Low-Resolution Electrical Tomography of the Brain During Psychometrically Matched Verbal and Spatial Cognitive Tasks

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Abstract: EEGs were recorded from 75 normal, young, female subjects during psychometrically matched verbal (WF) and spatial (DL) cognitive tasks to elicit the differences in the electrical source distribution inside the brain. Recordings were obtained using 43 EEG and 3 guard electrodes then visually edited and spatially filtered to remove extracerebral artifacts. Twenty 1-sec artifact-free epochs were obtained and analyzed from 42 and 60 subjects during WF and DL respectively. Of these subjects, 20 were placed in a training set and the remainder into a test set. The baseline for the comparison of the two tasks was established by factoring the average cross-spectral matrices of the training-set EEGs, computed in the theta, alpha, and beta frequency bands into spatial patterns common to the two tasks. Only those spatial patterns that contributed to the correct classification of subjects in the test set were included in the source analysis. The source-current density distributions were obtained using the LORETA-KEY[®] algorithm. The results show that the source-current density distribution is related to the putative functional activity in the brain in all three frequency bands. The electrical effects of the tasks are both most highly localized and lateralized in the theta band. The effects in the alpha and beta bands are much more generalized and are strongly lateralized only during one and the other of the tasks respectively. The conclusion is that WF is mainly a left central and bilateral frontal cerebral process while DL is mainly a right central and bilateral posterior cerebral process. *Hum. Brain Mapping* 12:144–156, 2001. © 2001 Wiley-Liss, Inc.

Key words: electroencephalography; pattern recognition; cognitive function; source localization

INTRODUCTION

In the past 30 years, research interest in the relationship between features in the EEG and the cortical

regions associated with specific cognitive activity has been considerable. The quantitative approach to the study of this relationship was probably first taken by Galin and Ornstein in 1972. More recently, Davidson et al. [1990] published a study designed to elicit EEG differences in normal subjects during the execution of psychometrically matched verbal and spatial cognitive tasks. These tasks, called Word Finding (WF) and Dot Localization (DL), putatively engaged the left and right cerebral hemispheres of the brain, respectively. The two tasks were matched for difficulty level and yielded differential performance scores that were independent of the subjects' functional capabilities [Fujioka, 1986; Miller, 1986]. To record the EEG, Da-

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vidson et al. [1990] used 6 active electrodes located at two mid-frontal, two central, and two parietal homologous sites. They recorded EEGs from some 21 right-handed undergraduate female subjects and analyzed the data both with respect to a common vertex reference and with respect to an averaged-ears reference. The analysis utilized the spectral power at each electrode site in the delta, theta, alpha and beta bands during the nonmotor phases of the tasks. The main result of their study was that, with respect to the vertex reference, there was a significant shift in the measure of right-left power symmetry in all of the frequency bands concomitant with the execution of the two tasks. Furthermore, the direction of this shift was the same in all of the bands. With respect to the averaged-ears reference, the shift was only significant in the alpha and beta bands. Based on an examination of the spectral powers from each hemisphere underlying these shifts, it was concluded that, at least for these tasks, a relative decrement in EEG power in any of the bands can be interpreted as increased functional activity in that region of the brain. Given the spatial distribution of these decrements, it was further concluded that WF is probably centered in the left central region of the brain whereas DL is centered in the right parietal region.

The study reported here is essentially a repeat of Davidson et al. [1990]. However, in order to examine the distribution of the electrical activity associated with WF and DL more precisely, the measurements were obtained using 43 EEG electrodes and three additional guard electrodes for detecting and eliminating eye movement, muscle, and other artifacts. Included in the study were some 75 young female subjects and the EEGs characterized by their full cross-spectral matrices rather than just by the power spectral values at the individual electrode sites. It has been shown [Lind et al., 1997, 1999] that the cross-spectral matrix is a better description of the EEG for discriminating between WF and DL than are just the diagonal values of this matrix (the power spectral values). To examine the differences in the distribution of source current densities inside the brain underlying the EEGs during these tasks, the cross-spectral matrices in the theta, alpha and beta frequency bands were used as the input to the LORETA-KEY® algorithm. The source-current densities at each volume element (voxel) in the LORETA solution space were compared between the two tasks to determine which brain regions were involved.

LORETA is an acronym for low-resolution electromagnetic tomography [Pascual-Marqui et al., 1994]. It is one of a class of so-called minimum-norm algo-

rithms used to obtain solutions to the inverse problem in electroencephalography. These solutions provide an estimate of the 3D distribution of the source-current density inside the brain underlying the electrical activity measured on the scalp. With LORETA, the nonuniqueness of the solution of the inverse problem is overcome by assuming that the true source-current density distribution is spatially smooth and that it has minimum spatial energy in the solution space inside the brain (usually the gray-matter) that can account for the EEG measurements on the scalp. This indicates that, in order to be seen by LORETA, the source activity inside the brain must, on the scale of the assumed smoothness, be spatially synchronized. Unlike dipole fitting algorithms such as MUSIC [Mosher et al., 1992; Koles et al., 1998], which can provide higher spatial resolution, LORETA requires no assumptions about the number or the geometry of the active sources inside the brain. Indeed, simulations have shown that, given adequate spatial separation, LORETA will locate multiple nondipolar sources accurately, and almost identically, irrespective of whether these sources are generating correlated waveforms [Lind et al., 1999].

One of the appealing aspects of the source-current density distribution in the brain over the potential distribution on the scalp is that the former is a function only of location in the brain and not of the reference used to record the EEG. Therefore, the ambiguities such as those seen in the results of Davidson et al. [1990] related to the recording reference are avoided.

In this work, the EEGs obtained during WF and DL were compared only to each other and not to some resting state. This was done because the resting state is difficult to control and therefore likely to be highly variable across individual subjects. This variability could obscure any differences between the cognitive tasks. Instead, a baseline for the comparison was established from an average of the cross-spectral matrices obtained during the two tasks. The averaged cross-spectral matrices were factored into spatial patterns in the EEGs common to the two tasks but which accounted for maximally different proportions of the variance in the EEGs in the two tasks. To set the baseline for the comparison of the tasks and to exclude brain sources not involved in the verbal/spatial processing, those spatial patterns that did not contribute significantly to the discrimination of the EEGs between the two tasks were excluded. In other words, those spatial patterns that accounted for the same variance in the EEG in both tasks were used as the baseline for the comparison of the tasks. Therefore, only those components of the source-current density

distribution in each subject and task underlying the deviations of the EEG from this baseline were examined with LORETA.

METHODS

Participants

Data was recorded from a total of 75 dextral female subjects. The mean age of the subjects was 25.4 ($SD = 8.4$). All subjects were completely right-handed as determined by the Chapman and Chapman [1987] handedness questionnaire. EEGs were recorded from all subjects during the Word Finding (WF) and Dot Localization (DL) tasks. Recordings lasting until the end of the two tasks (at least 3 min) were obtained. These tasks were developed by Miller [1986] and Fujioka [1986] and have been psychometrically matched on item difficulty, item-scale correlations and internal consistency reliability using a sample of 350 normal subjects by these researchers. In the present work, the test questions were presented to the subjects as slides projected from the rear of the recording chamber. Having formulated an answer to a question, the subjects were asked to press a button to indicate that they were about to verbalize a response. By using the recording of the button signal, the EEGs were separated into cognitive and motor phases. Generally, the subjects required at least 5 sec to formulate their answers and neither the first nor the last second of the EEG recorded during this period was selected for analysis. Also, to ensure compliance, only those EEGs corresponding to correct responses to the test questions were utilized. No rest period was allowed the subjects between the questions.

The DL task contained 25 items with each item consisting of two vertically arranged open rectangles, the top rectangle containing a pair of dots and the bottom rectangle, slightly offset to either the right or the left, containing an array of numbers. The offset of the bottom rectangle differed randomly among items such that half of the items were offset to either the right or the left side. Subjects were asked to indicate which two numbers in the lower rectangle corresponded to the location of the dots in the upper rectangle. Item difficulty is determined by the size of the number arrays, which varies in five levels from 8 to 50 numbers. In the WF task, subjects were asked to correctly identify an object when presented with a written definition of the object. For example, the correct answer for the item "a very large piece of floating ice" is iceberg. The WF task consisted of 30 items that differed in an ascending order of difficulty.

All potential subjects were administered a pretest interview. Any who responded in the affirmative to having any history of neurological disease, birth complications, head trauma, psychiatric illness, or substance abuse were excluded from the study. In addition to the pretest interview, the subjects received the Quick Diagnostic Interview Schedule [Marcus et al., 1989] and any participants with positive symptom categories were excluded from the study.

Recordings

EEG recordings were obtained using a 43-lead stretchable electrode cap containing tin electrodes. The 43 electrode sites represented standard electrode positions described in the American Electroencephalography Society Guidelines [Sharbrough et al., 1990]. The lead sites were AF_3 , AF_4 , FC_5 , FC_6 , FC_1 , FC_2 , C_3 , C_4 , C_1 , C_2 , TP_7 , TP_8 , CP_5 , CP_6 , CP_1 , CP_2 , P_3 , P_4 , P_1 , P_2 , PO_3 , PO_4 , AF_z , F_z , FC_z , C_z , CP_z , P_z , PO_z , FP_1 , FP_2 , F_7 , F_8 , F_3 , F_4 , FT_7 , FT_8 , T_7 , T_8 , P_7 , P_8 , O_1 , and O_2 . All leads were referenced to the left ear and the impedance at each electrode was adjusted to be below 5 K Ω . Three additional channels were recorded; the electrocardiogram (EKG), a bipolar recording over the external canthus to the supra-orbit of the right eye to monitor vertical and horizontal eye movements (EOG), and one bipolar electromyogram (EMG) channel recorded from the temporomandibular region on the right and left sides. All channels were amplified using a Grass Neurodata system and digitized with a 12-bit RC Electronics analog to digital converter at a rate of 256 samples/sec. The band pass was set at 3–80 Hz with the high pass controlled by a Grass Model 12A5 two-pole Butterworth filter with the 3-dB point set at 3 Hz. The anti-aliasing filter was an eight-pole Bessel function filter with the 3-dB point set at 80 Hz.

Spectral analysis

The digitized EEG records were visually edited offline to select from each subject, 20 nonoverlapping, 1-sec data segments corresponding to correct responses to the tasks. These were selected randomly from all of the 1-sec segments available from the subject. Segments that contained voltage spikes, large eye movements, or muscle activity were not selected for analysis. Rejection of segments was frequent and resulted in only 42 and 60 subjects finally being able to contribute EEGs to this study during WF and DL, respectively.

The Fast Fourier Transform (FFT) was applied to each raw data segment including the EKG, EMG, and

EOG channels resulting in a frequency resolution of 1 Hz. Prior to the application of the FFT, each data segment was preprocessed by applying a 50% Hamming taper [Brillinger, 1981]. Following FFT, the twenty 46×46 complex-valued cross-spectral matrices were averaged together to provide, for each subject, at each frequency, the measure of her cross-spectral matrix. Only the theta band (4–7 Hz), the alpha band (8–13 Hz) and the beta band (14–20 Hz) were investigated in this study. Therefore, a further averaging of four, six, and seven cross-spectral matrices respectively corresponding to these frequencies was performed in order to provide the final measure. The correlated effects of the EKG, EOG, and EMG with the EEG were removed using the match filtering technique described before [Brillinger, 1981; Lind et al., 1999], resulting in a single 43×43 complex-valued cross-spectral matrix for each subject, for each frequency band and for each task. Finally, each cross-spectral matrix was normalized with respect to the sum of its diagonal elements to remove the confounding effects of an individual's skull thickness on EEG power [Wheeler et al., 1993].

Baseline for the comparison of the EEGs

To establish a baseline from which to compare the EEGs during the two tasks, the subjects finally included in the study were divided into training and test sets. Given that the number of subjects able to provide EEGs for WF was 42, 20 who provided EEGs for both tasks were selected for the training set. The individual cross-spectral matrices obtained from these subjects were averaged in each frequency band to form a cross-spectral matrix for the task. The task cross-spectral matrices were then factored as [Lind et al., 1999]:

$$\Sigma_a = C\Psi_a C' \quad \text{and} \quad \Sigma_b = C\Psi_b C' \quad (1)$$

where Σ_a and Σ_b are the averaged cross-spectral matrices for the training set during WF and DL, respectively, in one of the frequency bands. In these equations, the $N \times R$ matrix C contains R spatial factors common to the two tasks in the subspace $R \leq N$. Here, $N = 43$, the number of electrodes used to record the EEG, while Ψ_a and Ψ_b are $R \times R$ diagonal (eigenvalue) matrices that contain the proportion of the combined variances in Σ_a and Σ_b accounted for by each of the columns in C in the subspace R . The columns of C are scaled so that:

$$\Psi_a + \Psi_b = I \quad (2)$$

To determine which of the spatial factors present in the EEGs of the training set should be used in setting the baseline for the comparison of the two tasks, these factors were used in combination to classify the cross-spectral matrices from the subjects in the test set as either WF or DL. To classify an unknown EEG with covariance matrix Σ_u into either group a or group b, the classical complex domain quadratic discriminant function was used [Shumway, 1982]. This function can be written as [Lind et al., 1999]:

$$QDF = \text{trace}(P(\Psi_a^{-1} - \Psi_b^{-1})P'\Sigma_u) \quad (3)$$

where P is the $N \times R$ transformation matrix corresponding to C and is given by $P = (C')^*$ where $'$ and $*$ are the transpose and pseudoinverse operators respectively. Large positive values for QDF would place the unknown EEG in group "a" while large negative values would place it in group "b." To obtain the expected (mean) QDF for each group, we let $\Sigma_u = \Sigma_a$ or Σ_b . It is obvious from equation (3) that the greatest contribution to the QDF will be made by the largest and smallest eigenvalues in Ψ_a and Ψ_b . Given the constraint imposed by equation (2), eigenvalues in Ψ_a that are, for example, close to 1 must be accompanied by eigenvalues that are close to 0 in Ψ_b . Because of the inverse operations in equation (3), values of Ψ_a close to 1 will push the QDF strongly in the negative direction. The opposite would be true for values of Ψ_a that are close to 0. On the other hand, those eigenvalues in Ψ_a and Ψ_b that are close to 0.5 will make only small contributions to the QDF .

To eliminate components of the EEGs and their corresponding sources inside the brain that did not factor heavily in the discrimination between the tasks and to thereby identify the components for the baseline from which to compare the tasks, our approach was to use only those eigenvalues from Ψ_a and Ψ_b that contributed significantly to the QDF . Therefore, in the classification of EEGs, the common spatial factors matrix C , transformation matrix P and corresponding eigenvalues Ψ_a and Ψ_b for the two training sets were found initially with $R = N$ so that $P = (C')^{-1}$. The diagonal elements of Ψ_a were then sorted from largest to smallest and the columns of C and P rearranged to correspond. Then, beginning with the first and last columns from P and the corresponding eigenvalues from Ψ_a and Ψ_b , the individuals in each of the test sets were classified using equation (3). This was done by finding a decision line that best separated the QDF s obtained for the individuals in these sets into their correct groups [Morrison, 1990]. Columns from each

end of $\mathbf{P}$ and the corresponding eigenvalues from Ψ_a and Ψ_b were then added one at a time to determine the maximum classification rate for the dimension R . The value of R was then reduced by one and the process of finding the vectors from $\mathbf{P}$ that best classified the test sets was repeated. The entire process was then repeated until it was clear that reducing R any further would not result in any better classification of the test sets. The main objectives here were first, to make R as small as possible so that the classifier was less dependent on individual EEGs, and second, to make the number of factors in R small to eliminate those sources that did not contribute to the classification.

The matrix of spatial factors common to the cross-spectral matrices to Σ_a and Σ_b used in this work is given by [Koles et al., 1995]:

$$\mathbf{C} = \mathbf{B}_c \lambda_c^{1/2} \mathbf{B}_t \quad (4)$$

where $\mathbf{B}_c$ and λ_c contain the eigenvectors and eigenvalues of the composite cross-spectral matrix:

$$\Sigma_c = \Sigma_a + \Sigma_b \quad (5)$$

and $\mathbf{B}_t$ contains the eigenvectors of the whitened covariances matrices:

$$\Gamma_a = \mathbf{W}' \Sigma_a \mathbf{W} \quad \text{or} \quad \Gamma_b = \mathbf{W}' \Sigma_b \mathbf{W} \quad (6)$$

where

$$\mathbf{W} = \mathbf{B}_c \lambda_c^{-1/2} \quad (7)$$

λ_c is an $R \times R$ diagonal matrix containing the largest R eigenvalues of Σ_c while the corresponding eigenvector matrix $\mathbf{B}_c$ is of dimension $N \times R$.

Estimation of the source-current density

In LORETA the function:

$$f^2 = \|\mathbf{K}\mathbf{j} - \mathbf{v}\|_2 + \alpha \|\mathbf{L}\mathbf{W}\mathbf{j}\|_2 \quad (8)$$

is minimized with respect to $\mathbf{j}$, the primary source current density vector [Pascual-Marqui, 1995]. The vector $\mathbf{j}$ is of dimension $3M \times 1$ and contains the x , y , and z components of the current density at each of the M LORETA voxels in the brain. The vector $\mathbf{v}$ is the $N \times 1$ potential vector on the scalp (at a single time point), $\mathbf{K}$ is the $N \times 3M$ head transfer matrix, $\mathbf{W}$ is the diagonal $3M \times 3M$ depth-weighting matrix, $\mathbf{L}$ is the

$3M \times 3M$ Laplacian matrix and α is a scalar smoothing parameter. The transfer matrix $\mathbf{K}$ is reference dependent because it relates current sources inside the head to potential differences on the scalp. For this work, $\mathbf{K}$ was determined with respect to the average reference and the potential vector $\mathbf{v}$ transformed to correspond.

The solution to the minimization problem expressed by equation (8) has the form:

$$\mathbf{j} = \mathbf{T}\mathbf{v} \quad (9)$$

where $\mathbf{T}$ is the $3M \times N$ LORETA transformation matrix. To obtain a solution, α is chosen as a compromise between the spatial smoothness of the source-current density inside the brain and the proportion of the variance accounted for in $\mathbf{v}$. In this work, α was chosen to be 1×10^{-5} .

The source current density given by equation (9) for a single time slice is usually averaged over many time slices as:

$$\begin{aligned} \mathbf{q}_3 &= E(\text{diag}(\mathbf{j}'\mathbf{j})) = E(\text{diag}(\mathbf{T}\mathbf{v}\mathbf{v}'\mathbf{T}')) \\ &= \text{diag}(\mathbf{T}\Sigma\mathbf{T}') \end{aligned} \quad (10)$$

where Σ is the $N \times N$ cross-spectral matrix of the scalp potentials in some frequency band. The $3M \times 1$ vector $\mathbf{q}_3$ is then summed along all sets of three consecutive elements (the x , y , and z components) to form the $M \times 1$ source-current density vector q at each voxel. Since q is a mean-squared quantity, its values are always positive. The relationship between q_3 and q is expressed as:

$$q = \text{sum3}(\mathbf{q}_3) = \text{sum3}(\text{diag}(\mathbf{T}\Sigma\mathbf{T}')) \quad (11)$$

Having found the subspace dimension (R) and the subset (s) of columns from $\mathbf{C}$ and $\mathbf{P}$ that best classifies the test sets in groups a and b , the source current power density for each individual in both groups was computed from:

$$q_i = \text{sum3}(\text{diag}(\mathbf{T}\mathbf{C}_{Rs}\mathbf{P}_{Rs}'\Sigma_i\mathbf{P}_{Rs}\mathbf{C}_{Rs}'\mathbf{T}')) \quad (12)$$

In this equation, the subscript Rs indicates the column subset of $\mathbf{C}$ and $\mathbf{P}$ obtained from the classification of the test sets in the subspace of dimension (R). It should be noted that $\mathbf{C}\mathbf{P}' = \mathbf{I}$ if $R = N$ and s includes all of the columns in $\mathbf{C}$ and $\mathbf{P}$. In this case, equation (12) would be the same as equation (11) for the i^{th} individual. If, on the other hand, $R \neq N$ and s does not include all of the columns in $\mathbf{C}$ and $\mathbf{P}$, then the components of Σ_i ,

which factor heavily in the classification are extracted by pre- and postmultiplication with $\mathbf{P}_{Rs}$ and the cross-spectral matrix reconstructed in the reduced space by pre- and postmultiplication with $\mathbf{C}_{Rs}$. The net effect of this is to remove the baseline for the comparison of WF and DL from Σ_i . Therefore, the source current density inside the brain obtained using equation (12) is actually the deviation from the baseline established for the two tasks.

The measure of source-current density from each of the subjects doing each of the tasks was subjected to statistical analysis to determine which brain regions contained the significant differences. The method used was that of randomization [Holmes, 1996]. This method yielded an adjusted threshold statistic that was used to implement a pairwise t test on the mean source-current density vectors obtained from those subjects who completed both of the tasks. This test is exact in that it does not rely on any distributional assumptions of the data, it exhibits Type I error exactly as specified and hence is always valid.

LORETA-KEY uses the three-shell spherical head model registered to the Talairach Human Brain Atlas [Talairach and Tournoux, 1988] available as digitized MRI from the Brain Imaging Centre, Montreal Neurologic Institute (MNI). Registration between spherical and realistic head geometry uses the reported EEG electrode coordinates [Towle et al., 1993]. The solution space is restricted to the cortical gray matter and hippocampus in the Talairach Atlas, as determined by the corresponding digitized Probability Atlas available from the MNI. A total of $M = 2,394$ voxels at 7 mm spatial resolution is produced under this neuroanatomical constraint.

RESULTS

Table I shows the mean-square values (powers) of the EEGs from the 43 recording sites in the theta, alpha, and beta frequency bands from the 20 subjects assigned to the training set. The numbers in the table are the means and standard deviations of the EEG powers from these subjects during the WF and DL tasks. Application of paired t tests to the power values obtained from the individual subjects indicates that in both tasks there was significantly less ($P < 0.01$) beta power than alpha or theta power in the EEGs and that there was significantly less ($P < 0.01$) beta power in DL than in WF. There were no other significant differences between the powers in the tasks, nor was the total power in the three bands significantly different between the tasks.

TABLE I. Mean (std) global EEG power (mean-squared value or variance) in arbitrary units by frequency band in the Word Finding (WF) and Dot Localization (DL) tasks*

	WF	DL
theta	20.7 (5.9)	18.4 (8.5)
alpha	20.8 (10.3)	19.2 (9.2)
beta	13.4 (6.5)	10.1 (3.9)
total	54.8 (17.9)	47.7 (18.2)

* The EEGs used to obtain these results were obtained from the subjects placed in the training set ($n = 20$). A paired t test indicates that there was significantly less power ($P < 0.01$) in the beta band than in either the theta or alpha bands in both tasks and significantly less power ($P < 0.01$) in the beta band during Dot Localization than during Word Finding.

The subspace dimension (R) and the number of spatial patterns (s) from that subspace required to obtain the maximum classification rate of the subjects assigned to the test set is shown in Table II. The smallest subspace dimension was 9 in the theta band while the smallest number of spatial patterns was 3 in the beta band, whereas the largest subspace dimension was 40 and largest number of spatial patterns was 6 in the alpha band.

Table III shows the classification rates obtained using the subspace dimension and spatial patterns given in Table II for each frequency band. As expected, the training set is classified better than the testing set in all bands. Generally, classification in the theta and alpha bands is better than it is in the beta band with the test sets in these bands classified at the minimum rate of 82%. The minimum classification rate of the test set in the beta was less at 73%. In light of the very high rate of classification of the training sets ($\geq 80\%$), the discriminant scores of the subjects in the training set were examined to determine if the same individuals were being misclassified in all of the frequency bands. This analysis indicated that none of the subjects were misclassified in all three frequency bands.

TABLE II. The subspace dimension R and spatial factors s from the subspace that best classified the test sets in each frequency band*

	R	s	No.
theta	9	[1:2 8:9]	4
alpha	40	[1:2 37:40]	6
beta	26	[1:2 26]	3

* The number of subjects in the test sets was 22 for Word Finding and 40 for Dot Localization.

TABLE III. Classification of the EEGs by frequency band and by training/test sets in the Word Finding and Dot Localization tasks

	Set	WF	DL	Totals
theta	training	18/20 (90%)	18/20 (90%)	36/40 (90%)
	testing	18/22 (82%)	33/40 (83%)	51/62 (82%)
	total	36/42 (86%)	51/60 (85%)	87/102 (85%)
alpha	training	18/20 (90%)	19/20 (95%)	37/40 (92%)
	testing	18/22 (82%)	33/40 (83%)	51/62 (82%)
	total	36/42 (86%)	52/60 (87%)	88/102 (86%)
beta	training	16/20 (80%)	18/20 (90%)	34/40 (85%)
	testing	16/22 (73%)	30/40 (75%)	46/62 (74%)
	total	32/42 (76%)	48/60 (80%)	80/102 (78%)

Table IV shows the results of scattering the discriminant scores used to obtain Table III in a multidimensional space with each of the dimensions corresponding to one of the frequency bands. Given the results of Table III, it was expected that the scores would form clusters in this space corresponding to the two cognitive tasks. If the different bands contribute new information to the classification, a decision line placed between the clusters should separate the tasks better than it does with only one of the frequency bands. Table IV shows the results of doing this for all possible pairs of frequency bands and for the three frequency bands together to determine if this is the case. The diagonal cells in the table contain the results for a single frequency band as taken from Table III, the lower off-diagonal cells contain the results for pairs of frequency bands and the upper off-diagonal cell contains the result for all three frequency bands. An examination of the entries in the table indicates that with all three frequency bands (top right-hand corner), the rate of correct classification rate is 93% and therefore greater than with any of the frequency bands alone. When only two of the frequency bands are utilized, the classification rate is better than with a single band only when the theta band is involved. The two-band classification rate is however never as high as the three-band classification rate. Figure 1 shows the two-dimensional scatter plot and decision line for the alpha-theta band classification and indicates that of the 102 cases shown, 93 correctly cluster on the two sides of the decision line.

Figures 2, 3, and 4 show the LORETA-KEY images of the source-current densities in the theta, alpha, and beta frequency bands respectively during the two cognitive tasks relative to the baselines established by the classification process. The slices through the Talairach head shown are spaced 7 mm apart with the white LORETA solution space colored red or green to indicate regions of significantly different source current

TABLE IV. Multiple band classification rates of the 42 Word Finding and 60 Dot Localization cases using scatter plots (an example of a scatter plot is shown in Fig. 1)

Bands	Theta	Alpha	Beta
theta	87/102 (85%)	95/102 (93%)	
alpha	93/102 (91%)	88/102 (86%)	
beta	91/102 (89%)	88/102 (86%)	80/102 (78%)

density in WF and DL. To obtain these figures, LORE-TAs were calculated for each of the 33 subjects (including all 20 from the training set) who completed both tasks. Each of the 2,394 voxels in the solution space was then compared on a pairwise basis to determine if the mean source-current density in that voxel was different between the tasks. The red hues show the source-current density in those brain regions where it is significantly greater during WF than during DL, while the green hues show the source-current density where it is significantly greater during DL than during WF. Only those regions are colored where the statistical significance of the difference is at the $P < 0.05$ level of probability. The critical paired-t statistic required to achieve this level of significance was obtained using the method of randomization [Holmes et

Figure 1.

Scatter plot of the alpha and theta band discriminant scores. The asterisks denote the Word Finding cases while the circles denote the Dot Localization cases. Of the 102 cases shown, 93 fall on the correct sides of the decision line.

Figure 2.

Tomographs of the source-current density distribution in the brain during the Word-Finding (WF) and Dot Localization (DL) tasks in the theta (4–7 Hz) frequency band. The red hues indicate the source-current density in regions where it is significantly

greater ($P < 0.05$) during WF than during DL and the green hues indicate the source-current density in regions where it is significantly greater ($P < 0.05$) during DL than during WF.

al., 1996]. This method provides a statistic that is corrected for multiple comparisons.

An examination of Figures 2, 3, and 4 indicates that there are regions of significantly different source-current density between WF and DL in all three frequency bands. These regions are most highly localized and most completely lateralized in the theta band (Fig. 2). In the alpha band (Fig. 3), the significantly greater source-current density distribution during WF is almost completely lateralized to the right hemisphere, while in the beta band (Fig. 4), the greater source-current density distribution during DL is almost com-

pletely lateralized to the left hemisphere. In these two bands, the source-current distribution during the opposite task is not strongly lateralized. The general picture from Figures 2, 3, and 4 appears to be that brain regions with significantly greater source-current density during one task in one band will not also have significantly greater source-density during the other task in another band. The most notable exceptions to this picture are the right temporal lobe in the alpha and beta bands (upper left slices, Figs. 3 and 4) and in the left occipital lobe in the theta band (rightmost slices, second row from the top).

Figure 3.

Tomographs of the source-current density distribution in the brain during the Word-Finding (WF) and Dot Localization (DL) tasks in the alpha (8–13 Hz) frequency band. The red hues indicate the source-current density in regions where it is significantly

greater ($P < 0.05$) during WF than during DL, and the green hues indicate the source-current density in regions where it is significantly greater ($P < 0.05$) during DL than during WF.

Table V contains a list of the locations of the peaks in the source-current density distribution from Figures 2–4 along with their relative intensities and anatomical locations in the Talaraich Atlas [Talairach and Tournoux, 1988]. These centers of source-current density are indicated with yellow arrows on the figures and their locations are given with respect to a coordinate system with x axis oriented toward the right ear, y axis toward the nose and z axis toward the vertex. In the theta band, the centers of source-current density are located in the left hemisphere during DL and in the right hemisphere during WF. During DL, the cen-

ters are located in Brodman areas 44 and 19 generally considered to be Broca's motor speech area and a visual association area, respectively. During WF, the most intense center is located in area 39, also a visual association area. In the alpha and beta bands, the centers of source-current density identified in DL are frontal while in WF they are more posterior. Brodman area 6 (the premotor cortex) in the right hemisphere is a center of source-current density in both bands, during DL in the alpha band and during WF in the beta band. During DL however, the center is located some 20 mm above that during WF in area 6.

Figure 4.

Tomographs of the source-current density distribution in the brain during the Word-Finding (WF) and Dot Localization (DL) tasks in the beta (14–20 Hz) frequency band. The red hues indicate the source-current density in regions where it is significantly greater ($P < 0.05$) during WF than during DL, and the green hues indicate the source-current density in regions where it is significantly greater ($P < 0.05$) during DL than during WF.

DISCUSSION

The results of this work are considered to be convincing demonstrations of the relationship between electrical activity and cognitive function in the human brain. Unlike previous findings, those presented here are completely free of the ambiguities in the EEG caused by the recording reference. These ambiguities have, at times, acted to actually hide the electrical effects of some cognitive functions [Davidson et al., 1990]. Here, elimination of recording ambiguities was achieved by transforming the scalp potentials of the

EEG to source-current densities inside the brain using the LORETA algorithm. The tomographic images of the source-current densities provide a picture of how the relationship between electrical activity and cognitive function is distributed in the brain.

In the end, the results of this work support the conclusions of Davidson et al. [1990] insofar as there is a lateralization of the EEG in relation to the putative functional activity of the brain. It is notable that while these researchers reported the same task-related effects in all of the delta, theta, alpha, and beta frequency bands, these effects were not significant in the

TABLE V. Centers of source-current density and their locations (taken from Figs. 2 to 4)*

Band	Task	Intensity	X, Y, Z	Anatomy
Theta	DL	-1.0	-38, -88, 22	BA 19—Middle Occipital Gyrus
	DL	-0.74	-52, 10, 8	BA 44—Precentral Gyrus
	WF	0.69	46, -67, 29	BA 39—Angular Gyrus
	WF	0.67	60, -32, 1	BA 21—Middle Temporal Gyrus
Alpha	DL	-1.0	-59, 3, -6	BA 21—Middle Temporal Gyrus
	DL	-0.90	39, 3, 29	BA 6—Precentral Gyrus
	WF	0.76	46, -60, 8	BA 37—Middle Temporal Gyrus
	WF	0.37	18, -74, 29	BA 31—Precunius
Beta	WF	1.0	46, -67, 8	BA 37—Middle Temporal Gyrus
	WF	1.0	60, 3, 8	BA 6—Precentral Gyrus
	DL	-0.90	39, 38, 36	BA 9—Middle Frontal Gyrus
	DL	-0.86	-31, 3, -41	BA 38—Middle Temporal Gyrus

* The centers are the peaks in the source-current density distribution. Their locations are marked with yellow arrows in the figures. Numbers in the anatomy column indicate the respective Brodman Areas. The centers of the distributions are arranged in order of decreasing intensity. Locations are given with respect to a coordinate system with x axis in the direction of the right ear, y axis in the direction of the nose, and z axis in the direction of the vertex.

delta and theta bands when the recording reference was changed to that of averaged ears. Our results show similar statistically significant effects in the theta, alpha, and beta frequency bands with these being most localized spatially in the theta band. The fact that some of the theta-band effects were posterior temporal might explain why it was not seen by Davidson et al. [1990] with the averaged-ears reference.

To our knowledge, this work is the first demonstration of a right greater than left/left greater than right effect in the electrical activity of the brain associated with the verbal or spatial nature of the cognitive task. In other studies, lateralization is deduced from some measure of asymmetry in the EEG at homologous recording sites. Usually, the pattern seen is a shift in this measure, in one direction or the other. In many cases, the direction of the right/left asymmetry in the EEG remains the same in both tasks. To set a baseline for the comparison in this work, those components in the EEGs that were common to the two cognitive modes were removed. In an attempt to ensure that the removed components were truly characteristic of the general population, they were selected from one group of subjects and verified on another. Those components that did not contribute to the classification of the test group of EEGs were excluded. By factoring out those components from the EEGs that did not contribute to the classification, a baseline from which changes in electrical activity could be measured in both tasks was established. It should be noted at this point that without this factoring, attempts to find regions of significantly different source-current density in the two tasks yielded nothing in the theta band and compar-

atively small regions with significant differences in the alpha and beta bands. Also, comparison of the EEGs during the two tasks to EEGs recorded from the same subjects during a passive resting state showed regional differences in source-current density that were essentially the same for both tasks in all three frequency bands. Evidently, differences in the source-current density distributions between WF and DL are so subtle that the two tasks must be compared to one another to detect any differences.

LORETA provides a measure of the source-current density distribution inside the brain underlying the EEG. Of the infinite number of source-current density distributions that can account for the EEG, LORETA provides one that, in some sense, is spatially the smoothest. Individual EEG electrodes see only the synchronized activity of many thousands of cellular generators and multiple electrodes tend to see different groups of generators. LORETA creates a composite picture of what all of the electrodes see and fills in what they don't see well by blurring everything together. The conclusion is that LORETA images are images of synchronized generator activity inside the brain. Regions of high source-current density therefore represent regions of synchronized cellular electrical activity. It is generally assumed that in regions of synchronized electrical activity, functional activity is low. Our conclusion therefore is that, in our comparisons of WF and DL, those regions where the functional activity is lower in WF as evidenced by greater source-current density, actually represent regions of higher functional activity in DL and vice versa. In other words, instead of describing Figures 2–4 as re-

gions of greater synchronization in the first task compared to the second, they could just as well be described as regions of greater desynchronization in the second task compared to the first. To the extent that the two tasks are psychometrically matched, this logic should apply to the actual intensities of the source-current densities and their spatial distributions as well.

Because of the relationship between source-current density and functional activity in the brain, comparison of the present results with those obtained using fMRI and PET requires that the association of the centers of source-current activity with WF and DL in Figures 2–4 and Table V be reversed. That is, the centers of source-current density labeled WF in Table V are actually associated with centers of functional activity in DL and vice versa. Similarly, to indicate functional activity, the green regions in Figures 2–4 should actually be associated with WF and the red regions with DL. Now, the center of source-current density in the theta band (Fig. 2) in the left motor speech area associated with WF is as expected. With respect to the alpha and beta bands (Figs. 3 and 4), one could say that almost all of the brain regions are involved functionally in one task or the other. WF involves much more of the brain than DL in the alpha band (Fig. 3) whereas the opposite is true in the beta band (Fig. 4). The conclusion is that WF is more an alpha-band effect and DL is more a beta band effect and that WF involves the left central and frontal parts of the cerebrum and DL involves the right central and posterior parts of the cerebrum. We recall that it is only in the beta band that there is significantly less global power in the EEG during DL than in WF (Table I).

The lateralization of cognitive function has been demonstrated with the emission tomographies and with functional magnetic resonance imaging. Probably the most impressive results related to the lateralization of verbal and spatial processing were obtained by Smith et al. [1996] using PET. Their results showed that a particular verbal memory task activated primarily left-hemispheric regions whereas a particular spatial memory task activated only right hemispheric regions. Ojemann et al. [1998] have shown that consistent results are obtained with blood oxygen level measurements obtained with fMRI and blood flow measurements obtained with PET. Both modalities show strong bilateral occipital activation during a visually presented word-stem completion task and strong left hemisphere activation in the motor speech area. Similar results were obtained for PET and fMRI by Xiong et al. [1998] using a verb generation task that

was also visually presented. The results presented here show a strongly lateralized occipital effect in the theta-band source-current density during visually presented verbal and spatial tasks.

The finding that the effects of verbal and spatial cognitive tasks occur in different frequency bands is contrary to the commonly held belief that this occurs only in the alpha band. Our results related to multiple-band classification suggest that not only is there an effect in all three frequency bands but that there is independent information related to cognitive function in each them. Given the usually large statistical variation in EEG parameters, it is interesting that, when all three frequency bands were used, 95 out of 102 cases of WF and DL were correctly classified (Table IV). This suggests that the brain patterns in 93% of the subjects tested showed the patterns of brain activity seen in Figures 2–4. It is worth noting that Cohen et al. [1996] have pointed out significant problems associated with inter-subject variability in PET.

The methods used in this work are similar to those used by Lind et al. [1999] except that the methods of removing those components from the EEG that are not related to the differences in the processing of verbal and spatial tasks have been improved. In the present study, the approach was to find and to use only those spatial factors in the EEG common to the two tasks that were maximally discriminatory. This procedure eliminated components that were equally present in the two tasks and created a baseline from which to measure shifts in source-current density specific to the two tasks. Another way of doing this would have been to record the resting EEG [Hoptman and Davidson, 1998]. However, this procedure is less sensitive to the specific nature of the tasks because of the additional variance in the measurements introduced by the instability of this baseline over the subjects. In Lind et al. [1999], the MUSIC algorithm was used to estimate the centers of electrical activity associated with each of the tasks. MUSIC is a dipole-fitting procedure, and while it was demonstrated that dipole fitting can be used to find the centers of electrical activity in the brain even if the actual sources are not point sources, it was also demonstrated that the estimated centers may sometimes not be in the brain part of the head. This happens when the volume of source activity is larger than roughly one the cerebral lobes. With LORETA, this is not a problem as assumptions about the source model are not required and the solution space can be constrained to be in just the gray matter of the cerebrum. Also, unlike MUSIC, LORETA does not produce an estimate of the goodness of fit of a point dipole source but of the actual primary source current density un-

derlying the EEG. As such, the spatial distribution of the source density is more amenable to comparison with measurements of brain function obtained with the other imaging modalities.

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