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Temporoparietal Cortex in Aphasia

Evidence From Positron Emission Tomography

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• **Forty-four aphasic patients were examined with (F^{18})-fluorodeoxyglucose positron emission tomography in a resting state to determine whether consistent glucose metabolic abnormalities were present. Ninety-seven percent of subjects showed metabolic abnormalities in the angular gyrus, 89% in the supramarginal gyrus, and 87% in the lateral and transverse superior temporal gyrus. Pearson product moment correlations were calculated between regional metabolic measures and performance on the Western Aphasia Battery. No significant correlations were found between the Western Aphasia Battery scores and right hemisphere metabolic measures. Most left hemisphere regions correlated with more than one score from the Western Aphasia Battery. Temporal but not frontal regions had significant correlations to the comprehension score. The left temporoparietal region was consistently affected in these subjects, suggesting that common features in the aphasias were caused by left temporoparietal dysfunction, while behavioral differences resulted from (1) the extent of temporoparietal changes, and (2) dysfunction elsewhere in the brain, particularly the left frontal and subcortical areas.**

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A fundamental issue in aphasiology is whether the disorder consists of single or multiple syndromes. Over the past 100 years, two basic schools of thought have evolved. A unitary, holistic, or nonsyndrome approach championed by Marie and Head[1] has been supported by behavioral similarities between aphasic patients. It has been proposed, for instance, that all aphasic patients, regardless of site of lesion, have similar language problems (eg, anomia, paraphasia) but differ primarily in severity.[1,2] Pathoanatomic correlations have not been of primary concern in these arguments, although supporters have noted that it is difficult to predict aphasic symptoms from lesion data, suggesting that there is no one-to-one mapping between lesion location and symptom. The implication of these data is that there is no strong evidence for a model of strict localization of language function.

The second school of thought developed around the seminal work of Broca, Wernicke, and others, which has argued for the existence of multiple, distinct aphasic syndromes. Evidence for this position has been the observation of clinical differences between aphasic patients. Further, damage to specific brain regions has been associated with distinct symptoms, and these observations have been used to support theories of strict localization of language function. In this model, no single brain region is critical for language, but rather, various regions contribute different language functions, and connections between these regions are essential for intact language ability.[3,4]

One difficulty with attempts to associate lesion site with behavioral changes is that correlations have been based solely on the site of structural damage (through autopsy, computed tomography, or magnetic resonance imaging). Evidence of structural brain damage reveals where the brain has been injured, but little about the functional consequences of the injury. A structural lesion may have minor or major influence on other brain regions that may be critical in the aphasia. Most localization models ignore the effects of the damage on other brain regions, although some include the notion of disconnection of cortical regions based on white matter lesions.[5] Inconsistencies in anatomically based models may in part have resulted from the lack of a means for evaluating the remote effects of structural damage.

Positron emission tomography (PET) using (F^{-18})-fluorodeoxyglucose allows for the examination of glucose utilization within the brain and the study of remote regional effects.[6] Glucose is one of the two major energy substrates used by the brain. The amount of glucose used is directly proportional to the amount of neuronal activity.[7] Preliminary observations[8] have suggested that the left temporoparietal cortex is consistently abnormal in aphasic patients. If a common metabolic abnormality were present in all aphasic patients, it would argue that aphasia may arise from dysfunction in the abnormal region, supporting a unitary-holistic model. In such a model, subjects would be differentiated by the interplay between struc-

Table 1.—Percentage of Patients With Regional Glucose Hypometabolism Based on Left to Right Ratios and Regional Structural Abnormalities as Measured by Computed Tomography in 45 Aphasic Patients*

	Percentage With Abnormalities	
	Glucose Metabolism	Structural Damage
Prefrontal	56	11
Broca's region	67	24
Parietal lobe	82	67
Wernicke's area	87	67
Posterior middle temporal	80	58
Caudate	58	27
Thalamus	69	13

*Reference 10.

Table 2.—Distributions of Clinical Features*

Aphasia Type					
Conduction	Anomia	Broca	Wernicke	Global	Transcortical
8	19	10	5	1	1
Aphasia Quotient (WAB)					
0-20	21-40	41-60	61-80	81-100	
2	6	6	13	17	
Age, y					
30-39	40-49	50-59	60-69	70-79	
1	2	11	23	7	
Months After Onset					
1-3	4-6	7-12	13-36	>36	
6	7	12	10	9	

*The table shows the number of aphasic patients who meet the descriptive criteria. WAB indicates Western Aphasia Battery.

tural and functional abnormalities in different brain regions and their cumulative effects on behavior. Such observations were seen in Wernicke's Broca's, and conduction aphasias where the three syndromes were differentiated by the extent of left subcortical structural damage and left prefrontal hypometabolism.[9]

The question addressed in this study is whether there is a constant glucose metabolic abnormality across all major syndromes of chronic aphasia. In a preliminary study,[10] we compared the extent of structural damage with different brain regions with metabolic changes in the same regions (Table 1). The left temporoparietal region was found to have a consistent metabolic abnormality, but the study was not designed to examine specific temporal or parietal gyri. In this study, we have refined the analysis of regional glucose metabolism for specific gyri and subcortical structures using the method developed by Mazziotta et al.[11] This method allows for an accurate and detailed mapping of the brain cortex and some subcortical structures. This approach allows for better definition of the location of metabolic abnormalities most commonly associated with the presence of aphasia.

PATIENTS AND METHODS

Patients

Forty-four aphasic patients were studied by (F^{18})-fluorodeoxyglucose PET more than 1 month after onset of aphasia. The patients have been previously described in a number of studies.[9,10,18,20-22] They were administered the Western Aphasia Battery (WAB),[12] the Porch Index of Communicative Ability,[13] as well as several experimental batteries assessing various aspects of linguistic knowledge, and an analysis of their spontaneous speech. For the purpose of this study, all tests confirmed the presence of a language abnormality in all patients. Table 2 presents clinical information on the patients. The patients had a variety of aphasias and differing degrees of severity from mild to very severe. The distribution of aphasia type was comparable with other studies[4,14,15] having no specific selection criteria. Our sample consisted of relatively fewer patients with global aphasia, and relatively more with Broca and conduction aphasia. The number of subjects with conduction aphasia was consistent with the experience of Benson[3] who noted that 10% to 15% of aphasic patients have this type of aphasia. In general, the patients in this study represent the general distribution of aphasia severity and type as presented in the literature.

PET

Patients were studied in a resting state with eyes and ears unoccluded using a PET (NeuroECAT device, CTI, Knoxville, Tenn), with a resolution of $9 \times 9 \times 11$-mm full-width half-maximum. Following the injection of the isotope, patients lay quietly on the scanner bed for 40 minutes while the isotope equilibralized and arterialized venous blood samples were drawn, then scanning was begun. Patients were reliably positioned in a consistent manner in the scanner using the techniques developed by Mazziotta et al.[16]

Scans were analyzed using an interactive program that allowed for measures of local cerebral metabolic rates of glucose in milligrams per 100 g of tissue per minute.[17] Multiple regions of the brain were analyzed using the atlas developed by Mazziotta et al.[11] Regions were initially drawn by a nuclear medicine technician well trained in using the regional atlas. The technician was responsible for drawing regions for many PET projects in the laboratory, so that regions drawn from one set of studies were directly comparable with other studies in the laboratory. The regions were prepared independent of the analysis for which they would be used. The goal was consistency in regional measures independent of patient population or study. The scans were then reviewed by one of us (E.J.M.) and finally by the program director (J.C.M.) who compared them with the standards used for all scans analyzed in the laboratory. Only after this extensive review were local metabolic rates of glucose calculated on the final regions. From the large number of regions produced by this method, 20 were selected that had likely relevance in aphasia. These regions were more specific, measuring specific gyri, than data that we have published previously.[9,10]

For comparison with normal subjects, all regions were divided by the mean right hemisphere metabolic rate to give a regional metabolic ratio. Previous studies[18] have shown that the right hemisphere LCMRGlc in these aphasic patients did not significantly differ from normal. Each regional metabolic ratio from the aphasic patients was compared with 95% confidence limits derived from 22 control subjects. A region was considered abnormal if it was outside the confidence limits.

RESULTS

Table 3 presents the percentage of aphasic patients who had abnormal glucose metabolism for each region. The striking observation was that 97% of patients showed decreased metabolism in the left angular gyrus, 87% had abnormalities in the supramarginal gyrus, and 85% in the posterosuperotemporal (Wernicke's) area. When all temporoparietal regions were considered together, 100% of patients showed left temporoparietal hypometabolism. In the right hemisphere, the inferotemporal gyrus had the greatest number of patients with hypometabolism (25% of patients), but when means of the ratios were compared between the aphasic patients and the control subjects, they were not different at $P < .05$.

The constancy of metabolic abnormalities in the left temporoparietal region argues a role in the resulting aphasia. If the level of metabolic abnormality reflects the degree of func-

Table 3.—Percentage of Patients With Abnormal Metabolic Ratios for Each Region

Region	Hemisphere	
	Left	Right
Precentral gyrus	78	6
Laterosuperior frontal gyrus	59	0
Middle frontal gyrus	59	0
Inferofrontal gyrus	54	0
Medial prefrontal gyrus	24	2
Superoparietal lobule	38	...
Supramarginal gyrus	89	13
Angular gyrus	97	13
Posterocentral gyrus	63	4
Laterosuperior temporal gyrus	87	4
Transverse superior temporal gyrus	87	4
Middle temporal gyrus	2	2
Inferotemporal gyrus	70	25
Occipitotemporal gyrus	9	6
Laterosuperior occipital gyrus	70	10
Lateroinferior occipital gyrus	38	9
Caudate head	69	12
Caudate body	31	13
Putamen	71	0
Thalamus	85	9

Table 4.—Correlations Between Left Hemisphere Regional Measures of Glucose and Scores on the Western Aphasia Battery

	Aphasia Quotient	Spontaneous Speech	Comprehension	Repetition	Naming	Read	Write
Laterosuperior frontal gyrus	.51*	.65*	.20	.39*	.45*	.49*	.52*
Medial superior frontal gyrus	.31	.38*	.13	.18	.35	.30	.31
Middle frontal gyrus	.53*	.66*	.18	.41*	.49*	.48*	.52*
Inferofrontal gyrus	.57*	.69*	.25	.48*	.53*	.51*	.53*
Parietal precuneus	.22	.26	.18	.14	.20	.19	.30
Superoparietal lobule	.31	.34	.27	.24	.27	.31	.45*
Inferoparietal lobule	.42*	.47*	.20	.39*	.38*	.43*	.52*
Supramarginal gyrus	.42*	.45*	.29	.41*	.34	.39*	.41*
Angular gyrus	.38*	.31	.46*	.36	.34	.32	.36
Laterosuperior temporal gyrus	.60*	.59*	.44*	.58*	.53*	.50*	.49*
Transverse superior temporal gyrus	.47*	.49*	.30	.46*	.40*	.36	.31
Middle temporal gyrus	.57*	.47*	.60*	.53*	.54*	.53*	.47*
Inferotemporal gyrus	.46*	.44*	.45*	.39*	.41*	.42*	.38*

*$P < .01$ for $P = .01$, $r = .38$.

tional impairment for a region, then correlation to performance on aphasia tests should reflect on any regional brain-behavior relationship. Pearson product moment correlations were determined for standard combined scores from WAB subtests[12] and regional metabolic ratios (Table 4). Correlations were considered significant at $P < .01$, $r = .38$. Significant correlations were found to most left hemisphere regional metabolic measures except for the parietal-precuneus. The only WAB measure that distinguished frontal from temporoparietal regions was the correlations of comprehension to the latter regions. No significant correlations of the WAB scores to the right hemispheric metabolic ratios were found, so these regions were not included in Table 4.

COMMENT

The high percentage of patients with glucose hypometabolism in the left angular, supramarginal, and posterosuperior temporal gyri, suggests that these areas are essential (but not necessarily specific) for the development of aphasia. These observations are consistent with a common underlying functional abnormality in these brain regions, thus supporting, at a pathophysiologic level, the concept of a unitary locus of functional abnormality in aphasia. The nature and extent of the aphasia appears to depend on a complex interplay between the regions of structural damage, their effects on temporoparietal function, and the interrelationship between structural and temporoparietal dysfunction on the remainder of the brain.[8,9,18,19] Thus, although there may be a constant pathophysiology, the complex changes that occur in the brain result in individual differences in the severity and characteristics of the aphasia.

The correlation of most WAB scores to much of the left hemisphere is consistent with the roles of the left side of the brain in the aphasia, as is the correlation of the comprehension score to temporoparietal but not frontal measures. The temporoparietal correlations are similar to what we observed previously with the Porch Index of Communicative Ability and Boston Diagnositc Aphasia Examination.[19] The fact that the levels of correlation of language measures differed for different temporoparietal regions argue for related but not necessarily the same functions for each of these regions. Thus, differential involvement of temporoparietal regions, in part, is associated with differences in the aphasia. The temporoparietal regions appear to be critical for language features common to all aphasic patients.

We have noted elsewhere that behavioral differences between aphasic patients can be explained in part by changes in left frontal lobe metabolism, which are independent of structural damage to the frontal regions.[8,20] The degree of left prefrontal hypometabolism correlated with the extent of structural damage to subcortical regions (internal capsule, lenticular nuclei, caudate, and thalamus).[18] The damage to subcortical structures and prefrontal hypometabolism can be shown to have some common and independent effects on behavior.[21] In this study, the frontal metabolic measures were found to correlate with most WAB scores. Each of these scores is a complex measure that taps a number of underlying processes. This study has not explored the underlying makeup by looking at subtest changes.

Previously, we found for three major aphasic syndromes (Wernicke's, Broca's, and conduction aphasias) relatively similar levels of temporoparietal hypometabolism. The most striking differences were in the degree of prefrontal metabolic abnormalities.[9] We speculated that the agrammatic characteristics of Broca's aphasia and the fluent jargon of Wernicke's aphasia may reflect the differential involvement of the prefrontal areas. In Broca's aphasia the presence of marked prefrontal hypometabolism may imply functional impairment (ie, a loss of capability of the region to do its normal task). In Wernicke's aphasia there is only a mild to moderate degree of prefrontal hypometabolism that may result from a disruption of communication between temporal and

frontal regions. This poor communication (particularly feedback) between prefrontal and temporal cortex may result in the situation where the frontal lobe responds to a need to speak but without appropriate feedback and communication with the temporal lobe thus resulting in jargon.

The absence of correlations between WAB scores and right hemisphere metabolism can have at least three explanations. First, the degree of functional change in the right hemisphere in these aphasic patients was not associated with the performance on the WAB. Metabolic abnormalities were found in the right inferotemporal gyrus in 25% of patients. Any effects that this may have contributed to the aphasia may be masked by the more relevant changes in the left hemisphere. More subtle tests that focus on specific behavioral functions may demonstrate stronger correlations. Second, metabolic effects from transcallosal connections may have different functional meaning than intrahemispheric connections. Small intrahemispheric lesions can cause marked metabolic changes throughout the ipsilateral hemisphere. On the other hand, large lesions that damage large parts of a hemisphere cause only transient metabolic changes in the contralateral hemisphere. Clearly, the mechanisms causing changes in brain metabolism differ when the lesion is within the hemisphere or is dependent on transcallosal connections. For this reason, behavioral interpretations of the effect of an ipsilateral lesion on the contralateral hemisphere needs to be thoroughly investigated. Third, the role of the contralateral hemisphere may be in compensation rather than primary functional loss. The WAB may not adequately measure the consequences of compensation, thus masking the brain-behavior relationship.

Alternate explanations may exist for the constancy of the left temporoparietal hypometabolism in aphasic patients. The changes could be nonspecific resulting from residual ischemia in the temporoparietal regions. This does not seem likely as cortical hypometabolism was observed in patients with intracerebral hemorrhages,[22] and persist for at least 15 to 20 years. Also, the metabolic abnormalities do not respect arterial distributions, so that the persistent ischemia hypothesis does not seem likely.

The data demonstrate a high sensitivity for the temporoparietal region in aphasia. We have no data, though, to argue for its specificity. Nonaphasic patients with left hemispheric lesions are likely to demonstrate left temporoparietal hypometabolism. What will likely differentiate aphasic and nonaphasic patients will be the location and extent of the structural damage, as well as the extent of regional functional disruption by direct damage and from remote effects. Clearly, further studies comparing aphasic and nonaphasic patients are needed to understand these relationships.

The data from this study are consistent with a general two-compartment model of brain abnormality associated with aphasia: (1) temporoparietal, and (2) frontoparietal. Abnormality of the temporoparietal region is necessary for the presence and severity of aphasia as well as characteristics of the language disability. Changes in the frontoparietal compartment (through either direct structural damage or from distant effects of subcortical damage) are important for other features that differentiate individual aphasic patients. Presumably, the temporoparietal regions are responsible for the language deficit, through disruption of linguistic processes. The frontal lobe appears to be involved with the motor and planning factors associated with the ability to complete a language task. This model, in which aphasia results from dysfunction of temporoparietal areas, supports both a unitary concept of aphasia and multiple aphasic syndromes. In this model, multiple behavioral differences existing between aphasic individuals are dependent on differential changes in the temporoparietal region and the extent of subcortical structural damage and frontal lobe dysfunction.

References

1. Darley FL. *Aphasia.* Philadelphia, Pa: WB Saunders Co; 1982.
2. Head H. *Aphasia and Kindred Disorders.* New York, NY: Cambridge University Press; 1926.
3. Benson DF. *Aphasia, Alexia, Agraphia.* New York, NY: Churchill Livingstone Inc; 1979.
4. Kertesz A. *Aphasia and Associated Disorders: Taxonomy, Localization, and Recovery.* New York, NY: Grune & Stratton; 1979.
5. Geschwind N. Disconnection syndromes in animals and man: I and II. *Brain.* 1965;88:237, 585.
6. Kuhl DE, Phelps ME, Kowell AP, Metter EJ, Selin C, Winter J. Effect of stroke on local cerebral metabolism and perfusion: mapping by emission computed tomography of 18FDG and 13 NH3. *Ann Neurol.* 1980;8:47-60.
7. Yarowsky P, Kadekaro M, Sokoloff L. Frequency-dependent activation of glucose utilization in the superior cervical ganglion by electrical stimulation of cervical sympathetic trunk. *Proc Natl Acad Sci U S A.* 1983;80:4179-4183.
8. Metter EJ. Neuroanatomy and physiology of aphasia: evidence from positron emission tomography. *Aphasiology.* 1987;1:3-33.
9. Metter EJ, Kempler D, Jackson C, Hanson WR, Mazziotta JC, Phelps ME. Cerebral glucose metabolism in Wernicke's, Broca's, and conduction aphasias. *Arch Neurol.* 1989;46:27-34.
10. Metter EJ, Hanson WR, Jackson CA, Kempler D, Van Lancker D. Temporoparietal cortex: the common substrate for aphasia. In: Prescott T, ed. *Clinical Aphasiology Conference Proceedings.* San Diego, Calif: College Hill Press. In press.
11. Mazziotta JC, Phelps ME, Plummer D. Optimization and standardization of anatomical data in neurobehavioral investigations using positron CT. *J Cereb Blood Flow Metab.* 1983;3 (suppl 1):S266-S267.
12. Kertesz A. *Western Aphasia Battery.* New York, NY: Grune & Stratton; 1981.
13. Porch BE. *Porch Index of Communicative Ability.* Palo Alto, Calif: Consulting Psychologist Press; 1968.
14. Wertz RT, Deal JL, Robinson AJ. Classifying the aphasias: a comparison of the Boston Diagnostic Aphasia Examination and the Western Aphasia Battery. In: Brookshire RH, ed. *Clinical Aphasiology Conference Proceedings.* Minneapolis, Minn: BRK Publishers; 1984:40-47.
15. Metter EJ, Riege WH, Hanson WR, Kuhl DE, Phelps ME. Commonality and differences in aphasia: evidence from BDAE and PICA. In: Brookshire RH, ed. *Clinical Aphasiology Conference Proceedings.* Minneapolis, Minn: BRK Publishers; 1984:70-77.
16. Mazziotta JC, Phelps ME, Meadors K, Ricci A, Winter J, Bentson J. Anatomical localization schemes for use in positron computed tomography using a specially designed head holder. *J Comput Assist Tomogr.* 1982;6:848-853.
17. Phelps ME, Huang SC, Hoffman EJ, Selin CS, Sokoloff L, Kuhl DE. Tomographic measurements of local cerebral metabolic rate in humans with (F^{18})-2-fluoro-2-deoxyglucose: validation of method. *Ann Neurol.* 1979;6:371-388.
18. Metter EJ, Kempler D, Jackson CA, et al. Cerebellar glucose metabolism in chronic aphasia. *Neurology.* 1987;37:1599-1606.
19. Metter EJ, Riege WH, Hanson W, Camras L, Kuhl DE, Phelps ME. Correlations of cerebral glucose metabolism and structural damage to language function in aphasia. *Brain Lang.* 1984; 21:187-207.
20. Metter EJ, Hanson WR, Kempler D, Jackson CA, Mazziotta JC, Phelps ME. Left prefrontal glucose hypometabolism in aphasia. In: Brookshire R, ed. *Clinical Aphasiology.* Minneapolis, Minn: BRK Publishers; 1988:300-312.
21. Metter EJ, Riege WH, Hanson WR, Jackson CA, Kempler D, Van Lancker D. Subcortical structures in aphasia: an analysis based on ($F-^{18}$)-fluorodeoxyglucose positron emission tomography, and computed tomography. *Arch Neurol.* 1988;45:1229-1335.
22. Metter EJ, Jackson CA, Kempler D, et al. Left hemisphere intracerebral hemorrhage studied by ($F-^{18}$)-fluorodeoxyglucose PET. *Neurology.* 1986;36:1155-1162.

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