

**CHANGES IN HEMISPHERIC ASYMMETRY FOLLOWING EARLY BRAIN
DAMAGE AND ITS IMPACT ON COGNITIVE PROCESSING**

by

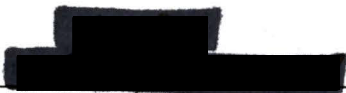
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We accept this thesis as conforming
to the required standard




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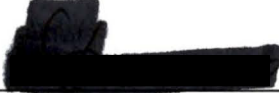
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ABSTRACT

Volumetric measurements of the hemispheres were derived using Magnetic Resonance (MR) images from patients with medical refractory seizures. Hemispheric asymmetry quotients were determined using the formula $100 \times (\text{left volume} - \text{right volume}) / (\text{left volume} + \text{right volume})$ and related to side of seizure origin, age of onset, hemisphere lateralization for speech, and IQ measures from the Wechsler Intelligence Scales (Wechsler Adult Intelligence Scale - Revised; and Wechsler Intelligence Scale for Children - Revised). Hemispheric asymmetry and side of seizure origin were associated, $(F(1,39) = 6.43, p < .005)$; that is, a larger left hemisphere occurred in the context of right, but not left-sided, seizure origin. Age of seizure onset, however, did not affect this asymmetry. In contrast to previous studies, there were no significant correlations between atypical asymmetry (right hemisphere > left hemisphere) and VIQ - PIQ scores. The relation between hemispheric speech dominance and anatomical asymmetry approached, but did not reach statistical levels of significance $(F(1,43) = 2.03, p < .08)$.


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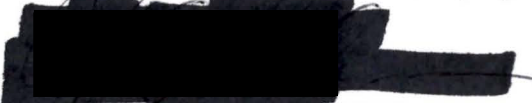
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INTRODUCTION

Ever since Broca (1865, cited in Heilman & Valenstein, 1985) first reported a left hemispheric dominance for speech, science has struggled to identify physical asymmetries between the hemispheres which might account for observed functional differences. Early studies, however, were restricted to crude, and often insufficient methodologies. Autopsies, for example, were plagued by the necessary, but unpredictable variance caused by the preparation of tissues, and the origin of death (Caviness, Filipek, & Kennedy, 1989). Furthermore, premortem behavioral characteristics could only be inferred with no chance of confirmation. Nonetheless, postmortem studies have shown conclusively the existence of many hemispheric asymmetries, and with the advent of computed tomography (CT) scans and magnetic resonance (MR) imaging, these (and other) differences have been confirmed in vivo and even linked to intellectual and behavioral attributes.

This chapter will begin by critically reviewing the methodologies used to ascertain the structural measurements of the brain. It will then review the literature regarding the brain's physical and intellectual asymmetries, and how they are believed to interact. Many studies in the animal literature have indicated that neonatal lesions may drastically affect the morphological and functional aspects of the brain. This literature will also be examined and the implications for human brain development discussed. Finally, this chapter concludes with a brief summary of the hypotheses and predictions examined in

this thesis.

Methods for Quantifying Anatomic Asymmetries

Historically, the only method available for quantifying hemispheric asymmetries was the direct examination of post-mortem brains. While this approach may provide numerous insights into the basic structure of the brain, it has several intrinsic drawbacks. For example, in order to measure "typical" asymmetries, it is essential to avoid using specimens which may have been affected by disease or by cortical atrophy, as these processes may affect the overall configuration of the brain (Caviness et. al., 1989; Filipek et al., 1989). Thus, it can be fairly difficult to acquire a significant amount of suitable, post-mortem brains. Assuming the desired samples can be collected, they must then be prepared before measurements can be made. This is typically a time consuming, and expensive task which may be damaging to the brain tissue as well (Caviness et al., 1989; Filipek et al., 1989). Finally, postmortem measurements generally prohibit researchers from correlating quantitative cognitive characteristics with brain structure, because premortem neuropsychological evidence is typically unavailable.¹

The advent of pneumoencephalography finally allowed researchers to observe the human brain in vivo. In this technique physicians introduce air into

¹ One exception to this is the brain collection held by Witelson and McCulloch (1991). Because their subjects underwent premortem neuropsychological testing, these authors are, in fact, able to compare postmortem measurements with cognitive functioning.

the cerebral spinal fluid through a lumbar puncture. An X-ray is then taken of the individual's head providing a clear picture of the participant's ventricles (Kolb & Wishaw, 1990). The invasive nature of this procedure is an obvious disadvantage, and is why its use was typically restricted to pathological populations. Another limitation, which greatly hinders research efforts, is the inability to directly examine cortical and subcortical structures (recall that the image only depicts the patient's *ventricles*). In fact, when using this method the physical aspects of the brain can only be inferred by the size and the shape of the ventricles. Nonetheless, many researchers have suggested that ventricular imaging can be a useful measure. It may, for example, be indicative of ventricular, and presumably, cerebral asymmetry (see Kolb & Wishaw, 1990). Others have even suggested that enlarged ventricles may represent cerebral atrophy (e.g., Cullum & Bigler, 1986; Roberts & Caird, 1976; Stafford, Albert, Naeser, Sandor, & Garvey, 1988; Takeda, & Matsuzawa). Regardless of its possible usefulness, however, newer, less invasive techniques have generally replaced pneumoencephalograms.

Most contemporary investigations of anatomic asymmetries rely upon computerized tomography (CT) scans and magnetic resonance (MR) imaging (Burke, Yeo, Delaney & Conner, 1993). The advantages offered by these imaging devices are many. For example, since both are non-invasive techniques, they pose little or no significant risk to neurologically impaired and intact participants (Andreason et al., 1993; Luchins, Weinberger & Wyatt, 1982).

Relative to their predecessors, these techniques also provide clearer and more accessible images of brain structures, and have allowed behavioral and structural studies to transpire concurrently (Andreason et al., 1993).

Comparatively, MR images provide superior and clearer pictures than CT scans as they display sharper delineations between grey matter, white matter, and cerebrospinal fluid (CSF) (Andreason et al., 1992; Caviness et al., 1989; Harris, Rhew, Noga, & Pearlson, 1991).

Although CT scans and MR images represent a significant improvement over postmortem measurements and pneumoencephalograms, they still possess some drawbacks. For example, images from both techniques are vulnerable to artifacts and blurred images caused by movements of the participant during examination (Caviness et al., 1989). When using images from a patient population other difficulties can arise. Specifically, the slices (i.e., images of brain structures) needed to determine pathology may not include the information needed for a particular study. Furthermore, the use of MR imaging presents a unique complication, because it can be modified to produce two different kinds of images, or spins. Those which are more suitable for medical diagnosis are often not appropriate for scientific research (Caviness et al., 1989). Therefore, studies which cannot produce images to their exact specification must make due with what is available.

Once the images have been acquired, there are 3 principal ways to determine the size of a particular structure: linear measurements, manual

tracing, and edge detection (Andreason et al., 1992; DeCarli, Kaye, Horwitz & Rapoport, 1990). Linear measurements generally refer to the distance between 2 points of interest, and can be used to determine, for example, the width or the length of a hemisphere (DeCarli et al., 1990). Although this method is relatively simple and expedient, there is a lack of consistent methodology between studies which makes it an unreliable method (Bird, 1982; DeCarli et al., 1990). For example the particular image which is measured (i.e. the MR/CT slice) often varies from study to study, which makes it difficult to replicate and refer to prior results. Furthermore, the determination of the length or the width of an area varies widely; e.g., some studies may take measurements 8 mm from each pole in order to determine the width of a lobe (e.g., Luchins et al., 1982), while others may take measurements 5 mm from the pole (e.g., Hier, LeMay, Rosenberger & Perlo, 1978). Finally, and most important, this method is unable to capture and quantify the variability seen within a brain's volumetric measurements. It is too simplistic, and often incorrect to assume that a single measurement of a complex and variable object can truly represent its entire structure (Aylward & Reiss, 1991)

Manual tracing involves outlining the structure of interest, generally with a track ball, or a mouse. A computer program then generates the area for the enclosed region of interest (De Carli et al., 1990). This can be a relatively time-consuming procedure, but can be quite accurate depending upon the expertise of the researcher (Andreason et al., 1992). The last

technique, edge detection, relies upon computer assistance to outline the specific region. The image is identified through an automated technique which localizes boundaries based on dramatic differences between the tissue densities. Each density is assigned a different shade of grey by the computer, and the program uses these shades to determine the outline and the area of the appropriate brain structure (Andreason et al., 1992). Difficulties occasionally arise in structures without clearly differentiated edges. The density of CSF, however, is strikingly different than the grey and white matter of the brain. Thus, this approach has been found to be exceptionally reliable when the boundaries are represented by CSF (Andreason et al., 1992; DeCarli et al., 1990).

Studies typically examine the overall hemispheric asymmetries either through planimetric or volumetric procedures. Both approaches rely upon one of the above mentioned techniques (i.e., linear, manual tracing, or edge detection), however, the number of measurements taken differs depending upon the approach used. Planimetric studies produce a single cross-sectional area of a region using one CT scan or MR image. Generally, the slice which contains the largest axial area is used to predict the physical characteristics of the entire structure (DeCarli, et al., 1990). Volumetric investigations determine the volume of a region by quantifying the area it occupies over several brain slices (DeCarli, et al., 1990). Volumetric evaluations are considered superior to planimetric measurements because they are more likely to pick up subtle

differences and are less influenced by variations in anatomy and by artifacts within the images (Aylward & Reiss, 1991; DeCarli et al., 1990; Raz et al., 1986). Furthermore, the area of a single brain slice may not be an accurate predictor for the overall volume of a structure. Although structural volumes may be related to the area of a particular slice, the relationship may be nonlinear, and, therefore, estimates may be incorrect and misleading. (Yeo, Turkheimer, Raz, & Bigler, 1987).

Overall, the research indicates that the best approach to quantify hemispheric differences is through the volumetric measurements of several slices. Boundaries are best determined either by manual tracing or by edge detection methods, depending upon the target structure and the available equipment.

Anatomical Asymmetries

In 1968 Geschwind and Levitsky were the first to quantitatively demonstrate the existence of a physical difference between the two hemispheres. Specifically, they dissected 100 human brains and showed that in 65% of the brains the left planum temporale, known as Wernicke's area, was larger than the right, (24% of the brains were symmetrical (demonstrating no anatomical asymmetry) and 11% showed a right hemispheric advantage). Geschwind and Levitsky's findings initiated a flood of research which has

focused on the determination of hemispheric differences.² As noted in Table 1, much of this literature has emphasized the asymmetries between the frontal lobes, the occipital lobes, and the overall hemispheres.

In her hallmark study LeMay (1976) utilized CT scans to measure the widths and the "petalia"³ of the frontal and the occipital lobes. Her initial findings demonstrated that out of 277 right handed individuals, the right frontal lobe was wider in 70% of the cases (only 8.6 % were wider in the left hemisphere, and 11.4% were equal). Moreover, she found that the right frontal lobe either protrudes as far as the left frontal lobe (63%), or farther (30%). Finally, LeMay reported that the left occipital pole was longer than the right in 69% of the cases and wider than the right in 63%. In summary, the general trends indicated that the left occipital lobe was larger than the right, and that the right frontal lobe was larger than the left.

Most of the literature to date has verified the presence of asymmetrical widths in the frontal and the occipital lobes (Burke et al., 1993; LeMay, 1977; LeMay & Kido, 1978; Pieniadz et al., 1983) (see Table 1). Those authors who have not found hemispheric differences (i.e., the occipital and frontal lobes were more commonly equal), still reported a higher prevalence of "typical"

²For a comprehensive review of the many hemispheric asymmetries within the brain see, for example, Davidson & Hugdahl, 1995; Geschwind & Galaburda, 1985; Kolb & Wishaw, 1990.

³ LeMay and Geschwind (1978) define "petalia" as "the forward or backward extension of one cerebral hemisphere beyond the other," (p. 312).

asymmetries than atypical or reversed patterns which is consistent with LeMay's (1976) study (Chui & Damasio, 1980; LeMay & Kido, 1978). The literature regarding the frontal and the occipital petalia is quite similar. Most authors have duplicated LeMay's findings in both adults, (Chui & Damasio, 1980; Deuel & Moran, 1980; Pieniadz & Naeser, 1984; Pieniadz, Naeser, Koff & Levine, 1983), and in children (Deuel & Moran, 1980). One exception to this was reported by Burke et al., (1993) who reported a higher incidence of equal, rather than asymmetrical lengths (in both the frontal and occipital lobes). Similar to the previously noted studies, however, when participants did demonstrate hemispheric asymmetries they were more likely to follow the general trends. Thus, the most common asymmetrical pattern noted in the literature is a longer and wider right frontal lobe and left occipital lobe. Further, when the morphological asymmetry differs from this pattern the hemispheres are more likely to be symmetrical (i.e., equal lengths or widths) than to demonstrate an atypical or reversed anatomical asymmetry.

Regardless of whether the asymmetries are due to differences in lengths or the widths, the measured volumes of MR images (Coffey et al., 1993; Glicksohn & Myslobodsky, 1993) and post-mortem brains (Weinberger, Luchins, Morhisa & Wyatt, 1982) have indicated that the right frontal lobes are significantly larger than the left frontal regions. Furthermore, the left occipital lobe occupies more space than the right occipital pole (Glicksohn & Myslobodsky, 1993; Weinberger et al., 1982). These results have also been

shown in fetuses as young as 20 weeks old (Weinberger et al., 1982). When the volumes of each hemisphere are measured, (without distinguishing the various lobes) the left hemisphere has been shown to be significantly larger than the right (Coffey et al., 1993; Yeo et al., 1987).

Thirty years of research have elucidated the nature of the anatomical asymmetries. These findings are valuable because they suggest that physical variations between the hemispheres may underlie their functional differences.

TABLE 1.
Anatomical Asymmetries

Study	Measure	Anatomical Asymmetries		
		Frontal Lobes	Occipital Lobes	Hemispheres
Burke et al. (1993)	Linear volumetric measurements of 2 CT scans per lobe assessed. Each asymmetry represented the average of 4 measurements taken per slice.	Right width > left width = frontal lengths	Left width > right width = occipital lengths	N/A
Chui & Damasio (1980)	Linear planimetric measurements of CT scans.	Right width ≥ left width Right petalia more common than left	Left width > right width Left petalia more common than right	N/A
Coffey et al. (1993)	Linear Volumetric measurements. Number of MR slices varied depending upon the structure measured (frontal lobes - 10-13; hemispheres - 30-35).	Total right frontal lobe > total left frontal lobe	N/A	Left hemisphere > right hemisphere
Deul & Moran (1980)	Linear planimetric measurements of CT scans (the scans used for the occipital and frontal lobes were often different).	Total right frontal lobe > total left frontal lobe in children aged 7 - 17.	Total left lobe > total right lobe in children aged 7 - 17.	N/A
Glicksohn & Myslobodsky (1993)	Edge detection, volumetric measurements of consecutive coronal MR images.	Total right frontal lobe > total left frontal lobe. Most prominent in dorsal aspects of lobe.	Total left lobe > total right lobe. Most prominent differences seen in ventral aspects of lobe.	N/A

TABLE 1.
Anatomical Asymmetries (Continued)

Study	Measure	Anatomical Asymmetries		
		Frontal Lobes	Occipital Lobes	Hemispheres
LeMay (1976)	Linear planimetric measurements of Ct scans (the scans used for occipital and frontal lobes were different).	Right width > left width Frontal lengths most often equal, however, if there were differences, the right was more likely longer than the left.	Left width > right width Left petalia more common than right	N/A
LeMay (1977)	Linear planimetric measurements of CT scans (scans used for occipital and frontal lobes were different).	Right width > left width Right petalia more common than left	Left width > right width Left petalia more common than right	N/A
LeMay & Kido (1978)	Linear planimetric measurements; 1 CT scan per area measured (scans used for occipital and frontal lobes were different).	Right width \geq left lobe (58% of cases > than left, 30% =) Frontal lengths most often equal, however, if there were differences, the right was more likely longer than the left.	Left width > right width Left petalia more common than right	N/A

TABLE 1.
Anatomical Asymmetries (Continued)

Study	Measure	Anatomical Asymmetries		
		Frontal Lobes	Occipital Lobes	Hemispheres
Pieniadz & Naeser (1984)	Linear volumetric measurements of 2 CT slices and post-mortem brain analysis.	N/A	Left petalia more common than right	N/A
Weinberger et al. (1982)	Postmortem brain analysis (subjects' ages ranged from 20 wks. gestation to 98 years)	Total volume of right lobe > left	Total volume of left lobe > right	N/A
Yeo et al. (1987)	Manually traced volumetric measurements of 8-9 CT scans per participant.	N/A	N/A	Left hemispheric volume > right hemispheric volume

Intellectual Correlates of Anatomic Asymmetries

Recent studies have shown that relative brain size (i.e., when body size is taken into account) is positively correlated with IQ (Andreasen et al., 1993; Willerman, Schultz, Rutledge & Bigler, 1991). Conversely, cortical atrophy has been associated in the decline of mental functioning in patients with head injuries (Bigler, et al., 1984; Cullum & Bigler, 1986) and in patients with dementia (Bigler, Hubler, Cullum & Turkheimer, 1985; Damasio et al., 1983). Thus, the literature has consistently reported that overall brain mass is significantly correlated with intelligence.

Other studies have attempted to clarify more specific relations between the morphology of the brain and intellectual functioning. For example, several studies to date have supported the premise that structural asymmetries may be associated with patterns of cognitive performance. In particular, variations in asymmetry seem to represent differences in verbal and nonverbal intellectual skills (see Table 2).

The typical asymmetrical pattern has repeatedly been associated with greater verbal cognitive functioning. For example, Burke et al. (1993) have demonstrated that a larger left occipital lobe is associated with faster language recovery one year post-stroke. The authors further noted that this asymmetry was correlated with a lesser initial impairment in their aphasic participants. Thus, a wider left occipital lobe appears to contribute to the preservation of speech following (left-hemispheric) stroke, and therefore, may play a role in the

verbal skills of non-damaged participants.

Raz et al. (1993) also found that the degree of left hemispheric asymmetry is significantly correlated with measures of cognitive skills. They found that both fluid and crystallized intelligence (as measured by the Culture Fair Intelligence Test and by an extended vocabulary test, respectively) were positively correlated with left hemispheric asymmetry. Since both of these tasks rely on some verbal processing, the left hemisphere is again placed in the role of supporting verbal functioning.

Conversely, reversed or atypical hemispheric asymmetries have been associated with reduced verbal skills. For example, Hier et al. (1978) examined the brain morphology and Verbal Intelligence Quotient (VIQ) from the Wechsler Adult Intelligence Scale (WAIS) of 24 patients with developmental dyslexia. Results indicated that 10 out of the 24 patients showed a reversed asymmetry (right hemisphere was wider than the left). It should be emphasized that this proportion of reversed asymmetry was strikingly different than what has been noted in the normal population (e.g., LeMay, 1976). Thus, dyslexia appears to be strongly associated with atypical hemispheric asymmetry patterns. Of further interest is that those patients with reversed asymmetry presented with lower mean verbal IQ's than the other developmental dyslexics in the study.

Others have supported the premise that, compared to controls, reversed asymmetry of the occipital region is significantly correlated with the difference between VIQ and Performance IQ (PIQ). Rosenberger and Hier (1980)

investigated the patterns of cerebral asymmetry in learning disabled children and young adults with exceptionally large discrepancies between their VIQ and PIQ scores (a difference of 15.8 ± 8.7 points). Their results indicated that 42 percent of their participants displayed a reversed asymmetry, and that the degree of reversed asymmetry was directly correlated with the extent of the VIQ-PIQ discrepancy (PIQ was significantly larger than VIQ; $r = 0.38$; $p < 0.02$).

Similar results were found in a study of CT scans of schizoaffective patients (Luchins et al., 1982). Their results suggest that schizoaffective patients have a higher rate of reversed asymmetry than controls. Moreover, unlike patients with normal asymmetry, those with reversed asymmetry have a higher PIQ than VIQ.

Still other studies have investigated this relation in healthy individuals (Willerman, Schultz, Rutledge, & Bigler; 1992; Yeo et al., 1987). The results within this population have also revealed an association between atypical asymmetry and a reduced VIQ-PIQ difference. Yeo et al. found that the larger the left hemisphere, the more the VIQ exceeded the PIQ, ($r = 0.57$; $p < .001$). Willerman et al. also found that a larger left hemisphere predicted higher verbal than nonverbal skills in their male participants. (The association between cognition and hemispheric asymmetries was reversed for their female

participants).⁴ It is important to note that none of the studies which have examined the relation between anatomical asymmetry and intellectual quotients have found a correlation between asymmetry and the Full Scale Intellectual Quotient (FSIQ), the VIQ or the PIQ. Thus, the association is more clearly dependent on the difference between the VIQ and the PIQ as measured by the Wechsler Intelligence Tests.

Intellectual quotients aside, there is some evidence that a person's hemispheric dominance for speech may be directly related to anatomical asymmetry. Charles et al. (1994) recently reported a significant correlation between atypical asymmetry in the occipital lobes (right > left) and atypical speech dominance (determined through sodium amytal tests). The converse was true for participant's with "typical" hemispheric asymmetry and left hemisphere language lateralization. Similar trends were seen within the parietal lobes, however, they did not reach significance within this sample.

In conclusion, the current literature suggests that the structural asymmetrical patterns of the brain are closely associated with patterns of cognitive performance and, possibly, language dominance. Specifically, the typical asymmetrical pattern (wherein the left hemisphere (or occipital lobe) is larger than the right) is associated with a VIQ-PIQ split, such that the VIQ is

⁴ This gender difference has not yet been replicated by other papers. In fact, Raz et al., (1993) were unable to replicate these results in their study. These two papers, however, relied upon different tasks to determine cognitive skills, thus it is still unclear what effects gender may play on the associations between cognition and hemispheric asymmetries.

equal to or slightly larger than the PIQ. Atypical asymmetrical patterns have been linked with impaired verbal skills such as language related learning disorders, dyslexia, poor recovery from aphasia, and a negative discrepancy between VIQ and PIQ (i.e. VIQ is less than PIQ). Finally, a reversed anatomical asymmetry has been associated with atypical hemisphere dominance for language. In short, the literature suggests that the relative size of the left hemisphere is predictive of an individual's verbal and nonverbal skills and is also associated with the lateralization of speech.

TABLE 2.
The Functional Correlates of Anatomical Asymmetries

Study	Method	Area Measured	Participants	Results
Burke et al. (1993)	Linear volumetric measurements of 2 CT scans per area assessed. Each asymmetry represented the average of 4 measurements taken per slice.	Frontal and Occipital width and length	Aphasics with unilateral left hemispheric infarcts (and normal controls)	Patients with traditional asymmetrical patterns recovered their language skills more quickly than those with atypical asymmetries and experienced lesser initial impairments.
Charles et al. (1994)	Linear volumetric measurements of 2 MR images per area assessed.	Frontal, Occipital and Parietal lengths	Epileptic patients being examined for surgical intervention	Asymmetry of the occipital lobe length was significantly correlated with hemisphere dominance for speech. Similar (but nonsignificant trends) were seen in the parietal lobes.
Hier et al. (1978)	Linear volumetric measurements of 4-6 CT scans. Measurements taken 5 mm anterior to the occipital pole.	Occipital width	Participants with developmental dyslexia	Participants with developmental dyslexia showed a higher frequency of reversed occipital asymmetry than is typically seen in normals. Those with reversed asymmetry also had a lower mean VIQ than the other dyslexic participants in the study.

TABLE 2.
The Functional Correlates of Anatomical Asymmetries (Continued)

Study	Method	Area Measured	Participants	Results
Luchins et al. (1982)	Linear volumetric measurements of 3 CT scans. Measurements taken 8 mm anterior to the occipital pole.	Occipital width	Schizophrenic and Schizoaffective patients (and normal controls)	Schizophrenic participants showed a higher frequency of reversed occipital asymmetry than controls. Those patients with reversed asymmetry also displayed a PIQ > VIQ. Conversely, participants with typical asymmetries displayed a VIQ > PIQ.
Raz et al. (1993)	Manually traced, volumetric measurements of 9 MR images.	Total hemispheric volumes	Normal Volunteers	The degree of left asymmetry positively correlated with measures of cognitive skills. (as determined by Culture Fair Intelligence Test & an extended vocabulary test) No difference was found between male and female participants
Rosenberger & Hier (1980)	Linear planimetric measurements (1 CT scan per participant) Measurements taken at 20% of the lobe's length anterior to the occipital pole.	Occipital width	Children and adults with learning disabilities, selected for large discrepancies between their VIQ and PIQ scores. (They also had normal controls).	Learning disabled participants showed a significantly higher frequency of reversed asymmetry than normal controls. The degree of left asymmetry positively correlated with measures of verbal cognitive skills (as determined by VIQ-PIQ)

TABLE 2.
The Functional Correlates of Anatomical Asymmetries

Study	Method	Area Measured	Participants	Results
Willerman et al. (1992)	Utilized an edge detection method to collect volumetric measurements of 4 MR images.	Total hemispheric volumes	College Student Volunteers	The degree of left asymmetry positively correlated with cognitive verbal skills (as determined by VIQ-PIQ) in male participants. Female participants showed the inverse correlation.
Yeo et al. (1987)	Manually traced, volumetric measurements of 8-9 scans.	Total hemispheric volumes	Neurologically normal individuals who had presented with somatic complaints	The degree of left asymmetry positively correlated with cognitive verbal skills (as determined by VIQ-PIQ).

Early Hemispheric Lesions and Their Relation to Structural and Functional Asymmetries

There is evidence (see Kolb and Wishaw, 1989 for review) that lateralized lesions in the neonatal rat cortex result in a brain that weighs less and has a smaller ipsilateral hemisphere than normal rats. Interestingly, similar lesions in adulthood do not produce such global effects. Further research has indicated that the effect of a lesion is, in fact, dependant upon the age of onset; the earlier the lesion occurs, the smaller the resulting brain size (Kolb, 1987; Kolb & Wishaw, 1981).

The fact that a lesion's effect on the rat's brain is dependent upon the age of onset, suggests that there are some stages of cortical development which are more vulnerable than others. The normal development of the cortex involves several stages, and the following is a brief summary of these steps. Initially, the cells must proliferate, migrate and then differentiate into their prospective types. Once this is established, there is a period of axonal and dendritic growth followed by the formation of synapses (synaptogenesis). Finally, unnecessary or redundant connections are terminated through synaptic death (Kolb & Wishaw, 1989).

Kolb and Wishaw (1989) propose that the development of the dendrites may play a significant role in explaining the effects of neonatal lesions. As dendrites develop they are profoundly affected by incoming information. If there is a lack of afferent stimuli during development, or while the dendritic arbor is being established, the dendrites will atrophy. Thus, Kolb and Wishaw

suggest that the entire ipsilateral hemisphere may be affected by even a small, isolated lesion through the process of dendritic atrophy.

These changes in cortical structures have been linked to behavioral consequences in rats. In particular, the thinner the cortex, the more behaviorally impaired the rat's behavior is (Kolb & Wishaw, 1989). Thus, the amount of cortex appears to be directly related to intact behaviors. Since the development of the human cortex parallels that of a rat's, it is plausible to assume that early damage to a human brain should have the same results. Kolb and Wishaw reported similar findings in the CT scan of a woman with early brain damage. To date, however, there have been no direct test of their notions in humans.

Summary and Goals of The Present Study

Over the past 17 years there has been a growing interest in quantifying the structural and the intellectual asymmetries of the human brain, and in determining their association with one another. The literature suggests that the most accurate way to measure structural asymmetries is through the use of volumetric studies of MR images. Volumes are best assessed through the edge detection or manual tracing of several MR images within each brain. This technique provides the most comprehensive determination of the volume of any given structure. Intellectual functioning is typically determined through neuropsychological testing.

Research has shown that the cortical hemispheres are both structurally

and functionally asymmetrical. In particular, the right frontal lobes are generally wider and longer than the left frontal lobes (right frontal > left frontal), and the left occipital lobes are generally longer and wider than the right occipital lobes (left occipital > right occipital). When hemispheres are measured as a whole, the left hemisphere is significantly larger than the right.

Structural asymmetries have been linked to differences in cognitive functioning. The typical asymmetrical pattern has been associated with a VIQ-PIQ split such that the VIQ is equal to or slightly larger than the PIQ. Reversed asymmetrical patterns have been linked with reduced verbal skills and a negative discrepancy between VIQ and PIQ (i.e. PIQ is greater than VIQ). In short, the relative size of the left hemisphere appears to be directly correlated to verbal intellectual capacity. There has also been some evidence to suggest that anatomical asymmetries are associated with hemispheric dominance for speech. Specifically, typical hemispheric asymmetries have been related to the left (or typical) hemisphere lateralization of language and "atypical" asymmetrical patterns have been associated with bilateral (or "atypical") speech dominance.

When rats are subjected to neonatal cortical lesions, the ipsilateral hemisphere is smaller than the non-damaged hemisphere, and this effect varies inversely with age of lesion. Adult rats who are lesioned in the identical area of the brain, do not demonstrate the same structural changes as their neonatal counterparts; rather, the damage is restricted to the area lesioned. Behavioral

deficits have also been correlated with the thickness of the cortex in those rats who were exposed to neonatal lesions. The purpose of the current study is to determine, in an epileptic population, whether structural asymmetries vary as a function of age of onset of damage. This thesis will also strive to determine the cognitive consequences of the resulting neuroanatomical patterns. Finally, it will attempt to replicate the previous finding that atypical language dominance is associated with reversed hemispheric asymmetries.

Predictions

- (1) Early damage to a person's left hemisphere will result in an atypical asymmetry, such that the right hemisphere is larger than the left.
- (2) Early damage to a person's right hemisphere will maintain the typical asymmetry with the left hemisphere being larger than (or equal) to the right.
- (3) Participants with atypical asymmetries (regardless of lesion location or age of onset) will display $PIQ > VIQ$; however, there will be no correlations between hemispheric asymmetry and FSIQ, PIQ, or VIQ.
- (4) The lateralization of language to the left hemisphere (as determined by sodium amytal tests) will be positively correlated with the "typical" asymmetrical pattern.

METHOD

Participants

The original sample consisted of 73 patients with medical refractory seizures who had been assessed for possible surgical treatment at the University of British Columbia Hospital. All participants had previously completed an extensive neuropsychological battery and underwent Magnetic Resonance (MR) Imaging as part of their evaluation. Participants met the criteria for inclusion in this study if their MR scans were performed using a spin which was appropriately differentiated by the digitizing program. Participants were excluded if (1) their MR images appeared to be distorted, (2) lesions appeared within the areas which were measured, or (3) the ventricles appeared to be significantly enlarged.

Forty-four participants met criteria (20 male, and 24 female), with a mean age at testing of 28.4 years ($SD = 11.6$). The breakdown of participants by hemispheric side of seizure origin and age at seizure onset is presented in Table 3. "Early" is defined as seizure onset (or age of damage when it is known) occurring before the age of 12 months.

TABLE 3. Number of participants by lateralization of seizure origin and age at seizure onset.

	<u>Early</u>	<u>Late</u>
Left Focus	10	14
Right Focus	5	15

Handedness was determined by a four-item inventory (Porac & Coren, 1980). Thirty-four of the participants were right-handed and 10 were left-handed. Thirty-eight of the participants underwent a carotid amygdal test to confirm their speech dominance. Twenty-nine were left speech dominant, and nine exhibited an "atypical" speech pattern (right or bilateral speech dominance). The remaining six subjects were not tested, but were suspected to be left-hemisphere dominant for speech, due to their right-hand preference. Table 4 presents the breakdown of language lateralization by seizure origin and age at seizure onset. Note that all of the participants with right hemisphere seizure foci displayed a left hemispheric speech dominance.

TABLE 4. Number of participants by seizure origin and age at seizure onset.

	<u>Left Seizure Foci</u>		<u>Right Seizure Foci</u>	
	<u>Early</u>	<u>Late</u>	<u>Early</u>	<u>Late</u>
Left Speech Dominant	4	11	5	15
Atypical Speech	6	3	0	0

Materials and Procedures

MR Analysis

All MR images were obtained using a Picker International Cryogenic Vista 2055 scanner operating at 0.15 Tesla. Two to four transaxial images were digitized for each participant. The first slice consisted of the image just above the third ventricle. Slices in which the third ventricle was not yet clearly visible

or distinguishable were measured as well. Any slices above this image were also digitized and used to determine the hemispheric volume. Because these participants were all patients with seizure disorders, the temporal lobes were the primary source of damaged tissue. In order to reduce the risk of including lesion mass in the measurement of brain tissue, the temporal lobe was avoided in all volumetric assessments.

Morphological analysis was performed by the author using the Microcomputer Imaging Device (Ramm, 1988). The laterality of the seizure foci and the age of seizure onset were unknown during the digitizing process. To determine the volumes of each hemisphere, the following procedure was employed for each MR image. First a line was drawn through the interhemispheric fissure to divide the two hemispheres. In slices where the fissure did not extend throughout the slice the line was drawn by connecting the two extreme ends of the fissure. Once this was completed, a thresholding function was used to determine the area of each hemisphere. In slices where the CSF was not distinct enough to outline the hemisphere or the ventricles, manual tracing was used in conjunction with the edge detection/thresholding method.

The area was taken of each slice and then added together to determine the volume of each hemisphere. Since the number of measurable slices differed from subject to subject, an average volume was calculated for each participant by dividing the overall volume by the number of slices measured.

An asymmetry quotient was then determined using the formula (as used by Yeo et al., 1987):

$$\frac{100 \times (\text{left volume} - \text{right volume})}{(\text{left volume} + \text{right volume})}$$

An asymmetry quotient of zero or greater was considered "typical asymmetry" and a negative quotient was termed "atypical."

In order to determine the reliability for the asymmetry measures, nineteen sets of MR images were measured on two separate occasions. A t-test determined that the volumetric measurements were highly reliable ($r = .90, p < .000$)

Intellectual Assessment

Cognitive functioning was evaluated using the age appropriate Wechsler Intelligence tests; the WAIS-R was administered to participants who were eighteen years or older (Wechsler, 1981), and the WISC-R was administered to those participants younger than eighteen (Wechsler, 1974). Ten patients were administered an abbreviated battery consisting of only the vocabulary and block design subtests. Full scale intelligence quotients (IQ's) for these participants were estimated based on IQ equivalents as presented in Spreen and Strauss (1991). The mean full scale intelligence quotient (FSIQ) for all of the participants was 90.25 (SD = 13.99). Because it is not possible to establish an individual's PIQ and VIQ with the abbreviated battery, these participants were not included in any analysis which examined the VIQ - PIQ ratio. Table 5 presents the breakdown of those participants whose VIQ - PIQ scores were used broken down by seizure origin and age at onset. For those individuals who completed the entire intelligence test, the mean verbal IQ (VIQ) was 90.47 (SD = 15.88) and performance IQ (PIQ) was 90.94 (SD = 16.26).

TABLE 5. Number of participants with complete intelligence testing by lateralization of seizure origin and age at seizure onset.

	<u>Early</u>	<u>Late</u>
Left Focus	8 (2)	11 (3)
Right Focus	4 (1)	11 (4)

Note. The number of participants without cognitive data is indicated in parenthesis.

RESULTS

Participants

Twenty-six out of the forty-four participants displayed an "atypical" hemispheric asymmetry (right hemisphere > left hemisphere) (see Table 6). The mean asymmetry quotient for those participants with a larger right hemisphere ("atypical" asymmetry) was -2.15 (sd = 1.52; ranging from .73 to 1.16). The mean asymmetry quotient for those who displayed the more typical left hemispheric advantage was 2.46 (sd = 1.36; ranging from .52 to 6.94). None of the participants demonstrated symmetrical hemispheres.

TABLE 6. Number of the participants' with hemispheric asymmetries by location of seizure origin and age at seizure onset.

	<u>Early Seizure Onset</u>		<u>Late Seizure Onset</u>	
	<u>Left</u>	<u>Right</u>	<u>Left</u>	<u>Right</u>
Typical Asymmetry (left > right)	2	4	4	8
Atypical Asymmetry (right > left)	8	1	10	7

1. The Effects of Seizure Origin on Anatomic Asymmetry

A 2x2 ANOVA was used to determine whether side of focus (left, right) and age of onset (early, late) would affect hemispheric asymmetry. It had been hypothesized that early lateralized damage (i.e., age of onset less than 12 months of age) would lead to a cerebral asymmetry such that the ipsilateral side would be smaller than the contralateral hemisphere. Thus, an early left hemispheric focus would result in an atypical cerebral asymmetry (right

hemisphere > left hemisphere) and an early right hemispheric focus would result in the typical asymmetrical pattern (left hemisphere ≥ right hemisphere). The analysis determined that the side of seizure origin did affect the resulting asymmetry quotient in the direction hypothesized, $F(1,39) = 6.43, p < .005$. Specifically, individuals with right-sided seizure origin displayed a (typical) left-sided advantage (mean asymmetry quotient = .62; SD = 2.73), while those with left sided foci displayed an atypical right hemisphere advantage (mean asymmetry quotient = -1.18; SD = 2.41). The main effect of age of seizure origin was not significant. Because the direction of the interaction (side of seizure origin by age of onset) had been predicted prior to analysis, a one tailed test of significance was used (Coldeway, 1989). In spite of this added power, the results indicated that the interaction approached, but did not attain conventional levels of significance, $F(1,39) = 1.25 p < .15$ (see Table 7). Similar results were found when the interaction was examined by multiple regression wherein the age of onset was defined by the person's age in terms of months, rather than by the divisions of "early" and "late".

TABLE 7. Means (and Standard Deviations) of Asymmetry Quotients Based on Side of Focus and Age of Onset.

	Left/Early	Left/Late	Right/Early	Right/Late
Asymmetry Quotient	-1.56 (2.50)	-.91 (2.41)	1.56 (1.72)	.30 (2.98)

Note. Early is defined as seizure onset occurring before the age of 12 months.

Note. Asymmetry Quotient = $\frac{100 \times (\text{left volume} - \text{right volume})}{(\text{left volume} + \text{right volume})}$

2. Effects of "Atypical" Anatomic Asymmetries on Cognitive Functioning

Based on a review of the literature it was predicted that the asymmetry quotient would be directly correlated with the VIQ-PIQ difference, yet asymmetry would not be correlated with FSIQ, VIQ, or PIQ. Pearson Product - Moment correlations were computed to examine the relations between anatomical asymmetries and cognitive functioning. Consistent with the hypothesis, there were no significant correlations between the asymmetry quotient and the basic measures of intelligence (FSIQ, VIQ, and PIQ). There were also no significant correlations between the asymmetry quotient and the VIQ - PIQ split (see table 8).

TABLE 8. Correlations Between the Asymmetry Quotient and the Basic Measures of Intelligence.

	<u>IQ</u>	<u>VIQ</u>	<u>PIQ</u>	<u>VIQ-PIQ</u>
Asymmetry Quotient (for all participants)	-.02	.03	.09	-.08
Asymmetry Quotient (by left side focus)	-.02	-.08	.13	-.27
Asymmetry Quotient (by right side focus)	-.08	.16	-.16	.32

Note. $p > .2$ for all correlations

3. The Effects of Language Dominance on Anatomical Asymmetry

It had been hypothesized that hemispheric dominance for language would be significantly associated with the anatomical asymmetry. A one-tailed,

simple factorial ANOVA indicated that the association between the pattern of speech lateralization and hemispheric asymmetry also approached, but did not attain conventional levels of significance ($F_{(1,43)} = 2.03, p < .08$). The mean asymmetry for the left speech group was -0.08 ($sd = 2.67$), whereas the mean asymmetry for the atypical (right and bilateral) speech group was -1.49 ($sd = 2.60$). Table 9 presents a breakdown of the number of participants by speech dominance and anatomical asymmetry.

TABLE 9. Breakdown of the participants by Speech Dominance and Anatomical Asymmetry

	<u>Anatomical Asymmetry Pattern</u>	
	<u>Left > Right</u>	<u>Right > Left</u>
Left Speech Dominance	15	20
Atypical Speech Dominance	2	7

DISCUSSION

Research Hypotheses and Findings

Part I: The Effects of Seizure Origin on Anatomic Asymmetry

It had been postulated that early lateralized damage to the developing human brain would significantly impact the brain's hemispheric asymmetry. Thus, although the typical asymmetry reflects a larger left hemisphere (Coffey, et al., 1993; Raz, et al., 1993; Yeo et al., 1987), early damage to this hemisphere would reduce or reverse this pattern. Conversely, early right hemispheric damage would exaggerate the typical asymmetrical pattern, resulting in an unusually larger left hemisphere.

This premise was based on Kolb and Wishaw's (1989) suggestion that early lesions may lead to a reduction of afferent stimuli to *developing* neuronal dendrites. This in turn, leads to the atrophy of the dendrites throughout the hemisphere. Consequently, if damage occurs during the development and expansion of dendrites, the entire hemisphere would be smaller than its healthy, contralateral counterpart. Because this theory emphasizes that general hemispheric damage only occurs during dendritic development, it was further hypothesized that later damage would not significantly affect the hemispheric asymmetry regardless of the site of damage.

Consistent with the proposed hypothesis, these findings suggest that there is a significant relationship between the side of seizure origin (left or right hemisphere) and hemispheric asymmetry. In particular, the side of epileptic focus was associated with a comparative reduction in the size of the ipsilateral

hemisphere. Contrary to the author's prediction, however, this finding occurred regardless of the age of onset. Thus, while individuals with left-sided foci generally displayed "atypical" hemispheric asymmetries, and individuals with right-sided foci presented with "typical" asymmetries, the timing of lateralized damage or seizure onset did not significantly relate to the asymmetrical patterns. There were, however, trends in the expected direction. That is, those with early left-hemisphere foci tended to show a right-sided advantage. Furthermore, those with late left-hemisphere foci also showed a larger right hemisphere, but, as predicted, the degree of asymmetry was comparably less. Similar trends were seen in the participants with early and late right-hemisphere foci.

These results differ from the animal literature which has clearly established an interaction between side of lesion and age of onset (Kolb, 1987; Kolb & Wishaw, 1981; Kolb & Wishaw, 1989). One possible reason for the contradictory results may lie in the nature of the observed population (patients with severe, long-standing epilepsy). It is conceivable that the pathology which results in epileptic seizures does not affect the brain tissue in the same manner that acute lesions do. In fact, there is some evidence which suggests that seizure activity may actually result in the growth and expansion of mossy fibers, axons and dendrites within the hippocampal formation (Babb, Kupfer, Pretorius, Crandall & Levesque, 1991; Sutula, 1990; Sutula, Cascino, Cavazos, Parada, Ramirez, 1989). Although there has been no similar findings within the

cerebral cortex, this research offers a possible explanation for my study's contradictory results.

What is striking about these results is that they contain a greater number of participants with atypical hemispheric asymmetries than a prediction based on the literature would suggest (26 out of 44 cases were "atypical"). If one were to assume that all of the individuals with atypical speech, and/or early left-hemispheric foci would also have "atypical" hemispheric asymmetries, then the predicted number of such participants would have been 13. Taking into account that, on the average, approximately 10 percent of the "normal" population also demonstrate "atypical" asymmetry patterns (LeMay, 1976) three more individuals could be included in this number (bringing the predicted number of individuals with atypical hemispheric asymmetries up to sixteen). Yet, within this sample, nearly twice that number displayed an atypical morphometry. Thus, it is clear, that there is something unique about this study. The difference between these results and other studies may, as noted above, lie in the nature of the participants or may be due to variations in the methodological approach (see below).

Part II: The Association Between Anatomical and Functional Asymmetry

A second issue addressed by this thesis is the relation between anatomical and functional asymmetries. The results from this study failed to support the premise that typical asymmetrical patterns are correlated with

verbal cognitive superiority (determined by the VIQ-PIQ difference from the Wechsler Intelligence Tests). The results did, however, confirm that simple cognitive scales (FSIQ, VIQ, and PIQ) are also unrelated to the asymmetry quotient.

The lack of correlation between the VIQ-PIQ difference and the asymmetry quotient is unique within the literature. Once again, the nature of the sample must be considered as a viable source of variance. Although others have studied pathological populations (e.g., Luchins et al., 1982; Rosenberger & Hier, 1980), no one has yet explored the interaction between anatomical asymmetries and intellectual performance within an epileptic population, or in patients with early, identifiable brain damage. There are some indications that those individuals who experience early left hemisphere damage can preserve basic language skills at the expense of other, nonverbal skills (Satz, Strauss, Hunter & Wada, 1994; Strauss, Satz & Wada, 1990). Perhaps a significant number of participants within this study do not follow the expected hypothesis because their language functioning (and, therefore, verbal intelligence) has been redistributed without affecting the gross structural hemispheric asymmetries.

Another difference may lie in the degree of anatomical asymmetry found within the subjects (as measured by the asymmetry quotient). For example, Yeo et al.'s (1987) findings indicated that the VIQ-PIQ difference was more likely to correlate with anatomical asymmetry when the asymmetry quotient exceeded a value of 4. Within this sample, however, very few cases actually demonstrated

this significant a degree of asymmetry (only one case was greater than 4, while two were less than -4). Thus, the inability to duplicate Yeo et al.'s findings may not be due to a difference in this sample's functional asymmetry. It may, instead, be associated with a smaller range of anatomical asymmetry quotients.

Part III: The Association Between Language Dominance and Anatomical Asymmetry

The final hypothesis examined the relation between lateralization of speech and hemispheric asymmetrical patterns. The results displayed some tantalizing, yet nonsignificant evidence that the side of language dominance (as determined by a sodium amytal test) is correlated with anatomical asymmetry. Specifically, the results indicate a trend in the predicted direction. Thus, it appeared that individuals with a left hemispheric dominance for speech may be more likely to demonstrate a left anatomical asymmetry. Conversely, individuals with atypical speech dominance may be more likely to display an "atypical" hemispheric asymmetry.

Because there were no significant findings, these results differ from those reported by Charles et al. (1994). This may, however, be due to differences between samples. Although both studies examined patients with retractable seizure disorders, the nature of the participants still differed. Specifically, Charles et al. examined nine participants with bilateral speech and only one who exhibited right hemisphere dominance for speech. This sample, however, consisted of 2 individuals with bilateral speech and 7 with right hemisphere

dominance. This difference is important because Charles et al.'s findings indicated that reversed asymmetries were significantly related to their bilateral language group, but **not** to the individual with right hemisphere dominance. In fact, this individual demonstrated a normal asymmetry pattern. Therefore, it is possible that this sample did not reach significance because atypical anatomical asymmetry is actually related to bilateral speech dominance and not "atypical" speech dominance as defined by this paper. It is difficult to rely upon this assumption, however, since the previous paper examined only one subject with left hemisphere dominance for speech, and it is possible that this patient was an exception to that seen in the general public. Future research in this area is necessary to clarify this issue.

Limitations and Suggestions for Future Research

Several explanations have already been offered to explain why some of the results may not have followed the predicted patterns. There are also some other potential methodological limitations which may have impacted the results of this study. First, there may have been some shortcomings within the MR process itself. Since the MR images were obtained from patient files, the goal for examination was to determine the location of the epileptic focus, rather than maintaining a consistent procedure from one patient to another. Thus, the location of the MR images varied from participant to participant. Furthermore, the number of usable MR images was also inconsistent. Although there was an effort to account for the number of slices used (recall, that the average volume

was taken for each participant) this may not have effectively reduced the variance. Finally, measurement error due to variable head rotation and subject movement during the MR process may have impacted the results as well.

The fact that the MR images were not collected strictly for experimental purposes also significantly reduced the number of viable participants for this study. Although there were initially 73 patients selected for the sample, only 44 had usable images. Because these trends followed the hypothesized direction, but did not reach significance, it is possible, therefore, that this study was limited by a small number of participants. Future studies, with larger subject pools, may be able to establish that these nonsignificant trends are, in fact, an accurate indication of the physiological results of early lesions and the correlations between anatomical and functional asymmetries.

The overall number of participants may not have been the only limitation in the design of this experiment. An examination of the number of participants in each group indicates that there was an uneven distribution within each category based on the variables: side of focus and age at onset (see table 3). Since this resulted in a situation with unequal n , and a cell with only five participants (those with early, right foci), the breakdown of the number of participants may have also reduced the significance of the results.

The small sample is even more conspicuous when the correlation between functional and anatomical asymmetries is examined. Since cognitive data were not available for each participant, the sample size for this hypothesis

is smaller and more unevenly distributed than had been expected. Table 5 indicated the breakdown of the number of participants with complete intellectual assessments based on lateralization of seizure and age of onset. An examination of this table demonstrates that although there seemed to be a fairly equal distribution among left-hemispheric early and late cases as well as the right-hemispheric late foci, only twelve percent of the participants (four out of 34) had early, right-hemispheric foci. Thus, once again, the grouping of the participants may have significantly affected the results.

Finally, the process used to determine anatomical asymmetries may have been limited. By attempting to avoid the temporal lobes (the presumed lesion site in most patients), some aspects of the occipital lobes could not be measured. It had originally been assumed that this would not significantly affect the hemispheric asymmetry quotient. This premise, however, may have been incorrect. Since there is some indication that the occipital pole represents the point of greatest hemispheric asymmetry (Glicksohn & Myslobodsky, 1993), the procedure used within this thesis may have reduced the accuracy of the hemispheric asymmetry quotient. In fact, what these measure may more accurately represent is the "typical" right frontal asymmetry tempered by some minor leftward occipital asymmetry. If the pathological nature of this population had not prevented these lower measurements, the resulting asymmetries may have been more closely related to the current literature. Thus, the inability to measure the full occipital lobes may have obscured the

results.

Since this limitation may have resulted in distorted asymmetry quotients, its effects may have impacted other hypotheses within this thesis. Specifically, the correlations between hemispheric asymmetry and intellectual skills may be based on inaccurate data. Previous studies which examined these questions were not restricted from measuring the temporal lobe or the full occipital lobe in determining their asymmetry quotients. In fact, while some studies measured the entire hemisphere (Willerman et al., 1992; Yeo et al., 1987), others based their correlations solely on the occipital asymmetry (Luchins et al., 1982) or the parietal-occipital asymmetry (Rosenberger & Hier, 1980). Therefore, it is conceivable that the intellectual correlations were based on inaccurate asymmetry quotients. If this is the case, then it is difficult to interpret the results of this research.

Similar complications may have arisen in the third hypothesis which examined the relation between anatomical asymmetry and language. Although this study was able to measure the upper portions of the planum temporale, it was not able to measure the structure in its entirety. Recall that this is the area that Geschwind and Levitsky (1968) first demonstrated anatomical asymmetries. They further postulated that their results confirmed that the left hemisphere's dominance in speech is directly associated with structural differences between the two hemispheres. Because the entire planum temporale could not be measured, there is a small possibility that the asymmetry quotient may not have

reflected the true structural differences in this critical part of the brain.

Summary and Directions for Future Studies

The results of this thesis indicate that there is a significant relation between side of epileptic focus and anatomical asymmetry. There were no significant associations, however, between anatomical asymmetry patterns and age at onset, intellectual variables or speech dominance. Future studies should investigate the role of the complete occipital lobes and their association with functional asymmetries. These studies should also incorporate control participants for comparison to a "typical" anatomical asymmetry in the population observed. Finally, analysis of larger sample sizes, with comparable groups size should be examined to determine whether the nonsignificant trends in this thesis were limited by a restricted population size.

REFERENCES

- Aylward, E. H., & Reiss, A. (1991). Area and volume measurement of posterior fossa structures in MRI. Journal of Psychiatric Research, *25*, 159-168.
- Andreasen, N. C., Cohen, G., Harris, G., Cizadlo, T., Parkkinen, J., Rezai, K., & Swayze, V. W. (1992). Image processing for the study of brain structure and function: problems and programs. The Journal of Neuropsychiatry and Clinical Neurosciences, *4*, 125-133.
- Andreasen, N. C., Flaum, M., Swayze II, V., O'leary, D. S., Alliger, R., Cohen, G., Ehrhardt, J., & Yuh, W. T. C. (1993). Intelligence and brain structures in normal individual. American Journal of Psychiatry, *150*(1), 130-134.
- Babb, T. L., Kupfer, W. R., Pretorius, J. K., Crandll, P. H., Levesque, M. F. (1991). Synaptic reorganization by mossy fibers in human epileptic fascia dentata. Neuroscience, *42*, 351-363.
- Bigler, E. D., Hubler, D. W., Cullum, C. M., & Turkheimer, E. (1985). Intellectual and memory impairment in dementia. The Journal of Nervous and Mental Disease, *173*(6), 347-352.
- Bigler, E. D., Paver, S., Cullum, C. M., Turkheimer, E., Hubler, D., & Yeo, R. (1984). Ventricular enlargement, cortical atrophy and neuropsychological performance following head injury. International Journal of Neuroscience, *24*, 295-298.
- Bird, J. B. (1982). Computerized tomography, atrophy and dementia: a review. Progress in Neurobiology, *19*, 91-115.
- Burke, H. L., Yeo, R. A., Delaney, H. D., & Conner, L. (1993). CT scan cerebral hemispheric asymmetries: predictors of recovery from aphasia. Journal of Clinical and Experimental Neuropsychology, *15*(2), 191-204.
- Caviness, V. S., Filipek, P. A., & Kennedy, D. N. (1989). Magnetic resonance technology in human brain science: blueprint for a program based upon morphometry. Brain and Development, *11*, 1-13.
- Charles, P. D., Abou-Khalil, R., Abou-Khalil, B., Wertz, R. T., Ashmead, D. H., Welch, L., & Kirshner, H. S. (1994). MRI asymmetries and language dominance. Neurology, *44*, 2050-2054.
- Chui, H. C., & Damasio, A. R. (1980). Human cerebral asymmetries evaluated by computed tomography. Journal of Neurology, Neurosurgery, and

Psychiatry, 43, 873-878.

Coffey, C. E., Wilkinson, W. E., Weiner, R. D., Parashos, I. A., Djang, W. T., Webb, M. C., Figiel, G. S., Spritzer, C. E. (1993). Quantitative cerebral anatomy in depression. Archives of General Psychiatry, 50, 7-16.

Coldeway, A. E. (1989). Using Basic Statistics in the Behavioral Sciences. Scarborough: Prentice-Hall Canada Inc.

Cullum, C. M., & Bigler, E. D. (1986). Ventricle size, cortical atrophy and the relationship with neuropsychological status in closed head injury: a quantitative analysis. Journal of Clinical and Experimental Neuropsychology, 8(4), 437-452.

Damasio, H., Eslinger, P., Damasio, A. R., Rizzo, M., Huang, H. K., & Demeter, S. (1983). Quantitative computed tomographic analysis in the diagnosis of dementia. Archives of Neurology and Psychiatry, 40, 715-790.

Davidson, R. J., & Hugdahl, K. (Eds.). (1995). Brain Asymmetry. Cambridge: The MIT Press.

DeCarli, C., Kaye, J. A., Horwitz, B., & Rapoport, S. I. (1990). Critical analysis of the use of computer-assisted transverse axial tomography to study human brain in aging and dementia of the Alzheimer type. Neurology, 40, 872-883.

Deuel, R. K., & Moran, C. C. (1980). Cerebral dominance and cerebral asymmetries on computed tomogram in childhood. Neurology, 30, 934-938.

Filipek, P. A., Kennedy, D. N., Caviness, V. S., Rossnick, S. L., Spraggins, T. A., & Starewicz, P. M. (1989). Magnetic resonance imaging-based brain morphometry: development and application to normal subjects. Annals of Neurology, 25, 61-67.

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

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

Glicksohn, J. & Myslobodsky, M. S. (1993). The representation of patterns of structural brain asymmetry in normal individuals. Neuropsychologia, 31(2), 145-159.

Harris, G. J., Rhew, E. H., Noga, T., & Pearlson, G. D. (1991). User-friendly method for rapid brain and CSF volume calculation using transaxial MRI images. Psychiatry Research: Neuroimaging, 40, 61-68.

Heilman, K. M. & Valenstein, E. (Eds.). (1985). Clinical Neuropsychology. New York: Oxford University Press.

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

Kolb, B. (1987). Recovery from early cortical damage in rats. I. Differential behavioral and anatomic effects of frontal lesions at different ages of neural maturation. Behavioral Brain Research, 25, 205-220.

Kolb, B. & Wishaw, I. Q. (1981). Neonatal frontal lesions in the rat: sparing of learned by not species-typical behavior in the presence of reduced brain weight and cortical thickness. Journal of Comprehensive Physiological Psychology, 95, 863-879.

Kolb, B. & Wishaw, I.Q. (1989). Plasticity in the neocortex: mechanisms underlying recovery from early brain damage. Progress in Neurobiology, 32, 235-276.

Kolb, B. & Wishaw, I. Q. (1990). Fundamentals of Human Neuropsychology (3rd ed.) (pp. 122-123; 347-382). New York: W. H. Freeman and Company.

LeMay, M. (1976). Morphological cerebral asymmetries of modern man, fossil man, and nonhuman primate. Annals. New York Academy of Science, 280, 349-366

Lemay, M. (1977). Asymmetries of the skull and handedness. Journal of the Neurological Sciences, 32, 243-253.

LeMay, M., & Geschwind, N: Asymmetries of the human cerebral hemispheres, in: Caramzza, A., Zurif, E.B. (Eds): Language Acquisition and Language Breakdown: Parallels and Divergencies. Baltimore, the Johns Hopkins University Press, 1978m oo, 311-328.

LeMay, M., & Kido, D. K. (1978). Asymmetries of the cerebral hemispheres on computed tomography. Journal of Computer Assisted Tomography, 2, 471-476.

Luchins, D. J., Weinberger, D. R., & Wyatt, R. J. (1982). Schizophrenia and cerebral asymmetry detected by computed tomography. American Journal of Psychiatry, 139(6), 753-757.

Pieniadz, J. M., & Naeser, M. A. (1984). Computed tomographic scan cerebral asymmetries and morphological brain asymmetries. Archives of Neurology, 41, 403-409.

Pieniadz, J. M., Naeser, M. A., Koff, E., & Levine, H. L. (1983). CT scan cerebral hemispheric asymmetry measurements in stroke cases with global aphasia: atypical asymmetries associated with improved recovery. Cortex, 19, 371-391.

Porac, C., & Coren, S. (1981). Lateral preferences and human behavior. Springer-Verlag, New York.

Ramm, P. (1988). Microcomputer Imaging Device (MCID). Imaging Research Inc., St Catherine, Ontario.

Raz, S., Raz, N., Weinberger, D. R., Boronow, J., Pickar, D., Bigler, E. D., & Turkheimer. (1987). Morphological brain abnormalities in schizophrenia determined by computed tomography: a problem of measurement? Psychiatry Research, 22, 91-98.

Raz, N., Torres, I. J., Spencer, W. D., Millman, D., Baertschi, J. C., & Sarpel, G. Neuroanatomical correlates of age-sensitive and age-invariant cognitive abilities: An in vivo MRI investigation. Intelligence, 17, 407-422.

Roberts, M. A., & Caird, F. I. (1976). Computerized tomography and intellectual impairment in the elderly. Journal of Neurology, Neurosurgery, and Psychiatry, 39, 986-989.

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

Satz, P., Strauss, E., Hunter, M., & Wada, J. (1994). Re-examination of the crowding hypothesis: Effects of age of onset. Neuropsychology, 8(2)255-262.

Spren, O., & Strauss, E. (1991). A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary. New York: Oxford University Press.

Stafford, L. L., Albert, M. S., Naeser, M. A., Sandor, T., & Garvey, A. J. (1988). Age related differences in computed tomographic scan measurements.

Archives of Neurology, 45, 409-415.

Strauss, E., Satz, P., & Wada, J. (1990). An examination of the crowding hypothesis in epileptic patients who have undergone the carotid amygdalotomy test. Neuropsychologia, 28(11), 1221-1227.

Sutula, T. P. (1990). Experimental models of temporal lobe epilepsy: insights from the study of kindling and synaptic reorganization. Epilepsia, 31, s45 - s54.

Sutula, T., Cascino, G., Cavazos, J., Parada, I., & Ramirez, L. (1989). Mossy-fiber synaptic reorganization in the epileptic human temporal lobe. Annals of Neurology, 26, 321-330.

Takeda, S., & Matsuzawa, T. (1984). Brain atrophy during aging: a quantitative study using computed tomography. Journal of the American Geriatric Society, 32, 520-525.

Wechsler, D. (1974). Wechsler Intelligence Scale for Children-Revised. New York: Psychological Corporation.

Wechsler, D. (1981). Wechsler Adult Intelligence Scale-Revised. New York: Psychological Corporation.

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. Annals of Neurology, 11, 97-100.

Willerman, L., Schultz, R., Rutledge, J. N., & Bigler, E. D. (1991). In vivo brain size and intelligence. Intelligence, 15, 223-228.

Willerman, L., Schultz, R., Rutledge, J. N., & Bigler, E. D. (1992). Hemispheric size asymmetry predicts relative verbal and nonverbal intelligence differently in the sexes: an MRI study of structure-function relations. Intelligence, 16, 315-328.

Witelson, S.F. & McCulloch, P. B. (1991). Premortem and postmortem measurement to study structure with function: A human brain collection. Schizophrenia Bulletin, 17(4), 583-591.

Yeo, R. A., Turkheimer, E., Raz, N., & Bigler, E. D. (1987). Volumetric asymmetries of the human brain: intellectual correlates. Brain and Cognition, 6, 15-23.

CHANGES IN ASYMMETRY

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