

Comparison of Regional Cerebral Metabolism (PET), Structure
(X-ray CT), and Language in Categories of Chronic Aphasia

Wayne R. Hanson

Veterans Administration Medical Center, Sepulveda, California

E. Jeffrey Metter and Walter H. Riege

Veterans Administration Medical Center, Sepulveda, California and
University of California-Los Angeles, School of Medicine

Daniel Kempler

Veterans Administration Medical Center, Sepulveda, California

Catherine A. Jackson, John C. Mazziotta and Michael E. Phelps
University of California-Los Angeles, California

In a large population of patients with aphasia due to stroke, subgroups of patients can be identified, based on recurring patterns of language impairment identified by the Porch Index of Communicative Ability (PICA), (Hanson, Riege, Metter and Inman, 1982). Many differences in the language behavior of these subgroups have been described, including differential response to long-term treatment (Hanson, Metter, Riege, 1985). How these behavioral differences may be associated with variations in underlying neuropathology is the topic of this report.

Traditionally, our understanding of functional neuroanatomy has been based primarily on studies that compared pathoanatomy and behavior. It has been assumed that an identifiable structural lesion was responsible for the behavioral differences displayed by aphasic patients. More recently, however, FDG positron emission tomography has shown metabolic abnormality extending beyond the zone of infarction, indicating that function in non-structurally-damaged tissue may not be normal (Metter, Waterlain, Kuhl, Hanson, and Phelps, 1981). Previously we have used PET to compare patients in different PICA subgroups and have found differences in overall cortical metabolism (Metter, Hanson, Riege, Kuhl, and Phelps, 1983). However, different patterns of regional hypometabolism for these patient categories have not been studied. It was to describe relationships that may exist between brain metabolism, structural damage, and language in different categories of chronic aphasic patients that the present study was undertaken.

METHOD

Forty-four consecutive aphasic subjects, 5 females and 39 males, were studied. The subjects had been selected based on the presence of aphasia secondary to a left cerebral infarct or hemorrhage with a history of only a single event. Language evaluation, PET, and CT studies were completed for each of the patients. Each subject was evaluated with the PICA and the Western Aphasia Battery (WAB). The PICA test data were used to classify the subjects into five aphasia categories determined from factor analysis scores of 118 aphasic subjects in a previous investigation (Hanson et al., 1982). Further group description of the subjects in each category is contained in Table 1. The WAB test scores were used to classify subjects into traditional aphasia syndromes, such as Broca's and Wernicke's aphasia.

Table 1. Patient descriptive data for aphasia categories.

	*Category 1 N=18	Category 2 N=4	Category 3 N=9	Category 4 N=6	Category 5 N=7
Mean Age (at time of testing)	60.47	60.25	61.00	62.16	63.43
Mean Months Post Onset	33.71	22.00	22.83	17.30	13.83
Mean PICA Overall Percentile	81.00	62.00	40.00	49.00	28.00
WAB Aphasia Types Included Per Category	Anomic Broca's Trans-cortical	Anomic Conduction	Broca's Conduction Wernicke's	Anomic Broca's Conduction Wernicke's	Broca's Conduction Global Wernicke's

*Patients were classified into five aphasia categories determined from factor-analysis scores of 118 aphasia subjects in a previous investigation (Hanson, Riege, Metter and Inman, 1982).

All subjects were studied with Pet (NeuroECAT) using (F-18) Fluorodeoxyglucose, in a resting state with eyes and ears unoccluded. Local cerebral metabolic rates for glucose were recorded for sixteen brain regions in each hemisphere (Figure 1). Twenty-two normal control subjects were also studied with PET thereby allowing each regional measure for each aphasic subject to be converted to a Z score. A Z score indicates the number of standard deviations a patient's score on each regional measure differed from the normal mean.

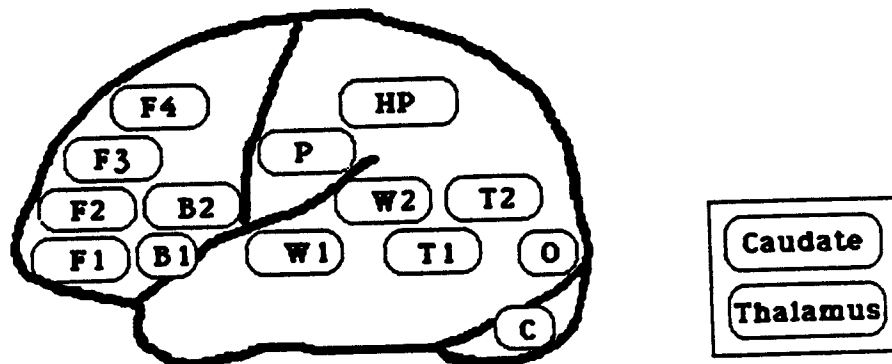


Figure 1. Sixteen regions of interest evaluated for glucose metabolism.

Each aphasic subject was also studied with X-ray CT, with scanning done parallel to the canthal-meatal line. Twenty-two regions were identified

based on the Atlas of Matsui and Hirano, which included 16 regions that corresponded to those measured on the PET scans plus the anterior internal capsule, posterior internal capsule, insula, lenticular nuclei, and the body of the caudate. Each region was rated on a 5-point scale by a neuroradiologist (blind to the rest of the data) and a neurologist familiar with the study (EJM). The scale was: 0 = normal, 1 = atrophy, 2 = damage but no loss of tissue (excluding atrophy), 3 = partial tissue loss, and 4 = complete tissue loss. The two readings for each region were averaged. Ninety percent agreement was found for all regions.

RESULTS AND DISCUSSION

Left Hemisphere Z-scores for metabolic measures for each brain region were averaged for patients in each aphasia category and plotted to provide a profile of regional hypometabolism for each group (Figures 2-6). Z scores, represented by the triangles, indicating the greatest metabolic depression are those the furthest to the left of zero (the normal mean). Downward pointing triangles represent Z scores showing impairment outside the range of 95% of the normal subjects. Comparison of the Z score profiles yields information along three dimensions: (1) the number of brain regions showing significant metabolic abnormality, (2) the location of the metabolically abnormal brain regions, and (3) the extent of hypometabolism per region. Comparison of the metabolic profiles reveals similarities and differences between aphasia categories in the location of brain regions showing extreme hypometabolism.

Figure 2 displays the metabolic profile for patients in PICA Category 1. Six regions show the most extreme hypometabolism for this group. However, these patients have the least severe metabolic abnormality of all the categories, as indicated by the number and position of the downward pointing triangles. Note in particular the measures for Wernicke's area. A shift to the left of these values tends to be associated with increasing overall severity of aphasia. Also, each of the categories show hypometabolism in the thalamus.

In Figure 3 can be seen the profile for category 2 patients, they have 7 regions showing greatest hypometabolism. Note the shift left in the values for Wernicke's area and both parietal regions. Category 2 patients tend to be more severely aphasic than patients in Category 1, particularly in writing.

Aphasia Category 3 patients have a metabolic profile that includes more significantly impaired regions than any other group (Figure 4). Here is shown substantial involvement of the frontal regions -- Broca's area, both subcortical structures, and the continuing leftward progression of the Wernicke's area Z scores. As might be expected, these patients are more severely aphasic than those in the previous categories. Furthermore, they have the most severe motor speech impairments of any patient group.

Patients in Category 4 (Figure 5) are of interest because, while their overall aphasia severity approximates that of Category 3, the metabolic profile has fewer regions with extreme hypometabolism. However, measures in Broca's, Wernicke's, and parietal regions are more extreme for this group than for Category 3. An important difference between the profiles of Categories 3 and 4 appears to be the greater involvement of frontal regions and the caudate in patients in Category 3 and greater severity in hypometabolism in the Wernicke's and parietal regions for Category 4.

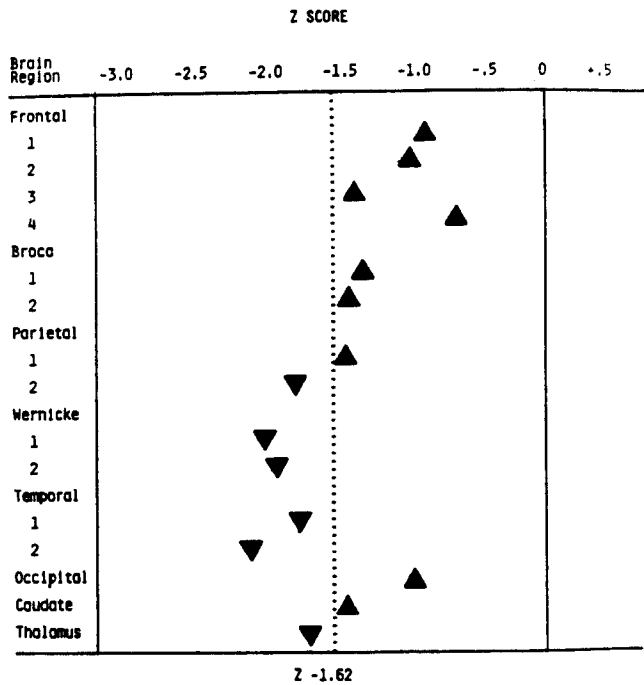


Figure 2. Mean Z score profile of regional cerebral metabolism (PET/FDG) for Aphasia Category 1.

Figure 3. Mean Z score profile of regional cerebral metabolism (PET/FDG) for Aphasia Category 2.

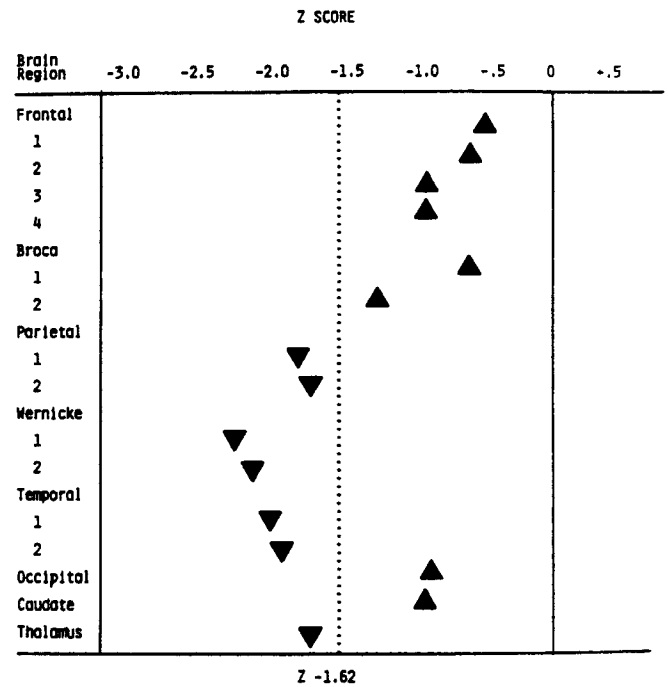
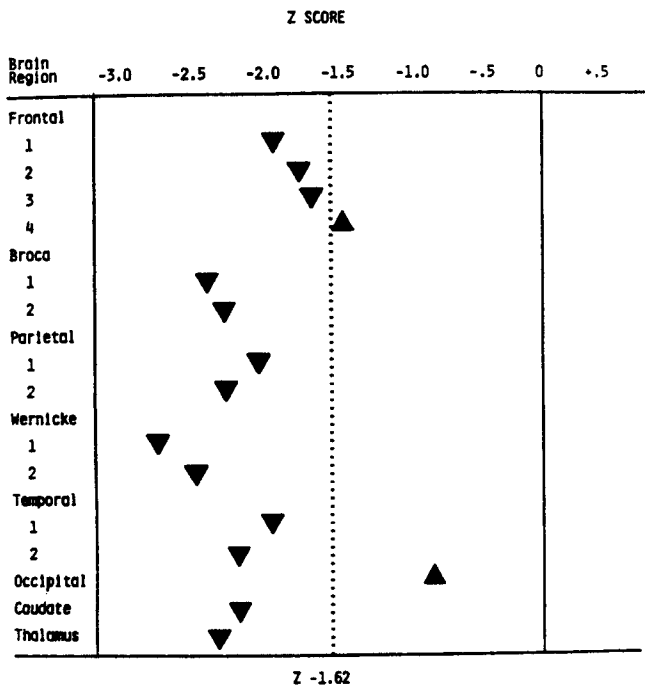


Figure 4. Mean Z score profile of regional cerebral metabolism (PET/FDG) for Aphasia Category 2.

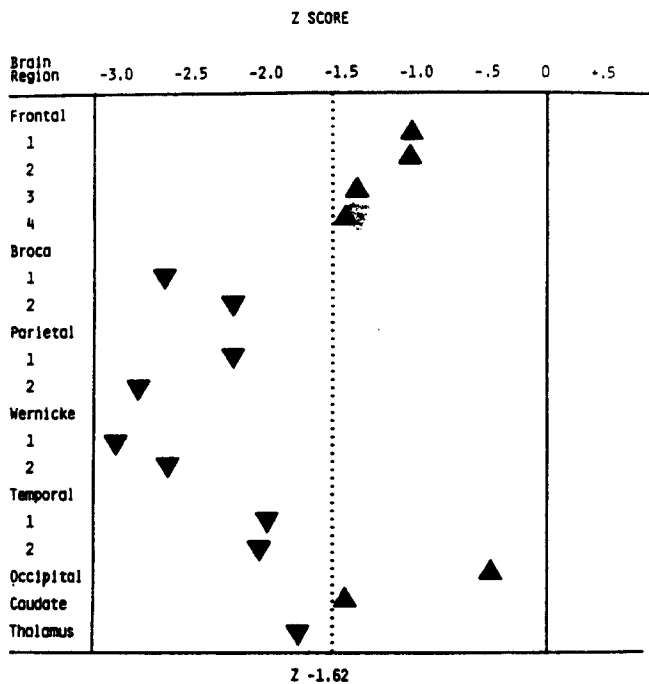


Figure 5. Mean Z score profile of regional cerebral metabolism (PET/FDG) for Aphasia Category 4.

The Category 5 profile indicates the most severe hypometabolism for Wernicke's area of any of the groups (Figure 6). All but four brain regions have substantial impairment and, behaviorally, patients in this group tend to be the most severely aphasic of all patients tested. "Global" aphasia is seen exclusively in this category. Some patients with severe motor speech impairments are also included in this group. Only Category 5 and Category 3 patients show substantial hypometabolism in the head of the caudate.

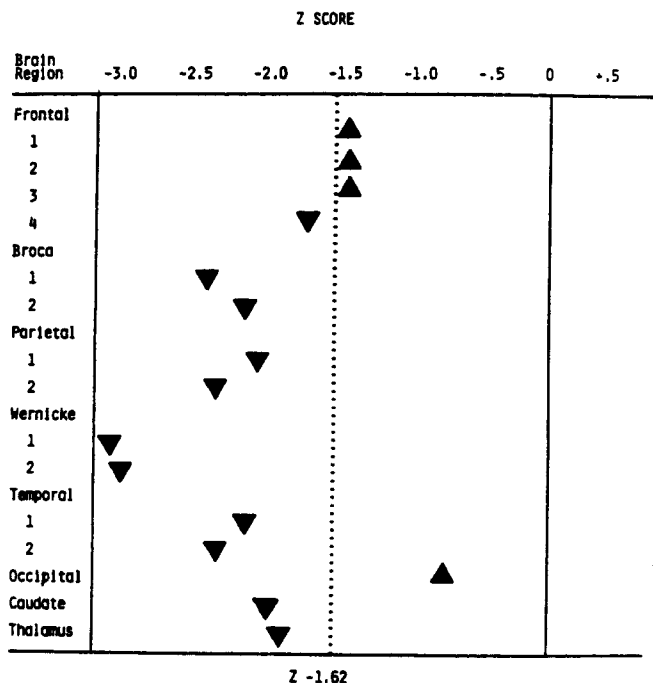


Figure 6. Mean Z score profile of regional cerebral metabolism (PET/FDG) for Aphasia Category 5.

CT ratings for regions corresponding to those studied with FDG PE have been averaged for each aphasia category and are presented in Figure 7. Damaged regions with mean CT ratings from 1 to 2 show diagonal lines. Regions with more severe damage, ratings greater than 2, are more completely filled in. Figure 7 shows CT findings for patients in Category 1. In none of the regions did the average rating exceed 1.9. Patients in this group had the least severe structural damage of any of the patients studied. Nine regions, 6 cortical and 3 sub-cortical, show mild damage. The cortical damage is temporo-parietal and the subcortical damage includes the body of the caudate, the insula, and the lenticular nucleus.

Category 2 patients, as a group, have more damage than those in Category 1, as indicated by the greater number of involved areas and by the three regions showing severe impairment, namely parietal, posterior temporal, and lenticular (Figure 7). Recall that Category 2 patients have a mild aphasia overall, with particularly poor writing ability.

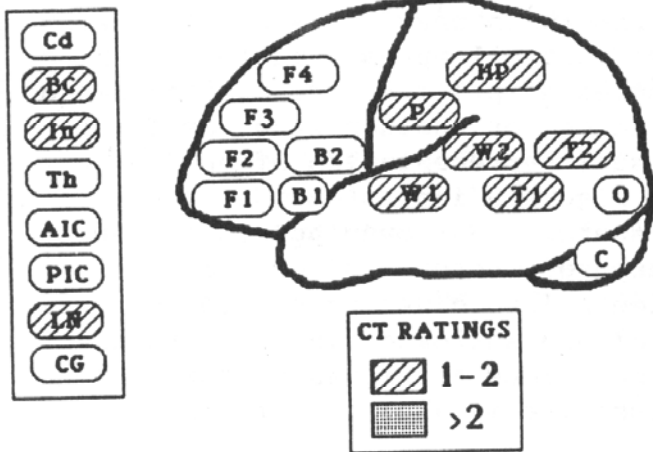
In Category 3 increased severity of structural damage over previous categories is apparent and, for the first time, we see structural damage to Broca's area (Figure 7). This group of patients has the most diffuse pattern of impairment of any of the groups, with the lesion extending frontally and involving more of the deep brain structures. Note, however, that for each patient category no structural damage to the thalamus is observed, whereas hypometabolically the thalamus was uniformly abnormal in each group.

Category 4 patients have fewer impaired regions than Category 3, but they have more severe damage in the temporo-parietal area (Figure 7). Their overall aphasia severity is equivalent to that of patients in Category 3 but their PICA modality scores are quite different.

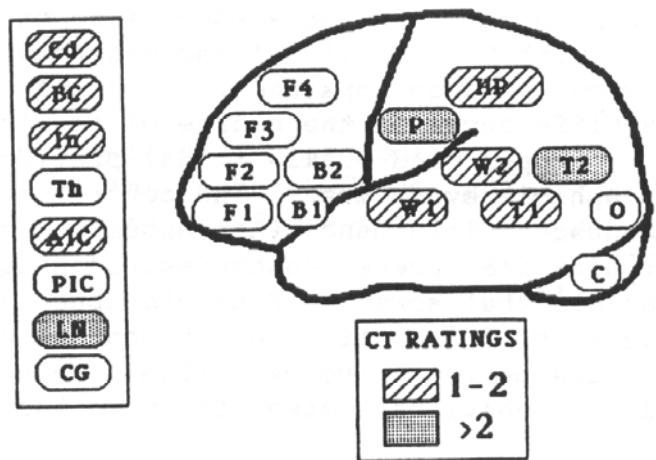
Category 5 patients display widely dispersed structural lesions with particularly severe damage to Wernicke's and parietal regions (Figure 7).

As anticipated, there was much consistency between our structural and metabolic results in these aphasic patients. When the regional Z scores for metabolism were compared to the CT ratings a correlation coefficient of .80 was obtained. Our most uniform finding was impairment of Wernicke's area, both structurally and metabolically, in every patient category. Increase in overall aphasia severity appeared to be associated with a greater extent of impairment to Wernicke's area and parietal regions. Although no evidence of structural damage was ever observed on CT, prefrontally marked hypometabolism did occur in these regions in some patients. These findings serve as evidence of remote effects whereby areas distant from a lesion show reduced metabolism.

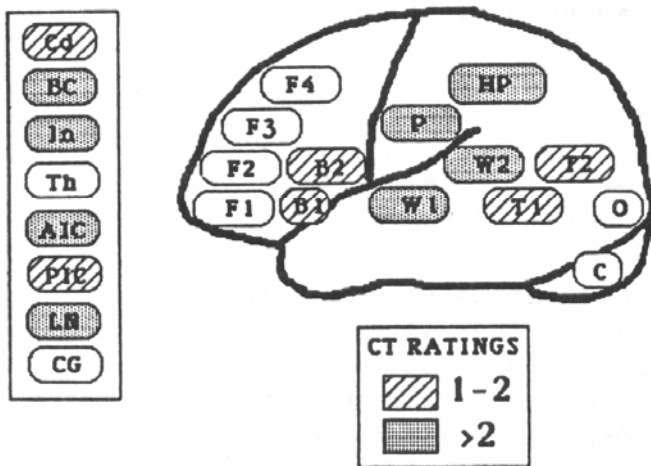
Kertesz (1979) has observed that the classification of aphasic patients is influenced by the tests used to measure the language deficit. Our results support this observation. When the WAB was used to classify patients into traditional aphasia groupings, more than one type of aphasia was included in each PICA category. Both Broca's and Wernicke's aphasia types were seen in each category except Categories 1 and 2. Patients with conduction aphasia were observed in all but Category 1. Global aphasia was confined to Category 5, and patients classified as "anomic" were predominant in Category 1. The two tests did show substantial agreement in their measures of overall severity of aphasia, with a correlation coefficient of .88 between the PICA OA percentile scores and the WAB aphasia quotients. Our data on regional cerebral metabolism indicate areas of overlap among patients in different aphasia categories--in particular, hypometabolism in Wernicke's area. However, each aphasia category is differentiated by a characteristic pattern of metabolic abnormality involving other brain regions.



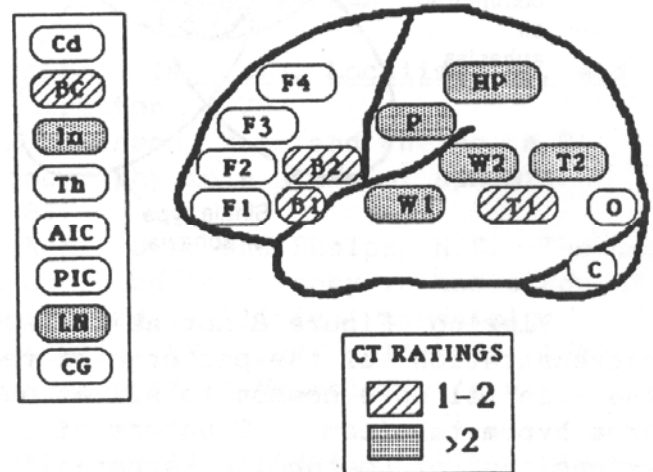
Category 1



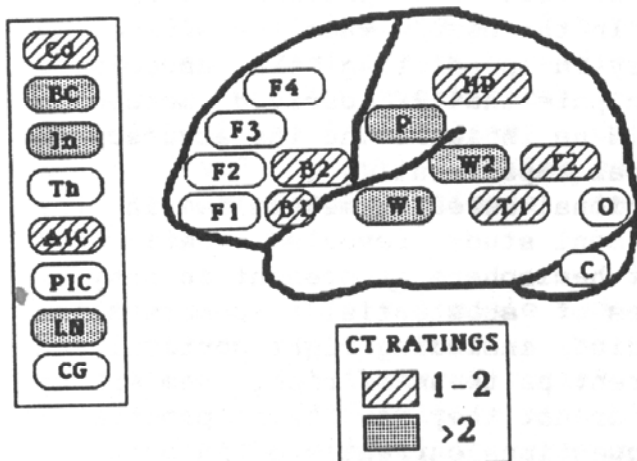
Category 2



Category 3



Category 4



Category 5

Figure 7. Cerebral regions showing structural damage on X-ray CT for Aphasia Categories 1 to 5.

We have stated previously (Hanson et al., 1982) that aphasic syndromes might usefully be conceptualized as vector space that overlaps, with each syndrome retaining some space independent from the others. We are in agreement with Schuell (1964) and others who feel that all aphasic patients share common language impairment--separate categories of patients are distinguished by differences in the degree of impairment on one or another language factor.

Hooper and Dunkle (1984) provide a visual representation of our concept of aphasia syndromes. The central area in Figure 8 indicates the overlap in language disturbance that aphasic persons share. Surrounding this common ground are areas encompassing unique language behaviors or performance factors that serve to separate aphasia patients into clusters or categories. Aware of the caution not to confuse clinical and anatomic classifications of aphasia patients (Poeck, 1983), we were nonetheless intrigued by comparisons of our behavioral categories with their respective metabolic profiles.

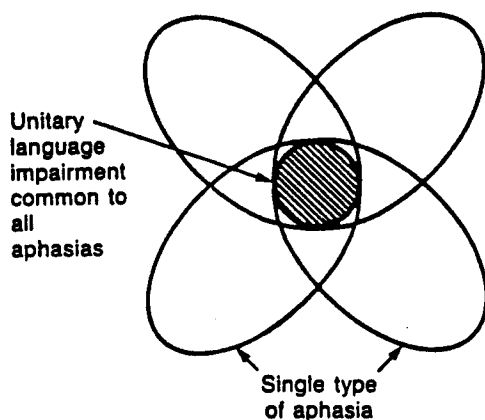


Figure 8. Visual representation of Aphasia Syndromes.

Viewing Figure 8 not as a visual representation of syndromes but as a representation of the patterns of regional hypometabolism in our subjects, the central core common to all of our patients would be the temporo-parietal area hypometabolism. Clusters of patients are then differentiated by their extensions of metabolic abnormality to other cortical and subcortical regions. This suggests that separate categories of patients may also be distinguished by differences in functional pathoanatomy. We think that our PET and CT findings support the hypothesis that the differences between the patient categories we have described are true differences related to the location and extent of neurological lesions as well as to patterns of aphasic impairment revealed by language testing. In the past, when the site of a structural lesion was known, the accuracy in predicting the associated aphasia syndrome was only fair. We anticipate that PET derived metabolic profiles, in addition to X-ray CT, will aid us in improving the accuracy in predicting aphasic syndromes from neurological impairment.

A preliminary look at Z scores for regional cerebral metabolism in the right hemisphere of the subjects in the present study revealed that: (1) marked regional hypometabolism in the right hemisphere is present in many of our patients but not in all. (2) Examples of substantial hypometabolism could be found for most of the 16 areas studied, including right cortical and subcortical regions. Whether or not different patterns of right hemisphere metabolic abnormality exist, and whether or not they may have prognostic significance for recovery from aphasia are questions currently of interest to us. To learn more about left and right hemisphere damage in aphasia, large

numbers of aphasic individuals need to be followed repeatedly with PET, CT, and language studies in order to document carefully the physiological and behavioral changes that may occur with time and treatment.

ACKNOWLEDGMENT

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DISCUSSION

- Q: I am very much in agreement with the idea of looking at metabolic measures of lesions but I have some problems with your study. Although I am not familiar with reading PET scans, I am familiar with reading CT scans and it is not clear to me what it means to have a damaged region without any tissue loss. (Category two of your CT scans.)
- A: A "two" on our CT rating scale would be a change in density without an obvious loss of tissue, indicating that the structure is there, but damaged.
- Q: Are those interval scale judgments? That is, is the difference between zero and one the same as the difference between one and two, and two and three, on an interval scale?
- A: There are difficulties with CT in indicating differences in the severity of damage to specific regions. There is no model that we are aware of to assist in interpreting CT results. It is a different situation with PET

in that we have a specific model, based on known biochemical and kinetic principles, that allows us to make observations from quantitative changes that occur. The difficulty with any anatomical CT study, even when you have the brain in front of you, is the generation of quantitative measures. There are no adequate models for this and our rating system represents our best attempt to deal with this situation.

- Q: From what I know about PET I agree with you. On the behavioral side, I am not at all sure what your aphasia categories represent in terms of deficit.
- A: The aphasia categories have been described extensively in previous publications and presentations so we did not detail those deficits today. The categories were derived from factor and cluster analyses of the PICA.
- Q: Those are formal and interesting analyses of test scores but they have to be translated into a statement of what is wrong with those patients. This methodology of taking very broad measures and factoring patients into heterogeneous groups and looking for lesions in those groups does not seem likely to solve the problem of what the neurologic locus of a particular process is.
- A: This study is a further description of five aphasia categories derived from PICA scores. We thought it would be of interest to generate these PET profiles and to present that information here.
- Q: What is your explanation of remote effects?
- A: A remote effect may result from damage that disrupts communication between brain regions that are functionally related. The remote effect is the lowering of metabolic rate in an area distant from a structural lesion.