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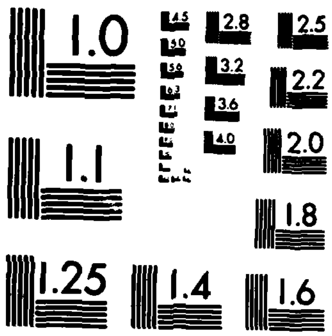

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ELECTROPHYSIOLOGICAL MEASURES OF REGIONAL NEURAL INTERACTIVE COUPLING+

(Linear and Nonlinear Dependence Relationships Among Multiple Channel Electroencephalographic (EEG) Recordings)

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ABSTRACT

Linear spectral coherence[1] measures have been used in the neurosciences to test hypotheses which address the question of whether multiple EEG recording sites are independent or whether they are activated by common sources of neurophysiological activity. This measure is appropriate when regional neural sources interact and thereby electrically activate several recording sites through linear transmission pathways which may or may not be different in their linear transformation properties. However, if the transmission media are nonlinear, then interactive dependency is not necessarily revealed by a linear coherence test. Therefore, if common sources are activating EEG recording sites through nonlinear media, evaluating the resulting relationships among the signals recorded from these sites requires a test which reveals the presence of such nonlinear relationships. In neurophysiological applications, a polycoherence cross-spectral measure provides such a test for nonlinear dependency (similar to the linear coherence test) among EEG recording sites. The data requirements and statistical properties of these linear and nonlinear measures are described and results of a linear coherence analysis are presented in the context of an EEG pilot study of learning-disabled children.

INTRODUCTION

Analysis of the relationships among multiple channel EEG signals[2] represents one of the challenging problems in the evaluation of brain electrical activity. One frequently used analysis procedure for the pair-wise comparison of multiple channel data is provided by the cross-correlation function, which measures the product moment correlation between two signals as a function of lag (i.e., the time displacement between the signals). However this procedure has the disadvantage of being insensitive to the presence of highly correlated low amplitude frequency components of activity which may be imbedded in uncorrelated high amplitude activity. Therefore the normalized Fourier transform of the cross-correlation function[a] is commonly employed to provide a means of deriving the degree of linear dependence or coherence between two signals over distinct frequency bands. This allows linearly dependent activity contained within particular frequency bands to be clearly observed in the presence of intense uncorrelated or linearly independent activity in other frequency bands.

The question of dependence between two signals can be broadened to include nonlinear dependence. However, to perform an analogous test for nonlinear dependence requires the use of polycoherence analysis which involves the computation of higher dimensional Fourier transforms. This paper will describe the analytical methodology for testing of both linear and nonlinear dependence. Illustrative pilot data from a study using EEG linear spectral coherence to test hypotheses involving shared brain activity in learning disabled children as compared to normal controls will also be described.

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[a] The normalized Fourier transform of the cross-correlation function is called the "spectral coherence function" or simply the "coherence function".

METHODOLOGY

The issue of neurophysiological interest examined in this paper can be stated as follows: can EEG activity recorded from multiple scalp locations give information about the level of shared or common electrical activity associated with the brain regions proximate to these recording sites? A basic method for addressing this question is to test whether a transformation exists which will map signal $S_1(t)$ into signal $S_2(t)$ where $S_1(t)$ and $S_2(t)$ represent EEG signals recorded from two scalp locations.

If the mapping can be done by a linear transformation then the signals in question are said to be linearly dependent. The degree of linear dependence (as a function of frequency) between the EEG signals associated with these brain regions is determined by applying spectral coherence analysis.

Similarly, if the mapping of $S_1(t)$ into $S_2(t)$ requires a nonlinear transformation then polyspectral (in particular cross-bicoherence)[4] analysis can be used to address the question of coupling or, stated another way, the degree of nonlinear dependence as a function of frequency.

The degree of dependence among signals can range from zero for independent signals to unity for totally dependent signals. In the context of EEG analysis this degree of dependence or connectivity is taken as a measure of shared electrophysiological activity among brain regions.

LINEAR DEPENDENCE

The numerical measure of linear dependence is derived from the coherence function whose magnitude ranges from zero to unity. The analytical and statistical methods involved in applying the coherence function to EEG data are outlined in the following paragraphs.

The coherence function is defined in terms of the normalized cross-spectrum of the two time series. The cross-spectrum can be expressed as the Fourier Transform of the cross-correlation function as follows:

Let $S_1(t)$, $S_2(t)$ denote the different time series and let $\phi_{12}(\tau)$ denote the cross-correlation function of $S_1(t)$, $S_2(t)$, where τ is the variable time shift between S_1 and S_2, then $\phi_{12}(\tau)$ is defined by the integral equation

$$\phi_{12}(\tau) = \frac{1}{T}\int_0^T S_1(t)\, S_2(t+\tau)dt \tag{1}$$

The cross-spectrum of $S_1(t)$ and $S_2(t)$, denoted as $P_{12}(f)$ is defined by (2), using the exponential form of the Fourier transformation,

$$P_{12}(f) = \int_{-\infty}^{+\infty} \phi_{12}(\tau)\, e^{-i2\pi f\tau} d\tau \tag{2}$$

(where f is frequency in Hertz and τ is time shift in seconds).

By substituting equation (1) into equation (2) and appropriately factoring the resulting double integral it can be shown that

$$P_{12}(f) = \overline{S}_1(f)\, \overline{S}_2^*(f) \tag{3}$$

where: $\overline{S}_1(f)$ is the Fourier transform of $\overline{S}_1(t)$ and $\overline{S}_2^*(f)$ is the conjugate Fourier transform of $S_2(t)$. Since $\overline{S}_1(f)$ and $\overline{S}_2^*(f)$ are complex numbers in general, therefore $P_{12}(f)$ is also complex. It simplifies subsequent analysis to represent them in polar form, as follows:

$$\overline{S}_1(f) = r_1 e^{i\theta_1} \tag{4}$$

$$\overline{S}_2^*(f) = r_2 e^{-i\theta_2} \tag{5}$$

Substituting (4) and (5) into (3) gives the cross-spectral density in polar form:

$$P_{12}(f) = r_1 r_2 e^{i(\theta_1 - \theta_2)} = r_1 r_2 e^{i\theta} \tag{6}$$

(where $\theta = \theta_1 - \theta_2$)

While not explicitly shown, note that the r's and θ's are functions of f. Now to arrive at the spectral coherence function we normalize equation

(6) by dividing by r_1r_2 and then average over a number of frequencies and/or over a number of time epochs of the two time series being analyzed.

Thus if the average is taken over $2N+1$ discrete frequencies we may write the spectral coherence as

$$C(f_0) = \frac{1}{2N+1} \sum_{k=-N}^{N} e^{i\theta(f_k)} \tag{7}$$

where f_0 is the center of the spectral window and uniform weighting is used in the window. If the average is taken over M time epochs at a specific frequency, f_k, (ensemble averaging) we may write the spectral coherence as

$$C(f_k) = \frac{1}{M} \sum_{m=1}^{M} e^{i\theta_m(f_k)} \tag{8}$$

where $\theta_m(f_k)$ is the phase angle between S_1 and S_2 at frequency f_k during the mth time epoch. If a combination of frequency and ensemble averaging is used then spectral coherence may be written

$$C(f_0) = \frac{1}{M(2N+1)} \sum_{m=1}^{M} \left(\sum_{k=-N}^{k=N} e^{i\theta_m(f_k)} \right) \tag{9}$$

Again, these expressions assume the use of uniform weighting in the spectral window.

It should be noted that for linearly independent signals the phase difference $\theta(=\theta_1-\theta_2)$ is a random function over both frequency and ensemble and therefore the expected value of coherence averaged over frequency and/or time (ensemble averaging) is zero.

Thus, when coherence deviates significantly from zero, one may conclude that the two signal processes in question are related through a linear transformation over the spectral region where such significant deviation occurs.

The statistical measure of significance of the deviation of a coherence estimate from its expected value depends on the number of independent samples of coherence which are used in arriving at the coherence estimate, and upon the probability distribution function of these coherence estimates as described below.

A coherence estimate is the average computed from samples of the normalized cross-spectrum. These samples can be represented as points on the unit circle in the complex plane, as illustrated in Figure 1. If these points are uniformly distributed over the unit circle, it is clear that the expected value of coherence lies at the origin $(\bar{x} = \bar{y} = 0)$. The normalized samples of cross-spectrum may be written:

$$x_k + iy_k = e^{i\theta_k} = \cos\theta_k + i\ \sin\theta_k \tag{10}$$

A random distribution of values on the circumference of the unit circle (as shown in Figure 1) is equivalent to the condition that the relative phase values between S_1 and S_2 be uniformly randomly distributed over an ensemble of time epochs and/or over a number of frequencies in a spectral window centered at frequency f_0. Under this condition the complex value of coherence may be written:

$$Coh(f_0) = \frac{1}{N} \sum_{k=1}^{N} x_k + i \frac{1}{N} \sum_{k=1}^{N} y_k \tag{11}$$

Since x_k and y_k lie on the unit circle

$$x_k = \cos\theta_k$$

$$y_k = \sin\theta_k$$

the PDF (Probability Distribution Function) of both x and y (given that θ is a uniformly distributed random variable) have the same form and are given by:

$$D(x) = \frac{1}{\pi\sqrt{1 - x^2}}\ ,\ D(y) = \frac{1}{\pi\sqrt{1 - y^2}} \tag{12}$$

The corresponding means, $(\bar{x}, \bar{y})$ and variances (σ_x^2, σ_y^2) are given b

$$\bar{x} = \bar{y} = 0 \tag{13}$$

$$\sigma_x^2 = \sigma_y^2 = \frac{1}{2N} \tag{14}$$

where N = number of samples.

From (13) and (14) the resulting mean and variance of the coherence magnitude $(|coh(f_0)| \equiv r)$ are:

$$\bar{r} = 0 \tag{15}$$

$$\sigma_r^2 = \frac{1}{N} \tag{16}$$

Thus, to test the hypothesis that $S_1(t)$ and $S_2(t)$ are linearly independent time series, one examines the probability that the empirically-obtained mean, computed from N samples, deviates from the expected value (zero in this case).

For example when the coherence magnitude, r, is obtained by a combination of ensemble averaging over 20 epochs and frequency averaging over 5 spectral components then

$$N = 20 \times 5 = 100$$

and the resulting standard deviation of the estimate is

$$\sigma_r = \frac{1}{\sqrt{N}} = \frac{1}{\sqrt{100}} = 0.10$$

Thus an empirically obtained value of coherence magnitude which exceeds 0.2 would be more than two standard deviations from the expected value for independent signals. Therefore, it would be statistically reasonable to conclude that the signals in question are not independent, but rather that they are linearly dependent or coherent over the spectral region where the coherence magnitude exceeds 0.2.

NONLINEAR DEPENDENCE

The test for a nonlinear relationship between $S_1(t)$ and $S_2(t)$ is similar in principle to the linear test, but it makes significantly greater demands on computer processing.

By analogy with the linear coherence test, the nonlinear test involves a multi-dimentional Fourier transform of a multiple lag product similar to the cross-correlation function, whose normalized Fourier transform is the coherence function. Specifically the double lag product is given by:

$$\phi(\tau_1,\tau_2) = \frac{1}{T}\int_0^T S_1(t)\ S_1(t+\tau_1)\ S_2(t+\tau_2)\ dt \tag{17}$$

The cross-bispectrum [(b)] is defined as the two dimensional Fourier transform of $\phi(\tau_1,\tau_2)$ as follows:

$$B(f_m,\ f_n) = \int_{-\infty}^{+\infty}\int_{-\infty}^{+\infty} \phi(\tau_1,\tau_2)\ e^{-j2\pi f_m\tau_1}\ e^{-j2\pi f_n\tau_2} d\tau_1 d\tau_2 \tag{18}$$

The cross-bicoherence is obtained by normalizing the cross-bispectrum as follows:

Cross-Bicoh $(f_m,\ f_n) \equiv$ Average over frequency and/or ensemble of the following triple product of F.T.'s

$$\frac{\overline{S}_1(f_m)\ \overline{S}_1(f_n)\ \overline{S}_2^*(f_m+f_n)}{|\overline{S}_1(f_m)|\,|\overline{S}_1(f_n)|\,|\overline{S}_2(f_m+f_n)|}$$

where * denotes complex conjugate and the vertical bars denote absolute value. It is instructive to write this triple product in polar form, as follows:

Denote

$$\overline{S}_1(f_m) = r_m\ e^{i\phi_m} \tag{19}$$

$$\overline{S}_1(f_n) = r_n\ e^{i\phi_n} \tag{20}$$

$$\overline{S}_2^*(f_m+f_n) = r_p\ e^{-i\phi_p} \tag{21}$$

where the r's and ϕ's are functions of frequency and $|\overline{S}_k(f)| = r_k$. Using the polar form in equations (19), (20) and (21), cross-bicoherence is given by

Cross-Bicoh $(f_m,\ f_n) \equiv$ average over frequency and/or ensemble of $e^{i\phi_k}$

(b) If $S_1(t) \equiv S_2(t)$, then $B\ (f_m,\ f_n)$ is called the bispectrum.

where $\phi_k = \phi_m + \phi_n - \phi_p$ compares the phase at the sum frequency $(f_m + f_n)$ in channel 2 with the sum of the phases at frequencies f_m and f_n in channel 1.

Thus for every pair of frequencies selected we obtain a value for ϕ_k which defines a point on the unit circle in the complex plane (just as in the case of linear coherence). Therefore if $(2N + 1)$ pairs of frequencies are selected over an ensemble of M time epochs, the bicoherence estimate is obtained by averaging the $(2N + 1)M$ samples as follows (assuming uniform weighting of the samples):

$$Cross\text{-}Bicoh\ (f_m, f_n) = \frac{1}{M(2N + 1)} \sum_{k=1}^{M(2N+1)} e^{i\phi_k} \tag{22}$$

Some detailed expansion is required to implement the above simplified expression. First, the bicoherence estimate for the frequency pair (f_m, f_n) is an average obtained from samples centered around (f_m, f_n) as follows:

$$Bicoh\ (f_m, f_n) = \frac{1}{2N+1} \sum_{k=-N}^{k=N} \frac{\overline{S}_1(f_m + k\Delta f)\ \overline{S}_1(f_n + k\Delta f)\ \overline{S}_2^*(f_m + f_n + 2k\Delta f)}{|\overline{S}_1(f_m + k\Delta f)|\,|\overline{S}_1(f_n + k\Delta f)|\,|\overline{S}_2(f_m + f_n + 2k\Delta f)|} \tag{23}$$

Using a subscript j to designate the time epoch over which the above estimate is obtained and Δf to designate the frequency increments, then when ensemble averaging as well as frequency averaging is used we may write

$$Bicoh\ (f_m, f_n) = \frac{1}{M(2N+1)} \sum_{j=1}^{M} \sum_{k=-N}^{N} \frac{\overline{S}_{1,j}(f_m+k\Delta f)\ \overline{S}_{1,j}(f_n+k\Delta f)\ \overline{S}_{2,j}^*(f_m+f_n+2k\Delta f)}{|\overline{S}_{1,j}(f_m+k\Delta f)|\,|\overline{S}_{1,j}(f_n+k\Delta f)|\,|\overline{S}_{2,j}(f_m+f_n+2k\Delta f)|} \tag{24}$$

The argument for the statistics of this estimator is similar to the previous discussion of linear coherence. Thus for two independent random processes the standard deviation (σ) of bicoherence magnitude from the expected value of zero is $\sigma = \frac{1}{\sqrt{M(2N+1)}}$

Thus, if one averages 5 pairs of lines $(N=2)$ and over 20 epoches $(M=20)$ then $\sigma = 0.1$, similar to the example for linear coherence.

COHERENCE ANALYSIS OF PILOT DATA

Linear coherence analysis was applied to pilot data from the EEGs of white male learning disabled children and normal controls. The objective of this analysis was to investigate whether differences in EEG multiple channel linear dependence provides a basis for separating these populations.

The coherence analysis results shown in Figure 2 represent E data recorded from a learning disabled child and an age and sex m ed normal control. The recording paradigm was designed to control t cognitive state of the subjects so that data could be obtained dur information processing. Although several tasks were employed, the typical results in Figure 2 were derived from EEG data recorded while the subject indicated whether sequentially presented pictures and words matched. The subject was instructed to delay the response until a tone was presented approximately three seconds after the second stimulus and then press a button if the stimuli matched. The coherence analysis is based on the 1.2 seconds of EEG in the middle of this delay interval. The most consistent finding which separated the 12 learning disabled from the 13 normal children in the pilot study was coherence magnitude at frequencies above 20 Hertz. It can be noted in Figure 2 that for frequencies above 20 Hertz the learning disabled child exhibits values of coherence[c] much less than 0.1 while the normal control exhibits values of coherence greater than 0.1 over most of this frequency range. The comparisons in Figure 2 are for coherence between left and right central leads in the test and control subjects, and similarly for coherence between left and right occipital leads.

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[c] As in the discussion of linear coherence the coherence estimates here are based on averaging over 20 epochs and 5 spectral lines. For linearly independent signals the standard deviation from zero of these estimates is 0.1.

These findings suggest that impaired sharing of high frequency EEG activity may be implicated in the neural processes associated with learning disability. More generally these spectral procedures for obtaining dependency measures among multiple EEG recording sites offer a quantitative basis for assessing regional electrophysiological interactions during mental processing or in response to medication or other clinical intervention.

CONCLUDING COMMENTS

In evaluating the EEGs of subjects it is important to not that major differences in EEG waveshape across subjects may be of no consequence[3,4] as far as revealing useful diagnostic or clinical differences. The essential property of multiple channel coherence analysis is that it measures the degree of communication or shared EEG activity among the channels recorded from a particular subject rather than waveshape per se. It is this coherence measure of shared activity which constitutes the criterion for comparing or categorizing subjects. Thus even though the EEG waveshapes across subjects may be quite different it is possible that the multiple channel shared EEG activity of such subjects may be quite similar. Ultimately it is hoped that the multiple channel measures described here can provide important information to aid in diagnosis and in the evaluation of treatment of conditions such as learning disability as well as provide a measure of mental processing or neurophysiological state which is independent of idiosyncratic differences in EEG waveshape.

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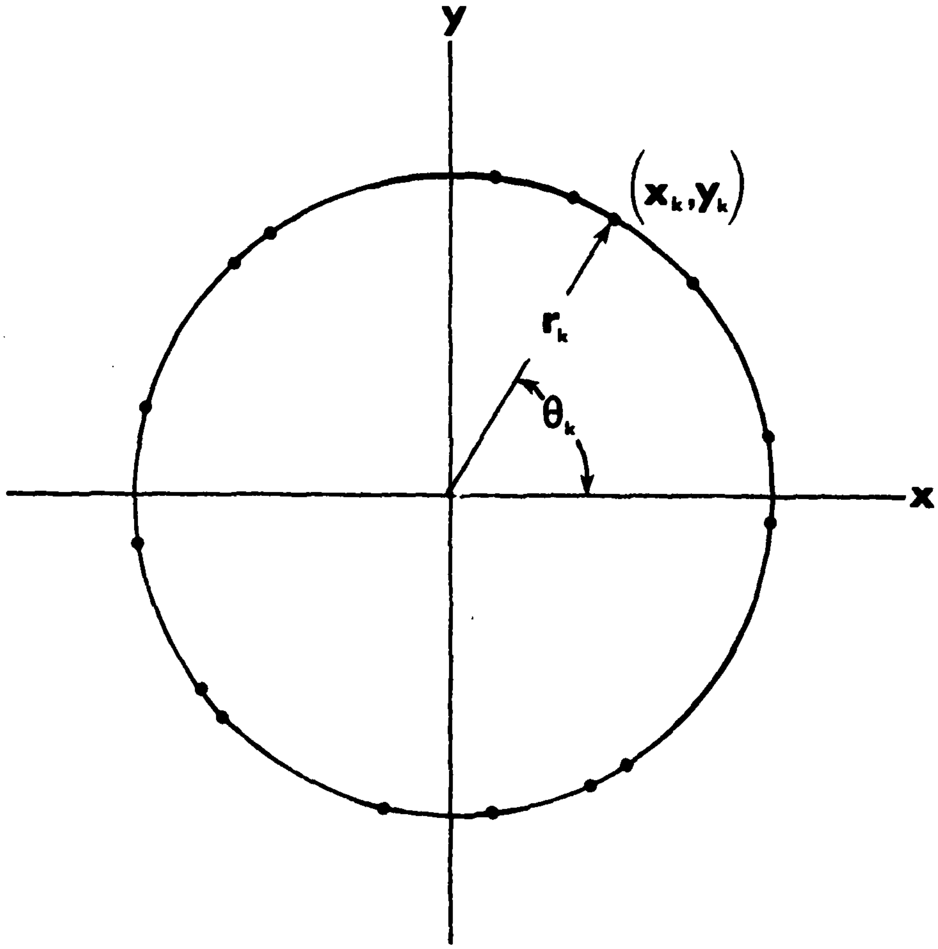

Figure 1. A coherence sample as a point on the unit circle in the complex plane. A coherence estimate is the average of such samples over a specified number of frequencies and/or a specified number of time epochs.

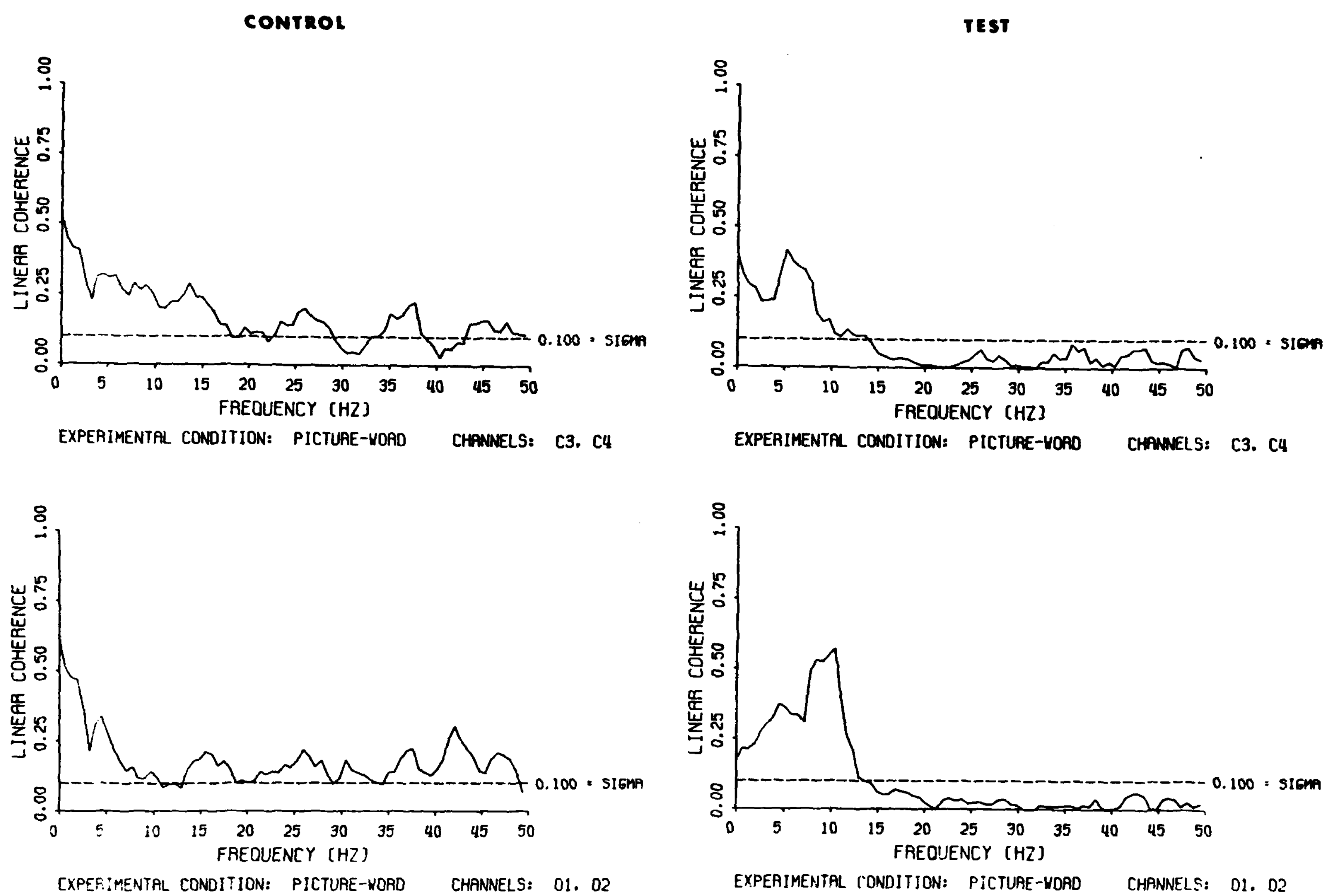
CONTROL
TEST
LINEAR COHERENCE
0.00
0.25
0.50
0.75
1.00
0
5
10
15
20
25
30
35
40
45
50
FREQUENCY (HZ)
0.100 : SIGMA
EXPERIMENTAL CONDITION: PICTURE-WORD
CHANNELS: C3. C4
CHANNELS: O1. O2

Figure 2

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