Fundamental Nature of Human Infant's Brain Asymmetry

JUHN A. WADA AND ALAN E. DAVIS

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.*

RÉSUMÉ: *L'asymétrie anatomique de la zone du langage chez l'homme ne peut pas être due à des facteurs environnementaux ou de développement survenant après la naissance. La signification fonctionnelle de ces découvertes n'est pas encore claire. L'asymétrie anatomique est accompagnée d'évidence électrophysiologique d'asymétries hémisphériques cérébrales. L'analyse de 50 nouveaux-nés révèle la similitude, mais non l'identité, chez le nourrisson des asymétries cohérentes occipito-temporales que l'on rencontre chez l'adulte. Ces asymétries sont activées par des stimuli sans contenu verbal chez des nourrissons sans capacité de langage. Il semble donc que le langage fait partie d'asymétries beaucoup plus fondamentales qui incluent l'analyse de l'information auditive et visuelle. Nos résultats appuient l'hypothèse qui veut que l'hémisphère gauche serve plus à faire la corrélation stimuli-expérience passée (à court ou à long terme), tandis que l'hémisphère droit sert à analyser des stimuli moins facilement dientifiables. Ces capacités qui ne seraient pas basées sur le langage se développeraient indépendamment et peut-être même avant le langage. Appuyant cette hypothèse est la démonstration que des stimuli non-verbaux dans les modalités visuelles et auditives peuvent, chez le nouveau-né, générer des asymétries électrophysiologiques réversibles.*

Supported by Medical Research Council of Canada grant to J. A. Wada.

Based on a paper given at the New York Academy of Science Conference on "Evolution and Lateralization of the Brain" October 12-15, 1976 at the Roosevelt Hotel, New York.

From the University of British Columbia, Health Science Center Hospital, Vancouver, Canada.

Reprint requests to: Dr. Juhn A. Wada, 2075 Wesbrook Place, U.B.C. Campus, Vancouver, B.C. V6T 1W5 Canada.

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, Lonbroso 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 sound (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 mid-portion 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

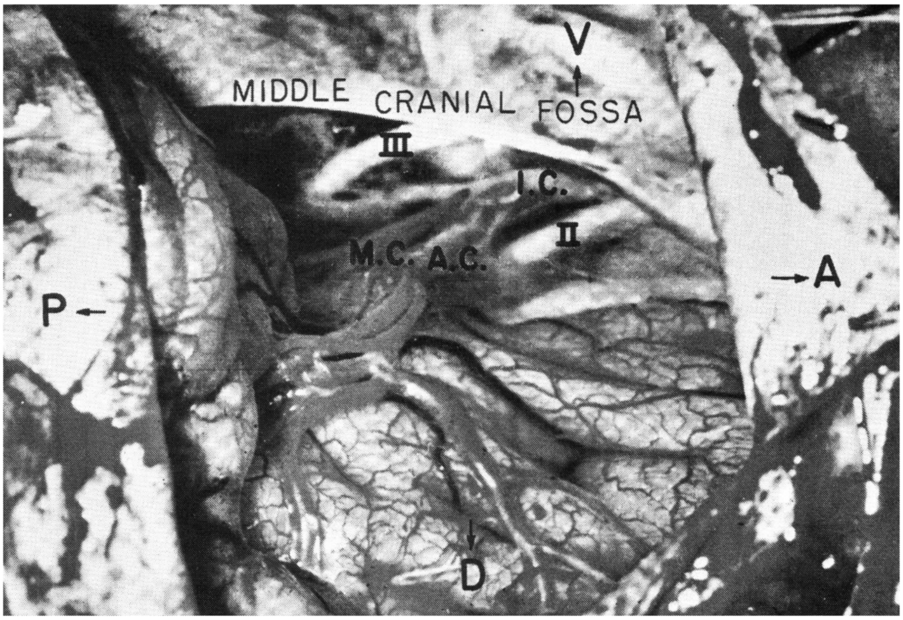

Figure 1—Agenesis of temporal lobe and a part of frontal lobe of speech dominant left hemisphere. (Courtesy of Dr. G. B. Thompson).
A: Anterior D: Dorsal P: Posterior V: Ventral.
II: optic nerve III: oculomotor nerve.
I.C.: internal carotid artery.
M.C.: middle cerebral artery.
A.C.: anterior cerebral artery.

lateralization (Wada et al., 1975), although alternative interpretation of such findings can be entertained. Geschwind, in 1966, confirmed the findings of Pfeiffer (1936) and von Economo and Horn (1930) with respect to the presence of gross morphological asymmetry in the temporal planum. But when does morphological asymmetry develop? 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 asymmetries appear early in life. However, a few facts should be mentioned which have some relevance to our understanding of brain asymmetry 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 measured 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 noninvasive 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 hemisphere, then the disclosure of this similar gross morphological asymmetry well before the development of linguistic capability suggests the fundamental nature of such asymmetry. Whatever functional significance the asymmetry may have, some aspect of it should be detectable objectively by noninvasive means. If fundamental asymmetry of the neurocircuit 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 domain 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 dominant hemisphere for flash. Discriminant analysis of coherence asymmetries of click and flash evoked potentials was 90% accurate as compared 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 potential coherence were significantly greater in the left hemisphere ($P < 0.005$). Of the 16 babies, 13 showed greater left hemisphere auditory evoked potential coherences, and 10 showed greater right hemisphere visual evoked potential coherences. 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 responses 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 significantly different among the four recording areas ($P < .005$) and was greater in the two occipital areas. Similarly, clicks produced significant ($P < .005$) variations among the four recording areas, but the temporal 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 significantly greater than the right temporal ($P < 0.005$), and the right hemispheric differences became insignificant.

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 Tables II and III, confirmed our previous results in 16 babies mentioned above.

DISCUSSION

The above results show hemispheric asymmetries of coherence and power spectra in neonatal evoked potentials. Click stimuli produce 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,

TABLE I

Lesion	Cases	Speech Lateralization		
		Left	Right	Bilateral
Left	19	7	7	5
Right	13	9	2	2
Total	32	16	9	7

Carotid Amytal Test results among patients with hemispheral insult before age 6.

TABLE II

Mean, 3-9 Hz., occipital to temporal coherence (± standard error) within each hemisphere, for flash and click. Average of 50 infants.

Hemisphere Stimulus	Left	Right
Fash	.52 ±.07	.59 ±.05
Click	.73 ±.05	.51 ±.06

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 referrable 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 referrable 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

TABLE III

Mean, 3.9 Hz., power spectra (± standard error) at the four recording areas, for flash and click. Average for 50 infants. Power in microvolts squared/Hz.

Site	Occipital		Temporal	
Hemisphere Stimulus	Left	Right	Left	Right
Flash	370 ±86	349 ±62	160 ±18	90 ±15
Click	87 ±14	71 ± 9	163 ±26	99 ±17

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.

ACKNOWLEDGEMENTS

Able and expert assistance provided by Dr. R. Clark, Miss Anne Hamm, Mr. Edward Jung and Mrs. Mary Mann is acknowledged. Grateful appreciation is expressed for many volunteer patients and their infants without whose willing participation this work would not have been possible.

REFERENCES

ADAMS, J. A. (1967). Human Memory. New York; McGraw-Hill.

BARTHOLOMEUS, B. (1974). Effects of task requirements on ear superiority for sung speech. Cortex, 10: 215-223.

BEVER, T. G. and CHIARELLO, R. J. (1974). Cerebral Dominance in Musicians and Non-musicians. Science 185: 137-139.

BISIACH, E. and FAGLIONI, P. (1974). Recognition of random shapes by patients with unilateral lesions as a function of complexity, association value and delay. Cortex 10/2: 101-110.

BOLLER, R. and De RENZI, E. (1967). Relationship between visual memory defects and hemispheric locus of lesion. Neurology 17: 1052-1058.

BUSCHBAUM, M. and FEDIO, P. (1970). Hemispheric differences in evoked potentials to verbal and non-verbal stimuli in the left and right visual fields. Physiology & Behavior, 5: 207-210.

COHEN, G. (1973). Hemispheric differences in serial versus parallel processing. Journal of Experimental Psychology, 97: 349-356.

DAVIS, A. E. (1973). Power spectral analysis of flash and click evoked responses. Electroencephalography and Clinical Neurophysiology 35: 287-291.

DAVIS, A. E. and WADA, J. A. (1974). Hemispheric Asymmetry: Frequency analysis of visual and auditory evoked responses to non-verbal stimuli. Electroencephalography and Clinical Neurophysiology 37: 1-9.

DAVIS, A. E. (1975). Spectral Analysis of Human Evoked Potentials. Unpublished doctoral dissertation. The University of British Columbia, Vancouver, B.C.

DAVIS, A. E. and WADA, J. A. (1976a). Hemispheric Asymmetries of Visual and Auditory Information Processing. Neuropsychologia: (accepted).

DAVIS, A. E. and WADA, J. A. (1976b). Hemispheric Asymmetries in Human Infants. Brain & Language: (accepted).

DAVIS, A. E. and WADA, J. A. (1976c). Lateralization of cerebral speech dominance by spectral analysis of evoked potentials. Journal of Neurology, Neurosurgery and Psychiatry: (accepted).

DAVIS, A. E. and WADA, J. A. (1976d). Speech dominance and handedness in the normal human. Brain and Language (submitted).

DIAMOND, S. and BEAUMONT, G. (1972). Processing in perceptual integration between and within the cerebral hemispheres. British Journal of Experimental Psychology 63: 509-514.

EIMAS, P., SIQUELAND, E., JUSCZYK, P. et al. (1971). Speech perception in infants. Science 171: 303-306.

GESCHWIND, N. and LEVITSKY, W. (1968). Left/right asymmetries in temporal speech region. Science, 161: 186-187.

GESCHWIND, N. (1970). The organization of language and the brain. Science 170: 940-944.

KIMURA, D. (1967). Functional asymmetry of the brain in dichotic listening. Cortex, 3: 163-178.

KIMURA, D. (1969). Spatial localization in the left and right visual fields. Canadian Journal of Psychology, 23: 445-458.

LENNEBERG, E. (1966). Speech development: Its anatomical and physiological concomitants. IN: The Brain Function. University of California Press, Berkeley, Vol. 3, pp. 37-66.

LENNEBERG, E. (1967). Biological Foundation of Language. Wiley, New York.

LENNEBERG, E. (1970). Brain correlates of language. IN: Neurosciences: 2nd Study Program, pp. 361-371.

LEVI-AGRESTI, J. and SPERRY, R. W. (1968). Different perceptual capacities of major and minor hemispheres. Proceedings of the National Academy of Sciences. Vol. 61: 1151.

LOW, M. D., WADA, J. A. and FOX, M. (1973). Electroencephalographic localization of connative aspects of language production in the human brain. Transactions of American Neurological Association 98: 129-133.

McADAM, D. W. and WITTAKER, H. A. (1971). Language production: electrophysiological localization in the normal human brain. Science, 172: 499-502.

MATSUMIYA, Y., TAGLIASCO, V., LOMBROSO, C. T. and GOODGLASS, H. (1972). Auditory evoked response: Meaningfulness of stimuli and interhemispheric asymmetry. Science, 175: 790-792.

MOLFESE, D. L., FREEMAN, R. B. and PALERMO, D. S. A. (1975). The ontogeny of brain lateralization for speech and non-speech stimuli. Brain and Language 2: 356-368.

MOFFITT, A. (1971). Consonant cue perception by twenty to twenty-four-week old infants. Child Development 42: 717-731.

MORRELL, L. K. and HUNTINGTON, D. A. (1971). Electrocortical localization of language production. Science, 174: 1359-1360.

MORRELL, L. K. and SALAMY, J. G. (1971). Hemispheric asymmetry of electrocortical responses to speech stimuli. Science 174: 164-166.

MORSE, P. (1972). The discrimination of speech and non-speech stimuli in early infancy. Journal of Experimental Child Psychology 14: 477-492.

NETLEY, C. (1972). Dichotic Listening Performance of Hemispherectomized Patients. Neuropsychologia 10: 233-240.

PFEIFFER, R. A. (1936). Pathologie des Hoerstrahlung duner der Corticalen Hoersphaere. IN: Bumke, O., Forester, O. (Eds.) Handbuch del Neurologie. Berlin, Springer 6: 533-626.

PENFIELD, W. and ROBERTS, L. (1959). Speech and brain mechanisms. Princeton University Press, Princeton, New Jersey.

SPERRY, R. W. (1974). Lateral specialization in the surgically separated hemispheres. IN: Schmidt, O., Worden, F. G. (Eds). The Neurosciences: Third Study Program, pp. 5-19.

TEZNER, D. (1972). Etude anatomique de l'asymétrie droit-gauch de planum temporale sur 100 cerveaux d'adultes. (Thesis) Université de Paris.

von ECONOMO, C. and HORN, L. (1930). Ueber Windingrelief, Masse und Rindenarchitek-tonik der supratemporalflache, ihre individuellen und ihre seitenunterschiede.

TREHUB, S. and RABINOVITCH, S. (1972). Auditory-linguistic Sensitivity in Early Infancy. Developmental Psychology 6: 74-77.

WADA, J. A. (1949). A new method for the determination of the site of cerebral speech dominance: A preliminary report on the intracarotid injection of sodium amytal in man. Medicine and Biology 14: 221-222.

WADA, J. A. and RASMUSSEN, P. L. (1960). Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. Journal of Neurosurgery 17: 262-282.

WADA, J. A. (1969). Interhemispheric Sharing and Shift of Cerebral Speech Function. Excerpta Medica, International Congress Series 193: 296-297.

WADA, J. A., CLARKE, R. and HAMM, A. (1975). Cerebral Hemispheric Asymmetry in Humans: Cortical Speech Zones in 100 Adult and 100 Infant Brains. Archives of Neurology 32: 239-246.

WITELSON, S. F. and PALLIE, W. (1973). Left hemisphere specialization for language in the newborn: Neuroanatomical evidence of asymmetry. Brain Research 96: 641-646.

WOOD, C. and GOFF, W. R. (1971). Auditory evoked potentials during speech perception. Science, 1973: 1248-1251.

WOODS, B. T. and TEUBER, Hans-Leukas (1973). Early onset of complementary specialization of cerebral hemisphere in man. Paper presented at the 98th Annual American Neurological Association meeting, June 12, Montreal.