

The Emergence of Cerebral Asymmetries in Early Human Development: A Literature Review and a Neuroembryological Model

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Ever since Broca's century-old discovery of cerebral asymmetries in human perceptual-cognitive functions, there has been speculation about the developmental emergence of those asymmetries. The basic question has been: Do the asymmetries first appear only at some point after birth, starting from an initial state of bilateral equivalence or symmetry at birth, or are the hemispheres instead functionally asymmetrical from the start? A related question is whether functional asymmetries can be traced to some lateral bias in the structural development of the hemispheres, such that one hemisphere matures in advance of the other. Thus, the term "emergence" in the title of this chapter might refer either to functional asymmetries in infants or to the embryological development of the hemispheres. An underlying assumption of this chapter is that the ontogeny of functional asymmetries is influenced by an asymmetry in the formation and physical maturation of the cerebral hemispheres. Both issues will be addressed in the following discussion, beginning with a review of behavioral evidence for perceptual-cognitive asymmetries in early infancy, and ending with a proposed model for a lateralizing gradient in the neuroembryological emergence of the cerebral hemispheres during prenatal development.

As for the development of functional asymmetries, Broca (1865) himself speculated that language becomes lateralized to the left hemisphere during language development (see Bever, 1978). Later, Samuel Orton (1937) expanded on this concept of "developmental lateralization" in his influential theory that dyslexic children suffer from a failure to developmentally establish cerebral dominance for language. More recently, Lenneberg (1967) further detailed the model of developmental change in lateralization of functions, proposing a critical period for language development, and hence for the progressive establishment of left-hemisphere language dominance, during the period between 2 years and puberty. More important for the present discussion, however, his model explicitly assumed that the child's cerebral hemispheres are equal in their capability to acquire language—a trait referred to as "equipotentiality"—until at least 2 years of age. In fact, the focus on language in theoretical discussions of those times, to the exclusion of other cognitive functions, led to the reasoning that since infants have not yet acquired language, they should not show any hemispheric specialization. Implicit in the equipotentiality concept has been the notion that the infant's hemispheres show functional symmetry, or lack of behavioral differentiation.

Since the mid-1970s, however, evidence of functional cerebral asymmetries in young infants has indicated that the assumption of functional symmetry between the hemispheres in early development cannot be correct. Generally, this literature suggests a pattern of functional cerebral asymmetries by at least 2 to 3 months of age, and possibly even before full-term birth, that is analogous to the adult pattern of left-hemisphere superiority for

language-related functions and right-hemisphere superiority for music and holistic perception of patterns and faces. The next part of the chapter will focus on perceptual-cognitive asymmetries in infants (for discussion of motoric asymmetries in infants, see Chapter 4 by Turkewitz, this volume), and particularly on behavioral evidence (electrophysiological data are presented in Chapter 6 by Molfese and Betz, this volume).

FUNCTIONAL ASYMMETRIES IN INFANTS

Before the specific findings are reviewed here, some preliminary qualifications are necessary. Up to this point, many questions about infant hemispheric specialization remain unanswered. It is not yet known, for example, whether infant asymmetries are fundamental responses to certain stimulus properties or classes, such as the physical characteristics of speech versus nonspeech, or whether, instead, they reflect different processing styles, such as feature-analysis versus holistic processing, as has been proposed for adults. In addition, the behavioral studies are actually quite few in number. Moreover, they have focused overwhelmingly on auditory asymmetries, particularly for human speech. This is due in part to a strong theoretical bias toward assessing language-related functions, but it is also due to pragmatic constraints. The dichotic listening procedure is more obviously amenable to infant research than are the lateralized behavioral measures of asymmetries in other modalities (e.g., the requirements of the visual split-field tachistoscopic technique are more difficult to adapt to infants).

Nonauditory Asymmetries

Thus far only two behavioral studies of infant cognitive-perceptual asymmetries in other, nonauditory modalities have been conducted, both of which assessed right-hemisphere advantages for pattern recognition. One of these was inconclusive regarding functional asymmetries during infancy; the other is not yet published. In the first, Rose (1984) tested 1-, 2-, and 3-year-olds for a left-hand advantage (right-hemisphere superiority) in haptic perception of shapes. After blind, unimanual palpation of a three-dimensional nonsense shape, children were tested for cross-modal shape recognition on a visual preference task in which they saw a picture of the palpated object presented alongside a picture of a different-shaped object. Although all children showed preferences for the novel figure, and hence recognition memory for the palpated object, only the 2- and 3-year-olds showed a left-hand/right-hemisphere superiority. The 1-year-olds—the only infants in the study—failed to show a right-hemisphere advantage. As Rose argues, however, this cannot be taken as evidence for a lack of infant right-hemisphere specialization, because the visual test phase of the task involved bihemispheric, or nonlateralized, visual input. In fact, even for the older children the left-hand effects were rather small. Perhaps some other, more sensitive and completely lateralized test measure would detect tactile asymmetries in infants.

In the other nonauditory behavioral study, Witelson and Barrera (Witelson, 1981, personal communication) tested visual asymmetries in 3-month-olds. They presented the infants with side-by-side slides of two identical photographs, both of which were either of the infant's mother, or of a female stranger, or of a standard black-and-white checkerboard pattern. The infants showed a fixation-time preference for the left-side photo of the mother, as well as for the left-side checkerboard, suggesting greater activation of their right hemispheres. However, they did not show any side preference for the stranger. The authors'

interpretation was that both mother and checkerboard constituted gestalt patterns to the infants, which they processed holistically, thus showing a right-hemisphere bias in activation. In contrast, the female stranger was not processed as a gestalt and thus not handled preferentially by the right hemisphere. This argument, at least with respect to the infants' responses to mother versus stranger, is consistent with developmental research on face recognition in children (Levine, 1985). Young children perceive unfamiliar faces in terms of salient features rather than holistically and show no hemispheric asymmetry for recognition of those faces. The same children, however, do perceive familiar faces holistically, as well as showing a right-hemisphere advantage for the familiar faces. Thus, the Witelson and Barrera results offer some suggestion of a right-hemisphere bias in holistic perception of faces (and patterns) by 3 months, which is compatible with the literature on visual asymmetries in adults. This suggestion, however, must be viewed as still tentative, given that it is based only on a single, unpublished finding.

Auditory Asymmetries

By comparison, the behavioral studies of auditory asymmetries have been more numerous, and have included assessments of both left- and right-hemisphere specialization in infants. The technique used is some modification of the dichotic listening procedure. In the first such study, reported at a conference held at Brock University in 1975, Anne Entus (1977) used a nonnutritive sucking measure with a dichotic habituation-dishabituation procedure. Two groups of infants, who averaged 2½ months in age, were tested for ear differences in discrimination either of musical notes played by different instruments, or of consonant differences in speech syllables. In the first phase of each test, the infants heard a rapidly repeated presentation of a dichotic pair of stimuli until they reached a criterion of habituation. At that point, the element in either the right or the left ear was changed to, respectively, a new music note or syllable, while the other ear continued to receive its original habituation stimulus. The infants in the speech condition showed a greater recovery of the sucking response when the syllable changed in the right ear (REA) than when it changed in the left, indicating left-hemisphere superiority. The music group showed the opposite pattern, a left-ear (LEA) or right-hemisphere advantage. However, Vargha-Khadem and Corballis (1979) subsequently failed to replicate with 2-month-olds the speech REA that Entus found, a point to which we will return later in the chapter. In this later study, the infants discriminated the speech syllable change equally well with both ears.

In a similar dichotic habituation study with 3-month-olds, Glanville, Best, and Levenson (1977) used the heart rate measure of a deceleratory orienting response, reflecting interested attention to a stimulus, in order to introduce a memory component to the task. Friedes (1977) has presented evidence that, in adults, memory retrieval is more strongly associated with dichotic ear asymmetries than is a simple input-processing dominance. Therefore, the intervals between presentations of the dichotic pairs in the Glanville *et al.* test were long enough ($M = 25$ sec) that the infants had to rely on short-term memory in order to learn the habituation pair and to recognize the stimulus change on the test trial. In each test block, the habituation pair was presented 9 times, and the stimulus change was then presented on the 10th and final trial. All infants received separate left- and right-ear discrimination test blocks each for speech syllables and for music notes. The results provided converging evidence with Entus's findings for an adultlike pattern among 3-month-olds of REA in response to speech syllable changes, and LEA in response to music changes (see Figure 1-1).

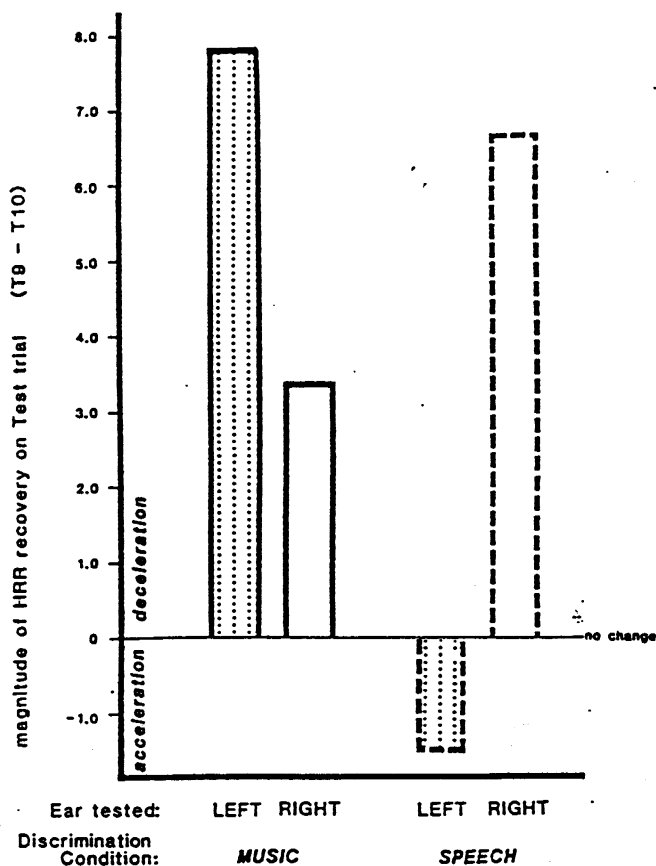


Figure 1-1. Ear differences in 3-month-olds' discrimination of speech syllables differing in initial consonant, and of music notes differing in instrument timbre. The task was a dichotic habituation-dishabituation task using heart rate deceleration as the response measure; represented here is the magnitude of dishabituation (cardiac deceleration) on the test trial (stimulus change in either right or left ear), relative to the cardiac response on the last habituation trial (trial 9). Redrawn from data reported in Glanville, Best, and Levenson (1977).

These first dichotic studies left several important questions unanswered, two of which were addressed by subsequent research with infants. First, there have been two attempts to obtain a better specification of the speech properties to which the infant's left hemisphere is preferentially responsive. Second, age changes in behavioral evidence of auditory cerebral asymmetries during infancy have been assessed.

THE BASIS OF LEFT-HEMISPHERE SPEECH SPECIALIZATION

For a more detailed understanding of the infant's left-hemisphere response to speech, Best (1978) used the dichotic heart rate habituation procedure to determine whether 3½-month-olds show different patterns of ear asymmetries for vowel versus consonant discriminations. Several studies with adults had suggested that the right-ear speech perception advantage is greatest for consonant perception, whereas there is often a weaker or absent ear advantage for vowel perception (e.g., Darwin, 1971; Studdert-Kennedy & Shankweiler, 1970; Weiss & House, 1973). This pattern may be related to the fact that consonants

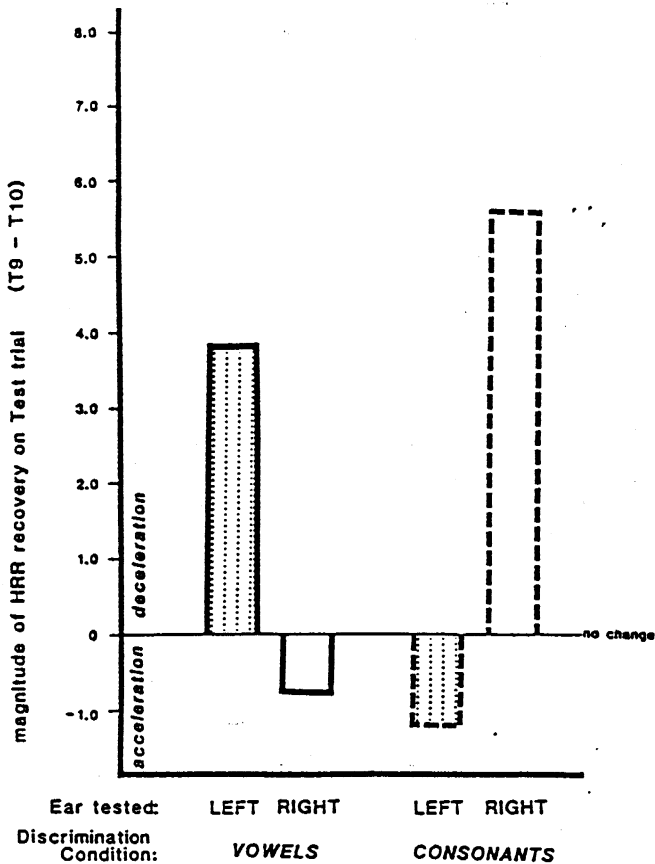


Figure 1-2. Ear differences in 3½-month-olds' discrimination of vowels and of consonants in computer-synthesized syllables. The method and response measure are the same as described for Figure 1-1. Based on data presented in Best (1978).

involve rapidly changing acoustic properties, whereas vowels are associated with much more slowly changing, or even steady-state, acoustic properties (see Cutting, 1974; Schwartz & Tallal, 1980). Therefore, Best developed a set of computer-synthesized syllables that exaggerated the rapidly changing acoustic properties versus steady-state characteristics associated with consonants versus vowels. The results revealed a REA for discrimination among the exaggerated consonants, consistent both with the earlier infant studies and with adult findings. The infants, however, unlike adults, showed an LEA for steady-state vowel discrimination (see Figure 1-2).

These findings suggest that the infant's left hemisphere may be particularly responsive to rapidly changing acoustic information, whereas the right hemisphere is more responsive to steady-state spectral information. The vowel LEA is compatible with John Sidtis's (1980) findings of a right-hemisphere advantage in adults' perception of steady-state harmonic information. The lack of an adult ear advantage for vowels suggests that this steady-state information may be easily transferred across the corpus callosum; the left-ear advantage in infants may be due to the immaturity of their corpus callosa (see also Molfese, Freeman, & Palermo, 1975; Molfese & Molfese, 1985; Studdert-Kennedy & Shankweiler, 1980).

MacKain, Studdert-Kennedy, Spieker, and Stern (1983) further explored the nature of the infant's left-hemisphere specialization for speech perception, in a bimodal-matching study with 5- to 6-month-olds. The infants viewed two side-by-side synchronous videotapes of a woman repeating two different two-syllable nonsense words, while they simultaneously heard a synchronous audio recording (over a centrally located loudspeaker) that corresponded to one of the two video displays. Infants detected the cross-modal equivalence, as indicated by a looking preference for the film that matched the audio presentation, but only when the correct video was in the right-side video monitor. This finding implies selective left-hemisphere activation, and suggests a left-hemisphere specialization for perception of the common underlying articulatory pattern that produced the disparate information in the two sensory modalities.

Together, these two studies on cerebral asymmetries for the properties of speech suggest that the infant's left hemisphere may be specialized for recognizing articulatory patterns in speech, and particularly the rapid acoustic changes resulting from the dynamic articulatory gestures that produce consonant sounds. However, this still leaves open the question: Why the left hemisphere? One possibility is a lateralized gradient in the maturation of the two hemispheres.

LATERAL DIFFERENCES IN HEMISPHERE MATURATION?

If a lateralized developmental gradient exists, uncertainty still remains as to whether the asymmetry in speech perception would result from earlier or later development of the left hemisphere relative to the right. Broca (1865) proposed a left-to-right gradient to explain language lateralization (see Bever, 1978); Corballis and Morgan (1978) seconded the notion of a left-right gradient. However, Taylor (1969); Crowell, Jones, Kapuniai, and Nakagawa (1973); and Brown and Jaffe (1975) have argued for a right-to-left gradient, which is also suggested by recent embryological evidence that cortical fissures appear consistently earlier in the right than in the left fetal hemisphere (Dooling, Chi, & Gilles, 1983).

To test the possibility of early age changes in asymmetrical function, Best, Hoffman, and Glanville (1982) tested for ear asymmetries in memory-based discriminations of speech syllables versus music notes by 2-, 3-, and 4-month-old infants. The 3- and 4-month-olds replicated the earlier findings of a right-ear/left-hemisphere advantage for speech and a left-ear/right-hemisphere advantage for music. The 2-month-olds, however, showed only the LEA for music; they did not detect the speech syllable change in either ear (see Figure 1-3). These results suggest an increase in functional maturity of the left hemisphere sometime between 2 and 3 months of age, at least for auditory discriminations that depend on short-term memory capacities. Such a change in cortical maturity around 2 to 3 months of age is consistent with reports of widespread biobehavioral changes and maturation of cortical influences over behavior around that time (Emde & Robinson, 1979).

This finding may also help explain the negative report by Vargha-Khadem and Corballis (1979), which had failed to replicate Entus's (1977) findings of a speech REA in infants. Although their infant subjects discriminated the syllable change in both ears, discrimination under the rapid-stimulus presentation conditions used in the sucking habituation procedure clearly does not depend solely on cortical involvement, since Frances Graham and her colleagues (Graham, Leavitt, Strock, & Brown, 1978) have found similar speech discrimination in a 6-week-old anencephalic infant. The conclusion of Best *et al.* (1982) was that the speech-specialized function of the left hemisphere may be insufficiently mature at 2 months to control behavioral responses in a memory-dependent discrimination task. In contrast, the analogous right-hemisphere function appears sufficiently mature at that age to effect a LEA for memory-based music timbre discrimination, suggesting a right-to-left

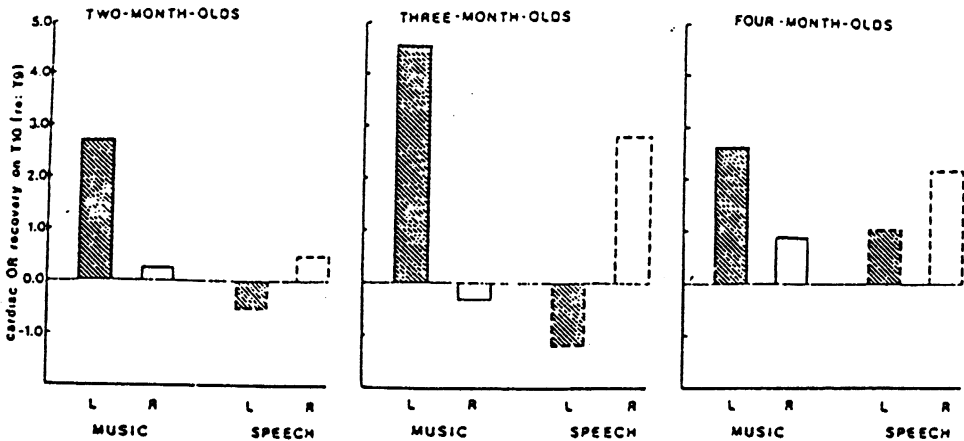


Figure 1-3. Age changes in ear differences for infants' discrimination of speech syllables and of musical timbre. Method and response measure are identical to the description of Figure 1-1. Reprinted with permission of the publisher from "Development of Infant Ear Asymmetries for Speech and Music" by C. T. Best, H. Hoffman, and B. B. Glanville, 1982, *Perception and Psychophysics*, 31, pp. 75-85. Copyright © 1982 by the Psychonomic Society.

gradient in the maturation of asymmetrical perceptual memory functions. This does not necessarily imply that cerebral lateralization itself develops out of an unlateralized substrate. Alternatively, cognitive and perceptual functions may mature developmentally at different rates, but within the context of a neural substrate that is already laterally specialized from the start (see Witelson, 1977, 1985; see also Kinsbourne, 1975).

If the latter view is correct, the question becomes: What is the source of this lateralized gradient in functional maturation? According to developmental biologists, morphologists, and particularly neuroembryologists, the patterns of embryological development are ultimately responsible for the structure and form of the adult organism, including the brain, at both the gross morphological level and the histological level. Given the basic neuropsychological assumption that variations in neuronal organization and development affect behavior and its development, then, fetal brain development should provide evidence of a lateralized developmental gradient. In the remainder of this chapter it will be argued that a right-to-left gradient in postnatal functional maturation parallels a similar gradient in the prenatal, embryologic development of the cerebral hemispheres.

PROPOSAL FOR A LATERALIZED GRADIENT IN NEUROEMBRYOLOGICAL DEVELOPMENT

Gross Morphological Asymmetries

The notion that morphological properties of the brain find their expression during embryogenesis can be traced back at least to the early neuroscientist Pernkopf (see Keller, 1942) and is consistent with general principles of contemporary theory in embryology and evolutionary biology. Thus, the patterns of morphological asymmetries found in adult brains should be attributable to embryological growth patterns. From a complementary perspective, we should be able to "read" adult asymmetries in brain structure as a record of the

forces in embryological growth. Presented in the following pages is a working model of just this sort of interpretive view of the various structural asymmetries in the cerebral hemispheres that have been reported in the past 15 to 20 years.

The best known asymmetry found in the majority of right-handed adults' brains was first reported by Geschwind and Levitsky (1968) and was replicated and extended in numerous subsequent reports (e.g., Galaburda, 1984; Galaburda, LeMay, Kemper, & Geschwind, 1978; Galaburda, Sanides, & Geschwind, 1978). The left hemisphere shows a larger surface area of the planum temporale (see Figure 1-4), which incorporates the auditory association area known as Wernicke's area that is central to language comprehension. This asymmetry is found in the majority of infant (Witelson & Pallie, 1973) and fetal brains as well (Chi, Dooling, & Gilles, 1977; Wade, Clarke, & Hamm, 1975).

Another language-specialized area in the left hemisphere is Broca's area in the frontal lobe, encroaching on the Sylvian fissure. The size of this crucial speech production area is paradoxically smaller in the left hemisphere than in the right in the majority of both adult and fetal brains, if measured as the visible surface area, according to Wada, Clarke, and Hamm (1975). However, several reports suggested that this region is more deeply fissurated in the left hemisphere. Following up on this suggestion, Falzi and colleagues (Falzi, Perrone, & Vignolo, 1982) measured the cortical surface area in the regions corresponding to Broca's area, pars triangularis and pars opercularis, in both hemispheres, such that their measurements included the cortex buried inside the sulci. They found this anterior speech region to be larger on the left than the right in three-quarters of their cases, when "hidden cortex" inside the sulci was taken into account in this manner (see Figure 1-5), thus implicating greater fissuration on the left, a point to which we will later return.

Let us focus now on another set of morphological asymmetries reported by Marjorie LeMay (1976, 1977, 1984; LeMay & Geschwind, 1978, LeMay & Kido, 1978), which exist in the majority of adults, children, and fetuses, as well as in corresponding measurements of prehistoric human skulls (LeMay, 1976, 1984). The pattern is a wider and more protruding right frontal lobe, a characteristic referred to as right frontopetalia; there is a converse left-hemisphere bias in the posterior portion of the brain, where a left occipitopetalia (greater backward protrusion) is found along with a wider left occipital region. These patterns are illustrated in Figures 1-6, 1-7, 1-8, and 1-9. Notice that the left occipitopetalia is generally more striking than the right frontopetalia. These characteristics are reflected in gross volumetric measures of frontal and occipital regions (Weinberger, Luchins, Morihisa, & Wyatt, 1982; see Figure 1-10) and by corresponding asymmetries in the skull itself. As mentioned earlier, they are also evident in fetal brains (Figure 1-11) and skulls (Figure 1-12—note the positions of the bone plates before the fontanelles have closed).

MORPHOLOGIC ASYMMETRIES AS EVIDENCE OF A LATERALIZED NEUROEMBRYOLOGIC GRADIENT

The argument put forth in this chapter is that these morphological asymmetries can be read as a record of a right-to-left gradient in the embryological emergence of the cerebral hemispheres. This proposal depends on several considerations: First, the brain develops in a general anterior-to-posterior direction. Second, this general gradient is complicated by interaction with other developmental gradients, in the ventrodorsal and primary → secondary → tertiary dimensions.¹ Third, it assumes (on the basis of reasoning and some indirect evidence which will be presented later) that earlier onset in the formation and growth of a given region of telencephalon will strongly tend to result in a larger volume of that region (e.g., greater hemispheric width, but not necessarily a larger measurement of cortical surface area of gray matter), relative to the homologous contralateral region. This hypothesis

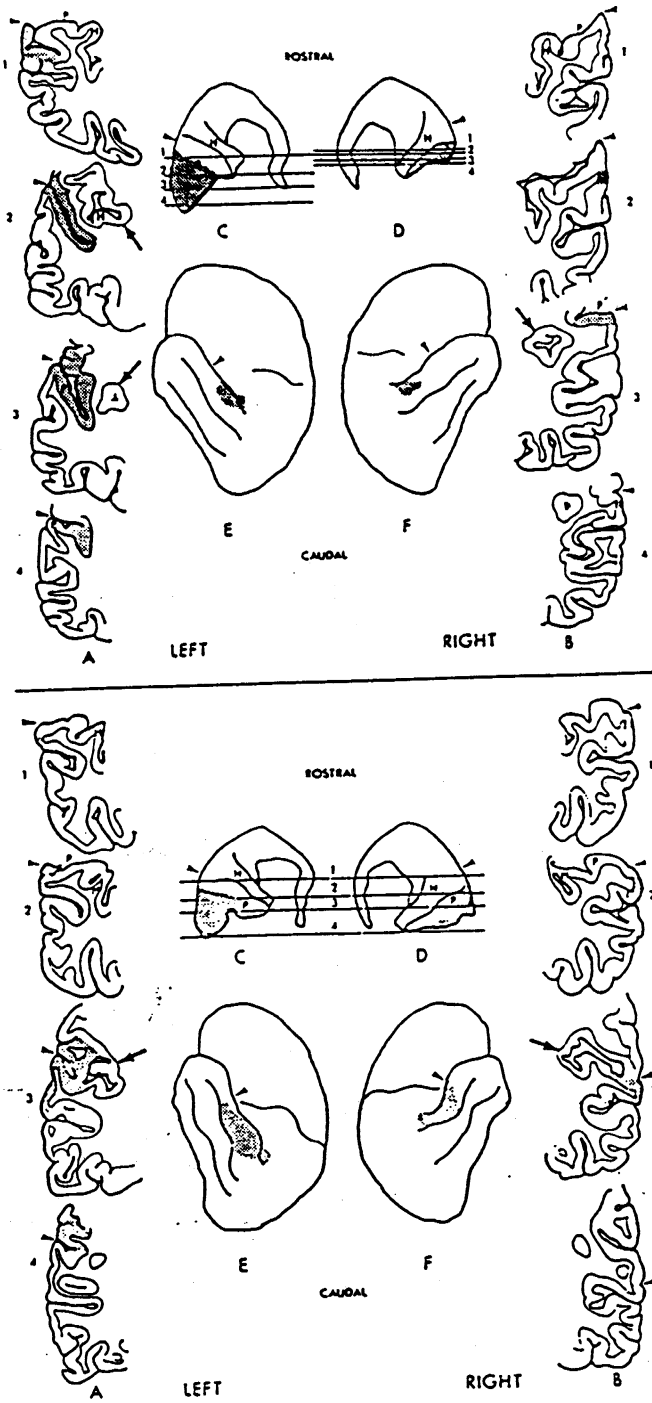


Figure 1-4. Anatomical analyses of two brains are shown here, illustrating the left-hemisphere bias in size of planum temporale. Coronal sections are shown in columns A and B; superior temporal plana in C and D showing planum temporale (P) and Heschl's gyrus (H); and lateral surfaces of brain showing area Tpt and P. Arrowheads point to Sylvian fissures. Note large asymmetry in Tpt and P. Also note buried temporal cortex on coronal sections (arrows). Reprinted with permission of the senior author and publisher from "Cytoarchitectonic Left-Right Asymmetries in the Temporal Speech Region" by A. M. Galaburda, F. Sanides, and N. Geschwind, 1978, *Archives of Neurology*, 35, pp. 812-817. Copyright © 1978 by the American Medical Association.

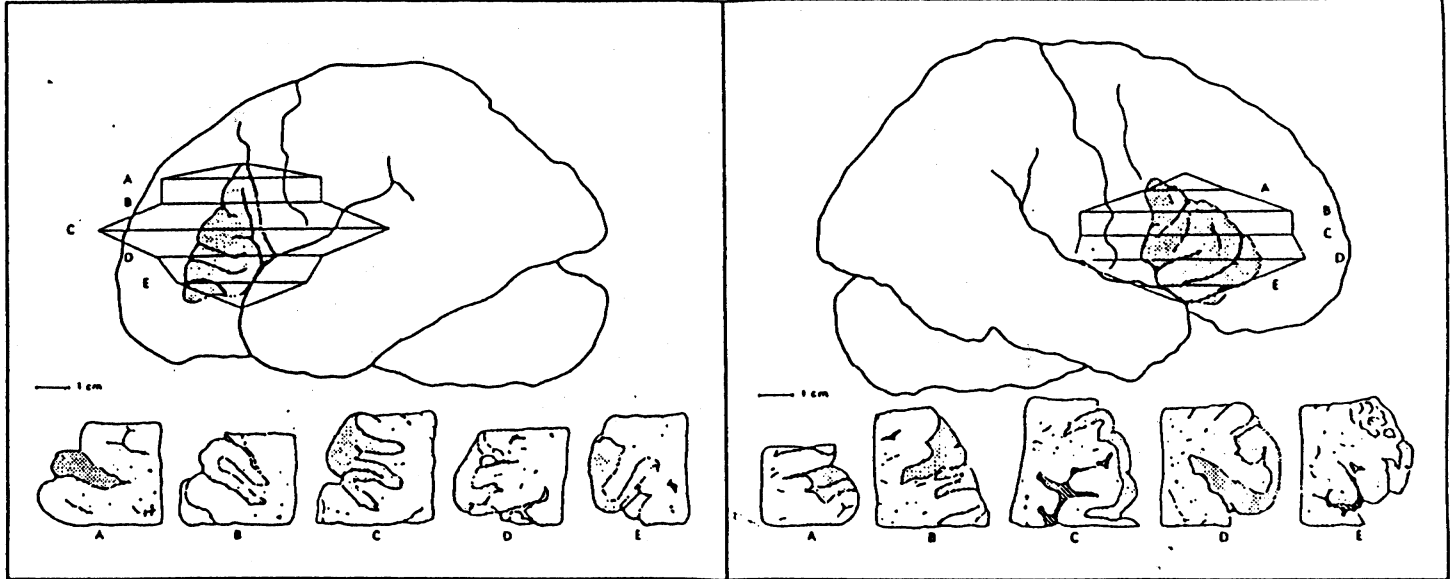


Figure 1-5. "Entire" anterior speech region (defined as pars opercularis and pars triangularis of the third frontal convolution), and its right-hemisphere homologue, shown here superimposed within the polygons on the surface of both hemispheres. The figure illustrates one of the 12 right-handed cases reported in Falzi, Perrone, and Vignolo (1982). The authors measured both the extrasulcal and intrasulcal cortex of these regions (the polygons superimposed on the hemispheres show the sections made in order to measure intrasulcal cortex). There was more *intrasulcal* cortex found in the left hemisphere in three-quarters of their cases, indicating greater fissuration on the left than on the right hemisphere. Reprinted with permission of the authors and publisher from "Right-Left Asymmetry in Anterior Speech Region" by G. Falzi, P. Perrone, and L. A. Vignolo, 1982, *Archives of Neurology*, 39, pp. 239-240. Copyright © 1982 by the American Medical Association.

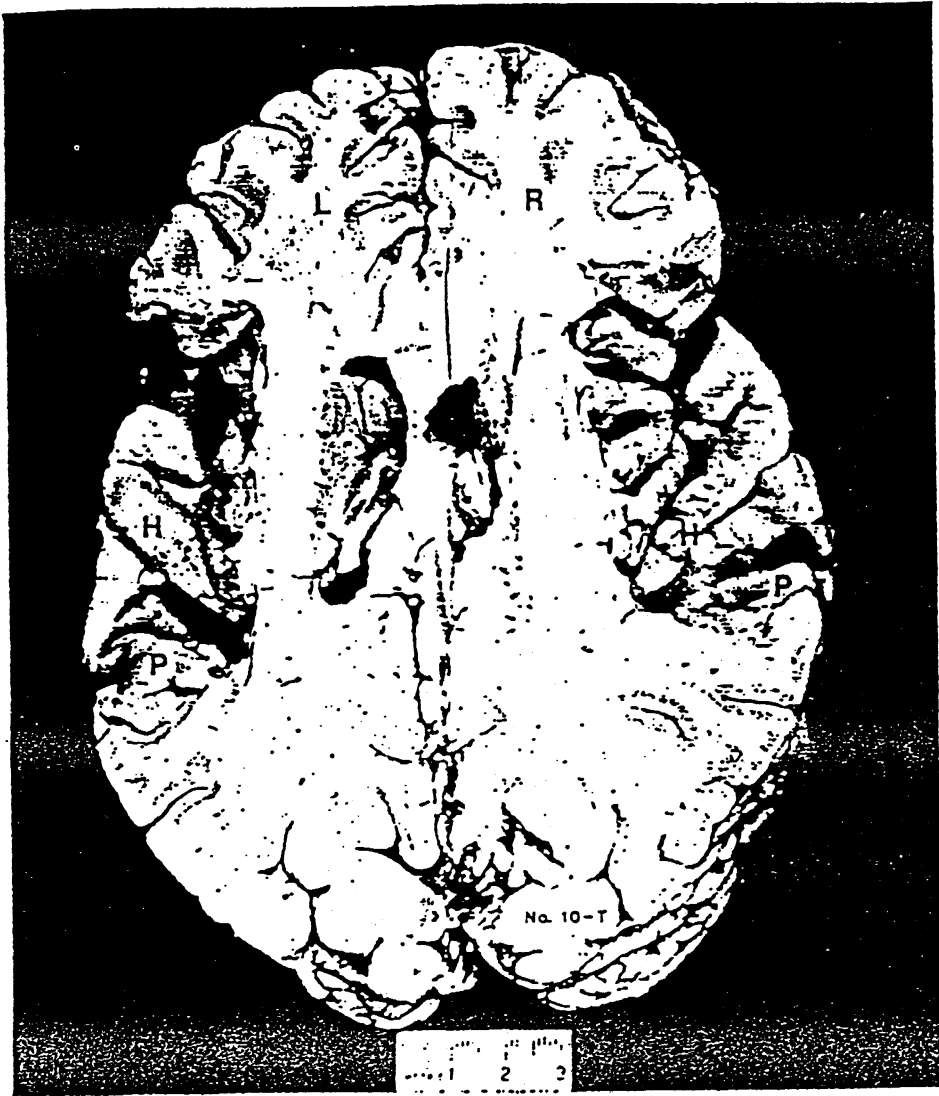


Figure 1-6. Horizontal section of an adult brain, exposing the plana temporale (P) and Heschl's gyri (H). Note both the larger planum on the left, and the right frontopetalia and left occipitopetalia. Reprinted with permission of the publisher from "Early Hemispheric Specialization and Interhemispheric Plasticity: An Empirical and Theoretical Review" by S. F. Witelson, 1977, *Annals of the New York Academy of Sciences*, 299, pp. 328-354. Copyright © 1977 by the New York Academy of Sciences.

of a right-to-left growth gradient is consistent with recent evidence that in fetal development, the major (primary-region) fissures appear 1 to 2 weeks earlier on the right hemisphere than on the left (Dooling, Chi, & Gilles, 1983).

The current proposal differs in one crucial respect from earlier proposals of a right-to-left or left-to-right gradient in brain growth. The earlier models assumed or implied that the earlier-maturing hemisphere would show advanced development over the other hemi-

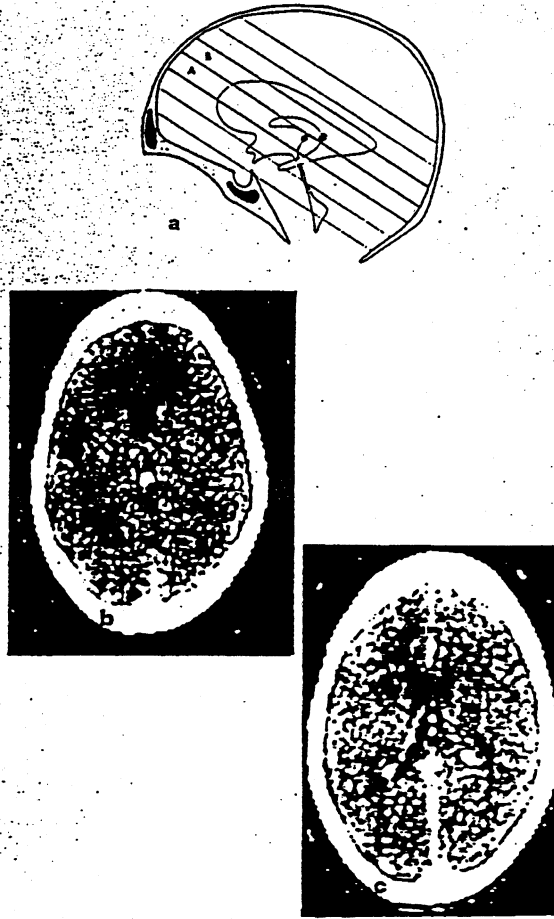


Figure 1-7. (a) Diagram of sections taken through the brain during routine examination by X-ray computerized axial tomography (CT). (b) CT scan through section A. (c) CT scan through section B. Note the left occipitopetalia and wider right frontal region. Reprinted with permission of the publisher from "Morphological Cerebral Asymmetries of Modern Man, Fossil Man, and Nonhuman Primate" by M. LeMay, 1976, *Annals of the New York Academy of Sciences*, 280, pp: 349-366. Copyright © 1976 by the New York Academy of Sciences.

sphere *throughout its extent*. If we combined that assumption with the assumption stated in the previous paragraph that there should be greater volume for earlier-emerging regions, the resulting prediction would be that the earlier-emerging hemisphere should end up larger overall, which is simply not the case. In fact, the simple-minded lateral gradients of earlier models would have to posit some sort of post hoc explanation (like Ptolemy's planetary epicycles) for the fact of larger right-hemisphere volume in the frontal regions but larger left-hemisphere volume in the posterior regions.

The present proposal refers to a dynamic, developmental gradient in the lateral right-to-left axis of the embryo; that is, it refers to a shift over time from right to left. The proposal also takes into account the fact that there are growth gradients along the other main axes of embryologic development—that is, that emergence of the hemispheres takes place *over time in three-dimensional space*. The right-to-left gradient is only one of several

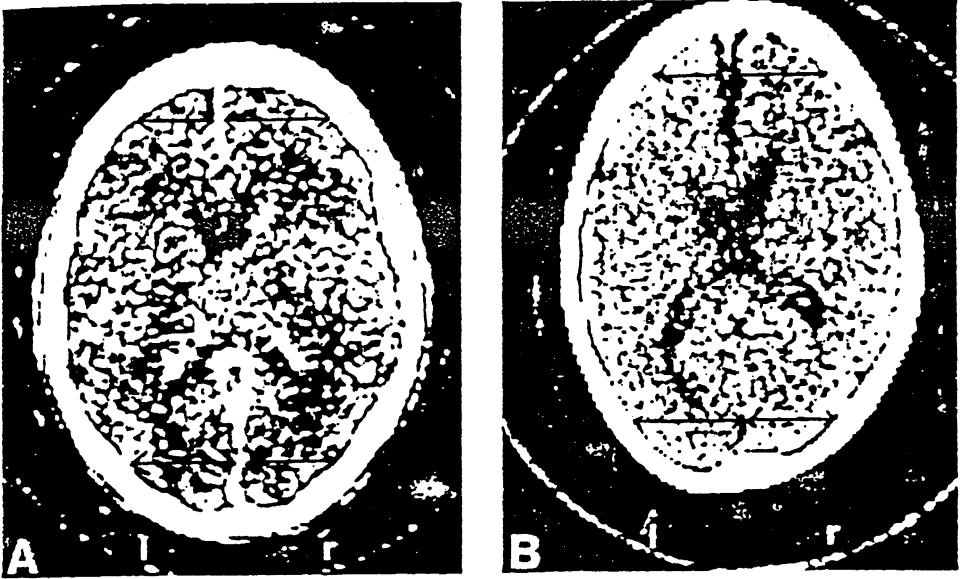


Figure 1-8. CT scans. The central arrows mark the interhemispheric region. Note the wider right frontal and left posterior parietal-occipital areas. (a) Note the slight left occipitopetalia. (b) Note the left occipitopetalia and slight right frontopetalia (patient B has slightly enlarged ventricles). Reprinted with permission of the publisher from "Asymmetries of the Human Cerebral Hemispheres" by M. LeMay and N. Geschwind, 1978, in *Language Acquisition and Language Breakdown*, edited by A. Caramazza and E. B. Zurif, Baltimore, MD: Johns Hopkins University Press. Copyright © 1978 by Johns Hopkins University Press.

axial growth gradients, and its influence on morphological asymmetries can only be understood in the context of the other gradients. In other words, we need to conceptualize a *growth vector* cutting through at least three dimensions over time; this vector represents a *wave of leading growth activity*. There are actually three other developmental gradients that should be accounted for in this hypothesized growth vector (see Figure 1-13 for general reference on human fetal brain growth). The anteroposterior gradient refers to the general direction of growth from the frontal region toward the occipital region (e.g., Gilles, Leviton, & Dooling, 1983). This gradient, however, is complicated by a growth gradient that moves in the following direction: from primary motor and sensory zones to secondary association areas, and finally to tertiary association zones. This is important to keep in mind, because although the motor and premotor zones of the frontal lobe are early-emerging, the forward extension of the *prefrontal* area is one of the last developments of the hemispheres, and is a tertiary association area (e.g., Rabinowicz, 1979; Yakovlev & Lecours, 1967). The third developmental gradient to consider is the ventrodorsal gradient (Jacobson, 1978), from basal regions toward upper or superior regions. In hemispheric development, however, the ventrodorsal gradient is distorted by the fact that the hemispheres develop radially around the core of the basal ganglia and the insula (considered to be the basal or floor region of the hemisphere), moving in an inverted C-shaped direction, folding down and under around the back of the head and then turning forward to form, respectively, the occipital and temporal poles.

The resulting prediction of a three-dimensional growth vector starts with an earlier



Figure 1-9. X-ray of a brain in which the blood vessels were injected with an opaque substance post-mortem. The tips of the occipital lobes are shown by white arrowheads. The ventricular outlines are shown by interrupted dark lines. The frontal and central portions of the right hemisphere are wider than those of the left. Note also the right frontopetalia and left occipitopetalia. Reprinted with permission of the publisher from "Morphological Cerebral Asymmetries of Modern Man, Fossil Man, and Nonhuman Primate" by M. LeMay, 1976, *Annals of the New York Academy of Sciences*, 280, pp. 349-366. Copyright © 1976 by the New York Academy of Sciences.

emergence of right primary motor (and premotor) and sensory regions that, at least initially, lie more frontal and ventral. With concurrent developmental shifts along all gradients, the advancing wave of the growth vector would then proceed toward *earlier* emergence of the *left* side for tertiary association regions (including Wernicke's area) that lie more dorsal and posterior (e.g., superior parietal), again at least initially (but recall the

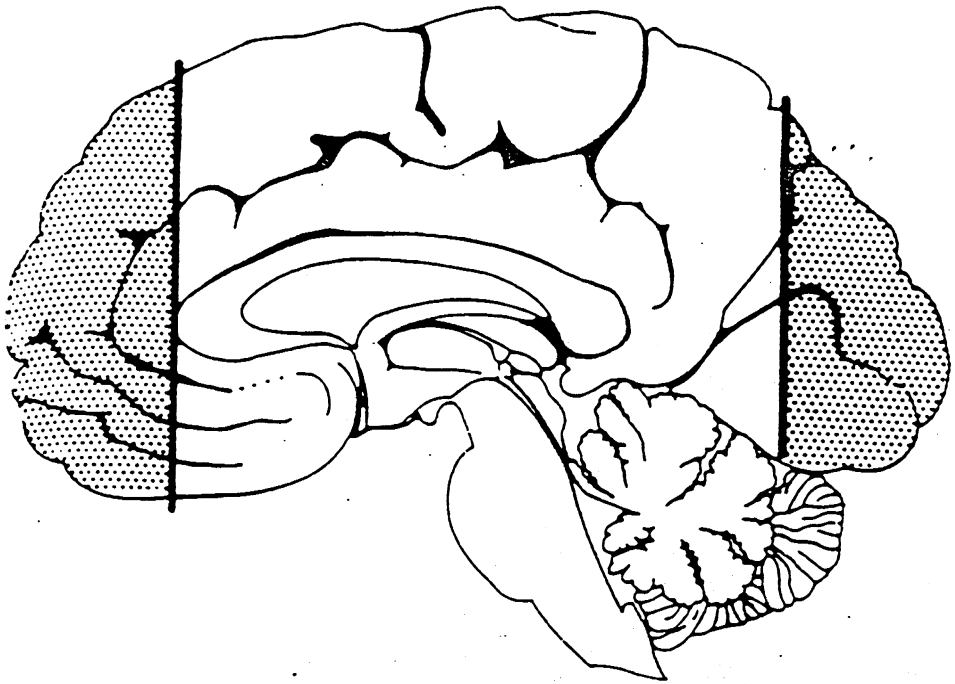


Figure 1-10. Sagittal section of the adult brain. Stipled areas were measured volumetrically. The anterior region was larger on the right, and the posterior region was larger on the left, in the majority of brains studied (taken from the Yakovlev collection). Reprinted with permission of the publisher from "Asymmetrical Volumes of the Right and Left Frontal and Occipital Regions of the Human Brain" by D. R. Weinberger, D. J. Luchins, J. Morihisa, and R. J. Wyatt, 1982, *Annals of Neurology*, 11, pp. 97-100. Copyright © 1982 by Little, Brown and Company.

late and presumed leftward bias in protrusion of prefrontal regions). At some point midway between these extremes, growth should reach equilibrium between the two sides (possibly in secondary association areas).

The effect of this growth vector is a counterclockwise torque evident in the shape of the developing as well as the adult brain. This can only be illustrated here in two dimensions at a time. Figure 1-14 shows a brain viewed from above (from LeMay, 1976), to illustrate the combined influences of the anteroposterior and right-left gradients, producing a counterclockwise torque, as though some force had molded the brain with a fore-to-aft twist on the left, concurrent with an opposing twist on the right. The counterclockwise torque resulting from the combined effects of the ventrodorsal and right-left gradients is seen in coronal views of fetal brains (from Dooling, Chi, & Gilles, 1983), as shown in Figure 1-15 (easiest to view in the 34-week brain at top).

The overall effect on the hemispheres is as though some force had twisted the left hemisphere rearward and dorsal, while twisting the right hemisphere forward and ventral. LeMay's (1984) observations of asymmetries in the positions and angles of the central (Rolandic) fissure and the Sylvian fissure are consistent with this image: The Rolandic fissure appears farther forward (and tilted more vertically) on the right hemisphere, even in fetal brains, whereas the Sylvian fissure slants more horizontally (i.e., lower) on the left, with a lower and more posterior endpoint (Sylvian point). The right Sylvian fissure angles more sharply upward and has a more anterior endpoint.

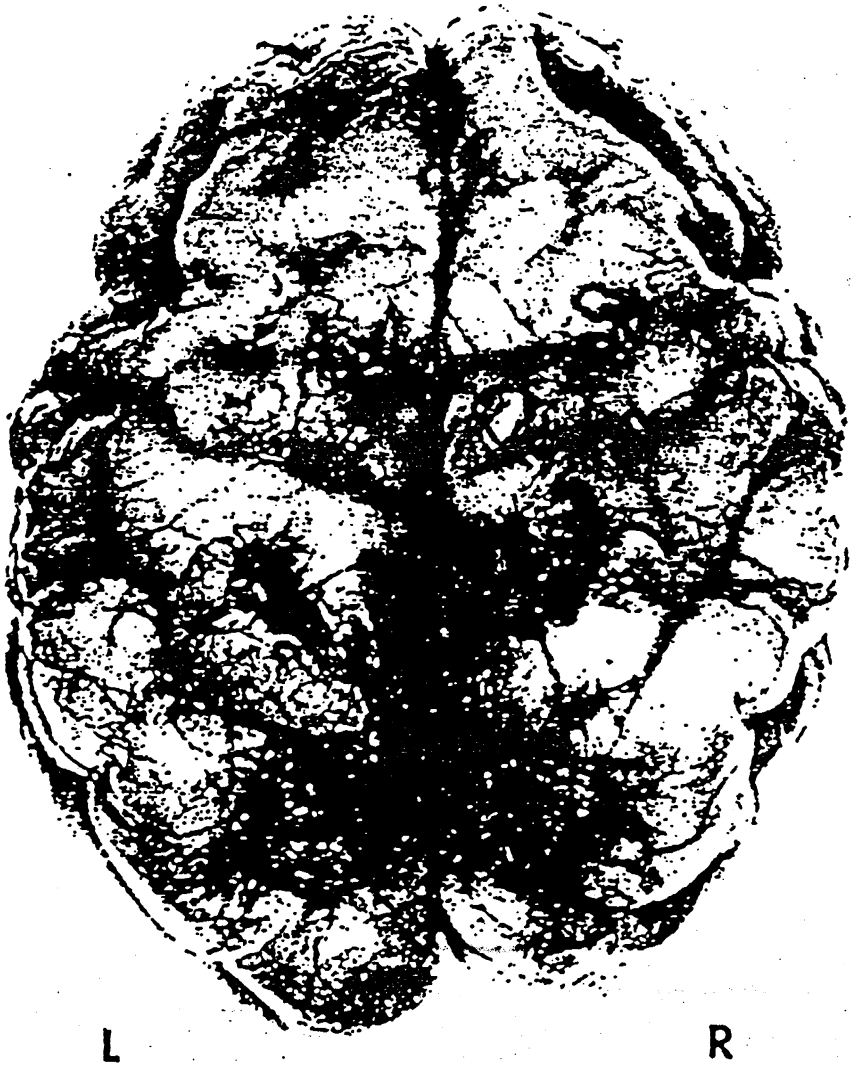


Figure 1-11. Photograph of superior surface of a 32-week-old fetal brain showing a slight right frontopetalia and a more striking left occipitopetalia. Reprinted with permission of the publisher from "Asymmetries of the Human Cerebral Hemispheres" by M. LeMay and N. Geschwind, 1978, in *Language Acquisition and Language Breakdown*, edited by A. Caramazza and E. B. Zurif, Baltimore, MD: Johns Hopkins University Press. Copyright © 1978 by Johns Hopkins University Press.

This model of embryological hemisphere development leads to several predictions. First, the gross morphological effect of earlier-emerging right frontal-motor regions may become attenuated by the later, *left*-biased growth of the tertiary association cortex in the prefrontal region. This would contrast with the convergence of the left-side bias for posterior regions and the left-side bias in the growth of the posterior tertiary association areas. The result should be a more striking left occipitopetalia than right frontopetalia, at least in adult brains. LeMay's (1976) data are in agreement with this pattern. Moreover, since the left-biased tertiary association areas are late to emerge in development, we should expect

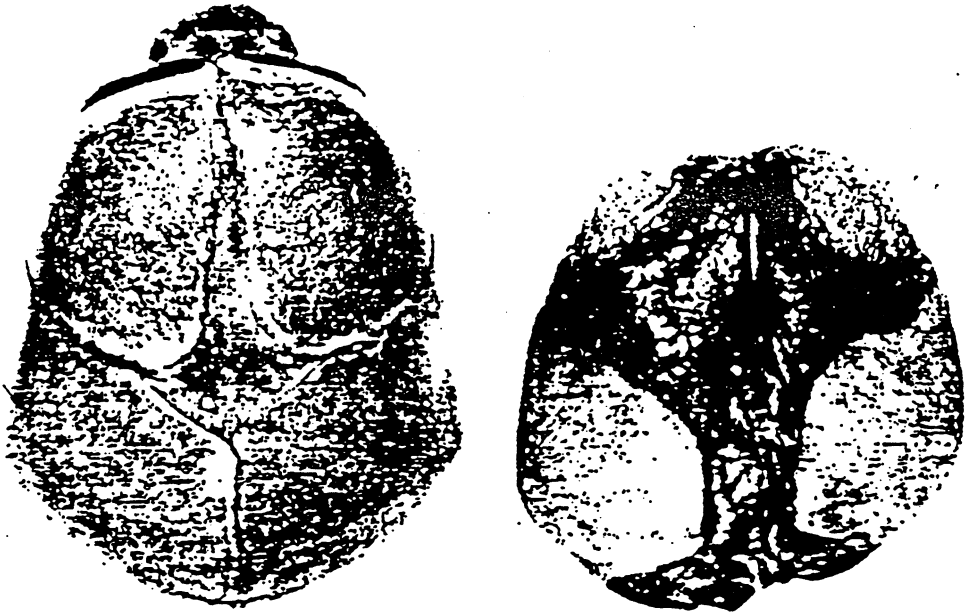


Figure 1-12. (a) Fetal skull. The bone over the right frontal region and the coronal suture, forehead, and lower rim of the orbit are farther forward than on the left side. The vault extends slightly more posteriorly on the left. (b) Upper surface of the skull of a young fetus. The fetus probably had hydrocephalus, but again note the forward position of the right frontal region, the posterior extension of the left hemisphere beyond the right, and the positions of the bony islands of the developing vault. Reprinted with permission of the publisher from "Radiological, Developmental, and Fossil Asymmetries" by M. LeMay, 1984, in *Cerebral Dominance: The Biological Foundations*, edited by N. Geschwind and A. M. Galaburda, Cambridge, MA: Harvard University Press. Copyright © 1984 by Harvard University Press.

to see *greater* evidence of right frontopetalia in fetuses than in adults, but *lesser* left occipitopetalia in fetuses than adults. Again, LeMay's data (1977) are in accord with these predictions. Also in accord is the Wada *et al.* (1975) finding of greater left-side bias in planum temporale among adult brains than among fetuses.

Another prediction is for a left-side bias in earlier emergence of tertiary sulci and gyri, in the tertiary association regions of prefrontal and posterior cortex. There are no data available on this possibility, because only primary sulci have been carefully mapped out on left versus right hemispheres in this manner (see Gilles, Leviton, & Dooling, 1983). In fact, the earlier right hemisphere appearance of fissures on the superior temporal surface actually refers to the formation of the transverse (Heschl's) gyrus, or primary auditory cortex, and not to the formation of Wernicke's association area (a tertiary area) itself (Dooling, Chi, & Gilles, 1983).

Effect of the Growth Vector on Neuronal Organization

The model also carries implications for asymmetries in neuronal organization of cortical areas, and hence for functional development and plasticity of the various regions on the two sides. The impact of the growth vector on neuronal organization must be understood

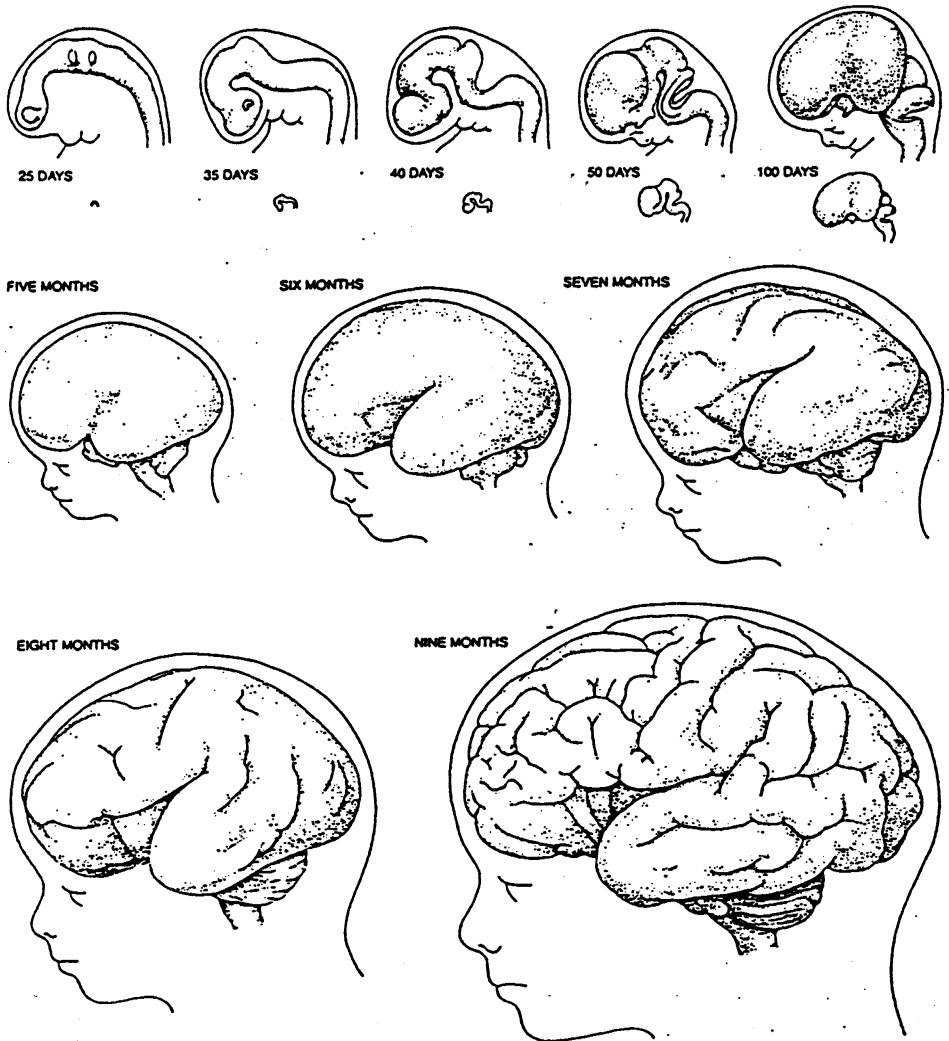


Figure 1-13. Developing human brain, seen from the left side in a succession of embryonic and fetal stages. The illustrations for the bottom two rows are approximately four-fifths life size, and drawn to scale. Those in the top row are enlarged to show structural details; the insets show four-fifths life size scale. Reprinted with permission of the publisher from "The Development of the Brain" by M. W. Cowan, 1979, *Scientific American*, 241, pp. 112-133. Copyright © 1979 by Scientific American, Inc. All rights reserved.

in the context of the sequential development of the six layers of neocortex and their differing contributions to the development of cortical fissuration and gyration, that is, the development of cortical folding. The five cortical layers that contain actual cell bodies of neurons develop in an inside-out sequence (Figure 1-16), with the cells of layer 6, the deepest inner layer, reaching their target positions and developing dendritic and axonal connections earliest (e.g., Rakic, 1980). The earliest-developing layers, 5 and 6, contain primarily efferent cells projecting to regions outside of cortex per se, and so give rise to long, myelinated axons, that is, subcortical white matter. Layer 4 is also directly associated with

PROPOSED GROWTH VECTOR

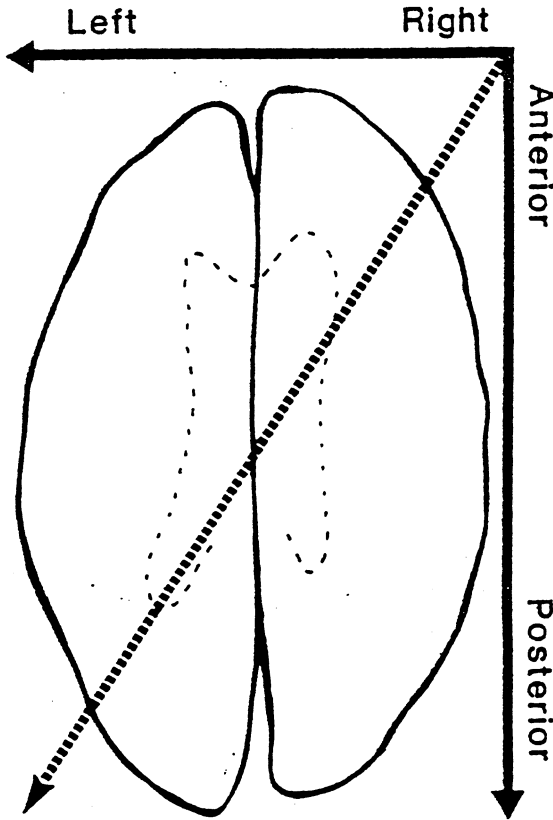
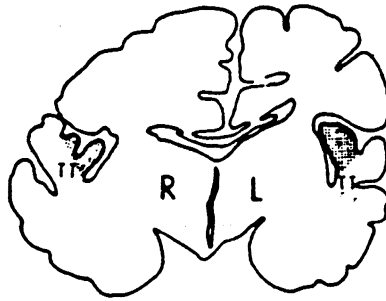


Figure 1-14. Schematic diagram of the proposed growth vector, proceeding from the right anterior to the left posterior region of the hemispheres. This diagram is a simplification of the vector, in that it shows only the left-right and anterior-posterior dimensions (it omits the primary → secondary → tertiary dimension and the ventral-dorsal dimension).

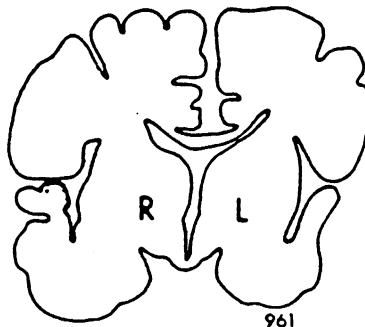
subcortical white matter, because in most regions of cortex it is the layer that receives initial, primary input from afferents to cortex. That is, its cells synapse with incoming long, myelinated axons that arise largely from subcortical areas or from other, relatively distant cortical regions. Thus, the lower layers 4, 5, and 6 of cortex contribute disproportionately to the "white matter" side of regional measurements of ratios of gray matter (aggregated neural cell bodies and short, unmyelinated axons within the cortical mantle itself) to white matter (subcortical myelinated axon bundles) (e.g., Gur *et al.*, 1980; Meyer *et al.*, 1978; McHenry *et al.*, 1978). For those areas with relatively higher proportions of subcortical white matter (low gray/white ratio), there should be a tendency toward greater width and/or volume than in areas with a higher gray/white ratio, given that white matter makes up more of the bulk of the width and volume of the hemispheres than does cortical gray matter.

Conversely, the cells of the most superficial cellular layer, layer 2, form latest. This latest-developing layer contains neurons that make predominantly local connections with



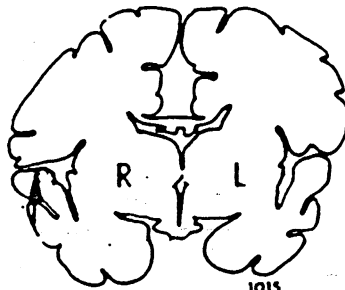
921

34 wks



961

36 wks



1015

39 wks

Figure 1-15. Tracings of photographs of sections in frontal plane of representative fetal brains of different gestational ages. Reprinted with permission of the publisher from *The Developing Human Brain* by F. H. Gilles, A. Leviton, and E. C. Dooling, 1983, Boston: John Wright, PSG. Copyright © 1983 by John Wright, PSG, Inc.

other cells lying within the nearby cortical layers. That is, it does not contribute substantially to subcortical white matter, and thereby contributes relatively more to cortical gray matter. Layer 3, which is next to last in development, also contributes more to gray matter than to subcortical white matter, in that its cells make mostly intracortical connections, including connections with the contralateral hemisphere via the corpus callosum. Thus, layers 2 and 3 contribute disproportionately to the gray matter side of the gray/white ratio. Furthermore, the late-developing, superficial layer 2 is primarily responsible for the process

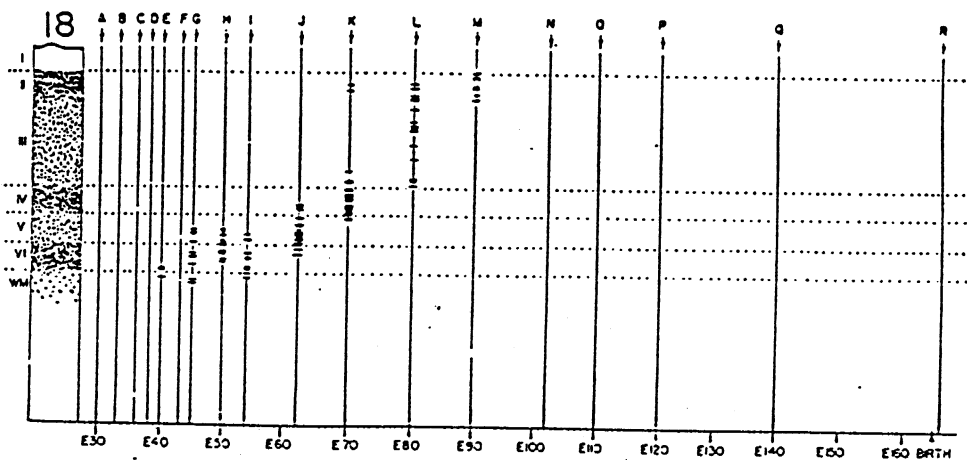
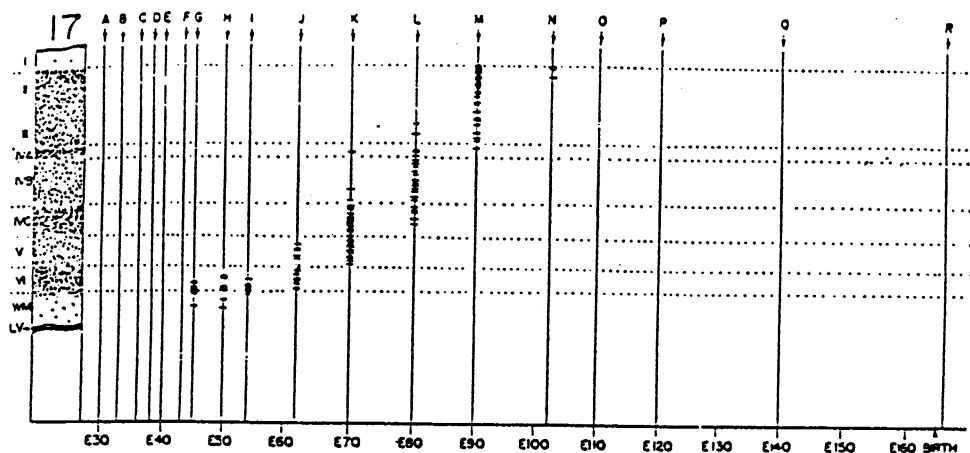


Figure 1-16. Diagrammatic representation of heavily labeled neurons in the visual cortex of juvenile monkeys that had been injected with $[^3\text{H}]\text{-TdR}$ at selected embryonic days. The top picture shows Brodmann's area 17, and the bottom shows area 18. On the left of each diagram is a drawing of cortex sections with cresyl-violet staining with Brodmann's layers indicated in roman numerals. WM: white matter; LV: lateral ventricles. Embryonic days (E) are shown on the X axis, starting with the end of the first fetal month (E27) and ending at term (E165). The vertical lines represent the embryonic days on which subsets of the animals received a pulse of $[^3\text{H}]\text{-TdR}$. On each vertical line, short vertical markers indicate the positions of all heavily labeled neurons. Since $[^3\text{H}]\text{-TdR}$ labels the cells undergoing mitosis at the time of injection, these diagrams indicate that cortex is built in inside-out order, with layer VI neurons generated earliest and layer II neurons latest. Reprinted with permission of the publisher from "Developmental Events Leading to Laminar and Areal Organization of the Neocortex" by P. Rakic, 1981, in *The Organization of the Cerebral Cortex*, edited by F. O. Schmitt, F. G. Worden, G. Adelman, & S. G. Dennis, Cambridge, MA: MIT Press. Copyright © 1981 by the Massachusetts Institute of Technology.

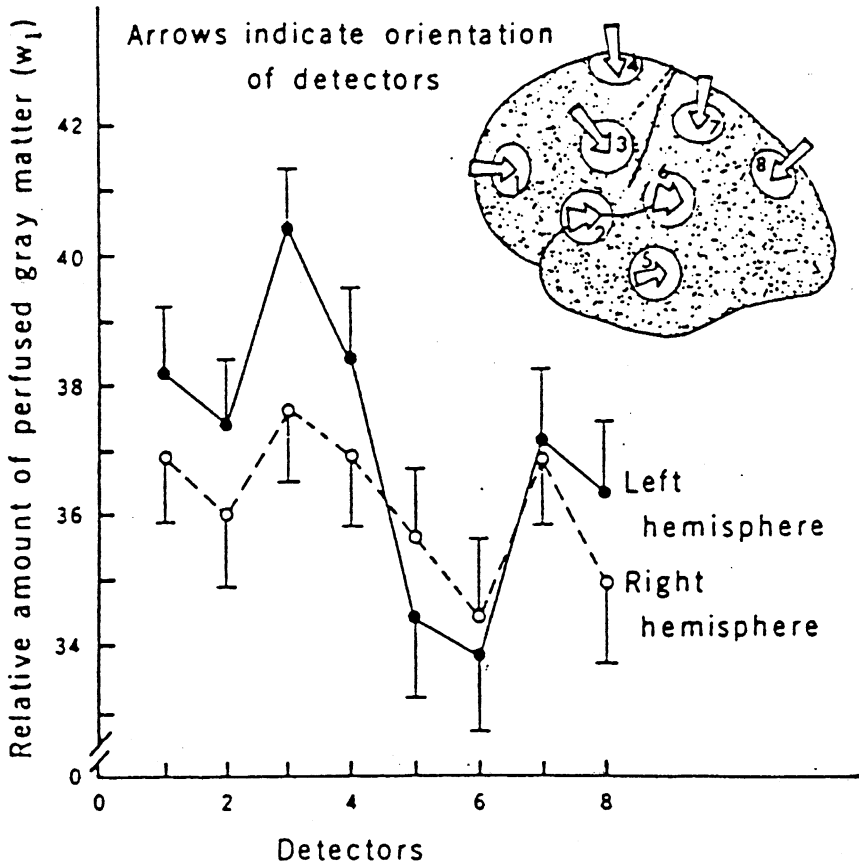


Figure 1-17. Relative amount (\pm standard errors) of perfused gray matter (w_1) plotted separately for 8 homologous regions in the left and right hemispheres. Reprinted with permission of the authors and publisher from "Differences in the Distribution of Gray and White Matter in Human Cerebral Hemispheres" by R. C. Gur, I. K. Packer, J. P. Hungerbuhler, M. Reivich, W. D. Obrist, W. S. Amarnak, & H. A. Sackeim, 1980, *Science*, 207, March 14, pp. 1226-1228, Copyright © 1980 by the American Association for the Advancement of Science.

of cortical fissuration and gyration, during the period of fetal ontogeny when that layer greatly expands in thickness relative to the lower layers, as a result of its developing dendritic processes and proliferation of glial support cells (Jacobson, 1978). Therefore, later development and higher gray/white ratios should be associated with deeper, denser fissuration but also with *lesser* width and volume in that area of the hemisphere, given the argument made in the previous paragraph.

The growth vector would be expected to have the following influence on the development of cortical gray and white matter: For earlier-developing cortical regions relatively greater growth emphasis would be seen in the earlier-emerging deeper cell layers, which should result in smaller ratios of gray matter to white matter and greater regional width/volume. Figure 1-17, taken from Gur and colleagues (1980), illustrates that indeed the gray/white ratio is smaller in the right hemisphere for at least the primary motor and sensory cortical regions. In contrast, later-maturing regions should reflect greater growth emphasis of the later-emerging, more superficial cortical layers, 2 and perhaps 3. This should

yield smaller width and volume but a more deeply fissurated region with higher gray/white ratios, which may imply a somewhat higher degree of local intracortical organization of neuronal connections. In accordance, there is a higher gray/white ratio in the left hemisphere for motor, premotor, and primary sensory areas, (Gur *et al.*, 1980), consistent with Semmes's (1968) claim (based on her studies of somatosensory deficits in unilateral brain-damaged patients) that the left hemisphere is focally organized, whereas the right is diffusely organized. Correspondingly, it is those same areas in which LeMay (1976) found smaller hemispheric width on the left, and Meyer *et al.* (1978) measured a smaller volume on the left. Also, at least for the anterior speech area in the premotor region (Broca's area), there is deeper fissuration on the left (Falzi *et al.*, 1982).

Interestingly, and consistent with the predictions of the growth vector model, there is a higher gray/white ratio in the right hemisphere for tertiary association areas in posterior cortex (parietal association areas, numbered 5 and 6 in Figure 1-17). Recall the model's prediction that tertiary association areas in posterior cortex would emerge later in the right than in the left hemisphere. Also, in posterior regions, LeMay (1976) found lesser hemispheric width, and Meyer *et al.* (1978) found smaller volume, on the right side.

As for development of dendritic processes and of neuronal connections, the influence of the growth vector should be a bias toward later-emerging characteristics in the later-maturing regions of the cortex. Scheibel (1984) has thus far provided the only data relevant to this issue, and it appears to corroborate one part of the hypothesis. In layer 3 of the anterior speech region in the left hemisphere (LOP in Figure 1-18), the dendritic trees of the neurons show relatively greater elaboration of the later-emerging dendritic features, such as proportionally more higher-order branching points, than is true of the homologous region in the right hemisphere (ROP in Figure 1-18).

Implications for Functional Development

This morphological growth vector should also have implications for the development of perceptual and cognitive functions, and for asymmetrical patterns in developmental plasticity. Gross morphological asymmetries of the adult brain, both *in vivo* (Ratcliff, Dilla, Taylor, Milner, 1980) and postmortem (Witelson, 1983), are associated, in fact, with at least some measures of functional asymmetries, notably speech lateralization and handedness. Development of regional functional maturity should proceed according to the same growth vector as already outlined for the morphological development of the hemispheres. Specifically, in the frontal motor and premotor regions, and in primary sensory regions, right-hemisphere functions should mature earlier than the left-hemisphere functions in homologous areas. This is supported by the Best *et al.* (1982) finding of a right-hemisphere advantage for memory-based discrimination of musical notes by 2 months, but no evidence of the homologous left-hemisphere ability for discrimination of speech syllables until 3 months (also compare the speech REA in Entus's 2½-month-olds, 1977, with the lack thereof in Vargha-Khadem & Corballis's 2-month-olds, 1979).² Moreover, it is consistent with numerous reports in the language acquisition literature that children comprehend and produce the emotional intonational properties of language earlier than they comprehend and produce words and word combinations (e.g., Lewis, 1936). Research with both brain-damaged and neurologically intact adults indicates that the right hemisphere is specialized for affective, or emotional, prosodic aspects of spoken utterances both in perception (e.g., Haggard & Parkinson, 1971; Heilman, Scholes, & Watson, 1975; Ley & Bryden, 1982; Papanicolaou, Levin, Eisenberg, & Moore, 1983; Safer & Leventhal, 1977; Tucker, Watson, & Heilman,

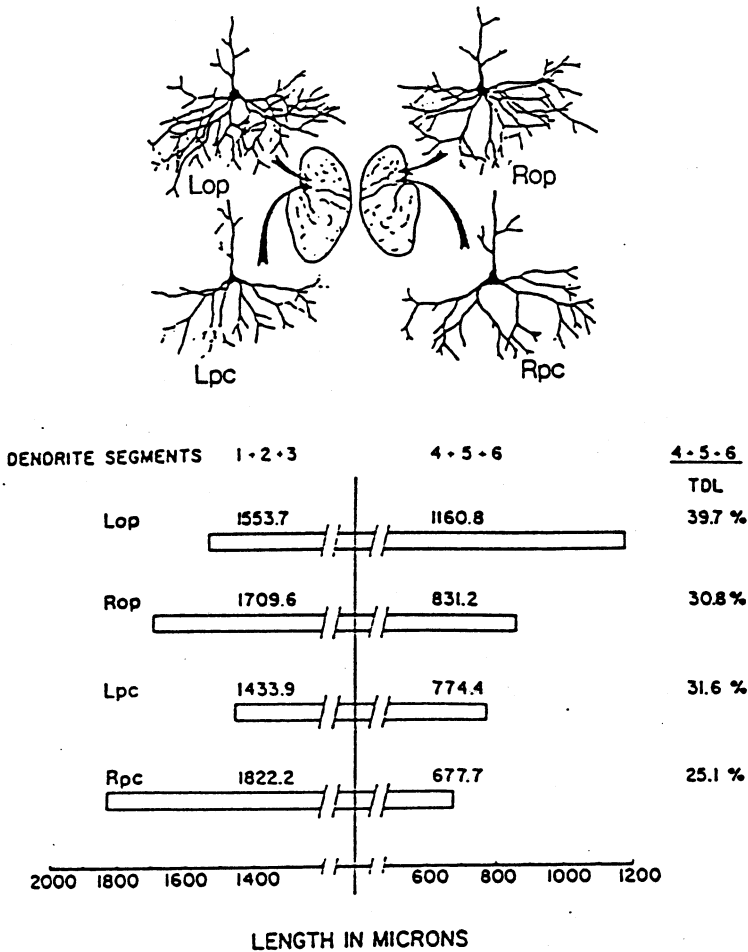


Figure 1-18. The top of the figure shows a somewhat schematicized drawing of typical dendritic ensembles from cells of the left and right frontal operculum and precentral regions in human cortex. Note the increased number of higher-order segments in left operculum (Lop) compared to the other three areas, and the relatively greater length of second- and third-order branches in the right operculum (Rop) and right precentral (Rpc) areas. The bottom of the figure shows dendritic length and proportion of the dendritic ensemble made up of lower-order (1,2,3) and higher-order (4,5,6) dendritic segments in left opercular (Lop), left precentral (Lpc), right opercular (Rop), and right precentral (Rpc) areas. The column of figures on the extreme right shows the percentage of total dendritic length (Tdl) occupied by higher-order dendrites in each region. Reprinted with permission of the publisher from "A Dendritic Correlate of Human Speech" by A. B. Scheibel, 1984, in *Cerebral Dominance: The Biological Foundations*, edited by N. Geschwind and A. Galaburda, Cambridge, MA: Harvard University Press. Copyright © 1984 by Harvard University Press.

1976; Wechsler, 1973) and in production (e.g., Benowitz *et al.*, 1983; Kent & Rosenbeck, 1982; Ross, 1981, 1984; Ross & Mesulam, 1979; Tucker *et al.*, 1976). In addition, according to the neuroembryological principle that later-maturing brain structures generally show greater functional plasticity than do earlier-maturing structures (Jacobson, 1978), the relative degree of plasticity of various cortical regions should be inversely correlated with their rate of maturation.

The proposed pattern of asymmetry in functional development should correspond to a greater plasticity of the later-maturing left frontal-motor, premotor, and primary sensory regions, relative to the plasticity of the homologous right-hemisphere regions. Conversely, there should be later development and greater plasticity on the right relative to the left side for posterior tertiary association area functions. Unfortunately, there are no published data relevant to this issue. Moreover, it will be difficult, to say the least, to match right- and left-hemisphere skills in terms of cortical areas involved, as well as for level of cognitive complexity and/or difficulty, in order to compare their development in normal children and their plasticity in brain-damaged children. For example, one might wish to compare the development and plasticity of reading ability, which depends on a tertiary association region of the left hemisphere in adults (angular gyrus), versus that of complex spatial and face-recognition abilities, which depend in adults on right tertiary association areas (parietal and inferotemporal). In our society, normal children begin reading around 6 years of age but do not develop the ability to solve complex mazes, or a right-hemisphere configurational-processing superiority for recognition of unfamiliar faces, until about 10 years of age (e.g., Kohn & Dennis, 1974; Levine, 1985). If we could assume that the criteria of comparability were met by these findings, the model would then predict greater ability of the *right* hemisphere to acquire reading skills, relative to the left hemisphere's ability to acquire spatial/facial skills, following early unilateral damage. However, there are several inherent problems. The comparability of cognitive levels for these skills is uncertain. The onset ages may be, at least in part, artifacts of our educational system. Finally, acquisition of a skill may call on different cortical regions in the child than those that underlie the execution of the already-acquired skill in the adult (see Kirk, 1985).

INDIVIDUAL DIFFERENCES IN FUNCTIONAL ASYMMETRIES

The growth vector is very likely influenced by hormonal and genetic factors, given the current understanding in neuroembryology that developmental gradients involve some sort of gradient(s) in biochemical influences on the prenatal guidance of neuronal migration and development of neuronal connections (Jacobson, 1978; Sperry, 1963). The possibility of hormonal influences on growth gradients may aid our understanding of the development of sex differences in brain organization and cognitive functions (see also Chapter 14 by Netley & Rovet, this volume), which may be mediated by sex differences in maturation rates (see Newcombe & Bandura, 1983; Waber, 1976, 1977; but see also Rovet, 1983; Waber, Mann, Merola, & Moylan, 1985).³ These sex differences are most apparent in the extreme cases of sexual anomalies, such as Turner syndrome (XO). Turner syndrome is associated with large deficits in spatial abilities (e.g., Waber, 1979), an increase in the rate of prenatal development (Netley & Rovet, 1981), and maldevelopment of tertiary association areas in the right hemisphere (Christensen & Nielsen, 1981). Sex differences in brain organization and function are also apparent in anomalies such as supernumerary-X syndrome (XXX and XXY), which is linked with low verbal relative to spatial abilities, and slow prenatal growth rates (Netley & Rovet, Chapter 14, this volume; Netley & Rovet, 1981, 1982, 1983; Rovet & Netley, 1983).

Hormonal and genetic influences on the growth vector may also be involved in heritable learning disorders. For example, Galaburda and colleagues (Galaburda & Eidelberg, 1982; Galaburda & Kemper, 1979; Galaburda, Rosen, Sherman, & Assal, 1986; Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Kemper, 1984) found symmetrical plana temporale in the brains of all four male dyslexics and the one female dyslexic that they have studied postmortem. The same brains showed abnormalities in cortical neuronal organization, which predominated in the left-hemisphere perisylvian regions. The nature of the latter abnormalities led them to posit a neuroembryological disturbance in the prenatal

migration of neurons during mid-gestation. Hormonal/genetic effects on the growth vector may be particularly relevant to understanding observed sex and handedness biases in the incidence of learning disabilities, for example, the suggestion that testosterone's effect on brain development forms the basis for the higher incidence of learning disabilities among males and left-handers (Geschwind & Behan, 1982, 1984; Marx, 1982).

CONCLUSION

What of the original question: Is the pattern of cerebral asymmetry developmentally invariant, or do functional asymmetries develop? Whether we refer to evidence of functional and/or structural asymmetries, even in very early development the extant data support "developmental invariance" (see also Kinsbourne, 1975; Witelson, 1985). Yet this does not necessarily imply that *nothing* is changing or developing. The timeless constancy of cerebral asymmetries coexists with continuous developmental change at many levels. Lateralized perceptual and cognitive functions *do* undergo developmental change (e.g., the child's language and spatial skills change both qualitatively and quantitatively); plasticity of function also undergoes developmental change (see Witelson, 1985); and the cerebral hemispheres supporting these abilities undergo change themselves (e.g., increases in dendritic arborization, neuronal connections, neurotransmitter functions, glial support cells, and myelination).

According to developmental biology, change and constancy are codeterminants of developmental growth in a biological system. The structural and functional properties of the two cerebral hemispheres do change developmentally, but always in different manners because they develop within the context of an ever-present lateralization of functions, which is continuous with a lateralized gradient of neuronal differentiation and maturation. The argument presented in this chapter is that the normal direction of this lateralizing gradient is from right to left, and that it interacts with gradients in the other main axes of embryologic development to result in a three-dimensional diagonal growth vector from right frontal-motor and primary sensory areas to left-posterior and tertiary association areas. This growth pattern has implications for hemispheric and regional differences in gross morphology and neuronal organization, as well as for differences in plasticity and in maturation of perceptual and cognitive functions.

ACKNOWLEDGMENT

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NOTES

1. There is also a general mediolateral gradient, but Jacobson (1978) states that it is less consistent than the other gradients; that is, in numerous regions it reverses to a lateromedial gradient, or else there is no obvious gradient in either direction along this dimension. Furthermore, it is difficult to conceptualize a vector of greater than three dimensions cutting through time without using some visualization aid such as computer animation modeling. Therefore, the mediolateral dimension will not be considered further in this discussion of the proposed model for hemispheric growth.

2. This is not meant to imply that music discrimination depends on *frontal* cortex in the right hemisphere. Presumably it would rely, in part, on primary auditory cortex (Heschl's gyrus) in the right hemisphere (see Shankweiler, 1966); the growth vector model does assume rightward bias in development of primary sensory areas. Indeed, a double Heschl's gyrus is more often encountered in the right hemisphere than in the left (Geschwind & Levitsky, 1968; but see also Witelson & Pallie, 1973). In addition, recall that the experimental paradigm required that the infants use short-term memory in order to make their discriminations. Short-term memory ability is largely dependent on the hippocampus, an early-emerging, ventrally located structure within the telencephalic hemispheres (Gilles, Leviton, & Dooling, 1983). Thus, the growth vector model would also predict a rightward bias in hippocampal maturation.

3. The effect of sex differentiation on the growth vector may also be related to sex differences in morphological asymmetries for other body parts, such as the hands and feet (Levy & Levy, 1978; Means & Walters, 1982); the latter asymmetries, in turn, appear to be traceable to prenatal development (Mittwoch, 1977).

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