

# NEUROBIOLOGICAL BASIS OF LEARNING DISABILITIES – AN UPDATE

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This paper reviews recent research in the field of learning disabilities and, in particular, developmental dyslexia. It summarizes findings from numerous studies employing widely divergent methodologies which have attempted to establish the neurobiological correlates of learning disabilities, including genetic, neuroanatomical, electrophysiological, and neuropsychological investigations. On the basis of the evidence compiled, it seems impossible to deny that learning disabilities are a manifestation of atypical brain development and/or function.

The Learning Disabilities Association of Canada convened the authors of this paper to summarize the considerable research literature which has provided evidence that learning disabilities represent a neurobiologically-based condition. Preparation of this paper was primarily motivated by the need to further inform people in education, politics, and social policy that learning disabilities are a condition based on atypical brain development and/or function. The understanding and acceptance of the neurobiological basis of learning disabilities is crucial to the development of programs and policies necessary to assist individuals with learning disabilities.

Important research efforts have focused mainly on developmental dyslexia, that is, reading disability, because it represents the most common and frequently identified learning disability. Reading is the primary academic problem in approximately 80% of children diagnosed with learning disabilities (Crago & Gopnick, 1994). Neurologically-based learning disabilities represent a heterogeneous group of disorders that involve both learning and behavioural components. Although learning disabilities may be exacerbated by other variables, such as ineffective teaching strategies or socioeconomic barriers, this paper supports the position that the essence of learning disabilities is neurobiological in nature.

Research into learning disabilities has been conducted through a variety of scientific perspectives. As discussed below, many studies show that reading disabilities have a familial transmission and that there is a genetic basis for the condition, with possible linkage to several chromosomes, especially 6 and 15 as well as 1 and 2. Research into toxicological, nutritional, and teratogenic agents, as well as prenatal, perinatal, and postnatal events indicates that these agents and events can have adverse effects on brain development and cause learning disabilities. Neuroanatomical studies (i.e. autopsy research, MRI and CT scan data) show that the brains of reliably diagnosed cases of developmental dyslexia lack ordinary temporal lobe asymmetry. Neuroimaging techniques (i.e. PET, rCBF, fMRI and SPECT) reveal atypical brain activity in specific areas directly correlated with developmental language disorders and reading subskill functions. Electrophysiological techniques (i.e. auditory brain stem evoked responses, EEG/Power Spectrum Analysis, control evoked response and magnetoencephalography) have also differentiated subjects with learning disabilities from controls. In addition, neuropsychological research indicates that phonological processing deficits are a primary difficulty in subjects with developmental dyslexia. Recent research, therefore, confirms the neurobiological basis of learning disabilities.

Following a brief historical perspective, this paper summarizes the research findings of the etiology of learning disabilities as well as the way in which brain structure and function has been related to learning disabilities.

## *Historical Perspective*

The association of learning disabilities with underlying neurological mechanisms has been noted in the early case studies of acquired alexia and developmental dyslexia, with the major contributions to this literature dating back to Dejerine in 1891 (Dejerine, 1891, 1892). Alexia refers to a syndrome in which an individual who is able to read, subsequently has a cerebral insult, such as a head injury or a stroke, and can no longer comprehend the written or printed word. This acquired reading deficit was correlated by Dejerine with pathological findings on postmortem examination, and because of this evidence, specific parts of the brain were localized as important to the task of reading. When an inability to develop fluent reading skills was initially recognized in children (Hinshelwood, 1896; Morgan, 1896), it was hypothesized that the functions subserved by the same areas of the brain affected in adults with acquired alexia must be implicated somehow in children and, therefore, cause difficulties in reading skill acquisition. Difficulty in acquiring the ability to read in individuals with normal intelligence was termed “developmental dyslexia.” The left angular gyrus; the left occipital lobe; the left calcarine, fusiform and lingual cortex; and the splenium of the corpus callosum were implicated as the likely areas of brain dysfunction in children with developmental dyslexia (Dejerine, 1891; Geschwind, 1979; Hinshelwood, 1896; Shallice, 1988).

Pathological findings observed in an acquired reading disorder cannot be linked directly to a developmental disability, for reasons such as neural plasticity and the possible transfer of functions from one part of the brain to another. Nevertheless, the anatomical discoveries from cases of acquired alexia in terms of localization of dysfunction, the kind and extent of reading disability and its associated neurolinguistic and neuropsychological symptoms, as well as other neurobehavioural correlations have served as a useful model upon which to base research in learning disabilities, particularly reading disabilities.

Since those early hypotheses were developed over a century ago, there has been an ever-growing body of evidence which continues to demonstrate the association of learning disabilities and neurobiological factors. This evidence includes research into the etiology of learning disabilities as well as evidence that the structure and function of the brain are related to learning disabilities.

## **Etiology**

### *Genetics of Learning Disabilities*

The familial nature of reading disability was first described by Thomas in 1905, and since then, pedigree analysis, sibling analysis, and twin studies have confirmed that it runs in families (DeFries & Gillis Light, 1996; Gilger, Pennington & DeFries, 1991; Hallgren, 1950; Lewis, 1992; Lewis, Ekelman, & Aram, 1989; Lewis & Thompson, 1992; Lubs et al., 1993; Tallal, Townsend, Curtiss, & Wulfeck, 1991; van der Lely & Stollwerk, 1996; Wolff & MeIngailis, 1994; Wolff, MeIngailis, Obregon, & Bedrosian, 1995). In fact, offspring risk rates are significantly elevated if a parent reports a history of reading disability, and the risks are sufficiently increased in families with parents who have a

reading disability to warrant use of family history as a component in clinical evaluation (Gilger et al., 1991). Hallgren (1950) reported that when one parent was affected, an average of 46% of the children were affected by dyslexia. Thirty-five years later, Vogler and colleagues reported essentially the same risk: if one parent was affected, 55% of the sons displayed reading deficits (though there may be reduced risk in daughters) (Vogler, DeFries, & Decker, 1984). Heritability estimates for various reading phenotypes have ranged from 0.51 to 0.93 (Bakwin, 1973; Olson et al., 1991; Stevenson, Graham, Fredman, & McLoughlin, 1987).

Results of twin studies and a comparison of monozygotic and dizygotic concordance rates have provided suggestive evidence of a substantial genetic etiology of reading disabilities. The Colorado twin study reported concordance rates of 68% for monozygotic twins and of 40% for dizygotic twins (DeFries et al., 1997; DeFries & Gillis Light, 1996). The difference between identical and fraternal twins was significant, further demonstrating that reading disability is caused in part by heritable influences.

Despite the certainty of the existence of a genetic basis, the mode of inheritance has not yet been proven. Some research has supported an autosomal (not sex-linked) dominant mode of transmission (DeFries, Gillis, & Wadsworth, 1993; Pennington, 1989); other work has indicated recessive, polygenic inheritance and genetic heterogeneity (Finucci, 1976; Hallgren, 1950; Lewitter, 1980; Pennington et al., 1991).

Potential explanatory modes of transmission of learning disabilities through genetics have been discussed in terms of three basic genetic models (Gilger, Borecki, DeFries, & Pennington, 1994; Gilger, Borecki, Smith, DeFries, & Pennington, 1996; Pennington & Gilger, 1996). A Mendelian genetic model stipulates that a single, major gene is responsible for a significant proportion of the variation present in reading. The multifactorial-polygenic model assumes that many genes, with additive and equal effect, act together along with a variety of environmental factors to produce the range of phenotypes observed. The model of Quantitative Trait Loci posits that genes of additive but unequal effect are responsible for the heritable aspects of the variance in a phenotype such as reading. Currently, the linkage data reviewed below tend to support the latter model; namely, that a number of genes at different loci may contribute to the range of reading ability/disability and that a simple locus is not likely (Gilger et al., 1996; Pennington & Gilger, 1996).

The first molecular genetics study of dyslexia was published in 1983, and reported linkage between reading disability and a region of chromosome 15 (Smith, Kimberling, Pennington, & Lubs, 1983); however, this finding has been disconfirmed by some (Bisgard et al., 1987). Subsequently, Smith, Kimberling, and Pennington (1991) added other families to their sample and reported additional linkage for a region on the long arm of chromosome 15. Single-word reading has more recently been linked, albeit weakly, to a region on the long arm of chromosome 15 by Grigorenko and her colleagues (1997). This region has also been studied by others, with both positive (Schulte-Körne, Deimel, Bartling, & Remschmidt, 1998) and negative (Sawyer et al., 1998) findings.

Chromosome 1 has also attracted some attention with respect to the genetic transmission of learning disabilities. Rabin et al. (1993) reported suggestive evidence of linkage on its short arm, as did Grigorenko et al. (1998). On the other hand, some have been unable to replicate this finding (Sawyer et al., 1998; Smith, Kelley, & Brower, 1998). The short arm of chromosome 2 has been implicated in a single large Norwegian family with dyslexia (Fagerheim et al., 1999).

Several studies on genetics and learning disabilities have reported a susceptibility locus on the short arm of chromosome 6 (Cardon et al., 1994; Fisher et al., 1999; Gayán et al., 1999; Grigorenko et al., 1997; Grigorenko, Wood, Meyer, & Pauls, 2000, Smith, Kimberling, Shugart., Ing., & Pennington, 1989). One of the groups that failed to replicate linkage to this region examined their large sample thoroughly using both a qualitative phenotype and a quantitative measure of reading disability (Field & Kaplan, 1998; Petryshen et al., 2000). Sawyer et al., (1998) also failed to find linkage to this chromosome 6 region. Most recently, a new region on the long arm of chromosome 6 has been identified (Petryshen, Kaplan, Lieu, & Field, 1999). No attempts at replication of this finding have yet been reported.

It is important to note that discrepant results in this type of research do not necessarily mean erroneous research. The increasing number of gene localizations may simply indicate the heterogeneity of the disorder, as well as the heterogeneity of the gene pools being investigated.

The gender ratio for reading disabilities has also provided some evidence of a genetic basis. The ratio may not be as disproportionate as commonly held in the past, since there may have been underidentification of females with learning disabilities (DeFries et al., 1993). It is clear that most of the male predominance in the previous rates of dyslexia was an artifact of the process of identification, and the male-female sex ratio across samples averages about 1.5:1.0 (Lubs et al., 1993; Pennington, 1995).

In summary, the influence of predisposing genes on the familial occurrence of dyslexia is now fully accepted, although much work is still needed to identify the contributing genes. In terms of the topic of this review paper, it is worth considering the fact that there probably are no genes that code specifically for dyslexia. In other words, the search for dyslexia-predisposing genes is actually a search for the genes that determine how the brain develops. It is likely that the molecular genetics findings reviewed above are particularly relevant to the language areas of the brain, yet it is still unlikely that any one of them influences reading and no other brain function. Roughly one-third of the estimated 60-100,000 genes in humans have some influence on the central nervous system. In view of this large number of genes, identifying those specific genes that influence learning disabilities continues to be a challenge. Sufficient evidence exists thus far, however, to conclude that there is a genetic component to the etiology of learning disabilities and, thus, their neurobiological basis.

In addition to the influence of genetics as an etiological factor of learning disabilities, several environmental factors also affect brain development. Prenatal, perinatal, and

postnatal events, as well as toxicological, nutritional, and teratogenic effects have all been shown to impact brain development and cause learning disabilities.

### **Adverse Effects on Brain Development**

Prenatal, perinatal, and postnatal events

Many biological factors can impact brain development and result in learning disabilities (Bonnet, 1989). Anatomical development of a child's brain prior to birth consists of cell proliferation and migration, axon and dendritic growth, synapse formation and loss, glial and myelin growth, and neurochemical changes (e.g., Kolb & Fantie, 1997). Not only is the brain's early development complex, but also growth continues over a prolonged period of time. Normal cortical growth can be disrupted by a wide range of events which influence not only early postnatal growth and development, but also later cognitive and behavioural development. The study of these events has been substantial, but methodological problems in the investigation of the fetal brain have made it difficult to determine exactly which event, or combination of events, leads to which specific outcomes. Furthermore, it is now well documented that postnatal growth and development do not simply follow a predetermined course based on cortical integrity at birth alone, but that environmental events and toxin exposure can significantly alter long-term outcome. Many studies have related stressful events in the prenatal, perinatal, and early postnatal phases of human development to later outcome and, in particular, to specific learning disabilities.

One of the most common consequences of early insult to the developing brain is birth before full gestational age or at less than full birthweight. The studies of very low birthweight infants (VLBW) have varied along the dimension of birthweight and gestation. Generally, more favourable outcomes have been associated with higher birthweights (Brooks-Gunn, & McCormick, 1994; Hack et al., 1994; Klebanov,). Some studies have indicated that VLBW children have a higher rate of learning disabilities (35%). Significantly poorer performance has been reported on a variety of measures of cognitive skills for VLBW in comparison to normal controls, including perceptual-motor and fine motor skills, expressive language, memory, hyperactive behaviour, and academic achievement, including reading and arithmetic (Cohen et al., 1996; Hack et al., 1992; Klein, Hack, & Breslau, 1989; Saigal, Hoult, Steiner, Stoskopf, & Rosenbaum, 2000). As well, the learning disabilities were less related to the more typical language-based learning disabilities than to arithmetic, perceptual motor, and attentional areas (Barsky & Siegel, 1992; Harvey, O'Callaghan, & Mohay, 1999; Low et al., 1992; Siegel et al., 1982; Taylor, Hack, Klein, & Schatschneider, 1995).

Other studies on early brain development have attempted to isolate the specific effects of related medical complications, specifically, bronchopulmonary dysplasia (oxygen dependence at or beyond 36 weeks gestation) (Robertson, Etches, Goldson, & Kyle, 1992; Singer, Yamashita, Lilien, Collin, & Baley, 1997; Vohr et al., 1991); perinatal asphyxia (Aylward, 1993; Handley-Derry et al., 1997; Korkman, Liikanen, & Fellman, 1996; Roth et al., 1997); intraventricular haemorrhage (Ross, Boatright, Auld, & Nass, 1996); and hydrocephalus (Dennis and Barnes, 1994; Dykes, Dunbar, Lazarra, &

Ahmann, 1989; Ishida, et al., 1997; Landry, Chapieski, Fletcher, & Denson, 1988). Children with these medical complications were demonstrated to be at risk for neurodevelopmental compromise and a variety of cognitive and academic difficulties. Transient Neonatal Hypothyroxinemia may also contribute to learning disabilities (den Ouden, Hille, Bauer, & Verloove-Vanhorick, 1993).

Research has also been conducted into the effects of neonatal seizures (convulsions) on neurodevelopment and later outcomes. Neonatal seizures in the first four weeks after birth are among the most common neurological emergency. They may be indicative of subtle neurodevelopmental vulnerability which may arise, at a later point, as a specific learning disability, with demonstrated difficulties in spelling and arithmetic as well as memory impairment for visual material (Temple, Dennis, Carney, & Sharich, 1995).

Many studies have used retrospective designs to determine correlations between perinatal events and later outcomes. Two specific categories of perinatal events that best predicted school achievement were gestational age and obstetrical history (Gray, Davis, McCoy, Dean, & Joy, 1992). Severe perinatal complications were significantly related to problems in cognitive and motor development (Korhonen, Vähä-Skeli, Sillanpää, & Kero, 1993).

### **Toxicological, nutritional, and teratogenic effects**

Many toxic agents are known to damage the developing, and unprotected, brain by interfering with those processes undergoing development at the time of the exposure (Rodier, 1995). Compared to the adult brain, the possibility that the developing brain is differentially sensitive to environmental agents was highlighted in a report by the U.S. National Research Council on pesticides in the diets of infants and children (1993). Loss of cells (microneurons) generated late in pregnancy is significant, because these cells are essential for establishing the balance between inhibitory and excitatory activities in critical brain areas such as the hippocampus (Morgane et al., 1993). Unlike other organ systems, the unidirectional nature of central nervous system development limits the capacity of the developing tissue to compensate for cell loss during specific time frames (Faustman, Silbernagel, Fenske, Burbacher, & Ponce, 2000).

Thyroid hormones regulate neuronal proliferation, migration, process outgrowth, synaptic development, and myelin formation in specific brain regions and are essential for normal behavioural, intellectual, and neurologic development (Porterfield & Hendry, 1998). A genetic syndrome, Resistance to Thyroid Hormone, is one of several hormone resistance syndromes which has been identified via molecular genetic studies and associated with poor school performance, learning disabilities, and symptoms of hyperactivity (Hauser et al., 1993b). Maternal and/or fetal thyroid deficiency in utero has also been linked to adverse neuropsychological development (Rovet, Ehrlich, Sorbara, & Czuchta, 1991). Children whose mothers had had abnormal thyroid levels, but who were not hypothyroid at birth, performed less well on all neuropsychological measures, and their IQ scores were lower.

PCBs and other dioxin-like compounds can affect neurodevelopment and learning, in that, they bear a striking resemblance to active thyroid hormones, can mimic or disrupt



their actions, and are known to cross the placenta and reach the fetus. A longitudinal study of children exposed to higher background levels of PCBs associated prenatal exposure with weaker reflexes at birth and less responsiveness, and with poorer visual recognition memory at 7 months of age (Jacobson & Jacobson, 1994). At 11 years of age, this cohort was twice as likely to be two years behind in reading comprehension, had problems in attention, planning, and organization, and had an average IQ deficit of 6 points (Jacobson & Jacobson, 1996). An ongoing follow-up study from Oswego, New York, (Lonky, Reihman, Darvill, Mather, & Daly, 1996) has replicated the early findings of the Jacobson study. Neonates whose mothers had higher exposures to contaminants in Lake Ontario fish had lower scores on three clusters of the Neonatal Behavioral Assessment Scales. Higher cord blood PCB levels were found to be predictive of lower performance on the Fagan test at 1 year of age and impairments on cognitive measures, including the memory subscales of the McCarthy Scales of Children's Abilities, in a follow-up study of the infants (Stewart, 1999). Hauser, McMillin, and Bhatara (1998) have suggested that the convergence of such studies could imply that these neurodevelopmental effects are mediated in part by alterations in hormone binding to the thyroid hormone receptor, and that other dioxin-like compounds could have the same effect.

The neuropsychological and cognitive effects of low-lead exposure was demonstrated in a ground-breaking study by Herbert Needleman and colleagues in 1979. Since that time a number of studies have found long-term effects from early exposure to lead (Feldman & White, 1992). Bellinger & Needleman (1994) reported that blood lead measured in the early postnatal period was the strongest predictor of effects on school age IQ. The increased absorption of lead in children may be a factor in attentional problems and aggressiveness (Riess & Needleman, 1992) and for delinquency (Needleman, McFarland, Ness, Tobin, & Greenhouse, 2000). A study using data from the National Health and Nutrition Examination Survey—III, found an inverse relationship between blood concentration levels as low as 2.5 micrograms per deciliter (ug/dL) and all cognitive function scores (Lanphear et al., 2000). (Ten ug/dL is currently the “alert” level for lead toxicity.)

The major classes of pesticides are inherently neurotoxic and can affect the developing brain. The first study to look at the possibility of effects on children from exposure to pesticides was conducted in Mexico quite recently (Guillette, 1998). This study compared 4- to 5-year-old children from agrarian and non-agrarian regions of Mexico who had very similar backgrounds and lives, except for pesticide use in their homes and environments. The children from the agrarian regions where pesticides were used had difficulty with eye-hand coordination, and social and emotional competence, as well as decreases in stamina and memory compared to matched control children from areas with very low pesticide use.

Alcohol has been found to have a significant impact on brain development in utero in several studies. Lower performance on IQ tests has been associated with two or more alcoholic drinks a day in mid-pregnancy (Carmicheal Olson, Barr, Sampson, Streissguth, & Bookstein, 1992; Streissguth et al., 1994; Streissguth, Barr, & Sampson, 1990), and 80% of clinically-diagnosed young adults with Fetal Alcohol Syndrome were found to

have attentional deficits (LaDue, Streissguth, & Randels, 1992). Coles et al., (1991) found significant deficits in sequential processing, mental composite scores, and academic skills in children who were exposed throughout pregnancy to low to moderate amounts of alcohol (11.80 oz. per week), and behavioural problems in play and social interaction as well as a specific pattern of attentional deficits on a computerized test of attention were also found with moderate amounts of alcohol intake during pregnancy (Brown et al., 1991). A recent experimental animal study (Ikonomidou et al., 2000) found that ethanol administered in just two doses, hours apart, during the time of synaptogenesis, resulted in a massive loss of neurons in the rat forebrain. This would coincide with fetal exposure during the last trimester of pregnancy.

The developmental effects of cigarettes, marijuana, and cocaine have been examined in several large prospective studies. Maternal smoking has been associated with altered auditory functioning and reading (Fried, Watkinson, & Siegel, 1997), impulsive behaviour (Fried, Watkinson, & Gray, 1992), lower IQ scores (Olds, Henderson, & Tatelbaum, 1994), and behaviour problems (Weitzman, Gortmaker, & Sobol, 1992). Prenatal marijuana exposure was related to increased omission errors in vigilance (Fried et al., 1997). The research on the effects of cocaine use in pregnancy has given mixed results, but in one study cocaine use in pregnancy was associated with multiple-risk factors and disruption in the discourse-pragmatics of language (Mentis & Lundgren, 1995).

Several studies have investigated the effects of malnutrition and undernutrition on cognition and behavior. Dietary precursors of neurotransmitters are critical to their regulation, and imbalances of neurotransmitters have been implicated in a number of conditions, including aggression, learning disabilities, and irritability (Fishbein & Meduski, 1987). Malnutrition has been shown to result in a number of syndromes involving attentional processes, adaptability, and learning disabilities (Morgane et al., 1993). Iron deficiency has been linked to negative effects on development, IQ, and achievement test scores which persist into childhood, even after supplementation (Lozoff, 1989). Several studies have followed children who were chloride deficient. Most of these children showed a neurobehavioural syndrome of language disorder as well as other academic and social deficits, despite average intellectual capability (Kalieta, Kinsbourne, & Menkes, 1991; Malloy et al., 1990; Silver, Levinson, Laskin, & Pilot, 1989).

In addition, research has accumulated which indicates that nutritional factors can affect the response to toxic exposures, but not abolish them (Hu, Kotha, & Brennan, 1995). Children who are deficient in calcium and iron are more susceptible to lead toxicity (Mahaffey, 1995), and these are the children who are possibly most exposed to lead from industrial sources and old housing.

In summary, the new insights gleaned from the research in the fields of developmental toxicology, environmental epidemiology, and nutrition present an important facet of etiology, and also an opportunity for prevention of some learning disabilities. Also, measurement of brain structure and function has provided information and a further understanding of the neurobiological basis of learning disabilities.

## *Measurement of Brain Structure and Function*

### **Neuroanatomical Studies**

Neuroanatomical investigations of brain morphology have provided strong evidence that there are differences in the brains of individuals with dyslexia (or reading disability) versus those without problems in reading (normal controls). Included in this category of investigation are postmortem or autopsy studies of the cytoarchitectonic features of the brain. Structural and functional neuroimaging techniques have also been applied to investigate these differences. The main findings of these three categories of neuroanatomical studies have been reviewed and are presented below.

### **Autopsy Findings**

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; Humphreys, Kaufmann, & Galaburda, 1990; Livingstone, Rosen, Drislane, & Galaburda, 1991; Rosen, Sherman, & Galaburda, 1993). 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 planum temporale is an area of the temporal lobe known to be language-relevant in normal controls (Steinmetz & Galaburda, 1991). The planum temporale lies on the supratemporal plane deep in the Sylvian fissure and extends from the posterior border of Heschel's gyrus to the bifurcation of the Sylvian fissure. It is believed to consist cytoarchitectonically of secondary auditory cortex (Shapleske, Rossell, Woodruff, & David, 1999). 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 than that of the right hemisphere. Between 20% and 25% of normal control brains show no asymmetry, with the remaining having asymmetry in favour 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 (discussed below) (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 centres of the brain are consistent with the functional deficits of dyslexia.

Because abnormal auditory processing has been demonstrated in individuals with dyslexia (as discussed later), 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, fibres 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).

Neuroanatomical 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.

In addition to the asymmetries anomaly, autopsy studies have also revealed multiple focal areas of malformation of the cerebral cortex located in the language-relevant perisylvian regions (Galaburda, 1989). The perisylvian cortices found to be affected by the minor malformations include the following: the frontal cortex (both in the region of and anterior to Broca's area), the parietal operculum, the inferior parietal lobule, and the temporal gyrus. Studies have shown that when scarring was dated according to the stages of brain development, it was determined that the abnormality in development had occurred sometime between the end of pregnancy and the end of the second year of life (Galaburda, 1989; Humphreys et al., 1990). These findings have been related to experimental animal research. 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.

### **Structural Neuroimaging Techniques**

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; Schultz et al., 1994). 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. 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. Njokiktjien, 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 midsagittal surface was larger, particularly in the isthmus.

Pennington (1999) summarized the findings of a structural MRI study of brain size differences in dyslexia, reportedly the largest dyslexic sample yet studied, in which he and his colleagues investigated 75 individuals with dyslexia and 22 controls involving twin pairs. The insula was significantly smaller, the posterior portion of the corpus callosum (isthmus and splenium) was marginally smaller, and the callosal thickness was smaller. On the basis of a preliminary test within twin pairs discordant for dyslexia, it was suggested that these size differences in the insular and posterior corpus callosum were not specific to dyslexia, but rather represented a neuroanatomical difference in dyslexic families. Further, it was concluded that genetic influences play a dominant role

in individual differences in brain size. The importance of controlling variance due to gender, age, IQ, and Attention Deficit/Hyperactivity Disorder was emphasized by Pennington. He did not find clear evidence of differences in the corpus callosum in a reading-disabled group. In view of the inconsistencies, more research to clarify the findings was recommended.

### **Functional Neuroimaging Techniques**

Functional neuroimaging techniques, including PET (positron emission tomography), rCBF (regional cerebral blood flow), fMRI (functional magnetic resonance imaging), and SPECT (single photon emission computed tomography) have added a unique dimension to the study of the neurobiological basis of learning disabilities, by measuring the activity in the brain of individuals with dyslexia while they are engaged in reading tasks. These are therefore “in vivo” studies of the brain. Using this method, atypical brain activity in specific areas has been identified and directly correlated with developmental language disorders and reading subskill functions.

Potentially confounding variables are associated with functional neuroimaging investigations, especially when studying young children. These include such factors as the effects of task difficulty in relation to developmental level of the subjects, necessity to account for changes in brain size and shape with development, as well as technical difficulties in providing a suitable testing environment for children. Regardless, impressive data have been collected. A significant difference in cerebral blood flow in children diagnosed with dyslexia has been reported (Flowers, Wood, & Naylor, 1991; Flowers, 1993). In these studies, controls showed activation to the left superotemporal region corresponding to Wernicke’s area, whereas the reading-disabled group showed activation of the immediately posterior temporoparietal region. Interestingly, the cerebral blood flow patterns of remediated subjects with dyslexia did not differ from those of subjects with persistent impairment. Further, an association between dyslexia and phonological awareness deficits has been demonstrated (Flowers, 1993; Paulesu et al., 1996).

Functional imaging studies have shown gender differences in patterns of brain activation during phonological processing and that separation of males and females is required in future studies (Lambe, 1999). There have been a number of findings of differences in individuals with reading disabilities. Hagman et al. (1992) reported significant differences in the medial temporal lobe with PET studies, and Logan (1996) indicated that individuals with dyslexia had significantly higher glucose metabolism in the medial left temporal lobe and a failure of activation of the left temporoparietal cortex.

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.

Nicolson et al. (1999) demonstrated a significant difference in rCBF activation in the cerebellum during motor tasks in a group of dyslexic adults. It was concluded that cerebellar deficits alone could not account for the reading disability but adversely affected acquisition of automatic, overlearned skills. An fMRI investigation supported the autopsy findings of abnormalities in the magnocellular pathway and implied a strong relationship between visual motion perception and reading (Demb, Boynton, & Heeger, 1998).

Rumsey (1996) reviewed functional neuroimaging studies of individuals with dyslexia compared to controls. All of the studies reported some differences in brain activity, and the differences were found in multiple brain sites, including: Wernicke's area, the temporoparietal junction, the lingual gyrus, the left insula (Paulesu et al., 1996), posterior perisylvian area (Rumsey et al., 1997), and ventral visual pathway (Eden et al., 1996).

Pennington (1999) has cautioned that the interpretation of these functional neuroimaging studies remains ambiguous, since the identified differences in brain activity could be secondary to dyslexia, or dyslexia could be secondary to the brain activity differences, or both dyslexia and the activity difference could be caused by a third factor. Pennington considered that differences in brain activation may be an indication of greater effort by the dyslexic group, may represent a compensatory strategy, or may reflect impaired processing capacity. Therefore, establishing causal links with this methodology is difficult. Nevertheless, it is apparent that there are significant differences in brain activity in individuals with dyslexia in comparison to normal readers.

In summary, 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. Electrophysiological investigations, although less isomorphic, have also substantiated this association.

### **Electrophysiological Studies**

Numerous variations in cortical and subcortical electrophysiological measurement techniques have been employed in the study of brain-behaviour relationships of individuals with learning disabilities. Measurement strategies have included auditory, brain stem evoked responses (ABR), EEG/Power spectral analysis, cortical evoked responses (ERPs) and, more recently, magnetoencephalography (MEG). Although the latter is not purely an electrophysiological recording technique it does involve the detection and localization of small magnetic fields associated with intra-cranial electromagnetic activity.

ABR studies have generally not yielded significant data, and there have been methodological weaknesses associated with these studies. With the advent of more powerful computing and statistical procedures, however, quantitative analysis of electroencephalographic recordings have shown promise as an investigative research tool. For example dyslexic children exhibited more energy in the 3-7 Hz band in the parieto-occipital region during rest conditions (Sklar, Hanley, & Simmons, 1972, 1973). This finding was replicated in a number of independent studies, but these studies were criticized for methodological reasons, and subsequently, there have been conflicting reports (Fein et al., 1986).

In contrast, significant results have been found in studies using quantitative EEG methods which examined carefully screened subtypes of individuals with learning disabilities while they carried out specific tasks. Dyslexic children with dysphonemic-sequencing problems showed an increase in alpha during a phonemic discrimination task, suggesting relatively poor orientation to the external stimuli. These children also showed a decrease in beta, suggesting differences in information processing in contrast to normal controls. The increased alpha-decreased beta was more evident over the left posterior quadrant, implicating the posterior speech region around Wernicke's area (Ackerman, Dykman, Oglesby, & Newton, 1995; Ortiz, Expósito, Miguel, Martin-Loeches, & Rubia, 1992). Proportionately less left hemisphere 40 Hz activity for a reading-disabled group, in contrast to normal controls or an arithmetic-disabled subgroup, was found, and conversely, the arithmetic-disabled subgroup exhibited proportionately less 40 Hz right-hemispheric activity than the reading-disabled subgroup during a nonverbal task (Mattson, Sheer, & Fletcher, 1992).

Several recent, well controlled, cortical evoked potential studies have shown significant differences on the P<sub>3</sub> waveform, with reading-disabled subjects having a longer P<sub>3</sub> and smaller amplitude to the target stimuli when compared with controls (Fawcett et al., 1993; Harter, Anllo-Vento, & Wood, 1989; Harter, Diering, & Wood, 1988; Taylor & Keenan, 1990). A larger amplitude for normal controls versus children with learning disabilities was demonstrated for a negative wave at 450 ms. in response to single words during initial learning and the same words in a subsequent recognition memory test series (Stelmack, Saxe, Noldy-Cullum, Campbell, & Armitage, 1988). Similar results on a



lexical task, involving distinguishing word pairs that rhymed or did not rhyme, have been reported (Ackerman, Dykman, & Oglesby, 1994). Using a probe technique, Johnstone et al. (1984) concluded that the language-dominant hemisphere was more involved in a reading task. With difficult reading material, reading-disabled groups generated a large bilateral central and parietal decrease in P<sub>300</sub> as they changed from easy to difficult material.

Although there is some emerging consensus from the ERP literature that phonological awareness is critical in the acquisition of reading and spelling, there remain some fundamental differences as to whether phonological processing problems are problems in their own right or whether they are problems because of a more fundamental sensory information processing difficulty (e.g. a temporal order information processing deficit). For example Schulte-Körne, Deimel, Bartling, & Remschmidt (1998) concluded that dyslexics have a specific phoneme processing deficit. This finding could help to identify children, at risk, as early as the preschool years. In contrast, Kujala, et al. (2000) presented evidence, observed in their sample of adults with dyslexia, which they suggest provides support for a more fundamental temporal information processing deficit.

ERP research has also been used in innovative ways to serve the needs of highly diverse patient populations. For example Byrne, Dywin, and Connolly (1995a) have made a case for its use with highly involved, difficult to assess individuals with cerebral palsy. Connolly, D'Arcy, Newman, and Kemps (in press) present a review of how ERPs have been used in the assessment of individuals with language impairment.

Research using auditory cortical evoked response technology has also yielded significant findings, particularly in identifying phonemic deficits as a significant variable in differentiating reading-disabled students from controls. Molfese and Molfese (1997) recorded neonatal auditory evoked potentials within 36 hours after birth to different sound contrasts. These same children, at follow up, were successfully classified into three language skill levels at 3 and 5 years of age, with 81% accuracy. This is a very impressive finding, since other perinatal predictors of later performance, e.g., Apgar score, the Brazelton Neonatal Assessment Scale, and low birth weight, were less effective as predictors of long-term developmental outcome.

Recently, research using MEG has uncovered interesting findings. MEG works on the principle that very weak magnetic fields are detected by means of an array of superconducting sensors. The superconductivity is preserved only at very low temperatures. These sensors are immersed into a helmet-shaped container of liquid helium that is brought close to the head for data collection. Salmelin et al. (1996) used whole-head MEG to track the cortical activation sequence during visual word recognition in individuals with dyslexia and controls. Within 200-400 msec. following stimulus onset, the left temporal lobe, including Wernicke's area, became involved in controls but not in individuals with dyslexia. The individuals with dyslexia initially activated the left inferior frontal cortex (suggesting involvement of Broca's area). Interestingly this area has been reported to be involved when normal subjects are required to perform a silent noun generation task. The authors suggested that individuals with reading impairment, in

order to compensate for their underdeveloped phonological skills, try to guess the word from whatever other limited information there may be available to them.

The usefulness of various electrophysiological and magnetoencephalographic measurement techniques is variable and a function of the type of technique employed as well as how well the targeted behaviour or cognitive process, under study, has been operationally defined. Although many of the research studies can be criticized for methodological problems, there is no question that the advances made in the measurement of higher cognitive functions over the past two decades have been impressive. Generally, those methodologically sound studies which have examined discrete skills in carefully selected subtypes of people with learning disabilities, have yielded results consistent with neuroanatomical and neuroimaging data. This converging evidence further strengthens the position that learning disabilities have a basis in neurobiology.

### **Neuropsychological Studies**

Neuropsychological investigations of learning disabilities have been based on psychometric testing of a variety of cognitive, sensory, motor and behavioural/emotional functions. These functions have been correlated with other types of measures of brain structure and function. This research, therefore, has provided a greater understanding of the neuropsychological profile of individuals with learning disabilities and also indirect evidence of underlying cerebral dysfunction. Within the neuropsychological literature, considerable attention has been focused on problems with either the acquisition of reading (developmental dyslexia) or math (dyscalculia) skills. The vast majority have focused on reading disabilities.

Deficient phonological awareness is now viewed as a primary problem in developmental dyslexia (Eden, Stein, Wood, & Wood, 1993; Heilman, Voeller, & Alexander, 1996; Ogden, 1996; Slaghuis, Lovegrove, & Davidson, 1993; Slaghuis, Twell, & Kingston, 1996). Evidence from neuroimaging (fMRI, PET, and SPECT scans) and electrophysiological studies have shown that the brains of those with reading disabilities respond differently from those of control subjects, particularly on tasks involving phonological awareness. Weaknesses in the activation of motor articulatory gestures may account for the difficulty in grapheme-to-phoneme conversion, which in turn impairs the development of phonological awareness (Heilman et al., 1996). Dysfunctions of the central auditory system (Katz & Smith, 1991) and temporal information processing deficits in both the auditory and visual modalities (Bakker, 1992; Eden, Stein, Wood, & Wood, 1995a) have also been identified. Independent deficits in speech and non-speech discriminative capacity have been reported as a significant factor in reading disabilities (Studdert-Kennedy & Mody, 1995). The critical work of Tallal, Miller, and Fitch (1993) has provided evidence of a basic temporal processing impairment in language-impaired children that affects speech perception and production and is thought to result in these phonological processing deficits. Visiospatial deficits have also been reported in a number of studies (Curley & Ginard, 1990; Eden et al., 1993; 1995a; Eden, Stein, Wood, & Wood, 1995b; Lovegrove, 1993; Slaghuis et al., 1993, 1996).

Irregular neurophysiological dynamics of the visual system may account for the random omissions and insertions of individuals with dyslexia during the reading process (Been, 1994). Differences in the control of saccadic eye movements have been found between individuals with dyslexia and controls (Lennerstrand, Ygge, & Jacobsson, 1993). A slow rate of processing of low spatial frequency information in the magnocellular channel of the lateral geniculate nucleus has been proposed as one deficiency accounting for some reading disabilities (Chase, 1996; Chase & Jenner, 1993). These results are consistent with the neuroanatomical findings. In the normal reader, the magnocellular pathway processes information more rapidly than the parvocellular route, providing the cortical maps with the global pattern information before information about the finer visual details arrives via the parvo pathway. When low spatial frequencies are processed too slowly, the ability to make rapid visual discriminations and to establish internal representations of letters and grapheme clusters in lexical memory is critically affected. This low spatial frequency deficit hypothesis has been supported by various studies (Chase, 1996; Chase & Jenner, 1993; Livingstone, 1993; Stein, 1994, 1996). It has been speculated that abnormality of the magnocellular system is not limited to the visual modality, but is generalized, affecting the auditory, somesthetic, and motor systems (Stein, 1996).

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, 1990), impaired comprehension and production of affective signals, and higher-order cognition about social behaviours (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 (Tranel, Hall, Olson, & Tranel, 1987; 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; Cossu, da Prati, & Marshall, 1995; Ogden, 1996), 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).

Several subtypes of reading disabilities have been reported (Boder, 1971; Doehring, 1978; Doehring & Hoshko, 1977; Doehring, Trites, Patel, & Fiedorowicz, 1981; Fiedorowicz, 1986; Fiedorowicz & Trites, 1991; Trites & Fiedorowicz, 1976). Research has shown that the locus of an abnormality in the brain is significant, in that, abnormalities in different areas of the brain relate to different reading problems. Therefore, the reason that one individual has difficulty reading may not be the same reason as another individual.

Not only have different subtypes of reading disabilities been identified, but also different learning disabilities, including the nonverbal learning disability (NLD) subtype (Gross-Tsur, Shalev, Manor, & Amir, 1995; Harnadek & Rourke, 1994; Rourke & Fuerst, 1992, 1995, 1996; Spafford & Grosser, 1993). Individuals with nonverbal learning disabilities typically have well-developed auditory perception (including phonological awareness) and simple motor skills, but have primary neuropsychological deficits involving visual perception, tactile perception, and complex psychomotor skills and psycho-social functioning, as well as difficulties in processing novel information (Rourke & Fuerst, 1992, 1995, 1996; Tranel et al., 1987). This pattern of strengths and deficits has now been identified in individuals with a wide variety of congenital and developmental disorders and is associated with diffuse brain dysfunction, leading some researchers to speculate that it is characteristic of white matter disease or dysfunction (Rourke, 1995).

Some specific areas of dysfunction have been identified in association with developmental dyslexia, namely, frontal lobe dysfunction (Heilman et al., 1996), underlying immaturity in the myelination within the central nervous system (Condor, Anderson, & Sailing, 1995), left temporal lobe dysfunction (Cohen, Town, & Buff, 1988), and cerebellar impairment (Fawcett, Nicholson, & Dean, 1996). The attentional problems associated with some cases of learning disabilities appear to have a widely distributed neurobiological basis ranging from the brainstem reticular activating system to the basal ganglia and on into the frontal cortex (Bakker, 1992).

In summary, these investigations have demonstrated that neuropsychological characteristics are associated with learning disabilities. They offer indirect evidence of localization of dysfunctions which is consistent with the neuroanatomical, neuroimaging, and electrophysiological findings

## *Conclusion*

Recent advances in neuroscience technology as well as the development of innovative research designs have enabled scientists to answer some intriguing questions involving brain-behaviour relationships. Of particular relevance to this review is that this has provided compelling scientific evidence in support of the neurobiological basis of learning disabilities. Studies employing widely divergent methodologies, e.g., research using genetic analysis, neuroanatomical neuroimaging, electrophysiological recording, the pathological analysis of brain tissue at autopsy, and neuropsychological evaluation, have yielded highly convergent conclusions in support of a neurobiological etiology. The fields of behavioural toxicology and teratology have provided evidence that many preventable biological factors can negatively affect brain development, brain functioning, and subsequent learning and behavioural abilities.

It would be a formidable task to review every study that demonstrates the neurobiological basis of learning disabilities: instead, the literature was reviewed from many perspectives to demonstrate the breadth of the available evidence that bears on this subject. Although there are still many unanswered questions, it seems impossible to deny that learning disabilities are a manifestation of atypical brain development and/or function.

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 caregiving (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.

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