CHAPTER

7

Brain Glucose Metabolism in Aphasia: A Model of the Interrelationship of Frontal Lobe Regions on Fluency

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We have been interested in the role of the left frontal lobe in aphasia. In previous studies, we have found left prefrontal glucose hypometabolism (in regions that lack obvious structural damage) associated with changes in fluency measures in aphasic subjects based on studies using (F-18)-fluorodeoxyglucose with positron emission tomography (FDG PET) (Metter et al., 1987a). We assume that changes in glucose metabolism reflect changes in regional capabilities to carry out specific functions. This assumption can be supported by observations that correlations of glucose metabolism to behavioral measures in aphasic subjects are better than correlations of structural damage to the same measures (Metter et al., 1984). In this study, we have expanded our examinations by using information from the literature on two clinical syndromes known to involve frontal lobe and speech to propose and test a model of the interplay of frontal lobe regions on fluency.

Aphemia consists of abnormalities in speech production with preservation of language comprehension. It has been associated with damage to Broca's area, white matter immediately underlying Broca's area, and inferior aspects of the precentral gyrus (Schiff et al., 1983). Kushner and colleagues (1987) studied a 74-year-old man with aphemia using FDG PET. Hypometabolism was found in the inferior precentral cortex, superior insula that extended deep into the caudate, thalamus, and lenticular nuclei. Broca's region was initially involved but improved with time. The conclusion from these and other studies is that the cortical motor generator or motor programming is damaged in aphemia, and this involves Broca's region and/or the precentral gyrus and its outflow to basal ganglia, thalamus, and brainstem nuclei.

Transcortical motor aphasia (TCM) is characterized by severe dysfluency and stumbling in speech but good repetition. It is associated with structural damage anterior and superior to Broca's region in the left frontal lobe. One hypothesis is that TCM results from a disconnection of the supplementary motor area (SMA) with Broca's area or the precentral gyrus (Freeman, Alexander, and Naeser, 1984). The supplementary motor cortex (SMA) is argued to be the initiator of the speech process, while Broca's area is involved with the actual process of completing the act. This model argues that in TCM a dissociation occurs between the general speech initiator (SMA) and the motor generator in Broca's area. Thus it has been hypothesized that SMA initiates speech through its action on Broca's region. Alternately, the lesion data would be consistent with the SMA having a direct effect on the precentral gyrus.

The two syndromes, aphemia and TCM, appear to disrupt frontal lobe functions, including speech initiation, motor programming, and higher decision-making issues regarding whether or not to complete an action. The syndromes demonstrate that perhaps these mechanisms can

be differentially disrupted and result in somewhat different speech disturbances.

From the TCM and aphemia models, we hypothesize that a strong relationship occurs between the supplementary motor area and Broca's area or the precentral gyrus that is involved with fluency of speech in aphasia. We have modeled the interrelationship between the SMA and Broca's region on fluency with path analysis using regional glucose metabolism as a marker of regional function. For completeness in considering the lateral aspects of the frontal lobe, we have included a prefrontal measure. In our previous studies, prefrontal cortex was found to be important in explaining behavioral discrepancies between aphasic subjects (Metter et al., 1989). The goal was to identify a plausable general model that explains the relationship of these frontal regions in fluency.

To accomplish this end, we assume that regional glucose metabolism reflects the ability of the region to complete its behavioral functions. We have shown in a number of studies that this assumption appears to be reasonable [see Metter (1987) for a review]. Path analysis applies regression and partial correlation techniques to evaluate the acceptability of a specific model (Duffy, Watt, and Duffy, 1981). The model shows causality between two variables if three criteria are met: (1) time precedence (one event clearly precedes the other), (2) temporal priority (variables need to be reasonably associated in time, space, and function), and (3) nonspuriousness (there isn't a third variable causing the change in the other two). For the models presented in this chapter, we do not believe that causality can be argued. Rather, the focus is on looking at the functional (metabolic) relationships between the areas based on current thinking regarding the functional roles of the regions in speech.

METHODS

Forty-eight aphasic subjects were studied by FDG PET in a resting state with eyes and ears unoccluded. Clinical descriptions of these subjects have been published previously (Metter et al., 1987b; Metter et al., in press). They had mild to severe aphasias and were tested greater than 1 month after onset, with the vast majority being tested more than 6 months after onset.

Subjects were scanned on the NeuroECAT scanner with resolution of about 10 mm full-width–half-maximum. They were injected with 5 to 10 mCi FDG and then lay quietly for 40 minutes, during which time serial arterialized venous blood samples were drawn. Scanning was then com-

pleted. Regions of interest were analyzed using a standard approach, and local cerebral metabolic rates for glucose (LCMRglc) were reported in milligrams per 100 gm tissue per minute (Phelps et al., 1979).

Four regions were analyzed, including the supplementary motor area (SMA), prefrontal regions of the middle and inferior frontal gyrus (PF), Broca's area (posteroinferior frontal gyrus), and precentral gyrus (PC). Regions were analyzed using left-to-right ratios for each measure to reduce intersubject variability. In previous studies, we have demonstrated that right-hemisphere regional glucose metabolism in these aphasic subjects did not differ from that of normal control subjects (Metter et al., 1987b). Models were generated based on our understanding of the relation of the four anatomic regions. Data were analyzed using path analysis, as previously described (Metter et al., 1988b). Path coefficients were estimated as the beta scores derived from multiple regression analysis. A coefficient was accepted as being important if it accounted for 5 percent of the total variance (i.e., a pathway coefficient of .22).

Each subject was administered the Western Aphasia Battery (WAB) by one of the speech pathologists on the project (Kempler or Jackson). No test-retest data were determined to verify the reliability of scoring on this test. The fluency measure was used as the behavioral endpoint.

RESULTS AND DISCUSSION

Model 1 (Fig. 7-1) assumed that the SMA had an effect on the function of the prefrontal, Broca's, and the precentral regions, as well as a direct action on fluency. We also assumed that the prefrontal cortex acted through Broca's area, the precentral cortex, and had a direct effect on fluency. Broca's area was assumed to affect fluency either directly or indirectly through its action on the precentral gyrus. This model assumes a hierarchical directionality, with the supplementary motor area being the most independent operator and the initiator of speech. This is implied in Figure 7-1 by the directionality of the arrow. The arrow from the SMA to the prefrontal cortex (PF) implies that the SMA is acting on the prefrontal cortex, and the strength of the action is represented by the path coefficient. For example, if the coefficient were 1.0, then for every unit change in the SMA there would be a unit change in the prefrontal cortex. Model 1 is consistent with that proposed by Freeman et al. (1984) based on their study of TCM. Blood-flow data also support this assumption, since the supplementary motor area becomes active

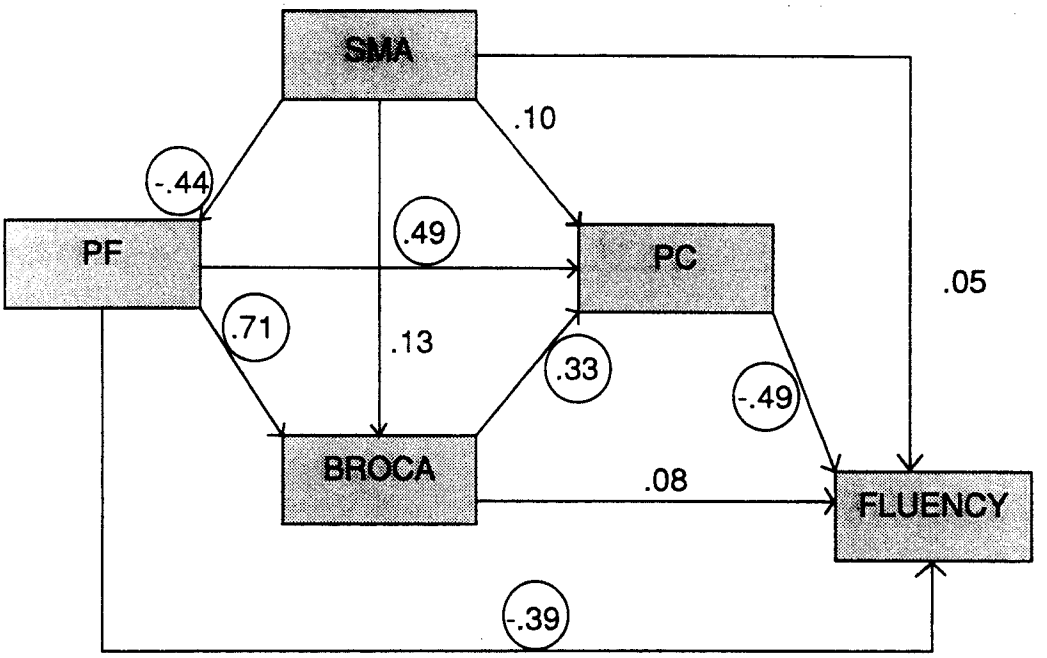

Fig. 7-1. Model 1. This model presents the SMA = supplementary motor area, the PF = prefrontal area, the *PC* = precentral gyrus and their affects on fluency. The model assumes that the supplementary motor area is the initiator of action. The calculated pathway coefficients derived from multiple regression analysis are shown along each arrow. A coefficient greater than .22 is assumed to be important. A pathway coefficient represents a strength of association between the two measures. The direction of the arrow states the direction of the action and is important in the model and the resulting regression equations.

when one plans an action, while the prefrontal and precentral gyri become activated only during the action (Roland, 1984).

Figure 7-1 shows model 1 and the pathway coefficients. Important coefficients are circled. The SMA was found to have little direct influence on Broca's area, the primary motor cortex, or fluency; its major action was on the prefrontal cortex. The adequacy of model 1 was tested by using the path coefficients to calculate correlations and then comparing them to actual Pearson's product moment correlations. Table 7-1 shows calculated and actual Pearson correlations between the four regions and fluency. Note that the correlations between the supplementary motor cortex and other measures were not accurately predicted by the path coefficients. This argues that model 1 cannot be accepted as being a reasonable explanation for the data.

Model 2 (Fig. 7-2) does not include a direct effect of the SMA on the primary motor cortex (PC) or fluency. It assumes that the SMA acts on prefrontal and Broca's areas, causing these areas then to complete the fluency task. A strong relationship was found between the SMA and the prefrontal cortex but not the SMA and Broca's area.

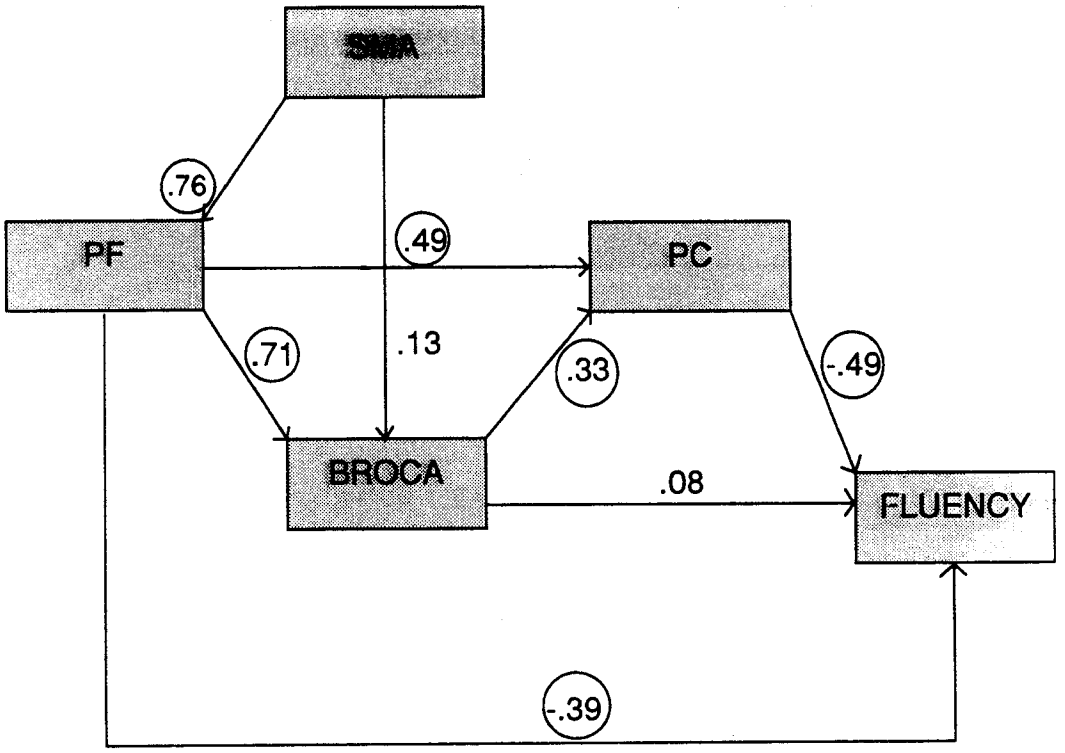

Fig. 7-2. Model 2. This model has been modified to eliminate any direct actions of the SMA on fluency and on the precentral gyrus.

Table 7-1 shows that calculated correlations using the path coefficients from model 2 accurately predict the true Pearson correlations between these measures. Therefore, model 2 represents a plausable explanation for the relationship between the four regional measures and fluency. It argues that the SMA affects fluent speech production through its association with the prefrontal cortex and not through the functioning of Broca's region; that is, the path SMA to Broca's region has a low value (0.13), while the path SMA to prefrontal has a high value (76). Prefrontal regions have both a direct and indirect influence on speech production. The precentral gyrus has a major direct role on fluency and is influenced by both prefrontal and Broca's regions. Interestingly, Broca's area had no direct influence on fluency.

Model 2 does not support the concept of a direct disconnection between the SMA and Broca's region. This does not disprove such a disconnection as the cause of transcortical motor aphasia, as proposed by Freeman et al. (1984). The data they present, though, would be consistent with disruption of the effect of the supplementary motor area on prefrontal function or disruption of the role of the prefrontal cortex on speech production as the cause of the fluency changes. The model is

TABLE 7-1. COMPARISON OF CALCULATED CORRELATION COEFFICIENTS AND PEARSON CORRELATIONS

	Model 1	*Model 2*	*Pearson*
SMA with PF	−0.44	0.76	0.76
SMA with Broca	−0.17	0.67	0.67
SMA with PC	−0.18	0.67	0.71
SMA with fluency	0.23	−0.60	−0.60
PF with Broca	0.65	0.67	0.67
PF with PC	0.68	0.84	0.84
PF with fluency	−0.66	−0.73	−0.74
Broca with PC	0.69	0.75	0.80
Broca with fluency	−0.53	−0.61	−0.64
PC with fluency	−0.65	−0.73	−0.76

Note: Pearson refers to the standard Pearson product-moment correlation. Based on the two models that we studied, the Pearson correlation can be estimated by considering all pathways that can lead from one measure to the next. By adding these products, an estimate of the Pearson correlation can be derived. For a model to be valid, a reasonable estimation of the correlations should be obtained. Model 1 poorly estimates the correlations for all SMA pathways, while model 2 accurately estimates the correlations.

consistent with the concept that aphemia results from disruption of the final pathways involved with speech planning and production.

The data extend current concepts to suggest that prefrontal regions are important in the planning and processing of the final speech product. Two points need to be made. First, the fluency score on the WAB is influenced by a variety of different speech, language, and cognitive functions. We have elected to study a general measure of fluency and not individual components, because our goal was to examine the pathoanatomy rather than those specific factors which result in the fluency measure. Second, the two models studied show that the SMA behaves different from the prefrontal region, Broca's region, and the precentral gyrus in relationship to fluency. However, this is not an exhaustive analysis of all possible models.

The strong presence of prefrontal regions in these analyses raises the question as to whether all speech behavior observed in aphasic patients results directly from language dysfunction. The prefrontal regions are considered to be involved with decision factors and executive types of functions, which include the desire to communicate and other aspects of motor control. Alteration in such control mechanisms may add another factor to the overall behavior that is observed in spontaneous speech.

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