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Quantitative Assessment of Covariation between Neuropsychological Function and Location of Naturally Occurring Lesions in Humans*

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ABSTRACT

Studies of localization of brain function in humans depend on analysis of covariation between the location of naturally occurring lesions and measures of neuropsychological ability. Such an analysis presents two problems: how to represent numerically the infinite variety of lesion locations, sizes, and shapes; and how to assess covariation between the location measure and performance. We present a mathematical model of lesion location and its relationship with performance. To demonstrate its utility, the model is applied to a sample of 53 patients with naturally occurring brain lesions who were administered a standard battery of neuropsychological tests. Importance functions derived for the neuropsychological measures generally conform to expectations. Sensory and motor abilities were localized correctly within the contralateral hemispheres, and language functions were localized in the left frontal region. Lesion location accounts for substantially more variation in performance than does lesion volume, with location accounting for more than 50% for some left-hemisphere functions.

Localization of brain function is one of the classic problems of neuroscience. Theories of localization have ranged from elaborate mappings of functions onto small regions of cortex to assertions of complete equipotentiality of all brain tissue (Kertesz, 1983a). The truth almost certainly lies somewhere between these extreme positions. Moreover, there is probably considerable variability in the extent to which different behavioral functions are localized (Knopman, Selnes, & Rubin, 1989).

*The authors gratefully acknowledge the assistance of Rebecca Hoag and William Reiter in taking measurements from the CT scans. Jim Pisano wrote the computer program that produced the graphic images.

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Localization of function is particularly difficult to demonstrate in humans because the most productive experimental paradigm involves intentional lesioning of animal brain tissue. Modern developments in brain imaging, particularly computer assisted tomography (CT) and magnetic resonance imaging (MRI), offer an opportunity to use naturally occurring brain lesions as a means of extending the lesion experiment to the study of localization in humans.

The analogy between surgical lesions in animals and naturally occurring lesions in humans is not simple, however. The effectiveness of the lesion paradigm in animals is founded on the experimenter’s ability to place lesions in carefully controlled, anatomically circumscribed areas, in accordance with the principle of double dissociation (Teuber, 1955). Naturally occurring lesions are unique, often large, irregularly shaped, and unevenly distributed across the brain.

Considerations such as these render it difficult to make precise inferences about brain function on the basis of naturally occurring lesions. Whereas other applications of brain imaging to human neuropsychology (such as the study of atrophic processes in psychopathology and dementia) have seen the development of precise techniques for quantification of brain-behavior relationships (Turkheimer, 1989), localization studies continue to rely on largely subjective methods.

It has sometimes been questioned whether inferences about localization of function are possible on the basis of lesion studies of any kind, even when lesion locus is under experimental control. Diaschisis, recovery of function, and the effects of disruption of complex functional systems all present interpretive difficulties (see Luria, 1966, for a thorough review). We wish to take a straightforward empirical approach to this complex theoretical issue. Whatever the implications for our understanding of the functional organization of the brain, whether or not lesions in different locations produce different functional deficits is an empirical matter and can be investigated as such. When we refer to “localization of function” in this paper we are referring to this empirical relationship between lesion location and performance, rather than “the function” of a brain region, elucidation of which requires converging results across several methodologies, including human and animal lesion studies, physiological and metabolic methods (e.g., PET), and cognitive approaches.

Using naturally occurring lesions to study localization of function is essentially a problem in covariation. If all areas of the brain have equal importance for a function, then variation in lesion location among subjects will not be associated with variation in the function. Conversely, if particular brain areas are more important than others for a particular function, lesions involving these areas will produce greater deficits than lesions elsewhere, resulting in covariation between location and function. Assessing this covariation presents two problems: how to measure lesion location quantitatively, and how to compute the covariation between such a measure and an index of performance.

Existing methods of quantifying lesion location have been reviewed recently (Turkheimer, 1989). Briefly, these methods may be divided into qualitative and
quantitative approaches. Qualitative methods represent lesion location graphically or by reference to anatomical landmarks of the brain. By far the most common approach is to divide patients into groups characterized by damage to gross structures such as hemispheres or lobes. Localization of function is measured in terms of behavioral differences between the groups (e.g., Warrington, James, & Maciejewski, 1986). Some researchers have classified lesion location on the basis of finer anatomical details, but the resulting analysis of relationships between damage to small areas and particular behavioral deficits is extremely complex. Naeser and colleagues carefully code brain images for damage to a large number of cortical and subcortical structures (Naeser, 1983), but the analysis of relationships between damage to these structures and behavior is conducted on a case-by-case basis.

Graphical methods involve schematic diagrams showing the overlap of lesions from patients with similar deficits (Kertesz, 1983b; Mazzocchi & Vignolo, 1979). These diagrams can provide an impression of how function is localized, but their interpretation is entirely subjective.

Quantitative approaches involve numerical measures of location that can be employed in statistical analyses. It has proven difficult, however, to represent the complexities of lesion location and shape with a single number. One attempt in this direction is the series of studies by Robinson and his colleagues (e.g., Parikh, Lipsey, Robinson, & Price, 1988) of mood disorders in stroke patients. Robinson et al. measure the average distance between the anterior border of a lesion and the frontal pole as a percentage of the total length of the anterior-posterior dimension of the brain. This quantity is then correlated with behavioral measures of mood.

Although this measure succeeds in capturing some aspects of lesion location and has produced interesting results, it has several limitations. Most important, it only measures location in one dimension, along the anterior-posterior axis, whereas left-right differences are analyzed by comparing groups with left- and right-hemisphere lesions. This distance measure also has a complex relationship with lesion size, as larger lesions will in general show greater anterior extent. The use of linear correlations in the analysis is also problematic because there is no particular reason to expect lesion location along the anterior-posterior axis to be linearly related to behavioral deficits. Sinyor et al. (1986) have reported a curvilinear relationship between the location measure used by Robinson et al. and depression scores in right hemisphere patients.

Another quantitative approach has been proposed by Grafman, Salazar, Wiegartner, Vance, and Amin (1986). Subjects’ scans are coded for presence or absence of damage to 26 brain areas, resulting in 26 dichotomous variables coding for lesion location. Wechsler IQ scales are regressed on these variables and on estimate of lesion volume. The unique variance accounted for by the 26 location variable provides an estimate of the importance of location. The use of so many predictors in a regression equation requires very large sample sizes, however; Grafman et al. report the results of 27 predictors for groups of 98 and
84 left- and right-handed subjects, respectively. Therefore, the $R^2$ values they report include substantial capitalization on chance.

In earlier work, our group has explored a quantification approach that falls between the multiple-structure checklist approach and Robinson's single-variable index (Haaland, Yeo, & Knotuvalkku, 1987; Yeo, Melka, & Haaland, 1988). Each hemisphere was divided into four regions (anterior third, middle third, posterior third, and subcortical extent) and the proportion of each area lesioned allowed for a four variable description of lesion locus. While avoiding some of the simplification inherent in Robinson's approach and the statistical difficulties of that of Grafman et al., this method does not allow for a rigorous exploration of localization.

Here, we describe a new approach to covariation between behavior and lesion location. An early version of the method, quantifying location in two dimensions on a single slice, has been described in Turkheimer (1989). In the current paper, we provide a more complete mathematical account of the model including a description of lesion location in three dimensions. Furthermore, we provide new graphical methods for presentation of results, and report the preliminary application of the model to data obtained from a sample of brain-injured patients.

A Quantitative Model of Localization of Function

Consider a sample of images of the brains of $n$ subjects, with $k$ parallel, equally spaced horizontal slices per subject. Each subject has one continuous three-dimensional lesioned area, visible as a single enclosed region on a subset of the $k$ slices. For each subject, a measure is obtained of some behavioral deficit.

Every point on each subject's image may be represented as a unique cartesian coordinate $(x, y, z)$, with $x$ indexing the left-right axis from ear to ear, $y$ the anterior-posterior axis, and $z$ the inferior-superior axis across slices. On the $x$ axis, 0 is located on the interhemispheric fissure, on the $y$ axis it is located at the midpoint of the interhemispheric fissure, and on the $z$ axis it is located midway between the highest and lowest slice. Suppose an importance function, $I(x,y,z)$, associates every point $(x, y, z)$ with an importance value representing the importance of the point to the behavior in question. High importance values indicate that the point is crucial to the function, while low values indicate the point is irrelevant to the function. The three-dimensional importance function may be easier to visualize if it is represented as an importance surface over each slice. Highly localized functions are "peaked"; i.e., they have high importance values concentrated in a limited region of the three-dimensional space; completely unlocalized functions are flat in all dimensions.

According to the model, the expected deficit produced by any lesion is equal to the integral of the importance function over all lesioned areas. That is, for each subject, the expected functional deficit is approximated by the sum of the volumes between the slice and the importance surface, across all slices on which the lesion is visible.

This model conforms to intuition about localization of function. Large le-
sions in important regions produce the greatest expected deficits; small lesions in unimportant regions produce the smallest. Large lesions in unimportant regions or small lesions in important ones will produce intermediate deficits.

In this procedure, one is given a score for the behavioral deficit of each patient and a description of the location of each patient’s lesion. The task is to recover the importance function for the behavior on the basis of this information.

A Polynomial Solution

Suppose the importance function for some behavior is estimated by a polynomial function of the form

\[ I(x,y,z) = b_1 x^3 + b_2 y^3 + b_3 x^2 + b_4 y^2 + b_5 x + b_6 y + b_7 xy + b_8 z^2 + b_9 H(x) + b_{10} \]  

The exact form of the polynomial is somewhat arbitrary, and may be modified in form and complexity to suit the behavior being studied and the number of subjects in the study. For our purposes, we have found that polynomials cubic in \( x \) and \( y \), linear in \( z \), and including a term for the interaction between \( x \) and \( y \) are adequate. In addition, we include a term, \( H(x) \), that equals \(-1\) for \( x \) values in the left hemisphere and \(+1\) for \( x \) values in the right hemisphere. This term codes for mean differences in importance between the hemispheres.

To compute the expected deficit for a subject, we must compute the volume under this function over the area of the lesion in each slice. For one slice, the volume over the lesion may be expressed as an area integral of the importance function over the lesion

\[ \int I(x,y,z) \, dA 
\]

If the shape of the lesion is approximated as a rectangle extending from \( x_1 \) to \( x_2 \) and from \( y_1 \) to \( y_2 \) (see Figure 2 below), this integral may be computed as a double integral in \( x \) and \( y \) on each slice:

\[ \int_{y_1}^{y_2} \int_{x_1}^{x_2} I(x,y,z) \, dx \, dy \]

The expected deficit for each patient is the value of these integrals summed over slices,

\[ \sum_{s=1}^{S} \left[ \int_{x_{1s}}^{x_{2s}} \int_{y_{1s}}^{y_{2s}} I(x,y,z) \, dx \, dy \right] \]

\[ + b_9 H(x) (x_{2s} - x_{1s}) (y_{2s} - y_{1s}) + b_{10} (x_{2s} - x_{1s}) (y_{2s} - y_{1s}) \]
Equation 4 expresses the expected deficits in terms of known lesion parameters \((x_n, x_p, y_n, \text{ and } y_p)\) and unknown coefficients of the importance function. All that remains is to find a set of values for these coefficients that provides the best fit to the observed deficits. This is a simple matter of linear regression, as is demonstrated below.

When estimated from observed data, the model produces two instructive results. The first is the derived importance function which, especially when depicted graphically, provides a quantitative impression of the relative importance of different brain areas to the behavior being studied. The second is the \(R^2\) of the regression of observed deficits on the model parameters, which quantifies the percentage of variability in behavior that is accounted for by lesion location and volume.

The effects of lesion location and volume may be separated by examination of the terms of Equation 4. The rightmost term, derived from the integral of the intercept term in Equation 1, represents observed deficits as the sum across slices of the area of the lesion on each slice, which is a linear function of the volume of the lesion. Regressing observed deficits on this term alone provides an estimate of the percentage of variation in behavior accounted for by lesion volume regardless of location; the additional variation accounted for by the remainder of the model represents the percentage of variation in behavior uniquely accounted for by location, once volume has been held constant.

The estimated importance function can be graphed as a regression surface relating importance to \(x\) and \(y\). By convention, we represent these as a contour map over a horizontal brain slice, with the number of contours a function of the \(R^2\) explained by the model (\(R^2/0.5\); see Figures 3 to 9 below). We are able to represent importance functions on a single slice because location differences along the inferior-superior (\(z\)) axis have so far not made substantial contributions to our models of empirical data, a finding we consider in greater detail below. If the \(z\) axis did contribute to the model, a separate function would have to be drawn for each slice.

Subjects
Archival data were obtained for 53 patients examined in a neurological clinic who met the following criteria:

1. A CT scan had been performed.
2. A unilateral lesion was visible on the CT scan.
3. The patient was right-handed.
4. The patient was over 15 years of age.
5. There was no history of psychiatric disorder or drug abuse.

The sample included 26 males and 27 females. The mean age was 55 years and the mean time postlesion was nine months. Etiologies consisted of stroke (41), tumor (9), focal trauma (2), and abscess (1). The distribution of lesions is illustrated in Figure 1, in which lighter regions were more frequently lesioned than darker regions.
Neuropsychological Measures
Subjects were administered portions of the Halstead-Reitan Neuropsychological battery as a routine part of their examination. Tests included the Trail Making Test, Parts A and B, Reitan-Kløve Sensory Perceptual Exam, Reitan-Indiana Aphasia Screening Exam, Finger Oscillation Test, and strength of grip test (Reitan & Wolfson, 1985). Russell’s (Russell, Neuringer, & Goldstein, 1970) scoring system was used to score the Aphasia Screening Exam. Of the two scores produced (verbal and spatial), only the verbal score was included in the analysis. Trail Making Test, Parts A and B were also scored according to Russell et al. (1970). Total time was converted to a 6-point scale. If testing was discontinued, the subject was assigned the lowest score. For the auditory, visual, and tactile modalities of the sensory perceptual exam, the total score was the number of errors occurring during unilateral and double simultaneous stimulation. Left- and right-side performances were scored separately. Finger-tip number-writing and finger recognition scores were the number of errors made with each hand. Left- and right-finger tapping speed was determined as the mean number of taps in a 10-s interval over five separate trials with each hand. Left and right strength of grip was determined with a hand dynamometer (Stoelting Co.).
CT Analysis
CT scans were placed on a light box, and the outer perimeter of the cortex and the
lesioned area on each slice were traced onto tracing paper. Slices were then
coded according to the criteria of Naeser et al. (1983), which standardizes hori-
zontal slices according to prominent anatomical landmarks. Slices ranged from
B-3 (three slices below Broca’s area) to SM+8 (8 slices above the supramarginal
gyrus level) and were renumbered as -7 through +8, which constituted the z axis.
The greatest width and length of each slice was measured in centimeters. The
greatest left and right extensions of the lesion from the interhemispheric fissure
were measured, with leftward distances represented by negative numbers. These
were then divided by the width of the subject’s widest slice and multiplied by 10,
resulting in standardized left and right extension values (x1 and x2 in Equation 4)
ranging from -5 to +5. Similarly, the distance from the greatest anterior and
posterior extensions of the lesion to the midpoint of the interhemispheric fissure
were divided by the length of the longest slice and multiplied by 10, resulting in
anterior and posterior extension values (y1 and y2 in Equation 4) ranging from -5
to 5. These measurements are illustrated in Figure 2.

Figure 2: Distribution of lesions across subjects. Lighter regions indicate greater fre-
quency of lesions.
**Statistical Analysis**

The parameters of the model were estimated using polynomial multiple regression. One analysis was conducted to predict each neuropsychological measure, with a test score as the dependent variable and the independent variables computed from the known lesion parameters according to Equation 4. Each term of Equation 4 includes an unknown parameter from the importance function \((b_i, \ldots, b_n)\) and a term computed from the lesion parameters. The first term, for example, includes the unknown parameter representing the cubic effect of \(x\) in the importance function and the term

\[
\frac{1}{4} (x_{2}^{3} - x_{1}^{3}) (y_{2} - y_{1})
\]

that is computed directly from the measured characteristics of each subject's lesion and is an independent variable in the regression analysis.

**RESULTS**

Table 1 shows the sample means and standard deviations for the neuropsychological measures for subjects with left- and right-hemisphere lesions. Sample sizes vary somewhat because of missing data. Table 2 shows the results of the localization regressions. The first column of Table 2 gives the \(R^{2}\) resulting from the regression of the neuropsychological measures on age and sex. The next column gives the incremental \(R^{2}\) resulting from the addition of lesion volume to the age and sex regression. The next two columns show the unique contributions of lesion location along the left-right and anterior-posterior axes estimated by removing all \(X\) (linear, quadratic, cubic and \(H(X)\)) and \(Y\) (linear, quadratic, and cubic) terms in turn from the full model and noting the reduction in \(R^{2}\). The next column estimates the total contribution of lesion location by removing all nine location terms from the full model. The next column shows the variance accounted for by the full model, and the next to rightmost column is the total \(R^{2}\) corrected for the ratio of predictors to subjects. The above were tested for significance using an \(F\) test of the difference in \(R^{2}\) between the full and reduced models, with the numerator degrees of freedom equal to the number of terms removed from the full model, and the denominator degrees of freedom equal to \(df\) error for the full model, which is given in the rightmost column of Table 2.

Females had consistently poorer scores on the motor tests, a sex difference unrelated to lesion effects (Heaton, Grant, & Matthews, 1986). Males made more right-hand sensory errors. Neither age nor inferior-superior location differences contributed significantly to the results. Lesion volume did not contribute substantially to the regressions, except for left tactile errors. Left-hand sensory and motor functions showed consistently greater effects of lesion volume.

For all measures, lesion location accounted for more unique variance after
Table 1: Means and Standard Deviations of Neuropsychological Measures

<table>
<thead>
<tr>
<th>Test</th>
<th>Side*</th>
<th>M (SD)</th>
<th>n</th>
<th>M (SD)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength of Grip (kgs.)</td>
<td>R</td>
<td>20.6 (15.8)</td>
<td>19</td>
<td>28.3 (15.5)</td>
<td>23</td>
</tr>
<tr>
<td>Strength of Grip (kgs.)</td>
<td>L</td>
<td>27.3 (11.6)</td>
<td>18</td>
<td>14.5 (13.8)</td>
<td>23</td>
</tr>
<tr>
<td>Finger Tapping (# taps)</td>
<td>R</td>
<td>22.4 (19.5)</td>
<td>21</td>
<td>35.4 (15.2)</td>
<td>20</td>
</tr>
<tr>
<td>Finger Tapping (# taps)</td>
<td>L</td>
<td>32.4 (13.1)</td>
<td>20</td>
<td>21.9 (17.6)</td>
<td>20</td>
</tr>
<tr>
<td>Tactile Sensory Errors</td>
<td>R</td>
<td>3.1 (4.2)</td>
<td>21</td>
<td>0.3 (0.9)</td>
<td>28</td>
</tr>
<tr>
<td>Tactile Sensory Errors</td>
<td>L</td>
<td>0.3 (1.1)</td>
<td>21</td>
<td>3.8 (4.1)</td>
<td>28</td>
</tr>
<tr>
<td>Auditory Sensory Errors</td>
<td>R</td>
<td>1.3 (1.9)</td>
<td>20</td>
<td>0.6 (1.4)</td>
<td>27</td>
</tr>
<tr>
<td>Auditory Sensory Errors</td>
<td>L</td>
<td>0.9 (1.6)</td>
<td>20</td>
<td>1.9 (2.1)</td>
<td>27</td>
</tr>
<tr>
<td>Visual Sensory Errors</td>
<td>R</td>
<td>4.4 (6.6)</td>
<td>20</td>
<td>0.8 (2.2)</td>
<td>27</td>
</tr>
<tr>
<td>Visual Sensory Errors</td>
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<td>2.1 (4.7)</td>
<td>20</td>
<td>3.2 (4.2)</td>
<td>27</td>
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<tr>
<td>Finger Recognition Errors</td>
<td>R</td>
<td>4.4 (6.1)</td>
<td>19</td>
<td>1.3 (2.8)</td>
<td>28</td>
</tr>
<tr>
<td>Finger Recognition Errors</td>
<td>L</td>
<td>1.4 (2.5)</td>
<td>19</td>
<td>6.6 (8.2)</td>
<td>28</td>
</tr>
<tr>
<td>Finger-tip Number-writing</td>
<td>R</td>
<td>6.0 (7.0)</td>
<td>19</td>
<td>2.9 (4.4)</td>
<td>27</td>
</tr>
<tr>
<td>Finger-tip Number-writing</td>
<td>L</td>
<td>3.5 (4.1)</td>
<td>19</td>
<td>6.6 (7.7)</td>
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<tr>
<td>Trail Making Test, Part A</td>
<td>R</td>
<td>4.1 (1.7)</td>
<td>20</td>
<td>3.6 (1.7)</td>
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<tr>
<td>Trail Making Test, Part B</td>
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<td>4.3 (1.5)</td>
<td>20</td>
<td>3.5 (1.7)</td>
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<tr>
<td>Aphasia Screening Errors</td>
<td></td>
<td>34.0 (19.5)</td>
<td>21</td>
<td>8.6 (8.5)</td>
<td>25</td>
</tr>
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</table>

* Right = Right; L = Left.

Lesion volume had been controlled than was accounted for by lesion volume without any location terms in the models. The most localized functions were verbal aphasia errors, right and left tactile and right visual errors, for which lesion location predicted about one-half of the total variance. Differences in lesion location along the left-right axis accounted for substantially more variability than did differences along the anterior-posterior axis. Trail Making Test, Parts A and B and auditory sensory errors showed the smallest relationship with lesion location. The patterns of localization resulting from the analyses are presented graphically below.
Table 2: Variance Explained by Model

<table>
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<tr>
<th>Test</th>
<th>Side*</th>
<th>R² Age,Sex</th>
<th>R² Vol</th>
<th>R² X</th>
<th>R² Y</th>
<th>R² Location</th>
<th>R² Total</th>
<th>R² Corr error</th>
<th>df</th>
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<td>.30</td>
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<td>.70</td>
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<td>.01</td>
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<td>.43</td>
<td>.19</td>
<td>28</td>
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<tr>
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<td>.06</td>
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Underline — p < .1  
*L = Left; R = Right  
Italics — p < .05  
Italics and underline — p < .01

Figures 3 to 7 depict the importance surfaces in graphic form. The figures are analogous to horizontal CT slices, with anterior regions on top and posterior regions on the bottom. Importance is indicated by the grey contour bands, with lighter colors representing greater importance. One contour line has been drawn for each 5% of variance explained by lesion location. The boundaries between the bands are arbitrary. We depict only the importance functions for which lesion location contributed significantly (p < .10) to the model.

Figure 3 shows the importance function for right visual errors. The function for right errors shows the region of greatest importance in the left occipital region, and a substantial overall difference between the hemispheres. The differences along the Y axis (i.e., the greater importance of more posterior regions)
was not statistically significant (see Table 2) and should be interpreted cautiously as a trend.

Figure 4 shows the importance functions for left and right tactile errors. Both show regions of greatest importance contralaterally, posterior to midline. Left-right differences are significant for left and right tactile errors, but anterior-posterior differences are significant only for right-hand errors. Figure 5 shows the importance function for aphasia verbal errors. The region of greatest impor-
Figure 5: Importance function for verbal errors on the Aphasia Screening Exam. Lighter regions indicate greater importance.

tance is in the extreme posterior region bilaterally, with a second area of importance in the left anterior region. Only the left-right differences are significant.

The importance function for right finger tapping (Figure 6) shows the region of greatest importance in the extreme posterior regions, with a secondary region bilaterally frontal, with slightly greater importance in the left hemisphere. Left-right differences approach significance. The importance function for left strength of grip, shown in Figure 7, is somewhat difficult to interpret. The area of greatest importance is again in the extreme posterior region, with a secondary area in the right anterior region. Left-right and anterior-posterior differences are significant.

DISCUSSION

We have applied a new model for quantification of the relationship between lesion location and behavior. In considering the results of applying such a new model to actual data, it should be borne in mind that conclusive interpretation of results must await verification of the model’s validity. The results have been presented with the intent of demonstrating the validity of the model rather than
Figure 6: Importance function for right finger tapping. Lighter regions indicate greater importance.

Figure 7: Importance function for left strength of grip. Lighter regions indicate greater importance.
investigating substantive neuropsychological hypotheses. To that end, we have selected neuropsychological measures for which earlier work provides evidence for covariation with lesion location. It has been fairly well established, for example, that unilateral lesions produce contralateral deficits on sensory and motor functions; that left-hemisphere lesions produce greater language deficits than do right-hemisphere lesions; and that visual functions are particularly affected by posterior lesions. Although the results seem to provide some interesting possibilities for more detailed hypotheses, we will, in the main, limit our discussion to the conformity of results to these broad expectations.

Another reason for caution in interpretation of the results is the size of the sample. Although not especially small by the usual standards in this area, the application of more sophisticated statistical techniques requires greater samples for adequate statistical power and protection from Type I error. We have attempted to be as conservative as possible in deriving and interpreting the models. To the extent that results are in agreement with the expectations from earlier work mentioned above, they may be accepted as validation of the model. Deviations from expectations may (a) indicate the presence of previously undetected effects or (b) result from chance; in either case, further investigation with larger samples will be required once the model has been validated.

Bearing these cautions in mind, patterns of localization revealed by the analysis generally conform to expectations based on earlier work. Sensory measures show greater importance in the contralateral hemisphere. The area of greatest importance for tactile sensory errors is located just posterior to midline in both the left and right hemispheres. Right visual errors were localized in the left posterior region. The region of greatest importance for aphasia score was located in the left hemisphere.

Several results of the analyses, however, are not congruent with expectations and need to be examined more closely. The localization of aphasic errors, for example, shows increased importance in the most posterior extension of the cortex. Several factors contribute to a lack of confidence in this finding. First, regression surfaces have the greatest standard errors at the extremes of their range, and relatively few subjects had very anterior or very posterior lesions. Secondly, the results do appear to be an accurate description of this sample: The three subjects with lesions restricted to posterior regions of the left hemisphere had twice as many errors as did the entire sample. Thirdly, the Aphasia Screening Exam contains a substantial number of items that require visual abilities (e.g., reading, copying, naming), which may have been responsible for the posterior contribution to the importance function. Item scores were not available for analysis.

A final matter requiring discussion is the absence of effects along the inferior-superior axis. Several considerations may help to account for this finding. First, CT and MRI images consisting of axial slices have far worse resolution on this axis than on the anterior-posterior or left-right axes, and CT shows a great deal of artifact on inferior slices. Secondly, there was relatively little variation
along this axis in the sample, making independent effects of more inferior or superior lesions difficult to detect. Thirdly, the location of horizontal slices shows considerable variation across subjects in a sample of clinical images; this cannot be fully controlled, despite Naeser's (1983) method of standardization. Sagittal and coronal MRI images may prove particularly useful in detecting effects of variation in lesion location along the inferior-superior axis.

The quantitative model we have proposed here has several advantages over other methods of studying variation in lesion location. Most important, it combines much more information about the location of lesions. In the model, lesions are represented as rectangles on each slice on which they are visible. Other methods represent location as a single point on a single slice. The model is not limited to linear hypotheses, and combines information from all three dimensions of the brain.

The success of the model in predicting several neuropsychological measures from lesion characteristics measured from CT scans suggests that it may have some utility for predicting neuropsychological outcome of brain-injured patients in clinical settings. In particular, it could offer an alternative to the simple cutoff scores that have sometimes been used as indicators of “impairment” in neuropsychological test results. The sensitivity and specificity of the model for the identification of brain damage will depend not only on the strength of the relationship between lesion characteristics and neuropsychological tests, but also on the definition and base-rate of “impairment” in particular clinical settings.

An important characteristic of the model is that it ignores structural characteristics of the cortex. Analyses are based on coordinate locations of lesions, and implicitly assume that equivalent structures are located at the same coordinate locations across subjects. Some recent work has been directed toward improving correspondence between coordinate and anatomical locations (Fox, Perlmutter, & Raichle, 1985). It is also possible to include variables coding for damage to specific structures in the regressions; inclusion of a variable coding for hemispheric differences is an example of this.

The model also does not account for the possibility of joint effects of separate areas of the brain. In fact, hypotheses of this type could be investigated within the model if it were possible to obtain a sample of patients with a complete distribution of damage to pairs of brain areas. The enormous difficulties involved in assembling such a sample will plague any attempt to examine more complex hypotheses about localization of function.

REFERENCES


