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Chapter

CORTICAL ASYMMETRY AND LEARNING EFFICIENCY .A DIRECTION FOR THE REHABILITATION PROCESS*

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ABSTRACT

In numerous reviews that have appeared in the literature of learning disabilities over the past 100 years, Hynd & Willis (1988) concluded that by 1905 the number of observations that had emerged from the evolving literature was such that a number of tentative conclusions could be offered. Overall, the literature by 1905 supported the following: (I) reading disability (congenital word blindness) could manifest in children with normal ability, (2) males seemed to be more often affected than females, (3) children presented with varied symptoms, but all suffered a core deficit in reading acquisition, (4) normal or even extended classroom instruction did not significantly improve reading ability, (5) some reading problems seemed to be transmitted genetically, and (6) the core symptoms seemed similar to those seen in adults with left temporo-parietal lesions.

While no one would contest the idea that learning disabilities may differentially manifest in many areas of learning, including arithmetic, writing spelling, and so on, there is little doubt that it is with reading disabilities, or dyslexia, where most researchers have concentrated their efforts. For this reason and because so many researchers from Neuropsychology, neurology, and neurolinguistics have focused their efforts on reading

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disabilities, we will examine this literature in an attempt to draw some meaning from the volumes of research that have investigated brain-behavior relationships in this most common of learning disabilities. In fact, an understanding of this literature and the theoretical ideas concerning the meaning of lateralized function and potentially associated deviations in brain morphology may well assist future scholars in their investigation of the neurobiological basis of other forms of learning disabilities.

As the early case studies suggested, learning disabilities have always been thought to have a neurological origin and present definitions of learning disability reflect this perspective (Wyngaarden, 1987). However, the literature supporting this perspective has generated a great deal of controversy. As Golden (1982) and Taylor and Fletcher (1983) have pointed out, much if not most of the literature through the early part of the 1980s was correlational in nature. For example, some research indicates that reading-disabled children have an increased incidence of electrophysiological abnormalities (Duffy *et al.,* 1980) and perhaps differentially so in subtypes of reading disabilities (e.g., Fried *et al.,* 1981). Soft signs are also more frequently found in reading-disabled children (Peters *et al.,* 1975) and few would argue that reading disabled children have a higher incidence of left- or mixed handedness (Bryden & Steenhuis, 1991). Further, reading-disabled children are often inferred to have weak or incomplete laterality, as evidenced on perceptual measures such as dichotic listening (Obrzut, 1991). In fact, volumes summarizing the research in this area have been written (Bakker & van der Vlugt, 1989; Gaddes, 1985; Kershner & Chyczij, 1992; Obrzut & Hynd, 1991), but we are stiff to a significant degree left with inferential or correlative evidence supporting the presumption of a neurological etiology for learning disabilities. Typical of such inferential evidence were studies that found that children with learning disabilities performed more poorly than normal children on any given task (cognitive or perceptual) but did better than children with documented brain damage (e.g., Reitan & Boll, 1973). Needless to say, the inference was often made that the learning-disabled children suffered "minimal brain dysfunction" because their level of performance was somewhere between normality and known brain damage. This was clearly an inference and while not without merit theoretically, it did not directly correlate a known neurological deviation of any kind (e.g., developmental, traumatic) with observed behavioral or cognitive deficits, as we might find in learning-disabled children.

This absence of confirming evidence is certainly not due to a shortage of theories or research, however. Historically relevant is the theory of Orton (1928) who proposed that as children become more linguistically competent, the left cerebral hemisphere becomes progressively more dominant for speech and language. He believed that motor dominance and its evolution in the developing child reflected this process of progressive lateralization. Consequently, according to Orton, children who had mixed cerebral dominance, as might be reflected in poor language skills, reading words or letters backward and inconsistent handedness, were most likely delayed in cerebral lateralization and therefore neither cerebral hemisphere, particularly the left, was dominant for linguistic processes. While decades of research documented that learning-disabled children were indeed deficient in language processes, especially phonological coding, the model of progressive lateralization has not been supported by the research (Benton, 1975; Kinsboume & Hiscock, 1981; Satz 1991).

Most of the development and normal function of the cerebrum is dependent on subcortical structures especially the *cerebellum*and *basal ganglia*. A failure to develop and or a dysfunction in these areas can affect both the nonspecific arousal system as well as specific

transfer of information in the brain. Dysfunction in these areas will usually result in specific motor and sensory symptoms that are commonly seen in children with cognitive or behavioral disorders. These brain regions are often seen to be underactive or atrophied as well in these children. These cortical loci have been shown to be connected with the *prefrontal cortex*, which have also often been noted to be underactive or atrophied in children with the neurobehavioral developmental disorders. The underactivity and or atrophy is usually either restricted to the right or left side of the sub-cortex and cortex (Melillo & Leisman, 2004).

An imbalance of activity or arousal of one side of the cortex or the other can result in a functional disconnection syndrome similar to what is seen in split-brain patients, this could be an underlying source of many if not all of the symptoms that we see with children with behavioral and cognitive disorders. For example, post-mortem examinations have indicated structural differences between the brains of good and impaired readers. High concentrations of micro-dysgenesis are noted in the left temporoparietal regions of dyslexic brains. The concentration is most evidenced in the *planum temporale* region (Galaburda *et al.,* 1985; Kaufman & Galaburda, 1989; Duane 1989). These micro-dysgeneses seriously impair the normal pattern of architecture of dyslexics and remove the asymmetry normally observed between the enlarged language areas of the left temporoparietal region and the smaller homologous areas of the right hemisphere (Galaburda *et al.,* 1985; Leisman & Ashkenazi, 1980). The capacity for language is generally correlated with a significant development in the magnitude of the left temporoparietal region and an attrition of neurons in the right hemisphere. These neuronal casualties may produce the observed asymmetry between corresponding areas in the left and right hemispheres (Geschwind & Levitsky, 1968; Leisman & Ashkenazi, 1980). The relative symmetry in the dyslexics' brains might reflect their impaired linguistic development.

In one study, (Leisman, 2002; Leisman, and Melillo, 2004)) left parieto-occipital EEG leads recorded a frequency spectrum in dyslexics that was consistently different from the spectrum obtained from normals. It is suggested that these effects represent significant differences in the functional organization of these areas. EEG coherence values indicate that normals have significantly greater sharing between hemispheres at symmetrical locations. Dyslexics demonstrate significantly greater sharing within hemisphere than do normals as evidenced in Table 1. The data supports the notion that developmental dyslexia is a functional hemispheric disconnection syndrome. Other conditions in the spectrum of disorders that we are discussing yield similar results.

This spectrum of childhood disorders that we are discussing generally relates to an increase or decrease in activation of the brain and the balance of activation between brain regions. These conditions result from two primary system effects: 1) primary arousal deficit or imbalance, and 2) a specific activation deficit, imbalance, or asynchrony. The brain is driven by sensory input. We know that the brain receives more simultaneous sensory input than it can possibly consciously process (Heilman, 1995; Leisman, 1976; Broadbent, 1958; 1965) In general the more stimulation a brain cells receive the better their function allowing it to process more information faster, for longer periods of time (Venables, 1989; Pascual & Figueroa, 1996; Szeligo & Leblond, 1977; van Praag *et al.,* 2000). Therefore all sensory input is important although not all of it can be consciously processed and perceived. In fact, without subconscious baseline stimulation higher conscious processing of sensory stimuli would be difficult if not impossible.

Table 1.Average frequency (in Hz), power (in dB), left-right asymmetry of power (in dB) between hemisphere and within hemisphere coherence values at P_3-O_1/P_4-O_2 locations for dyslexics and normals

	Dyslexic					Normal				
S	Freq (Hz)	Power (dB)	L-R (dB)	Bilat. Coher.	W/in Coher.	Freq (Hz)	Power (dB)	L-R (dB)	Bilat. Coher.	W/in Coher.
1	09.2	12	-03	--	1.1	09.2	28	--	--	0.8
2	10.4	21	-04	--	1.8	10.8	24	--	2.4	--
3	11.7	22	10	--	2.4	12.7	18	--	1.9	--
4	09.8	18	04	--	1.6	10.9	20	-4	1.3	--
5	10.8	17	03	--	1.4	08.6	16	--	1.9	--
6	10.6	24	-01	--	0.8	08.9	08	--	1.8	--
7	10.6	28	-05	--	1.5	11.2	11	--	2.4	--
8	11.2	12	-07	--	2.1	11.7	13	-2	1.5	1.8
9	12.0	19	-04	--	1.9	10.0	12	--	1.3	--
10	09.8	14	--	0.7	0.6	10.7	15	-1	1.3	0.9
11	10.8	25	-02	--	1.0	10.6	11	--	1.2	1.4
12	11.7	22	--	1.0	--	12.0	09	--	0.8	1.1
13	08.7	13	-01	--	0.9	11.7	07	--	1.0	--
14	09.0	27	08	--	2.1	08.9	11	--	1.9	--
15	10.7	13	-04	--	2.4	09.5	10	--	1.7	0.6
16	10.3	08	-06	--	1.8	08.8	11	-2	2.1	--
17	09.5	22	-07	--	2.0	08.6	14	--	1.4	--
18	12.2	20	-07	--	1.9	09.3	09	--	1.8	--
19	11.9	09	-01	--	0.9	12.4	12	--	1.9	--
20	08.4	15	-04	--	1.6	11.6	10	--	0.9	--

Before higher brain centers can develop, the lesser supportive brain structures must develop. In the cortex, Luria (1973) thought that lateralized cortical functions progress from primary cortical areas to secondary and tertiary areas as the child matures (Luria, 1973). Going back even further we see that development of cortical areas and the cortex itself are dependent on the anatomic and functional development of subcortical areas especially the *cerebellum* and the *thalamus*. Studies suggest that intact *cerebellar* functioning is required for normal cerebral functional and anatomical development (Rae *et al.,* 1998; Llinas, 1995). The same has been seen for the *thalamus* - that intact *thalamic* function is necessary to cortical development and function (Castro-Alamancos, 2002; Scannell *et al.,* 1999; 2000; Gil *et al.,* 1999; Albe-Fessard *et al.,* 1983; Kalivas *et al.,* 1999). Developmental dysfunction of the same brain areas as seen in acquired disorders such as post-traumatic aphasia may be the basis of developmental learning disabilities and neurobehavioral disorders (Dawson, 1996; 1988; Obrzut, 1991).

As Orton (1928) had indicated, it is generally assumed that persons with learning disabilities have abnormal cerebral organization including atypical or weak patterns of hemisphere specialization (Bryden, 1988; Corballis, 1983; Obrzut, 1991). The developmental lag hypothesis proposed by Lenneberg (1967) suggested that learning-disabled persons are slower to develop basic language skills and demonstrate weak hemispheric specialization for language tasks. In a reformulation of the progressive lateralization hypothesis (Satz, 1991), it may be that subcortical and antero-posterior progressions have a differential developmental

course with learning disabled children and adults compared to control subjects or those with acquired syndromes.

Since learning disabled children exhibit deficient performance on a variety of tests thought to be a measure of perceptual laterality, evidence of weak laterality or failure to develop laterality has been found across various modalities (audio, visual, tactile) (Boliek & Obrzut, 1995). It is thought these children have abnormal cerebral organization as suggested by Corballis (1983) and Obrzut (1991). The basic assumption is that dysfunction in the the central nervous system either prenatally or during early postnatal development, results in abnormal cerebral organization and associated dysfunctional specialization needed for lateralized processing of language function and non-language skills. It is thought that cortical and subcortical dysfunction which results from aberrant patterns of activation or arousal (Obrzut, 1991), inter- and intrahemispheric transmission deficits, inadequate resource allocation (Keshner & Peterson, 1988), or any combination of these may compromise hemispheric specialization in those with cognitive and behavioral deficits (Bolick & Obrzut, 1995).

Development of higher processing areas in the *cerebellar* cortex would develop after other more primary areas. For example, the lateral *cerebellum* would be dependent on proper development of the more midline areas in the inter-medial and medial zones first. Similarly, any region to which lateral *cerebellum* projected would be dependent on the effective development of the lateral *cerebellum* and it in turn would be dependent on the more medial *cerebellar* development. Therefore, if the medial aspects of the *cerebellum* do not develop adequately, then the lateral areas would still grow however, they may be smaller or atrophic, and dysfunction would be expected.

The *cerebellum*is thought to be part of a neuronal system that includes the *thalamus basal ganglia*and *prefrontal cortex* (Thatch, 1980). Anatomic and functional development of the nervous system is dependent on sensory input, which is associated with growth of a given brain area and its associated connectivities with other brain regions. Brain area growth and the capacity to make functional connectivities is highly dependent on: continued regional stimulation and by global stimulation through connected and coordinated function. If specific regions are inadequately stimulated, then we may see failure of anatomic or functional development in that region with a preservation of basic lower level functionality. Higher functions that depend on greater areas of integrated stimulation may be lost or dysfunctional. If the sensory loss develops after a *critical period,* these areas may still be smaller due to atrophy or reverse plasticity, with either global or specific effects depending on the modality of dysfunction. In children with learning disabilities or affective disorders, there are specific areas of the nervous system that have been noted in imaging studies to be smaller than normal (von Plessen *et al.,* 2002; Frank & Pavlakis, 2001; Larsen *et al.,* 1990). Most often, these areas involve the *prefrontal cortex*, *basal ganglia*, *thalamus,* and *cerebellum*.

Some neurophysiologists regard the central nervous system as partly a *closed* and part *open* system (Llinas, 1995). An open system is one that accepts input from the environment, processes it, and returns it to the external environment. A closed system suggests that the basic organization of the central nervous system is geared toward the generation of intrinsic images and is primarily self-activating and capable of generating a cognitive representation of the outside environment even without incoming sensory stimuli. Although it is possible that a certain level of activation or stimulation will be intrinsic to single neuronal cells and the nervous system as a whole, this stimulation does not seem adequate to sustain a conscious,

awake, individual. Behaviorally, arousal is a term used to describe an organism that is prepared to process incoming stimuli. From a physiologic standpoint, arousal also refers to the excitatory state or the propensity of neurons to discharge when appropriately activated (neuronal preparation). A non-aroused organism is comatose (Heilman, 1995). Therefore, an aroused alert individual that is prepared to process information is in a state dependent on sensory input with an attendant intrinsic excitability. Remove stimulation and the individual will eventually lose conscious awareness and become comatose or at least inattentive. The majority of brain activity associated with arousal comes from the ascending *reticular activating system*. The majority of this activity is relayed by the non-specific *thalamic nuclei* or *intralaminar nuclei*.

All sensory perception is based on the effectiveness of the arousal level of nonspecific, mostly subconscious, activity of the brain. There can be no specific sensory modality perception like vision or hearing without a baseline arousal level. The more stimulation or greater frequency of stimulation the more aroused an individual will be. Low frequency stimulation of midline *thalamic non-specific nuclei* produces inattention, drowsiness, and sleep accompanied by slow wave synchronous activity and so called spindle bursts. High frequency stimulation on the other hand has been shown to arouse a sleeping subject or alert a waking organism (Tanaka *et al.,* 1975; Arnulf *et al.,* 2000; Halboni, 2000). Specific sensory perception and processing is dependent on specific *thalamic* relays, if one of the specific *thalamic* nuclei are damaged such as the *lateral geniculate body*, that specific sensory modality is lost (e.g. blindness) but it does not result in loss of other specific nuclei input like hearing. However, if lesions of the non-specific intralaminar nuclei exist, patients cannot perceive or respond to any input by the specific intact nuclei even though those pathways are intact. In essence, the person does not exist from a cognitive standpoint (Llinas, 1995).

Luria postulated that the brain was divided into three functional units: 1) the arousal unit, 2) the sensory receptive and integrative unit, and 3) the planning and organizational unit. He subdivided the last two into three hierarchic zones. The primary zone is responsible for sorting and recording incoming sensory information. The secondary zone organizes and codes information from the primary zone. The tertiary zone is where data are merged from multiple sources of input and collated as the basis for organizing complex behavioral responses (Luria, 1973). Luria's dynamic progression of lateralized function is similar to Hughlings Jackson's Cartesian coordinates with respect to progressive function from *brainstem* to cortical regions (Kinsbourne & Hiscock, 1983).

Satz (1991) suggested that developmental invariance describes the lateral (x-axis) dimension of asymmetry, whereas current formulation of equipotentiality and the *progressive lateralization hypothesis* better describes vertical (subcortical-cortical) and horizontal (antero-posterior) progression during infancy and early childhood. Interestingly it has been noted that most research designed to address laterality issues in developmental disabilities (i.e. learning disabilities) has not dealt systematically with subcortical-cortical development or antero-posterior progression, all based on the concept of arousal unit.

The arousal unit is really the *non-specific thalamic nuclei*. We know that arousal is dependent on external and internal environmental sensory input. The largest proportion of subconscious sensory input passes between the *thalamus*, *cerebellum*, and *dorsal column* from slowly adapting receptors found in muscles with a preponderance of slow-twitch fibers - or slowly adapting muscle spindle receptors. The highest percentage of these is found in anti-gravity postural muscles especially muscles of the spine and neck (Guyton, 1986). The

receptors, which provide the major source of input to the brain, only receive sensory information. These receptors only work when muscles are stretched or contracted with gravity being the most frequent and constant sensory stimulus.

In summary, brain development and the adequacy of it continued functioning is dependent on sensory input. Specific sensory perceptual processes like vision and hearing are dependent on non-specific sensory input. This, in turn, creates a baseline arousal and synchronization of brain activity (consciousness). This is a form of constant arousal and is dependent on a constant flow of sensory input from receptors that are found in muscles of the spine and neck. These receptors receive the majority of their stimulation from gravity, creating a feedback loop that forms the basis of most if not all of brain function. Sensory input drives the brain, and motor activity drives the sensory system. Without sensory input the brain cannot perceive or process input. Without motor activity provided by constant action of postural muscles a large proportion of sensory stimuli are lost to further processing. This loop is the *somatosensory system*.

Higher processing is also dependent on the baseline sensory functions. For example, it has been shown that when performing a complex task, it is likely that transfer of motor commands to produce a final output is preceded to some degree, by transfer of information between association areas, which in turn may precede transfer between sensory regions (Banich, 1995).

Actually, there is a growing body of evidence that indicates that very young children, including infants, are lateralized for language processing (Molfese & Molfese, 1986). Thus, none would refute the notion that in the majority of cases language is lateralized to the left cerebral hemisphere. However, while language abilities clearly develop over the course of human ontogeny, language remains lateralized, as it was early in infant development. What may devolve is the capacity for plasticity of function; i.e., the capacity for the other cerebral hemisphere to assume language functions when the dominant hemisphere is severely damaged may decrease significantly with the course of development (Piacentini & Hynd, 1988). What neurological structures or deficient neuropsychological systems underlie the behavioral and cognitive symptoms we associate with learning disabilities, particularly reading disabilities? While there are likely many different ways in which one could begin to address this question, we will approach this question from a neurolinguistic-neuroanatomic perspective. We first present a discussion of the lateralized system of language and associated reading processes and then examine its impact and relation to research that employs brain-imaging procedures to investigate morphologic differences in the brains of reading-disabled children and adolescents. In this fashion we hope to directly tie deviations in lateralized brain processes (e.g., language, reading) to potentially associated deviations in brain structure.

NEUROLINGULSTIC-NEUROANATOMIC MODEL

For over a century, those concerned with reading and language disorders have attempted to correlate observed functional deficits with the location of known brain lesions (Bastian, 1898; Dejerine, 1892; Dejerine & Vialet, 1893; Dejerme & Dejerine-Klumpke, 1901; Geschwind, 1974; Head, 1926; Kussmaul, 1877; Wemicke, 1910). These scholars and others interested in the lateralization and localization of language and reading processes contributed

to a literature that resulted in a neurolinguistic model of language and reading referred to by some as the Wernicke-Geschwind model (Mayeux & Kandel, 1985). While Wernicke and Dejerine deserve the most credit for the development of this model, it is clear that Geschwind (1974) did much to revive interest in the perspective first proposed in part by Bastian (1898), Liepmann (1915), Marie (1906), and others, whose ideas were controversial even when they were first proposed. As Head (1926) suggested over 60 years ago, "localization of speech became a political question; the older conservative school, haunted by the bogey of phrenology, clung to the conception that the 'brain acted as a whole,' whilst the younger liberals and Republicans passionately favored the view that different functions were exercised by the various portions of the cerebral hemispheres" (p. 25).

Even among the "diagram makers" (Head, 1926) controversy existed. For example, Bastian (1898) argued strongly against the popular perspective advocated by Dejerine whose views so influenced Geschwind in his thinking. Bastian proposed that bilateral visual word centers existed in the brain, each of which was involved in visual perception, low-level feature analysis, and cross-modal integration with the central language centers. Dejerine's views prevailed, however, as the accumulation of case studies supported the notion that there was indeed a left-lateralized "word center," most notably, it seemed, in the region of the angular gyrus. Figure 1 graphically contrasts Dejerine and Bastian's views on the posterior cortex involved in reading. Based on the contributions of Broca, Wernicke, and the others noted above, a more complete neurolinguistic model of language and reading evolved. This model presupposes that visual stimuli such as words are registered in the bilateral primary occipital cortex, meaningful low-level perceptual associations occur in the secondary visual cortex, and this input is shared with further input from other sensory modalities in the region of the angular gyms in the left cerebral hemisphere. This sequential neurocognitive process presumably then associates linguistic-semantic comprehension with input from the region of the angular gyms; a process which involves the cortical region of the left posterior superior temporal region, including the region of the *planum temporale*. The process is completed when interhemispheric fibers connect these regions with Broca's area in the left inferior frontal region. Figure 2 presents this model, and the Dejerine's theory of the left lateralized "word center" seen in the posterior aspect of the figure.

It was Geschwind (1974), of course, who revived interest in this neurolinguistic-neuroanatomic model. He contributed significantly, however, by focusing attention on the natural left-sided asymmetry of the region of the *planum temporale*. Reports by early investigators (Flechsig, 1908; von Economo & Horn, 1930) encouraged Geschwind and Levitsky (1968) to investigate asymmetries associated with the region of the *planum temporale*. They examined 100 normal adult brains and found that the region of the *planum temporale* (the most posterior aspect of the superior temporal lobe) is larger on the left in 65% of brains, whereas it is larger on the right in only 11 percent of brains. These findings were taken as evidence of a specialized and asymmetric neuroanatomical region in support of language functions. Studies by other investigators documented the finding of plana asymmetry in both adult and infant brains (Kopp *et al.,* 1977; Rubens, Mahuwald, & Hutton, 1976; Wada, Clarke, and Hamm, 1975; Witelson & Pallie, 1973). Figure 3 shows the left-sided asymmetry typically found in normal brains that is thought to subserve the evolution of higher-order neurolinguistic processes.

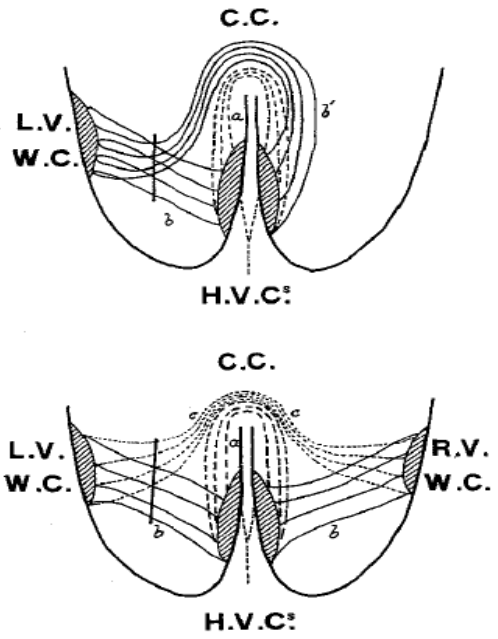

Figure 1: A comparison o Dejerine's and Bastain's views on the neuroanatomical basis of "pure word blindness" as presented by Bastian (1898). (Above) A simplified diagram representing Dejerine's views of the mode of production of pure word blindness. The dark line indicates the site of a lesion that cuts off the left visual word center (L.V.W.C.) from the Half vision center (H.V.C.) of each side. (Below) A diagram representing Bastian's views of the mode of production of pure word blindness. C.C., corpus callosum.

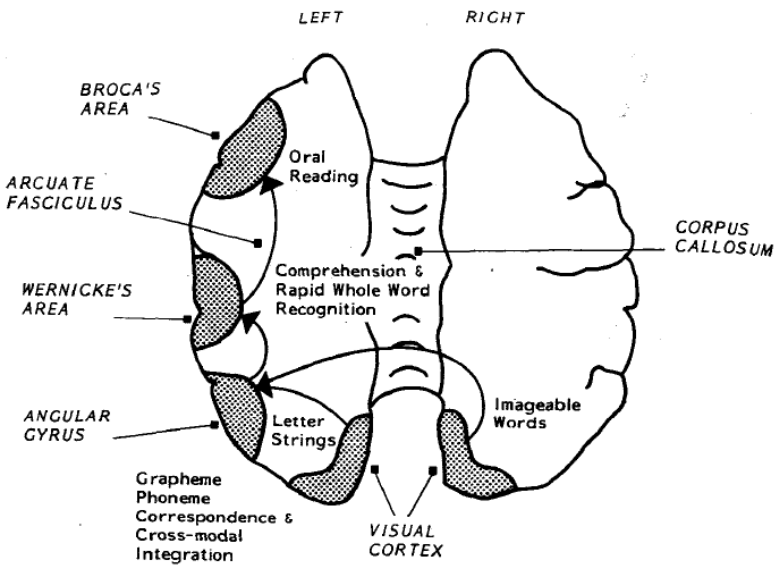

Figure 2. The brain as viewed in horizontal section. The major pathways and cortical regions thought to be involved in reading are depicted. neurolinguistic processes important in reading are also noted.

The research that was encouraged by the findings of Geschwind and Levitsky (1968) was significant in that other morphologic asymmetries in the human brain were soon reported. For example, Weinberger and colleagues (1982) found evidence that in approximately 75% of normal brains the right frontal volume (R) exceeds that of the left frontal cortex (L). Also this pattern of L < R asymmetry seems evident in fetal development as early as 20 weeks. Other documented asymmetries include the left anterior speech region (*pars opercularis* and *pars triangularis* of the third frontal convolution) favoring the left side (Falzi *et al.,* 1982) and cytoamhitectonic asymmetries favoring the left inferior parietal lobe (Eidelberg & Galaburda, 1984), the left auditory cortex (Galaburda & Sanides, 1980), and the posterior thalamus (Pidelberg & Galaburda, 1982).

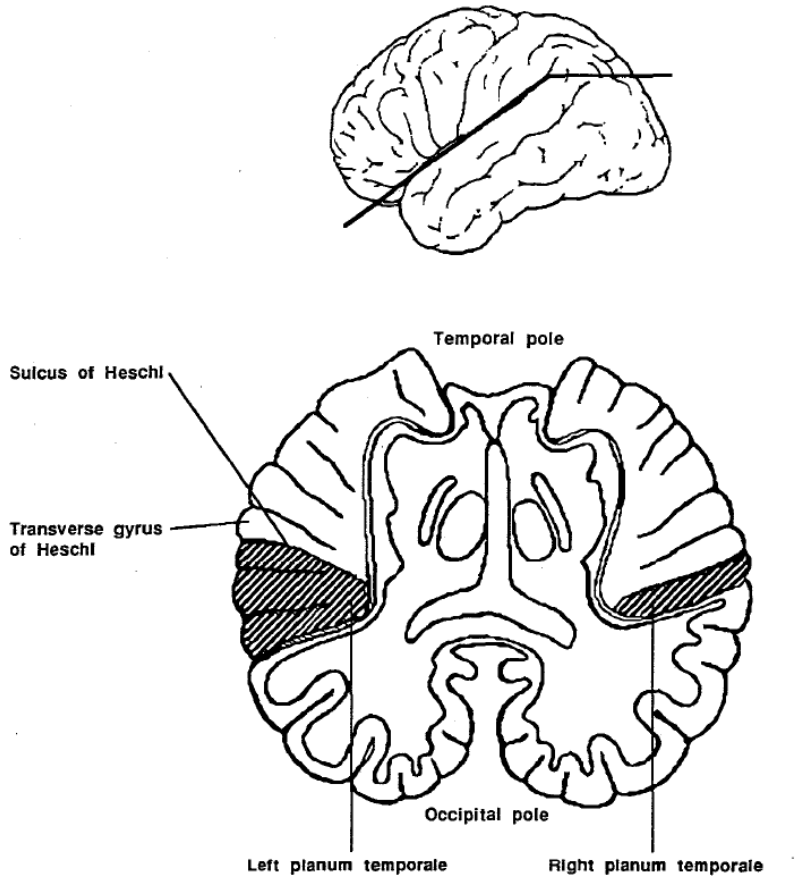

Figure 3 A graphic representation (top) of a slice up the sylvian (lateral) fissure exposing the posterior portion of the superior temporal region. The *planum temporale* is shaded bilaterally (bottom) and it can be seen that it is generally larger on the left.

Based on these as well as other research findings, Geschwind (1974, 1984) and especially Geschwind and Galaburda (1985a-c) argued that these natural asymmetries may be associated in a meaningful manner with language processes and, in cases of reversed asymmetry or symmetry, they ‘may underlie the deficits we observe in severe reading disabilities. While the theory outlined by Geschwind and Galaburda (1985a-c) addresses the possible relations between male gender differentiation, the effects of testosterone on neuronal assemblies, and

correlated asymmetries in brain morphology, immune function, and left-handedness, may indicate that deviations in natural brain asymmetries may be related to the deficient linguistic and reading processes observed in reading disabled children. Thus, in this context, the remainder of this chapter will address the brain-imaging literature and examine the findings in relation to whether or not evidence exists in support of the notion that deviations in natural asymmetries in the language-reading system in the brain are indeed related in some fashion to the cognitive or behavioral deficits observe in these children.

BRAIN IMAGING

Many methodologies have been employed to investigate laterality and asymmetries in human performance. Certainly, visual half-field and dichotic listening experiments have assisted us greatly in better understanding perceptual asymmetries that underlie linguistic and visuospatial perception. Dual-task paradigms have helped develop a better understanding of the lateralization of hemispheric attentional mechanisms and handedness-manual preference inventories have likewise helped in documenting variability in human laterality. All of these methodologies rely on the recording of a behavioral response that in turn leads to a measure of laterality. The documentation of morphologic asymmetries in the human brain that seemed to favor the left hemisphere central language zones encouraged speculation that variability in these patterns of asymmetry might be related to the behavioral deficits we see in such conditions as severe reading disability. Geschwind and his colleagues deserve much of the credit for encouraging this perspective. In this context then, measures of manual preference or perceptual asymmetries might still be of interest but they could not provide a window from which to actually view the brain and its associated morphology.

Computed tomography (CT) and magnetic resonance imaging (MRI) were obviously technologic advances that could help researchers examine directly structure-function relations in living humans. CT, of course, is considered an invasive procedure, as there is some limited exposure to radiation, whereas with MRI scans there are no known risk factors. Until MRl became more readily available, CT was the method employed to examine deviations in normal patters of asymmetry in the brains of reading-disabled children and adults. CT studies typically employed a scan between 0 and 25 degrees above the acanthomedial line to examine for posterior asymmetries. With the increased sophistication of MRI scanning procedures it became possible to obtain thinner slices and extreme lateral sagittal scans were used to examine sulcul topography as well. Most s canning facilities now have the capability to obtain three-dimensional volumetric scan data so that later reconstructions can be made on any plane desired. These technological advances have been accompanied by very significant methodological challenges with regard to head positioning, using a standardized grid system to normalize data acquisition across scans, and other difficulties in defining morphologic boundaries that may have functional significance. Nonetheless, these studies have been revealing and have encouraged increasing interest in using brain-imaging procedures to investigate many issues important to the study of lateralized functioning.

Table II Brain imaging studies of subjects with developmental dyslexia

Study	Type	No. of subjects	Mean age (yr)	Diagnostic criteria	Conclusions
Hier et al. (1978)	CT	24	25	Less than 5th-grade reading level on Gray Oral Reading Test or > 2-yr delay in reading while in school	Dyslexic subjects with reversed posterior asymmetry had lower verbal IQ 33% had normal L>R posterior asymmetry; 67% had symmetry or reversed (L<R) posterior asymmetry
LeMay (1978)	CT	27 dyslexic subjects[a] 317 controls	NR	NR	33% of dyslexic subjects had normal (L>R) posterior asymmetry compared to 70% of right-handed controls Left-handed controls evidenced more symmetry and reversed (L<R) asymmetry of posterior region
Leisman and Ashkenazi (1980)	CT	8 dyslexic subjects 2 controls	8.2—dyslexic subjects 7.6—normals	NR	100% of dyslexic subjects had symmetry or received asymmetry (L<R) of posterior region
Rosenberger and Hier (1980)	CT	53	6–45 (range)	Two grade levels below actual grade; large verbal-performance IQ discrepancy	42% of dyslexic subjects had reversed asymmetry (L<R) of posterior region Asymmetry index correlated with verbal-performance IQ discrepancy ($r = .38$, $P < .02$)
Haslam et al. (1981)	CT	26 dyslexic subjects 8 controls	11.7—dyslexic subjects 9.8—controls	Reading performance at least 2 yr below expected level based on IQ	46% of dyslexic subjects showed normal (L>R) posterior asymmetry while 87% controls did No relationship between IQ and posterior symmetry or asymmetry
Rumsey et al. (1986)	MRI	10	22.6	Childhood history of reading disability; median Gray Oral Reading Test was 3.7 grade equivalent	90% of dyslexic subjects showed symmetry of posterior regions
Parkins et al. (1987)	CT	44 dyslexic subjects 254 controls	57	Childhood history of reading and spelling disability, psychometrc evidence of dyslexia	Concluded that reversed posterior asymmetries are not characteristic of right-handed dyslexic subjects, but left-handed dyslexic subjects may evidence more symmetry
Larsen et al. (1990)	MRI	19 dyslexic subjects 19 normals	15.1—dyslexic subjects 15.4—controls	Highly significant difference between normals and dyslexic subjects in word recognition; selected prior to study by schools as dyslexic	Measured the patterns of asymmetry in the region of the planum temporale: 70% of dyslexic subjects evidenced symmetry, while only 30% of nondyslexic subjects did All dyslexic subjects with plana asymmetry demonstrated significant phonological coding deficits
Hynd et al. (1990)[b]	MRI	10 dyslexic subjects 10 ADDH children 10 normals	9.9—dyslexic subjects 10.0—ADDH children 11.8—normals	IQ ⩾85, positive family history, reading achievement ⩾20 standard score points below full-scale IQ on tests of word recognition and passage comprehension	Both dyslexic subjects ADDH children had smaller right frontal widths (more frontal symmetry than normals) 70% of normal and ADDH children demonstrated L>R plana asymmetry, while only 10% of dyslexic subjects did; plana symmetry or reversed asymmetry seems characteristic of dyslexia
Semrud-Clikeman et al. (1991)	MRI	Same as Hynd et al. (1990)	Same as Hynd et al. (1990)	NR	Frontal width symmetry/reversed asymmetry (L⩾R) associated with very significant delay in word attack skills Symmetry/reversed asymmetry of plana associated with poor confrontational naming, rapid naming, and passage comprehension
Leonard et al. (1993)	MRI	9 dyslexic subjects 10 relatives 11 controls	15–65 6–63 14–52	Primarily by clinical report and history	Dyslexic subjects had exaggerated left plana asymmetry for the temporal band and right asymmetry for the parietal bank Higher incidence of cerebral anomalies bilaterally

Modified from Hynd and Semrud-Clikeman (1989)

Key: ADDH, attention-deficit hyperactivity disorder; NR, not reported.

[a] LeMay (1981) used all subjects of Hier et al. (1978) adding three of her own in addition to the controls.

[b] Semrud-Clikeman et al. (1991) employed these subjects to examine the relationship between deviations in patterns of brain morphology and neurolinguistic ability in developmental dyslexics.

As can be seen in Table II, at least eleven studies using either CT or MRI have been conducted to examine whether or not deviations in normal patterns of asymmetry in brain morphology are associated with the manifestation of reading disabilities. The first such study was reported by Hier and colleagues (1978) who employed CT to investigate posterior asymmetries in 24 dyslexic subjects. They found that only 33 percent of the dyslexic group had a wider left posterior region while 67 percent had either symmetry or reversed asymmetry of the posterior region. Since fully 66 percent of the normal population is expected to show the expected L > R asymmetry, this lower incidence among the dyslexic group was taken as support for Geschwind's (1974) idea that patterns of asymmetry were meaningfully associated with linguistic functioning.

In a further study, Rosenberger and Hier (1980) found that a brain asymmetry index correlated with verbal performance intelligence quotient (IQ) discrepancies, whereas lower verbal IQ was correlated with symmetry or reversed asymmetry in the posterior region in the dyslexic subjects. This study actually was the first to examine whether there was any psychometric or behavioral relationship between asymmetry patterns and performance. In this respect this study was unique and an entire decade elapsed before several new studies also examined behavioral relationships to brain morphology data Thus, most of the early literature was characterized by examining the rather straightforward issue as to whether there was any deviation from normal patterns of brain asymmetry in subjects with severe reading disability. In 1981, Haslam and associates found in their sample of dyslexic subjects that 46 percent had L > R asymmetry similar to the normals, but in contrast to Rosenberger and Hier (1980), no relationship was found with regard to verbal ability. As Hynd and Semrud-Clikeman (1989) have pointed out, however, the-criteria employed by Haslam and colleagues for defining language delay were less strict than in the Rosenberger and Hier study. Nonetheless, Haslam's group (1981) did note that fewer dyslexic subjects had the normal L > R posterior asymmetry.

The mid-1980s marked a time of transition in that fewer CT studies were reported with increasingly more studies employing MRI procedures as MRI scanners became more available to the research community. In fact, the last CT study reported was by Parkins *et al.* (1987) who found that there existed some relationship of handedness to deviations from normal patterns of asymmetry by dyslexic subjects. They found in their older adult sample (mean age, 57 years) that symmetry of the posterior region was characteristic only in the left-handed dyslexic subjects. The results of this study are unusual because previously and in the studies to follow, handedness may have differentiated the normal from the severely reading-disabled sample, but no relationship was ever reported with handedness. The mean age of this sample is also unusual as these were reading-disabled adults who may represent an unusual part of the reading disability spectrum in that their reading disability persisted to such a severe degree well into advanced adulthood. Most other studies typically employed subjects in early adolescence through young adulthood.

The first reported MRI study was in 1986 by Rumsey and associates who found in their brief report that 90 percent of the dyslexic subjects showed evidence of posterior asymmetry. In a sense, this study was typical of the rather unsophisticated methodology that characterized the studies at that tie in that determination of asymmetry, symmetry, and reversed asymmetry of the posterior region most often relied on the clinical judgment of a radiologist or other expert in reading scans. Rarely were data presented as to the morphometric measurements that were obtained, if any, and for this reason it was difficult to compare results across

studies. About the only conclusion that could reasonably be advanced was that deviations in normal patterns of posterior asymmetry may be found more frequently in the brains of severe reading disabled persons. Based entirely on the Rosenberger and Hier (1980) study, there was limited but tantalizing evidence that symmetry or reversed asymmetry may somehow be associated with poor verbal-linguistic ability as is often found in dyslexic children.

To this point most studies had focused on posterior asymmetries, but theory had continued to emphasize the region of the *planum temporale* as being vitally important in verbal- their four consecutive autopsy cases and reported that the focal dysplasias clustered preferentially in the left superior posterior temporal region by a ratio of 2:I. Thus, there was good reason to shift the attention of researchers away from simple posterior asymmetries toward linguistic processes, particularly phonological coding. In fact, Galaburda *et al.* (1985) summarized attempts at measuring asymmetry of the region of the *planum temporale*. The focal dysplasias, Galaburda and colleagues reported, certainly could not be visualized on MRI scans, but different method could be employed in attempting to measure either the area or length of this region bilaterally in the brains of persons with dyslexia. Leisman & Ashkenazi (1980) present sample CT and Leisman & Melillo (2004) present sample MRI scans showing the anomalous cortex in the dyslexic subjects exemplifying measurement of asymmetry issues in dyslexia.

Two studies employed different methodologies aimed at investigating asymmetries in the region of the *planum temporale* in dyslexic persons. Using MRI to examine the size and patterns of asymmetry in this region in adolescents with dyslexia, Larsen, and colleagues (1990) found that 70 percent of their dyslexic group had symmetry in the region of the plana in contrast to 30 percent of the normals. In addition to the importance of this finding, Larsen *et al.* also found that when symmetry of the plana was present in dyslexia, the subjects demonstrated phonological deficits. They concluded that some relationship may exist between brain morphology patterns and neurolinguistic process, consistent with Rosenberger and Hier's (1980) conclusions.

That same year, Hynd *et al.* (1990) also reported a study employing MRI in which the relative specificity of patterns of plana morphology were investigated in relation to a population of normal controls and clinic control children. In this case the clinic control group comprised children with attention-deficit hyperactivity disorder (ADHD). For this reason, the study was unique in that of all studies reported previously, none had included a clinic contrast group but rather compared dyslexic subjects only with normal controls. While such an approach has value in determining whether a line of investigation might be productive, the results only suggested differences from normals. There was no way to address the specificity of deviations in brain morphology in relation to the behavioral deficits seen in any one clinical syndrome such as reading. Based on the previous literature, it was hypothesized that if differences existed in the brains of the dyslexic children in the region of the plana, similar differences would not be evident in the brains of the ADHD children who were carefully diagnosed so that this group did not include children with reading or learning disabilities.

Similar to Larsen *et al.* (1990), Hynd *et al.* (1990) found that the dyslexic group was characterized by either symmetry or reversed asymmetry (L < R) of the plana. Underscoring the importance of this region scientifically, they found that in 70% of the normals and ADDH children, L > R plana asymmetry existed. This is what would be expected according to the normative data provided originally by Geschwind and Levitsky (1968). Fully 90% of the dyslexic children demonstrated symmetry or reversed asymmetry of the plana. In a follow-up

study, Semrud-Clikeman and colleagues (1991) reported that symmetry and reversed asymmetry of the *planum temporale* was associated with significant deficits in confrontational naming, rapid naming, and neurolinguistic processes in general.

If one compares the Larsen *et al.* (1990) and Hynd *et al.* (1990) studies, differences seem evident in the way in which the plana were measured. Hynd *et al.* (1990) measured the length of the plana on extreme lateral sagittal MRI scans. Larsen *et al.* (1990), however, took measurements from sequential scans so that a measurement of area could be derived. Both studies found that significant indices of symmetry or reversed asymmetry characterized the brains of dyslexic children even though different methodologies were employed. A point to derive from this discussion is that there are no agreed-upon standardized methodologies, although the method employed by Larsen *et al.* (1990) most likely provides more reliable data. Further, in examining the literature regarding the neuroanatomical morphology of the ilana, one quickly realizes that there may be different sulcul patterns associated with whether or not a parietal bank of the *planum temporale* exists.

In a study reported by Leonard *et al.* (1993), the morphology of the posterior superior temporal region was examined bilaterally including the relative contribution of the temporal and parietal banks to an asymmetry index. The results of this study are particularly revealing in several ways. First, it turns out that nearly all dyslexic subjects and normals demonstrated a natural leftward asymmetry in the temporal bank and a rightward asymmetry in the parietal bank. When they examined intrahemispheric asymmetry, some dyslexic subjects had an anomalous intrahemispheric asymmetry between the temporal and planar banks in the right hemisphere because of an increased proportion of the plana being in the parietal bank What this suggests is that consideration must be given to measuring both the temporal and parietal banks of the *planum temporale* and the relative contribution of both banks bilaterally in deriving asymmetry indexes. To quickly illustrate this issue the reader may wish to refer to Figure 3, which illustrates the typical fashion in which the plana were described in the literature. By looking at the figure at the top where the slice location is noted, one can see at the end of the sylvian fissure where the slice line cuts horizontally that there is a small ascending ramus that is actually part of the planum. By not including this parietal aspect in lateral measures of asymmetry, the Larsen *et al.* (1990) and Hynd *et al.* (1990) studies were incomplete, although at the time they were published they were excellent studies. Finally, the Leonard *et al.* (1993) study documented that the dyslexic persons were more likely to evidence anomalies such as missing or duplicated gyri bilaterally in the region of the posterior end of the lateral fissure. These cerebral anomalies most likely evolve somewhere between the 24 and 30th week of fetal gestation when gyration occurs and represent a neurodevelopmental anomaly possibly related to a genetic etiology.

What does this literature suggest about cerebral morphology and lateralized function in reading-disabled or dyslexic children? First, it suggests that asymmetry may indeed be characteristic of most normal brains. Second, in the region of the *planum temporale* there may be an increased incidence of symmetry or reversed asymmetry if one only measures the temporal bank. If one measures the bilateral temporal and parietal banks in the dyslexic group one may actually end up with these persons having more leftward asymmetry because of intrahemispheric variation in the right hemisphere, at least according to Leonard *et al.* (1993). As the Leonard *et al.* (1993) study clearly indicates, measuring highly variable brain regions in different subject groups is fraught with complications, and decisions that must be made in terms of what to measure can dramatically influence outcomes. Finally, as Rosenberger and

Hier (1980) first suggested, there may indeed be relationships between deviations in brain morphology and neurolinguistic processes. The Larsen *et al.* (1990) and Semrud-Clikeman *et al.* (1991) studies provide further support for this important aspect of the theory advanced by Geschwind (1974,1984).

RECENT ADVANCES AND THE FUTURE AGENDA IN UNDERSTANDING THE RELATION BETWEEN CORITCAL ASYMMETRY AND LEARNING DISABILITY

There should be little doubt that brain-imaging procedures offer much promise in investigating issues related to possible relationships between brain structure morphology and behavioral observations, whether these observations be clinical or experimental. What needs to be kept in mind however is that across all of these studies in which over 200 subjects have been scanned, not one brain of a reading-disabled subject was judged to be abnormal in structure (other than asymmetry patterns). In other words, no evidence of brain damage was found. This should underscore the important findings of Galaburda and colleagues (1985) who find developmental anomalies in the brains of dyslexic persons. The anomalous cortex identified by Leonard *et al.* (1993) provides further data implicating neurodevelopmental processes as underlying the behavioral symptoms exhibited in dyslexia. It appears that reasonable evidence exists implicating unusual developmental processes sometime during the fifth to seventh month of fetal gestation in dyslexia. Clearly, the exact cause of these neurodevelopmental anomalies is one of the most important unanswered questions.

In autopsy research, Galaburda and his colleagues have been the main contributors to this area of investigation (Galaburda, 1988, 1989, 1993, 1994, 1997; Galaburda & Livingstone, 1993; Galaburda, Menard, & Rosen, 1994). These researchers have found areas of symmetry and asymmetry in normal brains that differ in individuals with reading disabilities. The autopsied brains of individuals with dyslexia show alterations in the pattern of cerebral asymmetry of the language area with size differences, and minor developmental malformations, which affect the cerebral cortex.

The work of Galaburda and colleagues has shown that about two-thirds of normal control brains show an asymmetry; the planum temporale of the left hemisphere is larger that that of the right hemisphere. Between 20% and 25% of normal control brains show no asymmetry, with the remaining having asymmetry in favor of the right side (Best & Demb, 1999). This asymmetry is thought to be established by 31 weeks of gestation (Chi, Dooling, & Gilles, as cited in Best & Demb, 1999), and Witelson and Pallie (1973) have shown hemispheric asymmetry of the planum temporale to be present in fetal brains.

In contrast, the brains of reliably diagnosed cases of developmental dyslexia have shown the absence of ordinary asymmetry; symmetry is the rule in the planum temporale of brains of dyslexic subjects studied at autopsy, and increased symmetry is also found in imaging studies (Best & Demb, 1999; Galaburda, 1993). These findings are relevant since individuals with dyslexia have language-processing difficulties, and reading is a language-related task. Therefore, anatomical differences in one of the language centers of the brain are consistent with the functional deficits of dyslexia.

Because abnormal auditory processing has been demonstrated in individuals with dyslexia, accompanying anatomical abnormalities in the auditory system have also been the focus of autopsy studies, specifically in the medial geniculate nuclei (MGN), which are part of the metathalamus and lie underneath the pulvinar. From the MGN, fibers of the acoustic radiation pass to the auditory areas in the temporal lobes. Normal controls showed no asymmetry of this area, but the brains of individuals with dyslexia showed that the left side MGN neurons were significantly smaller than those on the right side. Also, there were more small neurons and fewer large neurons in the left MGN in individuals with dyslexia versus controls (Galaburda & Livingstone, 1993; Galaburda et al., 1994). These findings are of particular relevance in view of the left hemisphere-based phonological defect in individuals with dyslexia (Tallal, Miller, & Fitch, 1993).

Neuroanantomical abnormalities in the magnocellular visual pathway have been reported (Galaburda & Livingstone, 1993), and these have been postulated to underlie functioning of the transient visual system in individuals with reading disabilities (Iovino, Fletcher, Breitmeyer, & Foorman, 1998). Jenner, Rosen, and Galaburda (1999) concluded that there is a neuronal size difference in the primary visual cortex in dyslexic brains, which is another anomalous expression of cerebral asymmetry (similar to that of the planum temporale) which, in their view, represents abnormal circuits involved in reading.

According to Galaburda, symmetry may represent the absence of necessary developmental "pruning" of neural networks, which is required for specific functions such as language. In other words, the pruning, which takes place in normal controls, does not take place in individuals with dyslexia (Galaburda, 1989, 1994, 1997), thereby resulting in atypical brain structures, which are associated with language-related functions.

MRI (magnetic resonance imaging) studies have substantiated the findings of autopsy studies; namely, individuals with dyslexia do not have the asymmetry or the same patterns of asymmetry of brain structures that is evident in individuals without dyslexia. A number of investigators have demonstrated a high incidence of symmetry in the temporal lobe in individuals with dyslexia. (Best & Demb, 1999; Hugdahl et al., 1998; Kushch et al., 1993; Leonard et al., 1993; Logan, 1996; Rumsey et al., 1996;). Duara et al. (1991) and Larsen, Høien, Lundberg, and Ødegaard (1990) showed a reversal of the normal leftward asymmetry in the region of the brain involving the angular gyrus in the parietal lobe. Dalby, Elbro, and Stodkilde-Jorgensen (1998) demonstrated symmetry or rightward asymmetry in the temporal lobes (lateral to insula) of the dyslexics in their study. Further, the absence of normal left asymmetry was found to correlate with degraded reading skills and phonemic analysis skills.

Logan (1996) reported that individuals with dyslexia had significantly shorter insula regions bilaterally than controls. Hynd et al. (1995) identified asymmetries in the genu of the corpus callosum of individuals with dyslexia and positively correlated both the genu and splenium with reading performance. This supports the hypothesis that, for some individuals with dyslexia, difficulty in reading may be associated with deficient interhemispheric transfer (Leisman & Melillo, 2004). Hynd and his colleagues (Hynd, Marshall, & Semrud-Clikeman, 1991) also reported shorter insula length bilaterally and asymmetrical frontal regions in individuals with dyslexia. The latter was related to poorer passage comprehension. Best and Demb (1999) examined the relationship between a deficit in the magnocellular visual pathway and planum temporale symmetry. They concluded that these two neurological markers for dyslexia were independent.

There has been substantial replication of findings, particularly with respect to the planum temporale. On the other hand, there have been conflicting reports regarding other areas, especially the corpus callosum (Hynd et al., 1995 versus Larsen, Höien, & Ødegaard, 1992). Methodological and sampling differences, such as slice thickness, orientation and position, and partial volume effects may account for this variability. In a review of the literature on the planum temporale, Shapleske et al. (1999) summarized the methodological concerns in operationalizing consistent criteria for anatomical boundaries when measuring the planum temporale and the need to use standardized measures of assessment and operationalized diagnostic criteria. They concluded that dyslexics may show reduced asymmetry of the planum temporale, but studies have been confounded by comorbidity. Njiokiktjien, de Sonneville, and Vaal (1994) concluded that, despite a multitude of developmental factors influencing the final size, total corpus callosal size is implicated in reading disabilities. In a study by Robichon and Habib (1998), in which more rigid methods were applied, MRI and neuropsychological findings of dyslexic adults were correlated and compared with normal controls. Different morphometric characteristics were positively correlated with the degree of impairment of phonological abilities. The corpus callosum of the dyslexic group was more circular in shape and thicker, and the midsaggital surface was larger, particularly in the isthmus.

Neuroanatomical investigations have substantiated what had been surmised from the early traditional studies of acquired brain lesions and associated changes in functions and have brought forward new evidence to support the neurobiological basis of learning disabilities. Advances in neuroimaging have permitted brain dissection "in vivo," a transparent window of brain functions, concurrent with neurological and neuropsychological evaluations. This methodology has supported previous findings and hypotheses while providing new evidence of brain structure/function relationships. Although the neuroanatomical correlates of dyslexia do not answer the question about whether dyslexia is a condition at one extreme in the normal distribution of reading skill (Dalby et al., 1998), the neuroanatomical and neuroimaging studies have provided evidence linking learning disabilities to neurobiological etiology. In a PET scan study, Horwitz, Rumsey, and Donohue (1998) demonstrated that in normal adult readers there was a correlation of regional cerebral blood flow in the left angular gyrus and flow in the extrastriatal, occipital, and temporal lobe regions during single word reading. In men with dyslexia, the left angular gyrus was functionally disconnected from these areas. Gross-Glenn et al. (1991) found regional metabolic activity measured with PET scan to be similar in individuals with dyslexia and those without dyslexia, reflecting that reading depends on neural activity in a widely distributed set of specific brain regions. There were also some differences concentrated in the occipital and frontal lobe regions. In contrast to controls, individuals with dyslexia showed little asymmetry. These findings correspond well with the reduced structural posterior asymmetry observed in the CT scan and postmortem studies. Prefrontal cortex activity was also symmetrical in individuals with dyslexia versus asymmetrical in normal controls. Higher metabolic activity (local utilization rate for glucose) in the lingual area (inferior occipital regions bilaterally) was reported by Lou (1992) with PET studies, and a SPECT (single photon emission computed tomography) scan showed striatal regions as hypoperfused and, by inference, under-functioning.

Numerous studies have attempted to identify the neurological basis of learning disabilities in terms of left–versus right–hemisphere dysfunction. Adult strokes were found to

affect cognitive abilities such as reasoning, perceptual speed and memory clusters, scholastic aptitude, written language (Aram & Ekelman, 1988), reading, language or verbal learning (Aram, Gillespie, & Yamashita, 1990; Eden et al., 1993; Leavell & Lewandowski, 1990), and arithmetic processing (Ashcraft, Yamashita, & Aram, 1992). It is hypothesized that, as a result of genetic or epigenetic hormonal and/or immunological factors, the cortical language areas are disturbed in their development through migration disorders and abnormal asymmetry, such that normal left hemisphere dominance does not develop, resulting in dyslexia in some children (Njiokiktjien, 1994).

Right hemisphere dysfunction has also been associated with specific learning disabilities. Damage to the right hemisphere in adults is associated with deficits in social skills, prosody, spatial orientation, problem-solving, recognition of nonverbal cues (Semrud-Clikeman & Hynd, 1991), impaired comprehension and production of affective signals, and higher-order cognition about social behaviors (Voeller, 1995). The right hemisphere is therefore implicated in the processing of social-emotional information in the same way that the left hemisphere is specialized for language (Voeller, 1995).

The association of chronic social difficulties coupled with deficits in producing and comprehending emotional expressions, in combination with left-hemibody signs, has been reported as the right hemisphere deficit syndrome (Voeller, 1995). Lower reading performance has also been associated with the right hemisphere (Aram & Ekelman, 1988; Aram et al., 1990; Branch, Cohen, & Hynd, 1995), as have mathematical problems (Ashcraft et al., 1992; Branch et al., 1995; Rourke & Conway, 1997; Shalev, Manor, Amir, Wertman-Elad, & Gross-Tsur, 1995), and visuospatial deficits (Tranel et al., 1987).

With regard to arithmetic disabilities, both the right and left hemispheres have been implicated (Ashcraft et al, 1992; Branch, Cohen, & Hynd, 1995; Rourke & Conway, 1997; Shalev et al., 1995). In the child, early damage or dysfunction in the right or left hemispheres has been reported to disrupt arithmetic learning, with very profound effects resulting from early right hemisphere insults, whereas in the adult, left hemisphere lesions predominate in the clinico-pathological analysis of acalculia or computation difficulty (Rourke & Conway, 1997).

The effective treatment of any condition or disease must be based on an adequate understanding of the etiology and genesis of that condition. Appreciating the neurobiological basis can facilitate the development of effective educational programs, with instructional goals, content, and pace of delivery designed to maximize success for individuals with learning disabilities. However, public policy makers have been slow to recognize the implications of this fact for the field of learning disabilities.

Recognition of the neurobiological basis of learning disabilities does not necessarily lead to a bleak outlook, because the individual's environment has the potential to reduce or amplify the impact of the learning disabilities. Supportive care giving (Kopp, 1990), quality of the home environment (Kalmar, 1996), and socioeconomic factors (Drillien, Thomson, & Burgoyne, 1980; Werner, 1990), as well as educational programs designed specifically to meet the needs of individuals with learning disabilities (Fiedorowicz & Trites, 1991; Lerner, 1989), have the power to mitigate the academic and cognitive deficits associated with the condition.

REFERENCES

Albe-Fessard, D. Condes-Lara, M. & Sanderson, P. (1983). The focal tonic cortical control of intralaminar thalamic neurons may involve a cortico-thalamic loop. Acts Morphologica Hungarica, 31, 9-26.

Aram, D. M., & Ekelman, B. L. (1988). Scholastic aptitude and achievement among children with unilateral brain lesions. *Neuropsychologia, 26* (6*),* 903-916.

Aram, D. M., Gillespie, L. L., & Yamashita, T. S. (1990). Reading among children with left and right brain lesions. *Developmental Neuropsychology, 6(4)*, 301-317.

Arnulf, I., Bejjani, B.P., Garma, L., Bonnet, A.M., Houeto, J.L., Damier, P., Derenne, J.P. and Agid, Y. (2000). Improvement of sleep architecture in PD with subthalamic nucleus stimulation. Neurology, 12, 1732-1734.

Ashcraft, M. H., Yamashita, T. S., & Aram, D. M. (1992). Mathematics performance in left and right brain-lesioned children and adolescents. *Brain and Cognition, 19,* 208-252.

Bakker, D. J., & van der Vlugt, H. (Eds.) (1989). Learning disabilities, vol 1. neuropsychological correlates and treatment. Amsterdam: Swets & Zeitlinger.

Banich, M. T. (1995). Interhemispheric processing: Theoretical considerations and empirical approaches. In: R. J. Davidson and K. Hugdahl (Eds.), Brain asymmetry. Cambridge, MA: MIT Press.

Bastian, H. C. (1898). A treatise on aphasia and other speech defects. London: H. K. Lewis.

Benton, A. L. (1975). Developmental dyslexia: Neurological aspects. In: W. J. Friedlander (Ed.) Advances in neurology. New York, NY: Raven Press.

Best, M., & Demb, J. B. (1999). Normal planum temporale asymmetry in dyslexics with a magnocellular pathway deficit. *NeuroReport, 10(3),* 607-612.

Branch, W. B., Cohen, M. J., & Hynd, G. W. (1995). Academic achievement and attention-deficit/hyperactivity disorder in children with left- or right hemisphere dysfunction. *Journal of Learning Disabilities, 28(1),* 35-43, 64.

Broadbent, D.E. (1958). Perception and communication. New York, NY: Plenum.

Broadbent, D.E. (1965). Applications of information theory and decision theory to human perception and reaction. Progress in Brain Research, 17: 309-20.

Bryden, M. P. (1988). Does laterality make any difference? Thoughts on the relation between cerebral asymmetry and reading. In D. L. Molfese & S. J. Segalowitz (Eds.), Brain lateralization in children: Developmental implications (pp 509-525). New York, NY: Guilford Press.

Bryden, M. P. & Steenhuis, R. (1991). The assessment of handedness in children. In: J. E. Obrzut & G. W. Hynd (Eds.), Neuropsychological foundations of learning disabilities: A handbook of issues, methods, and practice New York, NY: Academic Press pp 411-436.

Boliek, C.A. & Obrzut, J.E. (1995). Perceptual laterality. In: R. J. Davidson & K. Hugdahl (Eds.), *Brain asymmetry*. Cambridge, MA: MIT Press.

Castro-Alamancos, M. A. (2002). Role of thalamocortical sensory suppression during arousal: focusing sensory inputs in neocortex *The Journal of Neuroscience 22*, 9651-9655.

Corballis, M. C. (1983). *Human laterality*. New York, NY: Academic Press.

Dalby, M. A., Elbro, C., & Stodkilde-Jorgensen, H. (1998). Temporal lobe asymmetry and dyslexia: an *in vivo* study using MRI. *Brain and Language, 62,* 51-69.

Dawson, G. (1988). Cerebral lateralization in autism: Clues to its role in language and affective development. In: D. L. Molfese & S. J. Segalowitz (Eds.), *Brain lateralization in children: Developmental implications*. New York, NY: Guilford Press pp. 437-461.

Dawson, G. (1996). Brief report: neuropsychology of autism: a report on the state of the science. *Journal of autism and developmental disorders 26,* 179-84.

Dejerine, J. (1892). Contribution à l'étude de la localisation anatomopathologique et clinique des differentes variétés de cécité verbale. *Mémoires de las societé de Biologie 4*, 61-90.

Dejerine, J. & Dejerine-Klumpke, A. (1901). *Anatomie des centres nerveux, vol. 2*. Paris: Rueff et Cie., pp. 109-114.

Dejerine, J., & Vialet, P. (1893). Conhibution a l'étude de la localisation anatomique de la cécité verbale pure. *Comptes rendus des séeances de la societé biologie 45*, 790-793.

Drillien, C.M., Thomson, A.S.M., & Burgoyne, K. (1980). Low-birthweight children at early school-age: A longitudinal study. *Developmental Medicine and Child Neurology, 22*, 26-47.

Duane, D.D. (1989). Neurobiological correlates of learning disorders. *Journal of the American Academy of Child and Adolescent Psychiatry 28,* 314-318.

Duara, R., Kushch, A., Gross-Glenn, K., Barker, W. W., Jallad, B., Pascal, S., Loewenstein, D. A., Sheldon, J., Rabin, M., Levin, B., & Lubs, H. (1991). Neuroanatomic differences between dyslexic and normal readers on magnetic resonance imaging scans. *Archives of Neurology, 48,* 410-416.

Duffy, F. H., Denckla, M. B, Bartels, P. H, Sandini, G, & Kiessling, L. S. (1980). Dyslexia: Automated diagnosis by computerized classification of brain electrical activity. *Annals of Neurology 7*, 421-428.

Eden, G. F., Stein, J. F., Wood, M. H., & Wood, F. B. (1993). Dyslexia: A study of preserved and impaired visuospatial and phonological functions. *Annals of the New York Academy of Sciences, 682,* 335-338.

Eidelberg, D., & Galabuda, A. M. (1982). Symmetry and asymmetry in the human posterior thalamus: I. Cytoarchitectonic analysis in normal persons. *Archives of Neurology 39*, 325-332.

Eidelberg D., & Galaburda, A. M. (1984). Inferior paietal lobule: Divergent architectonic asymmetries in the human brain. *Archives of Neurology 41*, 843-852.

Falzi, G., Penone, P., & Vignolo, L. A. (1982). Right-left asymmetry in anterior speech region. *Archives of Neurology 39*, 239-240.

Flechig, P. (1908). Bemerkungen über die hemispheren des menschlichen gehirns. *Neurologisches Zentralblatt 27*, 50-57.

Frank, Y & Pavlakis, S. G. (2001) Brain imaging in neurobehavioral disorders. *Pediatric Neurology 25*, 278-87.

Fiedorowicz, C., & Trites, R. L. (1991). From theory to practice with subtypes of reading disabilities. In B. P. Rourke (Ed.), *Neuropsychological validation of learning disability subtypes*. New York: Guilford Press.

Fried, I., Tanguy, P. E., Boder E., Doubleday, C., & Greensite, M. (1961). Developmental dyslexia: electrophysiological evidence of clinical subgroups. *Brain and Language, 12*, 14-22.

Gaddes, W. H. (1985). *Learning disabilities and brain function: A neuropsychological approach, ed 2*. New York, NY: Springer-Verlag.

Galaburda, A. M. (1988). The pathogenesis of childhood dyslexia. *Research in Nervous Mental Disorders, 66,* 127-138.

Galaburda, A. M. (1989). Ordinary and extraordinary brain development: Anatomical variation in developmental dyslexia. *Annals of Dyslexia, 39,* 67-80.

Galaburda, A. M. (1993). Neuroanatomical basis of developmental dyslexia. *Neurologic Clinics, 11(1),* 161-173.

Galaburda, A. M. (1994). Developmental dyslexia and animal studies: At the interface between cognition and neurology. *Cognition, 50*, 133-149.

Galaburda, A. M. (1997). Neurobiology of developmental dyslexia: Results of a ten year research program. *Learning Disabilities*, *8(1)*, 43-50.

Galaburda, A., & Livingstone, M. (1993). Evidence for a magnocellular defect in developmental dyslexia. *Annals of the New York Academy of Sciences, 682,* 70-82.

Galaburda, A. M., Menard, M. T., & Rosen, G. D. (1994). Evidence for aberrant auditory anatomy in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America, 91,* 8010-8013.

Galaburda, A M., & Sanides, F. (1980). Cytoarchitectonic organization in the human auditory cortex. *Journal of Comparative Neurology 190*, 597~610.

Galaburda, A. M, Sherman, G. F., Rosen, G. D., Aboitiz, F., & Geschwind, N. (1985). Developmental dyslexia: four consecutive cases with cortical anomalies. *Annals of Neurology 18*, 222-233.

Geschwind, N. (1974). The development of the brain and the evolution of language. In: N. Geschwind (Ed.), *Selected papers on language and the brain*. Dordrecht, The Netherlands: D. Reidel, pp. 122-146.

Geschwind, N. (1984). Cerebral dominance in biological perspective. *Neuropsychologia 22*, 675-683.

Geschwind, N., & Galaburda, A M. (1985a). Cerebral lateralization: biological mechanisms, associations, and pathology, I. a hypothesis and program for research. Archives of Neurology, 42, 428-459.

Geschwind, N., & Galaburda, A M. (1985b). Cerebral lateralization: Biological mechanisms, associations, and pathology, II. A hypothesis and program for research *Archives of Neurology 42*,521-552.

Geschwind, N.. & Galaburda, A M. (1985c). Cerebral lateralization: Biological mechanisms, associations, and pathology. III. A hypothesis and program for research. *Archives of Neurology 42*, 634-654.

Geschwind, N., Levitsky, W. (1968). Human brain: left-right asymmetries in temporal speech region. *Science 161*, 186-187.

Gil, Z., Connors, B.W., & Amitai, Y. (1999). Efficacy of thalamocortical and intracortical synaptic connections: quanta, innervation, and reliability. *Neuron 23*, 385-97.

Golden, C. S. (1982). Neurobiological correlates of leaning disabilities. *Annals of Neurology 12,* 409-418.

Gross-Glenn, K., Duara, R., Barker, W. W., Loewenstein, D., Chang, J.Y., Yoshii, F., Apicella, A. M., Pascal, S., Boothe, T., Sevush, S., Jallad, B. J., Novoa, L., & Lubs, H. A. (1991). Positron emission tomographic studies during serial word-reading by normal and dyslexic adults. *Journal of Clinical and Experimental Neuropsychology*, *13(4)*, 531-544.

Halboni, P., Kaminski, R., Gobbele, R., Zuchner, S., Waberski, T.D., Herrmann, C.S., Topper, R. & Buchner, H. (2000). Sleep stage dependant changes of the high-frequency

part of the somatosensory evoked potentials at the thalamus and cortex. C*linical Neurophysiology 111,* :2277-2284.

Haslam, R H., Dalby, J. T., Johns, R D. & Rademaker, A W. (1981). Cerebral asymmetry in developmental dyslexia. *Archives of Neurology 38*, 679-682.

Head, H. (1926). *Aphasia and kindred disorders of speech*. Cambridge, England: Cambridge University Press.

Heilman, K.M. (1995). Attention asymmetries. In: R.J. Davidson & K. Hugdahl (Eds.) *Brain asymmetry*. Cambridge, MA: MIT Press, pp.. 217-234.

Hier, D. B., LeMay, M, Rosenbergen P. B., & Perlo, V. P. (1978). Developmental dyslexia: evidence for a subgroup with a reversal of cerebral asymmetry. *Archives of Neurology 35*, 90-92.

Hinshelwood, J. (1900). Word-blindness and visual memory. *Lancet 2*, 1564-1570.

Horwitz, B., Rumsey, J. M., & Donohue, B. C. (1998). Functional connectivity of the angular gyrus in normal reading and dyslexia. *Proceedings of the National Academy of Sciences of the United States of America. 95(15),* 8939-8944.

Hugdahl, K., Heiervang, E., Nordby, H., Smievoll, A. I., Steinmetz, H., Stevenson, J., & Lund, A. (1998). Central auditory processing, MRI morphometry and brain laterality: applications to dyslexia. *Scandinavian Audiology. Supplementum. 49,* 26-34.

Hynd, G. W., & Semrud-Clikeman, M. (1989). Dyslexia and brain morphology. *Psychological Bulletin 106*, 447-482.

Hynd, G. W, Semrud-Clikeman, M., Lays, A. R, Novey, E., & Eliopulos, D. (1990). Brain morphology in developmental dyslexia and attention deficit disorder/hyperacvity. *Archives of Neurology 47*, 919-926.

Hynd, G. W., & Willis, W. G. (1988). *Pediatric neuropsychology*. Needham Heights, MA: Allyn & Bacon.

Iovino, I., Fletcher, J. M., Breitmeyer, B. G., & Foorman, B. R. (1998). Colored overlays for visual perceptual deficits in children with reading disability and attention deficit/hyperactivity disorder: are they differentially effective? *Journal of Clinical and Experimental Neuropsychology. 20 (6),* 791-806.

Jenner, A. R., Rosen, G.D., & Galaburda, A.M. (1999). Neuronal asymmetries in primary visual cortex of dyslexic and nondyslexic brains. *Annals of Neurology. 46(2),* 189-196.

Kalmar, M. (1996). The Course of intellectual development in preterm and fullterm children: An 8-year longitudinal study. *International Journal of Behavioral Development, 19*, 491-516.

Kalvas, P.W., Churchill, L., Romainides, A. (1999). Involvement of the pallidal-thalamocortical circuit in adaptive behavior. *Annals of the New York Academy of Sciences 877,* 64-70.

Kaufmann, W.E. & Galaburda, A.M. (1989). Cerebrocortical microdysgenesis in neurologically normal subjects: a histopathologic study. *Neurology 39*, 238–244.

Kershner, J., & Chyczij, M. (1992). Lateral preference in six to nine year old children: relationships to language lateralization and cognitive ability. *Learning and Individual Differences 4*, 347-367.

Keshner, E.A. and Peterson, B.W. (1988). Motor control strategies underlying head stabilization and voluntary head movements in humans and cats. *Progress in Brain Research 76*:329-39

Kinsbourne, M.. & Hiscock, M. (1981). Cerebral lateralization and cognitive development: conceptual and methodological issues. In: G. W. Hynd & J. E. Obrzut (Eds.) *Neuropsychological assessment and the school-age child*. New York, NY: Grune & Stratton, Inc. pp. 125-166.

Kinsbourne, M. & Hiscock, M. (1983). The normal and deviant development of functional lateralization of the brain. In P. Mussen, M. Haith, & J. Campos (Eds.), *Handbook of child psychology, (ed 4.)*. New York, NY: John Wiley & Sons.

Kopp, C. (1990). Risk in infancy: Appraising the research. *Merrill Palmer Quarterly, 36,* 17-39.

Kopp, N., Michel, F., Carrier, H., Biron, A, & Duvillard, P. (1977). Étude de certaines asymétries hémisphériques de cerveau humain. *Journal of the Neurological Sciences. 34*,349-363.

Kussmaul, A (1877). A disturbance of speech. *Cylopedia of Practical Medicine*, 14, 581-875.

Kushch, A., Gross-Glenn, K., Jallad, B., Lubs, H., Rabin, M., Feldman, E., & Duara, R. (1993). Temporal lobe surface area measurements on MRI in normal and dyslexic readers. *Neuropsychologia, 31(8),* 811-821.

Larsen, J. P., Høien, T., Lundberg, I., & Ødegaard, H. (1990). MRI evaluation of the size and symmetry of the planum temporale in adolescents with developmental dyslexia. *Brain and Language, 39,* 289-301.

Leavell, C., & Lewandowski, L. (1990). Neurolinguistic deficits and the left hemisphere in the reading disabled. *Developmental Neuropsychology, 6(4),* 319-337.

Leisman, G. (1976), The role of visual processes in attention and its disorders. In: G. Leisman (Ed.) *Basic Visual Processes and Learning Disability*. Springfield, IL: Charles C. Thomas pp. 7-123.

Leisman, G. (2002). Hemispheric coherence function in developmental dyslexia. *Brain and Cognition 48*, 425-431.

Leisman, G, & Ashkenazi, M. (1980). Aetiological factors in dyslexia: IV. Cerebral hemispheres are functionally equivalent. *Neuroscience. 11*, 157-164.

Leisman, G. & Melillo R. (2004). Functional brain organization in developmental dyslexia. In: H. D. Tobias (Ed.) *Focus on dyslexia research*. Hauppauge, NY: Nova, pp.105-149.

Lenneberg, E. H. (1967). *Biological foundations of language*, New York, NY: John Wiley and Sons.

LeMay, M. (1981). Are there radiological changes in the brains of individuals with dyslexia? *Bulletin of the Orton Society. 31*, 135-141.

Leonard, C. M., Voeller, K. K. S., Lombardino, L. J., Morris, M., Hynd, G. W., Alexander, A W., Anderson H G., Garofalakis, M, Honeyman. J. C., Mao, J., Agee, 0. F, & Staab, E. V. (1993). Anomalous cerebral morphology in dyslexia revealed with MR imaging. *Archives of Neurology 50*, 461~469.

Lerner, J. (1989). Educational intervention in learning disabilities. *Journal of the American Academy of Child and Adolescent Psychiatry, 28*, 326-331.

Liepmann, H. (1915). Diseases of the brain. normal and pathological physiology of the brain. In: C. W. Burr (Ed.), *Text-book on nervous disease*. Philadelphia, PA: Blakistone, pp. 445-552.

Llinas, R .R. (1995). Neurobiology. Thorny issues in neurons. *Nature 373*, 107-108.

Logan, W. J. (1996). Neuroimaging and functional brain analysis. In J. H. Beitchman, N. J. Cohen, M. M. Konstantareas, & R. Tannock (Eds.), *Language, learning, and behavior*

disorders: Developmental, biological, and clinical perspectives (pp. 297-314). Cambridge, UK: Cambridge University Press.

Lou, H. C. (1992). Cerebral single photon emission tomography (SPECT) and positron emission tomography (PET) during development and in learning disorders. In I. Rapin & S. J. Segalowitz (Eds.), *Handbook of neuropsychology, Vol. 6: Child neuropsychology* (pp. 331-338). Amsterdam: Elsevier Science.

Luria, A. R. (1973) *The working brain*. New York, NY: Basic Books.

Marie, P. (1906). Revision de la question de l'aphasie: la 3 circonvolution frontale gauche ne joue aucn rôle spécial dans la fonction du langage. *Semaine Médicale 21*, 241- 247.

Mayeux R., & Kandel, E. R (1985). Natural language, disorders of language, and other localizable disorders of cognitive functioning. In: E. R Kandel & J. H. Schwartz (Eds.), *Principals of neural science*, (ed. 2). New York, NY: Elsevier, pp. 688-703.

Melillo, R. & Leisman, G. (2004). *Neurobehavioral disorders of childhood: an evolutionary approach*, New York, NY: Kluwer, 2004.

Molfese, D. L, & Molfese, V. J. (1986). Psychophysiological indices of early cognitive processes and their relationship to language. In: J. E. Obrzut & G. W. Hynd (Eds.), *Child neuropsychology: theory and practice. vol I* . New York, NY: Academic Press pp. 95-115.

Morgan, W. P. (1896). A case of congenital word-blindness. *British Medical Journal 2*, 1978.

Njiokiktjien, C. (1994). Dyslexia: A neuroscientific puzzle. Acta *Paedopsychiatrica, 56,* 157-167.

Obrzut, J. E. (1991). Hemispheric activation and arousal asymmetry in learning disabled children. In: J. E. Obrzut & G. W. Hynd (Eds.). *Neuropsychological foundations of learning disabilities: a handbook of issues, methods and practice*. New York NY: Academic Press pp. 179-198.

Obrzut, J. E., & Hynd, G. W. (Eds.) (1991). *Neuropsychological foundations of learning disabilities: A handbook of issues, methods and practice*. New York NY: Academic Press

Orton. S. T. (1928). Specific reading disability-strephosymbolia. *Journal of the American Medical Association 90*, 1095-1099.

Pascual, R., & Figueroa H. (1996) Effects of preweaning sensorimotor stimulation on behavioral and neuronal development in motor and visual cortex of the rat. *Biology of the Neonate 69*, 399–404.

Parkins, R, Roberts, R. J., Reinarz, S. J., & Varney, N. R (1987). Asymmetries in developmental dysics. Paper presented at the annual convention of the International Neuropsychological Society, Washington, DC, January 1987.

Peters, J. E, Romine, J. S., & Dykman, R A (1975). A special neurological examnation of children with learning disabilities. *Developmental Medicine and Child Neurology 17*, 63-78.

Piacentini, J. C., & Hynd, G. W. (1988). Language after dominant hemispherectomy: are plasticity of function and equipotentiality viable concepts? *Clinical Psychology Review 8*, 595-609.

Rae, C., Karmiloff-Smith, A., Lee, M.A., Dixon, R.M., Grant, J., Blamire, A.M., Thompson, C.H., Styles, P. and Radda, G.K. (1998). Brain biochemistry in Williams syndrome: evidence for a role of the cerebellum in cognition? *Neurology 51,* 33-40

Reitan, R M, & Boll, T. J. (1973). Neuropsychological correlates of minimal brain dysfunction. *Annals of the New York Academy of Sciences 205*, 65-68.

Robichon, F., & Habib, M. (1998). Abnormal callosal morphology in male adult dyslexics: relationships to handedness and phonological abilities. *Brain and Language, 62,* 127-146.

Rosenberger, P. B., & Hier, D. B. (1980). Cerebral asymmetry and verbal intellectual deficits. *Annals of Neurology 8*, 300-304.

Rourke, B. P., & Conway, J. A. (1997). Disabilities of arithmetic and mathematical reasoning: Perspectives from neurology and Neuropsychology. *Journal of Learning Disabilities, 30(1),* 34-46.

Rubens, A B., Mahuwold, M. W., & Hutton, J. T. (1976). Asymmetry of the lateral (sylvian) fissures in man.. *Neurology 26*, 620-624.

Rumsey, J. M, Dorwrt, R, Venness, M., Denckla, M. B., Kruest, M. J. P., & Rapoport, J. L. (1986). Magnetic resonance imaging of brain anatomy in severe developmental dyslexia. *Archives of Neurology 43*, 1045-1046.

Rumsey, J. M., Casanova, M., Mannheim, G. B., Patronas, N., DeVaughn, N., Hamburger, S. D., & Aquino, T. (1996). Corpus callosum morphology, as measured with MRI, in dyslexic men. *Biological Psychiatry, 39,* 769-775.

Satz, P. (1991). The Dejerine hypothesis: Implications for an etiological reformulation of developmental dyslexia. In J. E. Obrzut & G. W. Hynd (Eds.), *Neuropsychological foundations of learning disabilities: a handbook of issues, methods, and practice*. New York NY: Academic Press pp. 99-112.

Scannell, J.W., Burns, G.A., Hilgetag, C.C., O'Neil, M.A., & Young, M.P. (1999). The connectional organization of the cortico-thalamic system of the cat. *Cerebral Cortex 9*, 277-99.

Scannell, J.W., Grant. S., Payne, B.R., & Baddeley, R. (2000). On variability in the density of corticocortical and thalamocortical connections. *Philosophical Transactions of the Royal Society of London B Biological Science 355*, 21-35.

Semrud-Clikeman, M, Hynd, G. W., Novey, E, & Eliopulos, D. (1991). Dyslexia and brain morphology: relationships between neuroanatomical variation and neurolinguistic performance. *Learning and Individual Differences 3*, 225-242.

Shalev, R. S., Manor, O., Amir, N., Wertman-Elad, R., & Gross-Tsur, V. (1995). Developmental dyscalculia and brain laterality. *Cortex, 31*, 357-365.

Shapleske, J., Rossell, S. L., Woodruff, P. W. R., & David, A. S. (1999). The planum temporale: a systematic, quantitative review of its structural, functional and clinical significance. *Brain Research Reviews, 29,* 26-49.

Szeligo, F. and Leblond, C.P. (1977). Response of the three main types of glial cells of cortex and corpus callosum in rats handled during suckling or exposed to enriched, control and impoverished environments following weaning. *Journal of Comparative Neurology 172,* 247-263.

Tallal, P., Miller, S., & Fitch, R. H. (1993). Neurobiological basis of speech: A case for the preeminence of temporal processing. *Annals of the New York Academy of Sciences, 682*, 27-47.

Tanaka, T., Lange, H. & Naquet, R. (1975). Sleep, subcortical stimulation and kindling in the cat. *The Canadian Journal of Neurological Sciences 2*, 447-555.

Taylor, H. G., & Fletcher, J. M. (1983). Biological foundations of "specific developmental disorders": methods, findings, and future directions. *Journal of Clinical Child Psychology 12*, 46-65.

Thatch, W.T. Jr. (1980). The Cerebellum in: Mount Casgle DD, Ed. *Medical Physiology, 14th edition*. St. Louis: Mosby, 837-858.

Tranel, D., Hall, L. E., Olson, S., & Tranel, N. N. (1987). Evidence for a right hemisphere developmental learning disability. *Developmental Neuropsychology, 3(2),* 113-127.

Van Economo, C. & Horn, L. (1930). *Zeitschrift für die gesamte neurologie und psychiatrie, 130*, 678.

Van Praag, H., Kempermann, G. and Gage, F.H. (2000). Neural consequences of environmental enrichment. *Nature reviews, Neuroscience 1*, 191-198.

Venables, P.H. (1989). The Emanuel Miller memorial lecture 1987. Childhood markers for adult disorders. *Journal of Child Psychology and Psychiatry, and Allied Disciplines 30,* 347-364.

Voeller, K. K. S. (1995). Clinical neurologic aspects of the right hemisphere deficit syndrome. *Journal of Child Neurology, 10(Suppl. 1*), S16-22.

von Plessen, K., Lundervold, A., Duta, N., Heiervang, E., Klauschen, F., Smievoll, A.I., Ersland, L., Hugdahl. K. (2002). Less developed corpus callosum in dyslexic subjects: a structural MRI study. *Neuropsychologia 40*, 1035-44.

Wada, J. A, Clarke, R, & Hamm, A (1975). Cerebral hemispheric asymmetry in humans. *Archives of Neurology 32*, 239-246.

Weinberger, D. R, Luchins, D. J., Morihisa, J., & Wyatt, R J. (1982). Asymmetrical volumes of the right and left frontal and occipital regions of the human brain. *Neurology 11*, 97-100.

Wernicke, C. (1910). The symptom-complex of aphasia. In: A. Church (Ed.), *Modern clinical medicine: diseases of the nervous system*. New York, NY: D. Appleton & Co. pp. 265-324.

Wittelson. S. F., & Pallie, W. (1973). Left hemisphere specialization for language in the newborn. *Brain 96*, 641-646.

Wyngaarden, J. E. (1987). *Learning disabilities: A report to the Congress*. Washington, DC: National Institutes of Health, Interagency Committee on Learning Disabilities.