for identification. Then, as they gain a full understanding of the mapping of print to sound, children begin to decode words letter by letter in their entirety. Finally, as their vocabulary and automaticity improve, they consolidate common letter sequences, identifying them as a whole, and begin to read new words by analogy to known ones. Ehri (Ehri, 1999) describes this sequence of reading acquisition in 'phases' rather than stages, emphasizing that transitions between dominant reading strategies are not abrupt. Her model consists of four phases: pre-alphabetic, partial alphabetic, full alphabetic, and consolidated alphabetic. The partial alphabetic phase is unique to Ehri's model, while the other phases correspond to stages described by other investigators (see Chall, 1983; Frith, 1985; Hoien & Lundberg, 1988 for more detailed discussions).

Children's capabilities at phonological and related processing skills are critical determinants of future success at reading (Mann, 1993; Stanovich, 1988; J. K. Torgesen, Wagner, & Rashotte, 1994; J.K. Torgesen, Wagner, Simmons, & Laughon, 1990; Wagner, 1986; Wagner & Torgesen, 1987; Wagner, Torgesen, Laughon, Simmons, & Rashotte, 1993; Wagner et al., 1997; M. Wolf & Obregon, 1992). In particular, phonological awareness, the "awareness of and access to the sound structure of language" (Wagner & Torgesen, 1987), is causally related to learning in early stages of reading acquisition (Bradley & Bryant, 1983; Treiman, 2000; Wagner & Torgesen, 1987; Wagner et al., 1993; Wagner et al., 1997), and is considered the core deficit in developmental dyslexia (Felton, Naylor, & Wood, 1990). Common assessments include using phoneme segmentation tasks such as the Test of Auditory Analysis Skill (Rosner & Simon, 1971) ("say 'blend' without the /b/ sound"), or phoneme manipulation tasks such as the Lindamood Auditory Conceptualization Test (Lindamood & Lindamood, 1979), which requires children to represent speech sounds using colored blocks and manipulate them to depict changes in aural non-words ("if this says 'ip', show me 'pip'"). Two other phonological processing skills which independently contribute to reading success are (1) phonetic recoding in working memory, the sound-based coding of information for online maintenance in working memory, exemplified by the Digits Backwards subtest of the Digit Span; and (2) phonological recoding during lexical access, the efficiency of access to sound representations of words, assessed by rapid serial naming of items such as numbers or colors printed on a card (Denckla & Rudel, 1976; Wagner & Torgesen, 1987; Wagner et al., 1993). This latter skill may also be a critical area of deficit in severe cases of developmental dyslexia. Wolf has proposed a "double deficit" hypothesis of dyslexia, which posits that, in addition to the core phonological awareness deficit, a subset of severely impaired children also have a deficit in phonological recoding in lexical access (M Wolf, 1999).

The Biological Basis of Mature Reading

In the mature brain, literate adults rely on a network of neural structures to decode print. This network is widely distributed, including left lateralized regions of occipital, ventral temporal, posterior superior temporal, and inferior frontal cortices (Fiez & Petersen, 1998; Posner, Abdullaev, McCandliss, & Sereno, 1999; Price, 2000; Turkeltaub et al., 2002). When a printed word enters the visual field, striate and extrastriate cortices transmit visual information along a ventral occipito-temporal pathway to the left mid-fusiform gyrus. As discussed above, some have described this region as a "visual word-form area" (Cohen et al., 2000; Cohen et al., 2002; McCandliss, Cohen, & Dehaene, 2003), where the visual representations of words are stored. Phonological processing, the retrieval and assembly of the sound structure of words, relies on left superior temporal and dorsal inferior frontal cortical areas (Dietz, Jones, Gareau, Zeffiro, & Eden, Submitted; Fiez, 1997; Hagoort et al., 1999; Moore & Price, 1999; Poldrack et al., 1999; Pugh et al., 1996). Regions of the left anterior middle temporal gyrus, and the ventral inferior frontal gyrus have been implicated in semantic processing, the association of meanings with words (Fiez, 1997; Gorno-Tempini et al., 1998; Poldrack et al., 1999; Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996). Lesion and functional connectivity studies have implicated the left inferior parietal cortex in reading (Friedman et al., 1993; Horwitz, Rumsey, & Donohue, 1998), but it is unreliably activated during functional imaging studies (Fiez & Petersen, 1998; Turkeltaub et al., 2002). This area may be involved in a supporting function for reading, such as storage of phonological units for online processing in working memory (Becker, MacAndrew, & Fiez, 1999). Thus, the main areas commonly implicated in mature adult reading include the left fusiform gyrus in the ventral extrastriate cortex, the left superior temporal cortex, and the left inferior frontal gyrus. The developmental progression leading to this mature architecture, however, remains largely unknown.

Pediatric Brain Imaging

To some degree methodological constraints have made pediatric imaging studies of neural development spanning wide age ranges problematic. Physiological, anatomical and behavioral differences between subjects of different ages can confound results unless experiments are carefully controlled (Casey, Giedd, & Thomas, 2000; Gaillard et al., 2001; Poldrack, Pare-Blagoev, & Grant, 2002). Specifically, age-related differences in task performance, subject motion during scanning, and brain morphology must be accounted for if results are to be interpretable. To reduce confounds due to age-related differences in task performance, one can employ tasks individually tailored to subjects' abilities (Gaillard, Balsamo, Ibrahim, Sachs, & Xu, 2003), or select subgroups of subjects matched for task performance (Schlaggar et al., 2002). Differences between children and adults in brain morphology and physiology (i.e. heart rate, respiration) must also be addressed.

Neuroimaging studies of reading in healthy children have revealed activation of brain areas often associated with reading and language in adults, including those mentioned in the previous section (Gaillard et al., 2003; Gaillard et al., 2001). However, these studies have used either complex tasks such as story reading, prohibiting the inclusion of children with rudimentary reading skills, or silent reading tasks, ruling out performance measures during image acquisition, a critical consideration in data interpretation. Furthermore, story reading is likely to engage brain regions used for syntactic and semantic language processing in addition to those required for reading, per se (i.e. the decoding of printed words).

Despite these methodological difficulties, children have consistently exhibited less activity in the dorsal left inferior frontal gyrus than adults (Schlaggar et al., 2002; Simos et al., 2001), and children show a modest correlation between age and activity in this area when processing words semantically (Shaywitz et al., 2002). These findings may demonstrate developmental engagement of phonological or semantic processing units for reading (Fiez, 1997; Poldrack et al., 1999; Pugh et al., 1996), or may simply reflect a more general maturation of left inferior frontal cortex (Chugani, 1998; P. R. Huttenlocher & Dabholkar, 1997). Less consistent findings include differences between children and adults in left extrastriate activity (Schlaggar et al., 2002), and in the laterality of ventral temporal cortical activity during reading (Simos et al., 2001). As techniques for developmental neuroimaging are refined, findings from studies using various imaging paradigms will likely converge to reveal consistent mechanisms for reading acquisition. A cross sectional approach may offer unique advantages for examining the development of reading circuitry during childhood, and control for several of the confounding factors discussed above.

A cross sectional fMRI study of reading acquisition

To examine the development of neural mechanisms for reading, we studied 41 healthy, good readers between the ages of 6 and 22 (Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003). Their abilities in various reading and reading-related skills were assessed with cognitive testing, and brain activity during reading was assessed with fMRI. FMRI studies of cognitive skill acquisition require that tasks be designed such that novices and experts perform the activation task equally well. Differences in the effort required for accurate performance could masquerade as differences in brain activity even if the underlying neural circuitry is the same. To avoid this confounding performance effect, we employed an "implicit reading" task requiring detection of a visual feature (i.e. the presence of a tall letter) within words. Because the brain obligatorily processes visually presented words, this task elicits automatic, implicit activation of reading circuitry even though subjects are not instructed to read the words (Price et al., 1996). Furthermore, because performance of the task does not explicitly require reading, even non-readers can perform it accurately, and accuracy and reaction time can be equated across age groups. To isolate brain activity specifically related to implicit reading, a control task was employed in which subjects performed the same feature detection task on unreadable strings of false font (nonsense) characters matched to words for visual complexity and length (Figure 1).

While processing words, compared to false font strings, young readers (age 6-9) primarily activated a posterior area of the left superior temporal sulcus. Adult readers also activated this area, as well as the left inferior frontal gyrus, and other temporal and parietal areas. Neural changes associated with learning to read were evaluated by correlating brain activity during implicit reading with measures of reading ability, including the Gray Oral Reading Test and the Woodcock-Johnson Letter-Word Identification and Word Attack subtests. Increasing reading ability corresponded to decreasing activity in right hemisphere ventral extrastriate (visual) areas, and increasing activity in the left middle temporal and inferior frontal gyri (Figure 2A). To evaluate the relationship between important reading-related phonological skills and children's neural systems for reading, we explored the relationship between brain activity during implicit reading and measures of phonological awareness, phonetic retrieval, and phonological working memory. These three types of phonology, which independently predict future achievement in reading, were related to three different cortical networks (Figure 2B). Performance on a measure of phonological awareness, the Lindamood Auditory Conceptualization Test, was related to brain activity in the left superior temporal sulcus and the left inferior frontal gyrus. In contrast, performance on the Rapid Automatized Naming Letter subtest, a measure of phonetic retrieval, was related to activity in a distributed network of bilateral frontal and temporal cortical areas. Phonological working memory, as measured by the Digit Span, was related only to activity in an area of the left inferior parietal sulcus. Thus, the overall findings demonstrated that the left superior temporal sulcus is recruited early in schooling, and that its activity is related to children's phonological awareness ability; learning to read is associated with increasing activity in left hemisphere areas concerned with phonological processing, and decreasing activity in right hemisphere visual areas; three independent types of phonological processing modulate activity in independent cortical networks for reading.

An fMRI Case Study of Precocious Reading Acquisition

One purpose of normative studies such as the one above is to provide a neurodevelopmental context for the examination of children who learn to read differently from the norm. While the neural basis of impaired reading in dyslexia has been studied extensively, little is known about the neural basis of precocious reading. Despite their severe expressive and receptive language difficulties, children with autism spectrum disorders in some rare cases display surprisingly advanced "hyperlexic" reading skills (Aram, 1997; Healy, Aram, Horwitz, & Kessler, 1982; Nation, 1999; Silberberg & Silberberg, 1967). These children may learn as young as 18 months to identify words without explicit instruction (Sparks, 1995), but comprehend text at a level only appropriate for their verbal ability (Burd & Kerbeshian, 1989; Glosser, Friedman, & Roeltgen, 1996; Goldberg & Rothermel, 1984; P.R. Huttenlocher & Huttenlocher, 1973; C. M. Temple, 1990; Welsh, Pennington, & Rogers, 1987; Whitehouse & Harris, 1984). Investigation of the neural bases of hyperlexic reading may provide data on the impact of age of acquisition on reading circuitry, and on the mechanisms of extraordinary cognitive skill learning in autism. Also, comparisons between hyperlexia and dyslexia form an important dissociation for neuroimaging investigations of reading: i.e. advanced reading in the face of global delay versus delayed reading in the context of relatively normal neural function. To investigate the neurophysiology of hyperlexic reading, we utilized fMRI to examine the brain activity of a 9-year-old hyperlexic boy who began reading prior to using spoken language, and now reads 6 years in advance of the expected level (Turkeltaub et al., 2004). Using the same methods as those described above (Turkeltaub et al., 2003), we compared the hyperlexic boy's brain activity during implicit reading to two groups of control subjects: one matched to him for age in order to control for developmental level, and another matched for reading ability to control for text exposure and skill. This hyperlexic subject demonstrated greater activity than both age- and reading-matched control subjects in the left superior temporal sulcus and the left inferior frontal gyrus (Figure 2C). He also activated an area of the right ventral extrastriate cortex to a greater degree than reading-matched controls. Thus, this hyperlexic child hyper-activated normal left hemisphere phonological systems for reading, and retained use of right hemisphere visual areas which are normally disengaged over the course of learning to read.

Summary of the neurobiological basis of reading development

Based on the results of these studies, in the context of prior knowledge of neural systems for reading and their development, we can begin to surmise the roles of the three main reading areas in learning to read.

Left Superior Temporal Cortex

An area of the left superior temporal sulcus was active during implicit reading in both children and adults in our developmental study, demonstrating that it is recruited early in the course of learning to read and continues to be important for readers of all ability levels. Furthermore, children's reading activity in this region was related to their phonological awareness ability. The hyperlexic boy demonstrated hyper-activity of this area, even in comparison to older children at the same level of reading achievement.

The left superior temporal cortex is known to mature early in the course of development relative to other language areas (Balsamo et al., 2002; Simos et al., 2001). It is one of the few cortical regions capable of crossmodal auditory-to-visual mapping (Calvert, 2001), and is used for processing linguistic (Raij, Uutela, & Hari, 2000) as well as social (Hoffman & Haxby, 2000; Wright, Pelphrey, Allison, McKeown, & McCarthy, 2003) stimuli. Importantly, it is commonly implicated in phonological processing during reading (Price, 2000; Pugh et al., 2001; Simos, Breier, Wheless et al., 2000). Histological studies of dyslexic brains have revealed neural ectopias in left superior temporal cortex, suggesting developmental dysregulation of neural migration in this area (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985). Neuroimaging studies have shown reduced activity in left superior temporal cortex among dyslexic subjects during reading and phonological processing tasks (Brunswick et al., 1999; Rumsey, 1992; Shaywitz et al., 2002; Simos, Breier, Fletcher et al., 2000; E. Temple et al., 2001). Thus, activity in the left superior temporal cortex is decreased in cases of impaired reading (dyslexia), and increased in a case of precocious reading (hyperlexia). Together these findings implicate the superior temporal cortex as a fundamental phonological processing unit which is recruited early in the course of learning to read, but remains stable in its function with gains in reading achievement. Thus, one could envision this area as a dial which predicts a child's aptitude for reading at the onset of learning.

Left Inferior Frontal Gyrus

In contrast to the findings in the superior temporal cortex, activity in the left inferior frontal cortex does seem to increase developmentally over the course of learning to read. Many studies of reading-related processes discuss two functionally separate areas of the inferior frontal gyrus: the dorsal phonological area, and the ventral semantic area (Bokde, Tagamets, Friedman, & Horwitz, 2001; Fiez, 1997; Poldrack et al., 1999; Price, 1997; Price, 2000; Price, Moore, Humphreys, & Wise, 1997). During implicit reading, the group of children in our developmental study did not activate either the ventral or the dorsal left inferior frontal gyrus. In contrast, the adults activated both of these areas strongly. Likewise, activity in both areas correlated with reading ability. These findings confirm previous evidence that reading-related neural activity increases developmentally in the dorsal inferior frontal gyrus (Schlaggar et al., 2002; Shaywitz et al., 2002; Simos et al., 2001). Based on the ventral semantic/dorsal-phonological model of the inferior frontal gyrus discussed above, one would attribute these developmental changes in ventral and dorsal areas to maturation of semantic and phonological processors respectively. Indeed, our hyperlexic subject activated the left dorsal, but not ventral inferior frontal gyrus to a greater degree than control children. Given the dissociation between his decoding skill and his reading comprehension, this pattern supports the independent roles of dorsal and ventral inferior frontal gyrus in phonology and semantics respectively. Findings from the developmental study of reading acquisition and the study of hyperlexic reading support the theory that the dorsal inferior frontal gyrus is recruited for phonological assembly over the course of learning to read (Pugh et al., 2001; Pugh et al., 1996). The developmental study demonstrated that activity in this area increases throughout schooling, and that its activity is modulated by children's phonological awareness ability. Furthermore, a hyperlexic subject with exceptional phonological decoding skills activated this area to a greater degree than control subjects during implicit reading.

However, the correlations between brain activity and measures of phonology in our developmental study dispute the restriction of phonological processing to the dorsal inferior frontal gyrus. The measure of phonological naming (RAN) correlated with activity in ventral but not dorsal inferior frontal gyrus, and the measure of phonological awareness (LAC) correlated with activity in both ventral and dorsal inferior frontal gyrus. This suggests that both of these areas play a role in phonological processing during reading, but that their roles may differ. The correlations between phonological naming and the ventral inferior frontal gyrus suggest that this area may be recruited for retrieval of phonetic codes from lexical memory. This process could easily be confused with semantic processing because lexical retrieval is used only for known words, and hence only those with semantic referents. Alternatively, this area may indeed play a role in semantics, and semantic information may be used to aid in retrieval of lexical codes during reading. Experiments dissociating lexical retrieval from semantic processing will be needed to discriminate between these alternatives.

Together, these findings support the theory that the dorsal inferior frontal gyrus develops into a processor responsible for assembling phonological units into full phonetic codes over the course of learning to read (Pugh et al., 2001; Pugh et al., 1996). In contrast, the ventral inferior frontal gyrus may be recruited for semantic processing of words or lexical retrieval from memory.

Left Ventral Extrastriate Cortex

Adults consistently activate an area of the left fusiform gyrus during word reading. This "visual word form area" is commonly associated with holistic orthographic processing of words (i.e. direct lexical access or "sight reading"). Based on this role, some have hypothesized that activity in this area increases as children gain sufficient text exposure to access semantic and phonological codes for words directly from their orthography (Cohen et al., 2000; Cohen et al., 2002; Pugh et al., 2001). However, our developmental study showed no relationship between activity and reading ability in this area. Furthermore, no differences between the hyperlexic subject and controls were observed in the left ventral temporal cortex. Rather, in both studies differences were found in the right hemisphere ventral temporal cortex. These findings of stable left hemisphere visual activity and decreasing right hemisphere activity are consistent with behavioral models of learning to read. Young children begin to identify words based on visual features (Ehri, 1999; Frith, 1985; Hoien & Lundberg, 1988). The left fusiform gyrus may develop early in learning for this strategy, and adapt over the course of reading acquisition from a simple visual analysis system to its mature role in orthographic processing of whole words. Another possible explanation for this apparent stability is that the relationship between left fusiform gyrus activity and reading ability is non-linear. Children in the pre-alphabetic phase of reading acquisition may recruit bilateral fusiform cortex for visual recognition of text. Then, as they gain an understanding of the alphabetic principle, they may disengage these areas. When they begin to consolidate letter sequences and process words as wholes, the left fusiform gyrus would then be recruited again for this mature orthographic processing role. Such non-linear developmental patterns would not have been detected by the analysis performed on the normative developmental data. Although nonlinear analyses were attempted with these data, a lack of subjects in the middle age-range (12-18 years) prohibited reliable interpretation. Further investigations using larger numbers of subjects and longitudinal designs will be needed to confirm the developmental stability of activity in this region.

CAVEATS AND LIMITATIONS

Functional neuroimaging provides opportunities to study aspects of human cognition and learning which were previously inaccessible. However, certain limitations must be kept in mind when interpreting functional imaging data. Several of these factors will be addressed here.

(1) Changes in activity can be interpreted many ways. As we have seen, neural plasticity manifests in multiple ways, and care must be taken to interpret the changes in the context of behavior. For example, learning might be reflected as an increase in extent of activity as representations grow with experience, as a decrease in extent as representations become more efficient or focused, as changes in signal intensity, or as changes in temporal relationships between regions. These disparate possibilities present some interesting challenges for interpretation of the data. For example, if decreased activity is found for a given process, how do we know if the decrease reflects a more efficient representation or a deficit wherein compensatory activity is found in another region, not normally associated with the task?

(2) Experimental design is another issue that requires careful consideration. Tasks must be matched for performance as closely as possible across groups of different ages or different diagnoses, lest performance differences be confounded with changes in brain activity (Price & Friston, 1999). Likewise, it is important to control task parameters and attributes that might correlate with learning, such as differences in attentional resources. In such cases, correlational analyses may be useful to explore the relationship between activity and behavior. Careful selection of baseline tasks is paramount. One must also consider the time-course of learning, allowing for behavioral, morphological and molecular changes to emerge.

(3) Small cross sectional samples limit interpretation. Specifically in relation to the study of reading acquisition, future studies will benefit from samples with a much greater number of subjects, ideally 15-20 per grade level. A larger, more diverse sample will allow examination of relationships between brain activity and behavioral variables within small age ranges. Thus,

differences in brain activity related to reading could be isolated from those related to age. This method could also be used to determine if phonological variables modulate activity in different brain regions at different points in development. Likewise, detailed examination of more hyperlexic subjects are needed to determine how variable the neural basis of reading is in hyperlexia, and whether differences in brain activity in hyperlexia are due to the early age of reading acquisition, the current exceptional reading ability, or the severity of autism.

Future longitudinal studies will provide growth curves of brain development in individual subjects, reducing the noise from between subject variability, and allowing much more detailed examination of the data. Although developmental increases and decreases in brain activity observed in our cross sectional study appear linear, the stage models of reading acquisition predict stepwise changes in some brain areas. Cross sectional studies are insensitive to these nonlinear changes because the timing of the steps varies between subjects. Thus, stepwise changes can only be observed by studying each child repeatedly over the course of reading acquisition. Using a longitudinal design, one could also examine relationships between behavioral variables important to reading and developmental changes in brain activity. For example, measures of phonological awareness in kindergarten might predict the timing of a stepwise change in dorsal inferior frontal activity later in development. Conversely, young children's brain activity in certain areas, such as the left superior temporal sulcus, might predict reading outcomes later in schooling. Such relationships could yield early detection tools to identify pre-school children likely to experience reading difficulties later on.

(4) Application of different data analysis techniques will yield more information from a given data set as well. For example, inter-regional correlations could evaluate whether connectivity between frontal and temporal processing areas increases over the course of reading acquisition. Also, local cortical thickness measurements attained from anatomical images could assess whether developmental changes in neural function correspond with changes in cortical anatomy. Already, a comparison of MRIs of literate and illiterate adults has revealed differences in the corpus collosum, indicating a reading-related anatomical difference in the inter-hemispheric fibers connecting the parietal lobes (Castro-Caldas et al., 1999). Collection of blood and urine samples from subjects in future studies could also allow examination of genetic, metabolic, and hormonal effects on the development of neural mechanisms for reading.

(5) Finally, findings must be confirmed by multiple experimental modalities. It is important to interpret imaging data in light of complementary data from patient, lesion, and electrophysiological studies. Emerging techniques (diffusion tensor imaging, transcranial

magnetic stimulation, near-infrared optical imaging) will help to further refine our ideas about brain changes that occur with development and learning. We must be mindful that while imaging studies might inform us that certain brain regions are implicated in a given process, converging evidence from other modalities are often needed to determine the extent of their relevance.

CONCLUSIONS

Reading acquisition provides an interesting example of the neural plasticity associated with skill learning. Our understanding of the biological basis of reading can be informed by extrapolation from neuroimaging studies of acquisition of other skills. Conversely, neuroimaging studies of reading acquisition may imply mechanisms of cognitive skill learning in general. The studies of reading presented above illustrate that some areas of the brain, such as the left superior temporal sulcus, may house static processing units which determine one's aptitude for skill learning. Other areas, such as the left inferior frontal gyrus, seem to grow with the acquisition of skill and likely are responsible for changes in performance of reading tasks. If the processing systems subserved by these dynamic regions are not domain specific (i.e. they are used for multiple different tasks), this provides a mechanism by which learning to read effects the performance of non-reading tasks such as pseudoword repetition. The data from our hyperlexic subject suggest that some changes associated with learning, such as the decreasing activity in right extrastriate visual cortex, may represent shifts in strategy associated with, but not necessary to effective learning. Interestingly, no evidence of developmental changes in the VWFA was noted in our cross sectional study, nor was this area differentially activated by our hyperlexic subject during reading. The more general development of the brain occurring concurrently with learning to read may have obscured adaptive changes taking place in this critical region. Studies on the role of the right fusiform gyrus in face recognition suggest that tightly controlled training studies may clarify how this area develops to its mature role in reading. Along with these functional changes in brain circuitry, learning to read likely impacts the anatomy of the brain. While this has not been adequately demonstrated to date, anatomical differences between skilled musicians and non-musicians suggest that the same is true of literate and illiterate adults. As our understanding of neural plasticity and its manifestations during reading acquisition expands, this new knowledge will drive developments in educational strategies, and approaches to remediation of children with learning disabilities.

ACKNOWLEDGEMENTS

The authors are supported through the National Institutes of Child Health and Human Development (P50 HD40095). We thank Thomas Zeffiro, Lynn Gareau and Alyssa Verbalis for their contribution to the studies reported in this chapter and Alison Merikangas for her help with references.

FIGURE LEGENDS

Figure 1: Examples of word and false-font stimuli presented to subjects for the "implicit reading" task. For details of experimental design see (Turkeltaub et al., 2003).

Figure 2: (A) Cortical regions that displayed increases (light) and decreases (dark) in task-related-signal change underlying increasing reading ability; (B) brain areas where activity during reading correlated with the performance of verbal phonological awareness (light), phonetic retrieval (dark), and phonological working memory (dark and hashed), from (Turkeltaub et al., 2003). (C) Regions in the left hemisphere that demonstrated greater (light) and lesser (dark) activity in a hyperlexic boy compared to age matched (left) or reading level matched (right) controls. Reprinted from *Neuron, 41*(1), Turkeltaub, P. E., Flowers, D. L., Verbalis, A., Miranda, M., Gareau, L., & Eden, G. F. (2004). The neural basis of hyperlexic reading. An fMRI case study, 11-25, Copyright 2004, with permission from Elsevier.

REFERENCES

Allen, G., Buxton, R. B., Wong, E. C., & Courchesne, E. (1997). Attentional activation of the cerebellum independent of motor involvement. *Science, 275*(5308), 1940-1943.

Amunts, K., Schlaug, G., Jancke, L., Steinmetz, H., Schleicher, A., Dabringhaus, A., et al. (1997). Motor cortex and hand motor skills: Structural compliance in the human brain. *Human Brain Mapping, 5*(3), 206-215.

Aram, D. M. (1997). Hyperlexia: Reading without Meaning in Young Children. *Topics in Language Disorders, 17*(3), 1-13.

Balsamo, L. M., Xu, B., Grandin, C. B., Petrella, J. R., Braniecki, S. H., Elliott, T. K., et al. (2002). A functional magnetic resonance imaging study of left hemisphere language dominance in children. *Arch Neurol, 59*(7), 1168-1174.

Bavelier, D., & Neville, H. J. (2002). Cross-modal plasticity: where and how? *Nat Rev Neurosci, 3*(6), 443-452.

Becker, J. T., MacAndrew, D. K., & Fiez, J. A. (1999). A comment on the functional localization of the phonological storage subsystem of working memory. *Brain Cogn, 41*(1), 27-38.

Bokde, A. L., Tagamets, M. A., Friedman, R. B., & Horwitz, B. (2001). Functional interactions of the inferior frontal cortex during the processing of words and word-like stimuli. *Neuron, 30*(2), 609-617.

Booth, J. R., Burman, D. D., Meyer, J. R., Gitelman, D. R., Parrish, T. B., & Mesulam, M. M. (2002). Functional anatomy of intra- and cross-modal lexical tasks. *Neuroimage, 16*(1), 7-22.

Bradley, L., & Bryant, P. (1983). Categorizing sounds and learning to read: a causal connexion. *Nature, 301*(419).

Brunswick, N., McCrory, E., Price, C. J., Frith, C. D., & Frith, U. (1999). Explicit and implicit processing of words and pseudowords by adult developmental dyslexics: A search for Wernicke's Wortschatz? *Brain, 122*(Pt 10), 1901-1917.

Buchel, C., Price, C., Frackowiak, R. S., & Friston, K. (1998). Different activation patterns in the visual cortex of late and congenitally blind subjects. *Brain, 121 (Pt 3)*, 409-419.

Buchel, C., Price, C., & Friston, K. (1998). A multimodal language region in the ventral visual pathway. *Nature, 394*(6690), 274-277.

Bunge, S. A., Dudukovic, N. M., Thomason, M. E., Vaidya, C. J., & Gabrieli, J. D. (2002). Immature frontal lobe contributions to cognitive control in children: evidence from fMRI. *Neuron, 33*(2), 301-311.

Burd, L., & Kerbeshian, J. (1989). Hyperlexia in Prader-Willi syndrome. *Lancet, 2*(8669), 983-984.

Calvert, G. A. (2001). Crossmodal processing in the human brain: insights from functional neuroimaging studies. *Cereb Cortex, 11*(12), 1110-1123.

Casey, B. J., Giedd, J. N., & Thomas, K. M. (2000). Structural and functional brain development and its relation to cognitive development. *Biol Psychol, 54*(1-3), 241-257.

Castro-Caldas, A., Miranda, P. C., Carmo, I., Reis, A., Leote, F., Ribeiro, C., et al. (1999). Influence of learning to read and write on the morphology of the corpus callosum. *Eur J Neurol, 6*(1), 23-28.

Castro-Caldas, A., Petersson, K. M., Reis, A., Stone-Elander, S., & Ingvar, M. (1998). The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. *Brain, 121*(Pt 6), 1053-1063.

Chall, J. S. (1983). *Stages of Reading Development*. New York: McGraw Hill.

Chugani, H. T. (1998). A critical period of brain development: studies of cerebral glucose utilization with PET. *Prev Med, 27*(2), 184-188.

Cohen, L., Dehaene, S., Naccache, L., Lehericy, S., Dehaene-Lambertz, G., Henaff, M. A., et al. (2000). The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain, 123 (Pt 2)*, 291-307.

Cohen, L., Lehericy, S., Chochon, F., Lemer, C., Rivaud, S., & Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the Visual Word Form Area. *Brain, 125*(Pt 5), 1054-1069.

Denckla, M. B., & Rudel, R. G. (1976). Rapid "automatized" naming (RAN): dyslexia differentiated from other learning disabilities. *Neuropsychologia, 14*(4), 471-479.

Dietz, N., Jones, K., Gareau, L., Zeffiro, T., & Eden, G. (Submitted). The role of the left posterior fusiform cortex in phonological decoding.

Draganski, G., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: Changes in grey matter induced by training. *Nature, 427*(6972), 311-312.

Ehri, L. C. (1999). Phases of development in learning to read words. In J. Oakhill & R. Beard (Eds.), *Reading Development and the Teaching of Reading: A Psychological Perspective* (pp. 79- 108). Oxford: Blackwell Science Ltd.

Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B., & Taub, E. (1995). Increased Cortical Representation of the Fingers of the Left Hand in String Players. *Science, 270*(5234), 305-307.

Felton, R. H., Naylor, C. E., & Wood, F. B. (1990). Neuropsychological profile of adult dyslexics. *Brain Lang, 39*(4), 485-497.

Fiez, J. A. (1997). Phonology, semantics, and the role of the left inferior prefrontal cortex. *Hum Brain Mapp, 5*(2), 79-83.

Fiez, J. A., & Petersen, S. E. (1998). Neuroimaging studies of word reading. *Proceedings of the National Academy of Sciences, 95*, 914-921.

Flowers, D. L., Jones, K., Noble, K., VanMeter, J. W., Zeffiro, T. A., Wood, F. B., et al. (2004). Attention to single letters activates left extrastriate cortex. *NeuroImage, 21*(3), 829-839.

Friedman, R. F., Ween, J. E., & Albert, M. L. (1993). Alexia. In E. Valenstein (Ed.), *Clinical Neuropsychology* (3rd ed., pp. 37-62). New York: Oxford University Press.

Frith, U. (1985). Beneath the surface of developmental dyslexia. In K. E. Patterson, J. C. Marshall & M. Coltheart (Eds.), *Surface Dyslexia*. London: Routledge and Kegan Paul.

Gaillard, W. D., Balsamo, L. M., Ibrahim, Z., Sachs, B. C., & Xu, B. (2003). fMRI identifies regional specialization of neural networks for reading in young children. *Neurology, 60*(1), 94-100.

Gaillard, W. D., Pugliese, M., Grandin, C. B., Braniecki, S. H., Kondapaneni, P., Hunter, K., et al. (2001). Cortical localization of reading in normal children: An fMRI language study. *Neurology, 57(1) Jul 2001*.

Galaburda, A. M., Sherman, G. F., Rosen, G. D., Aboitiz, F., & Geschwind, N. (1985). Developmental dyslexia: four consecutive patients with cortical anomalies. *Ann Neurol, 18*(2), 222-233.

Gaser, C., & Schlaug, G. (2003). Brain structures differ between musicians and non-musicians. *Journal of Neuroscience, 23*(27), 9240-9245.

Gauthier, I., Tarr, M. J., Anderson, A. W., Skudlarski, P., & Gore, J. C. (1999). Activation of the middle fusiform 'face area' increases with expertise in recognizing novel objects. *Nature Neuroscience, 2*(6), 568-573.

Gilbert, C. D., Sigman, M., & Crist, R. E. (2001). The neural basis of perceptual learning. *Neuron, 31*(5), 681-697.

Glosser, G., Friedman, R., & Roeltgen, D. P. (1996). Clues to the Cognitive Organization of Reading and Writing From Developmental Hyperlexia. *Neuropsychology, 10*(2), 168-175.

Goldberg, T. E., & Rothermel, R. D. (1984). Hyperlexic Children Reading. *Brain, 107*, 759-785.

Gorno-Tempini, M. L., Price, C. J., Josephs, O., Vandenberghe, R., Cappa, S. F., Kapur, N., et al. (1998). The neural systems sustaining face and proper-name processing. *Brain, 121 (Pt 11)*, 2103-2118.

Green, C. S., & Bavelier, D. (2003). Action video game modifies visual selective attention. *Nature, 423*(6939), 534-537.

Hagoort, P., Indefrey, P., Brown, C., Herzog, H., Steinmetz, H., & Seitz, R. J. (1999). The neural circuitry involved in the reading of German words and pseudowords: A PET study. *Journal of Cognitive Neuroscience, 11*(4), 383-398.

Healy, J. M., Aram, D. M., Horwitz, S. J., & Kessler, J. W. (1982). A study of hyperlexia. *Brain Lang, 17*(1), 1-23.

Hier, D. B., Mondlock, J., & Caplan, L. R. (1983). Behavioral abnormalities after right hemisphere stroke. *Neurology, 33*(3), 337-344.

Hoffman, E. A., & Haxby, J. V. (2000). Distinct representations of eye gaze and identity in the distributed human neural system for face perception. *Nat Neurosci, 3*(1), 80-84.

Hoien, T., & Lundberg, I. (1988). Stages of Word Recognition in Early Reading Development. *Scandinavian Journal of Educational Research, 32*, 163-182.

Horwitz, B., Rumsey, J. M., & Donohue, B. C. (1998). Functional connectivity of the angular gyrus in normal reading and dyslexia. *Proc Natl Acad Sci U S A, 95*(15), 8939-8944.

Huttenlocher, P. R., & Dabholkar, A. S. (1997). Regional differences in synaptogenesis in human cerebral cortex. *J Comp Neurol, 387*(2), 167-178.

Huttenlocher, P. R., & Huttenlocher, J. (1973). A study of children with hyperlexia. *Neurology, 23*, 1107-1116.

Kanwisher, N. (2000). Domain specificity in face perception. *Nat Neurosci, 3*(8), 759-763.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *The Journal of Neuroscience, 17*(11), 4301-4311.

Karni, A., Meyer, G., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature, 377*(6545), 155-158.

Kujala, T., Alho, K., & Naatanen, R. (2000). Cross-modal reorganization of human cortical functions. *Trends in Neurosciences, 23*(3), 115-120.

Kumar, N., Verma, A., Maheshwari, M. C., & Kumar, B. R. (1986). Prosopagnosia (a report of two cases). *J Assoc Physicians India, 34*(10), 733-735.

Kwon, H., Reiss, A. L., & Menon, V. (2002). Neural basis of protracted developmental changes in visuo-spatial working memory. *Proc Natl Acad Sci U S A, 99*(20), 13336-13341.

Lindamood, C., & Lindamood, P. (1979). *Lindamood Auditory Conceptualization (LAC) Test*. Austin, TX: Pro-Ed.

Mann, V. A. (1993). Phoneme awareness and future reading ability. *J Learn Disabil, 26*(4), 259-269.

McCandliss, B. D., Cohen, L., & Dehaene, S. (2003). The visual word form area: expertise for reading in the fusiform gyrus. *Trends Cogn Sci, 7*(7), 293-299.

Moore, C. J., & Price, C. J. (1999). Three distinct ventral occipitotemporal regions for reading and object naming. *Neuroimage, 10*(2), 181-192.

Munte, T. F., Altenmuller, E., & Jancke, L. (2002). The musician's brain as a model of neuroplasticity. *Nature Reviews Neuroscience, 3*(6), 473-478.

Nardelli, E., Buonanno, F., Coccia, G., Fiaschi, A., Terzian, H., & Rizzuto, N. (1982). Prosopagnosia. Report of four cases. *Eur Neurol, 21*(5), 289-297.

Nation, K. (1999). Reading skills in hyperlexia: a developmental perspective. *Psychol Bull, 125*(3), 338-355.

Perrett, D. I., Hietanen, J. K., Oram, M. W., & Benson, P. J. (1992). Organization and functions of cells responsive to faces in the temporal cortex. *Philos Trans R Soc Lond B Biol Sci, 335*(1273), 23-30.

Petersen, S. E., Fox, P. T., Posner, M. I., Mintun, M., & Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature, 331*(6157), 585-589.

Poldrack, R. A., Pare-Blagoev, E. J., & Grant, P. E. (2002). Pediatric functional magnetic resonance imaging: progress and challenges. *Top Magn Reson Imaging, 13*(1), 61-70.

Poldrack, R. A., Wagner, A. D., Prull, M. W., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage, 10*(1), 15-35.

Posner, M. I., Abdullaev, Y. G., McCandliss, B. D., & Sereno, S. C. (1999). Neuroanatomy, circuitry and plasticity of word reading. *Neuroreport, 10*(3), R12-23.

Price, C. (1997). Functional Anatomy of Reading. In F. Frackowiak, Frith C, Dolan, Mazziotta (Ed.), *Human Brain Function* (1 ed., pp. 301-327). San Diego: Academic Press.

Price, C. J. (2000). The anatomy of language: contributions from functional neuroimaging. *J Anat, 197 Pt 3*, 335-359.

Price, C. J., & Devlin, J. T. (2003). The myth of the visual word form area. *Neuroimage, 19*(3), 473-481.

Price, C. J., & Friston, K. J. (1999). Scanning patients with tasks they can perform. *Hum Brain Mapp, 8*(2-3), 102-108.

Price, C. J., Moore, C. J., Humphreys, G. W., & Wise, R. J. S. (1997). Segregating semantic from phonological processes during reading. *Journal of Cognitive Neuroscience, 9*(6), 727-733.

Price, C. J., Wise, R. J., & Frackowiak, R. S. (1996). Demonstrating the implicit processing of visually presented words and pseudowords. *Cereb Cortex, 6*(1), 62-70.

Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., et al. (2001). Neurobiological studies of reading and reading disability. *J Commun Disord, 34*(6), 479-492.

Pugh, K. R., Shaywitz, B. A., Shaywitz, S. E., Constable, R. T., Skudlarski, P., Fulbright, R. K., et al. (1996). Cerebral organization of component processes in reading. *Brain, 119 (Pt 4)*, 1221-1238.

Raij, T., Uutela, K., & Hari, R. (2000). Audiovisual integration of letters in the human brain. *Neuron, 28*(2), 617-625.

Rauschecker, J. (1997). Mechanisms of compensatory plasticity in the cerebral cortex. In H. J. Freund, Sabel, B.A., White, O.W. (Ed.), *Brain Plasticity, Advances in Neurology* (Vol. 73, pp. 137-145). Philadelphia: Lippincott-Raven.

Rauschecker, J. P. (2002). Cortical map plasticity in animals and humans. In *Plasticity in the Adult Brain: From Genes to Neurotherapy* (Vol. 138, pp. 73-88). Amsterdam: Elsevier Science.

Rosner, J., & Simon, D. P. (1971). Test of Auditory Analysis Skill, TAAS. *Journal of Learning Disabilities, 4*(7), 40-48.

Rumsey, J. M., Andreason, P., Zametkin, A.J., Aquino, T., King, A.C., Hamburger, S.D., Pikus, A., Rapoport, J.L., and Cohen, R.M. (1992). Failure to activate the left temporopareital cortex in dyslexia. *Arch Neurol, 49*, 527-534.

Schlaggar, B. L., Brown, T. T., Lugar, H. M., Visscher, K. M., Miezin, F. M., & Petersen, S. E. (2002). Functional neuroanatomical differences between adults and school-age children in the processing of single words. *Science, 296*(5572), 1476-1479.

Sergent, J., Ohta, S., & MacDonald, B. (1992). Functional neuroanatomy of face and object processing. A positron emission tomography study. *Brain, 1*, 15-36.

Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, P., et al. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biol Psychiatry, 52*(2), 101-110.

Silberberg, N., & Silberberg, M. (1967). Hyperlexia: Specific word recognition skills in young children. *Exceptional Children, 34*, 41-42.

Simos, P. G., Breier, J. I., Fletcher, J. M., Foorman, B. R., Bergman, E., Fishbeck, K., et al. (2000). Brain activation profiles in dyslexic children during non-word reading: a magnetic source imaging study. *Neurosci Lett, 290*(1), 61-65.

Simos, P. G., Breier, J. I., Fletcher, J. M., Foorman, B. R., Mouzaki, A., & Papanicolaou, A. C. (2001). Age-related changes in regional brain activation during phonological decoding and printed word recognition. *Dev Neuropsychol, 19*(2), 191-210.

Simos, P. G., Breier, J. I., Wheless, J. W., Maggio, W. W., Fletcher, J. M., Castillo, E. M., et al. (2000). Brain mechanisms for reading: the role of the superior temporal gyrus in word and pseudoword naming. *Neuroreport, 11*(11), 2443-2447.

Snyder, A. Z., Abdullaev, Y. G., Posner, M. I., & Raichle, M. E. (1995). Scalp electrical potentials reflect regional cerebral blood flow responses during processing of written words. *Proc Natl Acad Sci U S A, 92*(5), 1689-1693.

Sparks, R. L. (1995). Phonemic awareness in hyperlexic children. *Reading and Writing, 7*, 217-235.

Stanovich, K. E. (1988). Explaining the differences between the dyslexic and the garden-variety poor reader: the phonological-core variable-difference model. *J Learn Disabil, 21*(10), 590-604.

Takada, T., Sakurai, Y., Takeuchil, S., & Sakuta, M. (1998). [Pure alexia due to a fusiform gyrus lesion]. *Rinsho Shinkeigaku, 38*(2), 154-156.

Tarr, M. J., & Gauthier, I. (2000). FFA: a flexible fusiform area for subordinate-level visual processing automatized by expertise. *Nat Neurosci, 3*(8), 764-769.

Temple, C. M. (1990). Auditory and Reading Comprehension in Hyperlexia: Semantic and Syntactic Skills. *Reading and Writing, 2*(297-306).

Temple, E., Poldrack, R. A., Salidis, J., Deutsch, G. K., Tallal, P., Merzenich, M. M., et al. (2001). Disrupted neural responses to phonological and orthographic processing in dyslexic children: an fMRI study. *Neuroreport, 12*(2), 299-307.

Thomas, K. M., King, S. W., Franzen, P. L., Welsh, T. F., Berkowitz, A. L., Noll, D. C., et al. (1999). A developmental functional MRI study of spatial working memory. *Neuroimage, 10*(3 Pt 1), 327-338.

Torgesen, J. K., Wagner, R. K., & Rashotte, C. A. (1994). Longitudinal studies of phonological processing and reading. *J Learn Disabil, 27*(5), 276-286; discussion 287-291.

Torgesen, J. K., Wagner, R. K., Simmons, K., & Laughon, P. (1990). Identifying phonological coding problems in disabled readers: naming, counting, or span measures? *Learning Disability Quarterly, 13*, 236-243.

Treiman, R. (2000). The Foundations of Literacy. *Current Directions in Psychological Science, 9*(3), 89- 92.

Turkeltaub, P. E., Eden, G. F., Jones, K. M., & Zeffiro, T. A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage, 16*(3 Pt 1), 765-780.

Turkeltaub, P. E., Flowers, D. L., Verbalis, A., Miranda, M., Gareau, L., & Eden, G. F. (2004). The neural basis of hyperlexic reading. An FMRI case study. *Neuron, 41*(1), 11-25.

Turkeltaub, P. E., Gareau, L., Flowers, D. L., Zeffiro, T. A., & Eden, G. F. (2003). Development of neural mechanisms for reading. *Nat Neurosci, 6*(7), 767-773.

Vaina, L. M., Belliveau, J. W., des Roziers, E. B., & Zeffiro, T. A. (1998). Neural systems underlying learning and representation of global motion. *Proceedings of the National Academy of Sciences of the United States of America, 95*(21), 12657-12662.

Vandenberghe, R., Price, C., Wise, R., Josephs, O., & Frackowiak, R. S. (1996). Functional anatomy of a common semantic system for words and pictures. *Nature, 383*(6597), 254-256.

Wagner, R. K. (1986). Phonological processing abilities and reading: implications for disabled readers. *J Learn Disabil, 19*(10), 623-630.

Wagner, R. K., & Torgesen, J. K. (1987). The nature of phonological processing and its causal role in the acquisition of reading skills. *Psychological Bulletin, 101*, 192-212.

Wagner, R. K., Torgesen, J. K., Laughon, P., Simmons, K., & Rashotte, C. A. (1993). Development of young readers phonological processing abilities. *Journal of Educational Psychology, 85*(1), 83-103.

Wagner, R. K., Torgesen, J. K., Rashotte, C. A., Hecht, S. A., Barker, T. A., Burgess, S. R., et al. (1997). Changing relations between phonological processing abilities and word-level reading as children develop from beginning to skilled readers: A 5-year longitudinal study. *Developmental Psychology, 33*(3), 468-479.

Welsh, M. C., Pennington, B. F., & Rogers, S. (1987). Word recognition and comprehension skills in hyperlexic children. *Brain Lang, 32*(1), 76-96.

Whitehouse, D., & Harris, J. C. (1984). Hyperlexia in infantile autism. *J Autism Dev Disord, 14*(3), 281-289.

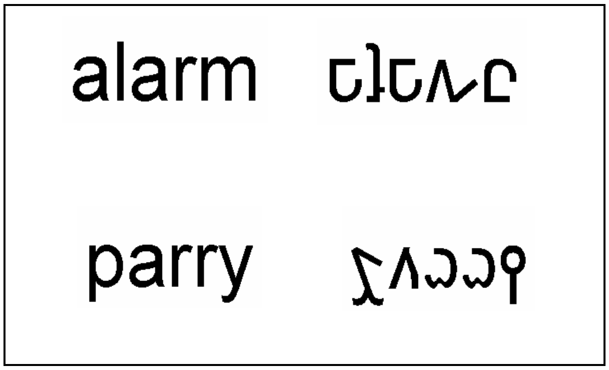
Wiesel, T. N., & Hubel, D. H. (1963). Single cell responses in striate cortex of kittens deprived of vision in one eye. *Journal of Neurophysiology, 26*, 1003-1017.

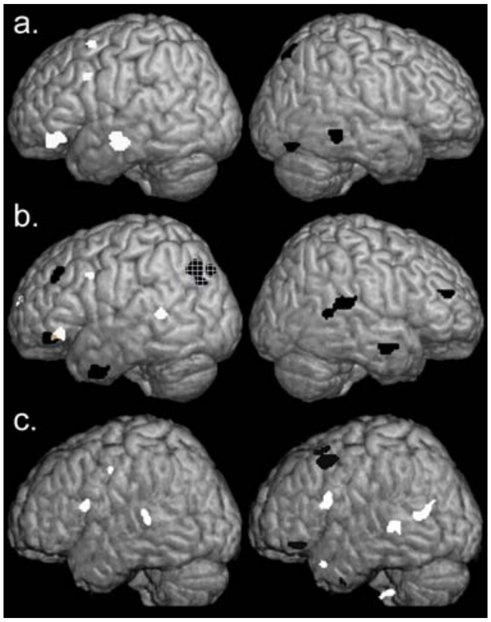
Wolf, M. (1999). What time may tell: Towards a new conceptualization of developmental dyslexia. *Annals of Dyslexia, 49*, 219-247.

Wolf, M., & Obregon, M. (1992). Early naming deficits, developmental dyslexia, and a specific deficit hypothesis. *Brain Lang, 42*(3), 219-247.

Wright, T. M., Pelphrey, K. A., Allison, T., McKeown, M. J., & McCarthy, G. (2003). Polysensory interactions along lateral temporal regions evoked by audiovisual speech. *Cereb Cortex, 13*(10), 1034-1043.

Zeki, S. (1999). *Inner vision: an exploration of art and the brain*. New York: Oxford University Press.


alarm
parry


a.
b.
c.