SUMMARY: Morphological speech zone asymmetry in man cannot be due to environmental or developmental factors after birth. The functional implication of such a finding is not yet clear. Morphological asymmetry of the human brain is paralleled by electrophysiological evidence of cerebral hemispheric asymmetries. The results of our analysis of 50 infants suggest that clear occipital-temporal coherency asymmetry similar, but not identical to the adult pattern, also exists at or near birth. These asymmetries are generated by stimuli with no verbal content and in infants who presumably have no or an undeveloped capability for language. It is suggested that language is only a part of much more fundamental asymmetries which include the processing of auditory and visual information. Our results, and those of others, are consistent with the assumption that the left hemisphere is more able to relate stimuli to past experience, either short or long-term, while the right hemisphere is more able to process stimuli which are not easily identifiable or referable. These capabilities would not be based on language, and hence would be expected to develop independently and possibly before speech. The demonstration that reversing electrophysiological asymmetries can be generated with non-speech stimuli in the visual and auditory modalities, and in neonates, supports such an assumption.

INTRODUCTION

During the past few decades we have learned a great deal more about the nature of lateralized human brain function. This has been based on the observations of patients with focal cortical lesion (Geschwind, 1970), bisected forebrain commissures (Sperry, 1974), human cortical stimulation (Penfield and Roberts, 1959) and the carotid amytal test (Wada, 1949; Wada and Rasmussen, 1960) and the findings in normal persons through sophisticated non-invasive neuropsychological procedures such as dichotic listening or tachistoscopic hemiretinal stimulation (Kimura, 1967; 1969) as well as various electrophysiological approaches (McAdam and Whittaker, 1971; Buchsbaum and Fedio, 1969; Wood and Goff, 1971; Matsumiya, Tagliasco, Lombroso and Goodglass, 1972; Morrell and Huntington, 1971; Morrell and Salamy, 1971; Low, Wada and Fox, 1973; Molfese, Freeman and Palermo, 1975). The observations have established our concepts of the left hemisphere’s functional predominance in language-oriented activities involving speech, reading and writing, and the right hemisphere’s superior non-language functions in spatial-perceptual capabilities. However, little is known about when and how the human brain develops its lateralization of hemispheric function.

The first theory defining the limits of the process of hemispheric lateralization was proposed by Lenneberg (1966, 1967, 1970). According to his 1966 paper, “no lateralization seems to be present before age two or three; then there is a period that lasts to about age ten or twelve, during which cerebral lateralization for speech is gradually established.
but may still be put back into the right hemisphere, if the left hemisphere is disturbed. After puberty, lateralization is normally firmly established to the left, and the right hemisphere is no further involved in the speech function; lesions to the left interfere with speech but lesions to the right do not” (Lenneberg, 1966, p. 47). Subsequently a series of observations was made suggesting that hemispheric lateralization may be established much earlier. More recently, Woods and Teuber’s study (1973) on the long-term effect of pre- or perinatal hemisphere lesions, suggested that left hemisphere lesions produce some subtle but definite linguistic loss while certain non-language capabilities are impaired in the right hemisphere lesions.

One assumes that receptive skills precede expressive language skills. Thus, before the child can use his first word meaningfully, he must isolate this word from the stream of speech he hears to form an association between it and its referent, and to learn the oromuscular adjustment necessary for producing this word. Admittedly, such a concept is oversimplified. However, some recent experiments suggest that the infant may be capable of refined perceptual discrimination and perceiving speech sounds (Eimas et al., 1971; Moffitt, 1971; Morse, 1971; Trehub and Rabinovitch, 1972). More recently, Netley reported a complex interaction in which the organization of a neonate’s (two to 14 days old) motor behavior is entrained by and synchronized with, the organized speech behavior of an adult. This suggests that an infant participates developmentally through a complex sociological entrainment process, in millions of repetitions of linguistic forms long before he uses them in speaking and communicating. If this receptive linguistic skill is being established throughout the first year of life and in normal children will later be established in association with the speech dominant hemisphere, it cannot be assumed that the two hemispheres have equal potential for speech at any time.

The major problem is to determine when the human cerebral hemisphere becomes lateralized in terms of structure as well as function. This is a difficult question to answer since no definitive microneuroanatomical study has been undertaken to differentiate the left and right hemispheres of infants. Similarly, most of the neuropsychological studies dealing with human brain lateralization differentiate the unique functional property of each hemisphere on the basis of response or mode of processing ‘verbal’ as against ‘non-verbal’ stimuli. Such differentiation is a pragmatic and convenient one, and yet it is difficult to define precisely the nature of cerebral processes differentiating such input.

In our work, a number of patients have been investigated for medically intractable seizure problems, and for consideration of alternative surgical treatment. Among these patients, 32 of them were found to have received hemispheric insults before the age of six. Patients with severe infantile hemiparesis were excluded. The carotid amytal test results are shown in Table 1. The extent, nature or location of the cerebral lesions as judged by clinical, electrographic and radiological examination did not always explain why, in some patients, speech dominance appeared to have ‘shifted’ and/or ‘shared’ while in others, it did not (Wada, 1969). As shown in Fig. 1, a 15-year-old boy whose cerebral speech dominance was clearly lateralized to the left hemisphere was found to have an extensive agenesis of the left temporal lobe and part of the frontal lobe. If some drastic event had taken place to produce such a profound structural aberration in the anterior to midportion of the speech dominant hemisphere at an early stage of its development, then it is surprising that speech dominance remained unchanged in that hemisphere. Admittedly, it could always be argued that such lesions left the critical speech area intact. On the other hand, the extent of bilaterality of the “speech area” in a number of infant and adult brains was suggested as one factor which might influence the ultimate pattern of cerebral speech.

![Figure 1—Agenesis of temporal lobe and a part of frontal lobe of speech dominant left hemisphere. (Courtesy of Dr. G. B. Thompson).](https://www.cambridge.org/core)
4. There may be sex differences, ever, a few facts should be men­
functional correlates.

3. Asymmetries are inborn, that is, asymmetries appear early in life. How­
function and structure of the human
sive techniques for studying the
findings of Pfeiffer (1936) and von
infant brains. Wada, Clarke and
Hamm, 1975) and confirmed by
Wada (1969) examined 26 infant
brains, as well as 51 adult brains and
was able to confirm the asymmetry found in adult brains by Geschwind
(1968) and showed that infant brains have a comparable asymmetry. This
was extended to 100 adult and 100
infant brains (Wada, Clarke and
Hamm, 1975) and confirmed by
Teszner (1972) and Witelson et al.
(1973).

It is clear that hemispheric asym­
metries appear early in life. How­
ever, a few facts should be men­
tioned which have some relevance to
our understanding of brain asym­
metry with respect to its possible
functional correlates.

1. Asymmetries are distributed on a
spectrum both in Geschwind’s and our series of 100 adult and 100
infant brains.

2. The left side is usually larger.
When this is so, the asymmetry is
greater and there may be no planum on the right. A larger
planum on the right is uncommon, but when this happens there is a
very evident planum on both sides.

3. Asymmetries are inborn, that is, planum asymmetries are present
and visible at the 20th week of gestational age and can be meas­
ured objectively at the 29th week.

4. There may be sex differences, although more work is needed to
verify this.

METHODS AND RESULTS
In the past decade, many noninva­
sive techniques for studying the
function and structure of the human
brain have become available. It is
becoming possible for us to learn the
range of human talents and capabilities in relation to the areas
and the pattern of morphological asymmetry.

If we assume that the presence of
a large temporal planum on the left
side of the adult brain is in some way indicative of the major speech and
language function in that hemis­
phere, then the disclosure of this
similar gross morphological asym­
metry well before the development
of linguistic capability suggests the
fundamental nature of such asym­
metry. Whatever functional signifi­
cance the asymmetry may have, some aspect of it should be detectable
objectively by noninvasive means. If fundamental asymmetry of
the neurotransmitter exists before the development of language and speech
function, then we ought to be able to
disclose such a difference without
using verbal stimuli.

During the past five years, we
initiated a series of studies in this
area. We shall briefly summarize our
findings and leave the details to a
number of papers which have been
published, or are now in press
(Davis, 1973; Davis and Wada, 1974;
Davis and Wada, 1976a, 1976b, 1976c,
1976d).

In contrast to many studies using
time-domain analysis, we attempted
to study coherence and power
spectra of both click and flash
evoked potentials by frequency do­
mains or spectral analysis (Davis
and Wada, 1973, 1974, 1976). In one
study of twenty-two amytal tested
patients (16 left speech dominant,
and 6 right speech dominant) occipital-temporal coherence or
similarity of form was largest in the
speech dominant hemisphere for
click and in the non-speech domi­
nant hemisphere for flash. Discrimi­
nant analysis of coherence asym­
metries of click and flash evoked po­
tentials was 90% accurate as com­
pared to the results of the carotid
amytal test. We have further studied
a group of 12 ‘pure’ right-handers
and 12 ‘pure’ left-handers. Both left­
and right-handed groups displayed
considerable evidence of bilateral
representation, i.e., 10% in pure
right-handed group, and 50% in the
pure left-handed group.

Extending our study to 16 infants
(mean age of 5 weeks), we found
asymmetries of visual and auditory
evoked potential coherences which
were similar to those of the adult.

Asymmetries of auditory evoked po­
tential coherence were significantly
greater in the left hemisphere
(P < 0.005). Of the 16 babies, 13
showed greater left hemisphere au­
ditory evoked potential coherences,
and 10 showed greater right hemi­
sphere visual evoked potential coher­
ces. The ratio of left over right
hemisphere coherence was used to
measure shift of asymmetry from
one hemisphere to the other. In 12 of
the 16 babies, this ratio increased for
click stimuli and decreased for flash
stimuli (significant at P < 0.01).

These results indicate that the
form of occipital and temporal re­
sponses to clicks are more similar
within the left hemisphere than
within the right, and that flash
stimuli cause this form similarity to
shift towards the right hemisphere.

Occipital to temporal asymmetries
were also seen in the power spectra,
which measured the amount of 3-9
Hz., amplitude-related energy in
each evoked potential. The flash
evoked potential power was signifi­
cantly different among the four re­
ording areas (P < .005) and was
greater in the two occipital areas.

Similarly, clicks produced signifi­
cant (P < .005) variations among the
four recording areas, but the tem­
poral amplitudes were greatest.

These results show that a flash
stimuli produces larger amplitude
occipital responses, while click
stimuli produces larger amplitude
temporal responses.

The power spectra were also
lateralized. For flash stimuli, the
right occipital power was signifi­
cantly greater than the right tem­
noral (P < 0.005), and the right hemi­
spheric differences became insig­
nificant.

Subsequent to the completion of
our initial study, we have extended
our study to 50 infants age 1 day to 5
weeks. These results, shown in Ta­
bles II and III, confirmed our pre­
vious results in 16 babies mentioned
above.

DISCUSSION
The above results show hemis­
phric asymmetries of coherence
and power spectra in neonatal
evoked potentials. Click stimuli pro­
duce a localized, coherent center of activity within the left temporal area. Flash stimuli produce a localized coherent center within the right occipital area.

These click and flash asymmetries correspond to verbal or left hemisphere effects, and non-verbal or right hemisphere effects. However, flashes and clicks have no obvious relationship to speech and generate opposing asymmetries in babies with no developed speech function. Consequently, hemisphere asymmetries may be related to more fundamental processes than language (Davis and Wada, 1974, 1975).

The nature of this more fundamental process is suggested by recent demonstrations of the nature of left hemisphere, verbal functions and right hemisphere, non-verbal functions. These results indicate that the predominance of one hemisphere in processing sensory input depends on the characteristics of both the stimulus, and the subject perceiving them. For example, Bever and Chiarello (1974) have shown that musically inexperienced listeners recognize melodies better with their left ear, and by inference their right hemisphere, while experienced musicians recognize the same melodies better with their right ear. Similarly, Bartholomeus (1974) has shown that recognition of the melody of a song is better within the left hemisphere. Therefore, innate characteristics of the stimulus do not uniquely determine cerebral lateralization. Rather, asymmetries can shift from the left to the right, depending the subject’s state, for instance the task he is involved in, or his experience.

We propose that the basis of this shifting asymmetry is the ease with which the stimulus can be related to the subject’s previous experience. With this criteria, the fundamental process occurring in the left hemisphere would be the association or recognition of a relationship between the stimulus or object and the subject’s previous experience. In contrast, the right hemisphere would be better able to process information which was not readily referable to previous experience. These comparisons could refer both to long term memories and to the short term processes associated with the recognition of a known sequence of sounds in a word.

As examples of this type of referential processing, the left hemisphere would be more involved than the right in the processing of speech by a human, melodies by an experienced musician and printed words by a literate person. In each of these, the locus of processing is defined by the characteristics of both the stimulus and the perceiver.

Meaningfulness as the fundamental process underlying lateralization has been proposed by Matsumiya et al. (1972) using evoked potentials, and by Boller and De Renzi (1967) and Bisiach and Faglioni (1974) on the basis of studies of patients with unilateral brain damage. However, our proposal resolved the ambiguity of ‘meaning’ to one of ‘recognition of relationship’ or ‘association with previous experience’.

Adams (1967) has suggested a similar hypothesis in which grasping the resemblance between a meaningless shape and a real object could aid recognition at a pre-verbal level. The attachment of labels, (coding of identified items) and consequently the entire process of language, would then be an epiphenomenon emerging from this more fundamental process.

The results of Molfese et al. (1975) for neonatal asymmetries can also be interpreted on the basis of this assumption. They showed that speech stimuli produced larger left hemisphere evoked potentials, while mechanical and piano chord stimuli produced larger right hemisphere evoked potentials. These asymmetries occurred in babies with a mean age of almost six months. By this time, they would certainly have become adept at recognizing speech sounds, but probably not so adept at recognizing mechanical noise or musical chords.

Our present results for neonatal asymmetries and our previous results for adults (Davis and Wada, 1974, 1975; Davis, 1975; Davis and Wada, 1976a, 1976b, 1976c, 1976d) can be similarly explained. From this viewpoint, a flash stimulus is unstructured visual information, but a click is highly structured auditory information. Consequently, the easily referable click stimuli would tend to be processed within the left hemisphere, while the unstructured flash would tend to be processed within the right hemisphere. This is supported by the observation that localized, coherent activity shifted to the left for clicks, and to the right for flashes.

The hypothesis of referential and non-referential processing modes for left and right hemispheric activity has been suggested in other forms by other authors (Levi-Agresti and...
Sperry, 1968; Diamond and Beaumont, 1972; Cohen, 1973). The comparative or relational processing of the left hemisphere could be described as analytic, sequential, serial or differential. In contrast, the non-referential mode of the right hemisphere could be termed holistic, gestalt-like, parallel or integrative.

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