

Clinical Neurophysiology 115 (2004) 2292-2307



Identifying true brain interaction from EEG data using the imaginary part of coherency

Guido Nolte*, Ou Bai, Lewis Wheaton, Zoltan Mari, Sherry Vorbach, Mark Hallett

Human Motor Control Section, NINDS, NIH, 10 Center Drive MSC 1428, Bldg 10, Room 5N226, Bethesda, MD 20892-1428, USA

Accepted 17 April 2004

Available online 10 July 2004

Abstract

Objective: The main obstacle in interpreting EEG/MEG data in terms of brain connectivity is the fact that because of volume conduction, the activity of a single brain source can be observed in many channels. Here, we present an approach which is insensitive to false connectivity arising from volume conduction.

Methods: We show that the (complex) coherency of non-interacting sources is necessarily real and, hence, the imaginary part of coherency provides an excellent candidate to study brain interactions. Although the usual magnitude and phase of coherency contain the same information as the real and imaginary parts, we argue that the Cartesian representation is far superior for studying brain interactions. The method is demonstrated for EEG measurements of voluntary finger movement.

Results: We found: (a) from 5 s before to movement onset a relatively weak interaction around 20 Hz between left and right motor areas where the contralateral side leads the ipsilateral side; and (b) approximately 2-4 s after movement, a stronger interaction also at 20 Hz in the opposite direction.

Conclusions: It is possible to reliably detect brain interaction during movement from EEG data.

Significance: The method allows unambiguous detection of brain interaction from rhythmic EEG/MEG data.

© 2004 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.

Keywords: Coherence; EEG; Connectivity; Motor control; Volume conduction; Time-lag

1. Introduction

The millisecond temporal resolution of electroencephalography (EEG) and magnetoencephalography (MEG) measurements make these techniques ideal candidates to study the brain as a dynamic system. Recently, much attention has been paid to interpreting rhythmic EEG/MEG activity in terms of brain connectivity. Probably the simplest and most popular measure of 'interaction' at a specific frequency is coherence, a generalization of correlation to the frequency domain (Nunez et al., 1997, 1999). Coherence is almost always studied as a relation between EEG or MEG channels while one is interested in relations between brain sites. Since the activity of a single generator within the brain is typically observable in many channels outside the head, with details of this mapping depending on the volume conductor (Sarvas, 1987), it is likely that a relation between

* Corresponding author. Tel.: +1-301-435-1578.

E-mail address: nolteg@ninds.nih.gov (G. Nolte).

channels is rather a trivial 'volume conduction artefact' than a reflection of an underlying interacting brain (Nunez et al., 1997). Mathematically similarly, for EEG one always needs a reference. If this reference is the same for the electrode pairs being studied, it can contribute significantly to the coherence, and thus, relative power changes may also affect coherencies without reflecting a change in coupling (Fein et al., 1988; Florian et al., 1998).

A plausible attempt to avoid artefacts from volume conduction is first to apply an inverse method (see Baillet et al. (2001) for an overview) to the data and then to calculate coherence or any other measure of interaction of the estimated source amplitudes (Gross et al., 2001). The problem is that a fully satisfactory inverse method does not exist and cannot exist (Sarvas, 1987). Any inverse method is based on prejudices about the underlying sources. If these prejudices are wrong (and sometimes even if they are correct) the separation of channel amplitudes into source amplitudes will be wrong (incomplete), and again it is likely

1388-2457/\$30.00 © 2004 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved. doi:10.1016/j.clinph.2004.04.029

that artefacts of volume conduction will be misinterpreted as brain interaction.

In this paper, we interpret brain interaction from a quantity, namely the imaginary part of coherency, which itself cannot be generated as an artefact of volume conduction as will be shown below. The fundamental assumption we make to arrive at this conclusion is that the the quasi-static approximation holds for EEG, i.e. that an observed scalp potential has no time-lag to the underlying source activity, which is indeed widely accepted (Stinstra and Peters, 1998). The imaginary part of coherency is only sensitive to synchronizations of two processes which are time-lagged to each other. If volume conduction does not cause a time-lag, the imaginary part of coherency is hence insensitive to artifactual 'self-interaction'.

It is conceivable that in many experiments this imaginary part is very small or even vanishing if the time-lag between two processes is small or even vanishing. Therefore, it is likely that our approach misses parts and in the worst case all of the brain interaction. However, because of this special property of being inconsistent with non-interacting sources, in our opinion, it deserves special attention. If we find a nonvanishing imaginary part, the interpretation as a reflection of true brain interaction is almost immediate.

Thus, the experimental question is whether an imaginary part of coherency can be observed in real data. We will exemplify this for EEG measurement of voluntary left and right-hand movements, which has been the objective of many EEG coherence studies (Andrew and Pfurtscheller, 1999; Florian et al., 1998; Gerloff and Andres, 2002; Ginter et al., 2001; Leocani et al., 1997; Manganotti et al., 1998; Mima et al., 2000; Pfurtscheller and Andrew, 1999). While an increased coherence at around 20 Hz (beta-activity) between electrodes over the left and right motor areas during movement and a decrease after movement is well known, it has been argued that these effects are essentially artefacts of volume conduction and that beta-activity is not involved in the connection between left and right motor areas (Andrew and Pfurtscheller, 1999; Pfurtscheller and Andrew, 1999). Regardless of whether this is right or wrong, of special interest to this paper is the debate itself. Coherence (as an absolute value) is ambiguous: any outcome is perfectly consistent with non-interacting sources. In contrast, such a debate is unnecessary when analyzing the imaginary part of coherency. We show here that in fact beta-activity is involved in the communication between left and right motor areas, but that the timing of these interactions differs from the one expected from 'standard' coherence analysis.

This paper is organized as follows. In Section 2.1 we recall the definition of coherence. A coherence matrix contains a large amount of information. Our solution as to how to visualize this information is presented in Section 2.2. In Section 2.3, we discuss the special role of the imaginary part of coherency, and in Section 2.4, we present the statistics of coherency including a method to control for

multiple comparisons. In Section 3, we give the results for a simple motor task. The paradigm is explained in Section 3.1 and the results of standard coherence and power analysis are presented in Section 3.2. Our main results are shown in Section 3.3, which contains the results for the imaginary part of coherency. Finally, we discuss our findings in Section 4.

2. Theoretical aspects of coherency

2.1. Definition of coherency/coherence

Coherency between two EEG-channels is a measure of the linear relationship of the two at a specific frequency. Here, we recall the basic definitions (Nunez et al., 1997). Let $x_i(f)$ and $x_j(f)$ be the (complex) Fourier transforms of the time series $\hat{x}_i(t)$ and $\hat{x}_j(t)$ of channel *i* and *j*, respectively. Then the cross-spectrum is defined as

$$S_{ii}(f) \equiv \langle x_i(f)x_i^*(f)\rangle \tag{1}$$

where * means complex conjugation and $\langle \rangle$ means expectation value. In practice, the expectation value can only be estimated as an average over a sufficiently large number of epochs. Coherency is now defined as the normalized cross-spectrum:

$$C_{ij}(f) \equiv \frac{S_{ij}(f)}{(S_{ii}(f)S_{jj}(f))^{1/2}}$$
(2)

and coherence is defined as the absolute value of coherency

$$\operatorname{Coh}_{ij}(f) \equiv |C_{ij}(f)| \tag{3}$$

We note that the terminology varies in different papers. Since it is the major objective of this paper to exploit phase structure as shown below, we use the two terms 'coherency' and 'coherence' to distinguish the full complex information from its magnitude.

In the case of 'event-related coherence', we are interested in the dependence of coherency as a function of the time relative to a given stimulus. We then divide a long epoch (typically in the order of a few seconds) into segments of length T (typically between 250 ms and 1 s) which are small enough for the desired time-resolution, given by Titself, and large enough for the desired frequency resolution, given by 1/T. Coherency then becomes a function of both frequency and time

$$C_{ij}(f) \to C_{ij}(f,t) \tag{4}$$

where *t* indicates the time of the center of the respective segment.

Coherency essentially measures how the phases in channel *i* and *j* are coupled to each other. In the following, frequency dependence is implicitly understood. If we write the Fourier transformed signals as $x_i = r_i \exp(i\Phi_i)$

and $x_i = r_i \exp(i\Phi_i)$ then the cross-spectrum becomes

$$S_{ij}(f) = \langle r_i r_j \exp(i\Delta\Phi) \rangle \tag{5}$$

where $\Delta \Phi = \Phi_i - \Phi_j$ is the phase difference between the signals in channel *i* and *j* at a specific frequency. The cross-spectrum is the average of $\exp(i\Delta\Phi)$ weighted with the product of the amplitudes r_i and r_j . For coherency, we merely normalize with respect to the 'global amplitudes' $\langle r_i^2 \rangle^{1/2}$ and $\langle r_j^2 \rangle^{1/2}$. If the signals in the two channels are independent, $\Delta\Phi$ is a random number and the coherency is zero.

It is worthwhile to compare coherency with (1:1) 'Phase-Locking' or 'Phase Synchrony' defined as an unweighted average

$$P = \langle \exp(i\Delta\Phi) \rangle \tag{6}$$

Lachaux et al. (1999) gave two arguments why phase synchrony is preferable to coherency.¹ First, it is argued that coherency can only be applied to stationary signals, and second, it is noted that phase synchrony specifically quantifies phase relationships. We disagree with the first argument. Coherency is a characteristic quantity of a stationary as well as a non-stationary process. Only if we interpret it as a parameter of a stationary process we actually assume stationarity. Similarly, we do not assume that the processes are linear by calculating a linear measure. We only look at the linear properties.

The second argument is more subtle. Phase synchrony is indeed a clearer measure of the phase relationship only, and if $\Delta \Phi$ is statistically independent of the amplitudes, there is no reason to weight with respect to amplitudes. However, the question is whether this is the case, and, if not, whether the weights result in statistically more robust estimators of phase relationships. Note, that independence of phases and amplitudes leads to

$$C_{ij} = \langle \exp(i\Delta\Phi) \rangle \frac{\langle r_i r_j \rangle}{(\langle r_i^2 \rangle \langle r_j^2 \rangle)^{1/2}}$$
(7)

and since

$$\frac{\langle r_i r_j \rangle}{(\langle r_i^2 \rangle \langle r_j^2 \rangle)^{1/2}} \le 1 \tag{8}$$

we find

$$|C_{ij}| \le |P_{ij}| \tag{9}$$

In our experience, this inequality is (slightly) violated in real data examples and the results for coherency are (slightly) more robust than for phase synchrony. To some extent, this is surprising since phase synchrony is obviously less sensitive to outliers. However, this result indicates a dependence of the phase difference on the amplitudes: if the signal is weak it is more likely that noise destroys the phase structure. We want to emphasize that we do not claim that this is always the case but we do believe that the question of what quantity is preferable is ultimately a statistical and not a conceptual one.

2.2. Visualising coherency

A coherence/coherency matrix contains an enormous amount of information. In order to assess this information, looking at *all* connections in one plot is very helpful. Our solution to this problem is presented in Fig. 1 where we show coherence in the alpha band at rest. The single large circle represents the whole scalp. At each electrode position, we place a small circle also representing the scalp and containing the coherence of the respective electrode with all other electrodes, i.e. the *i*th small circle contains the *i*th row of the coherence matrix $|C_{ij}|$. In Fig. 1, we observe strong coherence with all neighboring electrodes which is (at least qualitatively) consistent with a uniform distribution of independent sources in the brain.

In order to avoid overlapping circles, the positions have been slightly shifted. This transformation is shown in Fig. 2. Since it is very tedious to do this manually, we developed an (quite heuristic) algorithm to shift the electrodes: we regard them as a set of particles with a strong short-range repulsive force (to avoid overlaps) and a weak long-range force (to keep the circles together) attracting the circles to the overall center (typically at CZ). In an iterative procedure, the electrodes 'move' a small step proportional to the force until a satisfactory solution is found. The coordinate transformation only affects the position of the small circles within the large one but not the electrode locations within the small circles. Within each small circle, we placed a very small black dot marking the original electrode location. Without the transformation, the relative position of a dot within the small circle is the same as the relative position of that small circle within the large one. By looking at the positions of the small dots we can then qualitatively assess the impact of the transformation.

2.3. The special role of the imaginary part of coherency

We intend to interpret coherency between EEG channels as reflecting an interaction between different brain sites. Probably the biggest problem for that is the fact that the activity of a single source is measurable in many channels. This is usually referred to as 'volume conduction'. Especially close-by electrodes are highly coherent which reflects redundancies in the measurement rather than brain interaction. Formally speaking, any coherence matrix is consistent with non-interacting sources. Differentiating true brain dynamics from artifactual results caused by volume conduction is therefore a highly non-trivial task.

A way to avoid this problem could be to first estimate the activity at the brain sources instead of EEG/MEG channels using an appropriate inverse method. However, the inverse

¹ In that paper phase synchrony is defined as the absolute value of P which, however, is irrelevant for this discussion.



Fig. 1. Coherence in the alpha range for one subject.

problem is not solvable in principle. To end up with a mathematically unique solution, one has to impose a large number of constraints reflecting the researcher's prejudices about the underlying source rather than the unknown properties of the actual true source.

Here, we pursue a different approach. We isolate that part of coherency which necessarily reflects interaction and that is given by the imaginary part of the coherency. This does not replace the ultimate goal to also localize the sources of interaction, but the interpretation of observed synchronizations



Fig. 2. Original electrode locations (left) are slightly shifted to avoid overlapping spheres (right).

as brain interactions does not depend on the validity of the inverse method. To see this, let us assume that the signals in channel *i* and *j* arise from a linear superposition of *K* independent sources $s_k(f)$

$$x_i(f) = \sum_{k=1}^{K} a_{ik} s_k(f)$$
(10)

and similarly for $x_j(f)$. We further assume that mapping of sources to sensors is instantaneous, implying that the phases are not distorted resulting in real coefficients a_{ik} and a_{ik} .

We then have for the cross-spectrum

$$S_{ij}(f) = \langle x_i(f)x_j^*(f)\rangle = \sum_{kk'} a_{ik}a_{jk'}\langle s_k(f)s_{k'}^*(f)\rangle$$
$$= \sum_k a_{ik}a_{jk}\langle s_k(f)s_k^*(f)\rangle = \sum_k a_{ik}a_{jk}|s_k(f)|^2$$
(11)

which is real. Since the normalization is also real, it follows immediately that coherency is also real.

For the derivation, we assumed a linear superposition of sources which is certainly justified because the Maxwell equations are linear. The assumption that the mapping between sources and sensors is free of phase shifts is less trivial to assess. Note, that a phase shift in the frequency domain corresponds to a time-lag in the time domain. The imaginary part of coherency is insensitive to artifactual 'self-interaction' caused by volume conduction because a signal is not time-lagged to itself.

In fact, our assumption that volume conduction does not cause phase shifts follows from the validity of the quasistatic approximation of the forward problem, stating that one can ignore time-derivatives in the Maxwell equations, which actually depends on the frequencies under study. Plonsey and Heppner (1967) estimated the quasi-static approximation to be valid below 2 kHz. In a detailed study, Stinstra and Peters (1998) found no phase shifts for frequencies below 100 Hz for both EEG and MEG (higher frequencies were not analyzed). Since we are interested in frequencies in typical EEG bands (< 50 Hz), we believe that our assumption is justified.

At this point, we would like to make clear what we precisely mean by stating that the imaginary part of coherency is insensitive to artifacts of volume conduction. Since we still measure at channels and since the source amplitudes are 'volume conducted' to the electrodes, this volume conduction affects where we measure what interaction. Furthermore, the coherency is normalized with respect to the diagonal elements of the cross-spectrum which belong to the real part of it and are also affected by non-interacting sources. Adding non-interacting sources (e.g. noise) causes a decrease in the imaginary part of coherency. However, it can never cause an increase und thus it cannot 'create' a non-vanishing imaginary part of coherency. The situation is slightly different for the crossspectrum itself. While there, too, volume conduction affects what signal is observable at what channel, non-interacting

sources do not affect the result at all-apart, of course, from random fluctuations which vanish in the mean.

The above result is, in our opinion, a relatively trivial observation which just has not been exploited so far. Magnitude and phase of coherency are common measures of connectivity in many studies. Since the real and imaginary parts of coherency are just a different representation (Cartesian instead of polar) of the complex coherency, we do not calculate different quantities but rather we look at coherency from a different viewpoint.

Although magnitude and phase contain the same information as the real and imaginary parts, there are subtle but important advantages/lack of disadvantages to look at the imaginary part instead of the phase: (1) Non-interacting sources do not lead to small but rather to random phases. We cannot interpret a phase without having an estimate of its significance at the same time. (2) One usually calculates coherency with respect to a baseline (a rest condition). Since in the individual coherencies the real parts are typically much larger than the imaginary parts, the phase flips by π depending on whether the real part of coherency is larger in the rest or active condition. The interesting structure is easily obscured by this rather meaningless effect. (3) Phase is usually regarded as an additional information about time delay between two processes. However, volume conduction strongly affects the real part but does not create an imaginary part. Processes can appear to be synchronized with almost vanishing time delay while it is only the volume conducted copies of the signals which do not have a time delay.

An illustration of the imaginary part of the same data as for Fig. 1 is given in Fig. 3. In contrast to the absolute value of coherency, we observe interesting structure. Although very blurred, we can see interactions between occipital and left parietal electrodes. The imaginary part of coherency between parietal and occipital electrodes is positive (the central circles are red in occipital regions) which means the central activity precedes the occipital one.

For comparison, we also show the phase of coherency in Fig. 4. The structure now looks very different. Significant deviation from zero phase can be seen for very remote (here: frontal and occipital) pairs of electrodes. However, this does not necessarily reflect an interaction. In fact, similar patterns can be seen for all frequencies, and they are likely to be a consequence of anti-correlated 'self-interaction' due to opposite polarity of the electric potential of neuronal dipoles in remote electrode pairs. If the imaginary part is negligible, then anti-correlation leads to phases fluctuating near $\pm \pi$. Interestingly, although the imaginary part of coherency is easily calculated from coherence and phase, we see this occipital-parietal interaction neither in the coherence (Fig. 1) nor in the phase (Fig. 4) themselves which are both dominated by the effects of volume conduction. Finally, we note that the shown plots are actually based on one-quarter of the available data for this subject. The same plots for



Fig. 3. Imaginary part of coherency in the alpha range for the same subject as in Fig. 1.



Fig. 4. Phase of coherency in the alpha range for the same subject as in Fig. 1.

the other quarters are almost undistinguishable by eye from the ones shown.

2.4. Statistics

2.4.1. The statistics of a single pair of channels

The statistic for coherence is well known and described in detail; e.g. by Rosenberg et al. (1989) or by Amjad et al. (1997). If c is a coherence calculated from N Gaussian distributed observations, then for large N, the Fisher's Z transform $\arctan(c)$ is approximately Gaussian distributed with a standard deviation of approximately $1/\sqrt{2N}$. This is a very good approximation unless c is very close to zero. In this case, c is distributed like a radius of a two-dimensional Gaussian distribution and the standard deviation is overestimated.

We are interested in the statistic of (complex) coherency. The stabilizing Z-transform of a coherency C_{ij} then becomes a scale transformation in the complex plane:

$$C_{ij} \rightarrow \frac{C_{ij}}{|C_{ij}|} \operatorname{arctanh}(|C_{ij}|) \equiv \tilde{C}_{ij}$$
 (12)

and \tilde{C}_{ij} is approximately Gaussian in the two-dimensional complex plane. To discuss the covariance matrix, let us first assume that the true phase is zero and later perform a rotation to arbitrary phases. In this case, the imaginary part fluctuates randomly around zero and must be uncorrelated with the real part. For the variance of the real part, one obtains the usual result 1/2N. In contrast to coherence, the real part of coherency is not constrained to non-negative values and the approximation is also valid for real parts close to zero. The variance of the imaginary part is, in general, reduced due to the presence of a non-vanishing real part. The non-transformed imaginary parts have variance $(1 - |C_{ij}|^2)/2N$ which follows immediately from the variance of the phase approximately given by $(1/|C_{ij}|^2 - 1)/2N$ (Mima et al., 2000). Due to the transformation, the imaginary part is additionally scaled by a factor $\operatorname{arctanh}(|C_{ii}|)/|C_{ii}|$ and the total variance reads

$$\operatorname{var}(\operatorname{Im}(C_{ij})) = \frac{(1 - |C_{ij}|^2)}{2N} \frac{\operatorname{arctanh}^2(|C_{ij}|)}{|C_{ij}|^2}$$
(13)

For general phases, the same arguments as for the real and imaginary parts apply for the coordinates in the direction of the phase and orthogonal to it, respectively. In this case, the variances of real and imaginary parts are found by projection and read

$$\operatorname{var}(\operatorname{Re}(C_{ij})) = \frac{1}{2N}(g(C_{ij})\sin^2(\Phi) + \cos^2(\Phi))$$
(14)

$$\operatorname{var}(\operatorname{Im}(C_{ij})) = \frac{1}{2N} (g(C_{ij}) \cos^2(\Phi) + \sin^2(\Phi))$$
(15)

with the abbreviation

$$g(x) = (1 - |x|^2) \frac{\arctan^2(|x|)}{|x|^2}$$
(16)

To obtain an averaged coherency (over subjects) or a difference of coherencies, the average/difference is taken for the Z-transformed coherencies and the variances add accordingly. An exception to this rule is an average over time which is done for the cross-spectra since we can regard that as an increased number of epochs. A *P*-value is calculated from the number of standard deviations the measured quantity differs from zero. The averaged/differenced coherency is finally transformed with the inverse

$$\tilde{C}_{ij} \rightarrow \frac{C_{ij}}{|\tilde{C}_{ij}|} \tanh(|\tilde{C}_{ij}|) \tag{17}$$

2.4.2. Correction for multiple comparisons using the false discovery rate

To assess whether a specific spatial pattern in coherency is significant, we must correct for multiple comparisons. Because coherencies are largely redundant in neighboring channels with dense electrode settings, a Bonferroni correction is surely overconservative. Here, we adopt the False Discovery Rate (FDR), well established in functional magnetic resonance imaging (Benjamini and Hochberg, 1995; Benjamini and Yekutieli, 2001; Genovese et al., 2002).

FDR controls for the rate of true detections out of all detections. The general procedure is as follows: For *N* comparisons, the *P*-values are sorted in ascending order $(p_i, i = 1, ..., N)$ and one finds the maximum of the (p_i) which satisfies the relation

$$p_i < \frac{\alpha i}{Nc(N)} \tag{18}$$

where α is the level we control at. All *P*-values lower or equal to this maximum are regarded as significant detection. The function c(N) should be set according to the statistics of the *P*-values: for general distributions $c(N) = \sum_{i=1}^{N} 1/i$ and for positively correlated *P*-values, it is sufficient to set c(N) = 1. Here, positively correlated *P*-values mean that an increased deviation from the null-hypothesis in one electrode-pair does not lead to decreased deviations in other pairs. Regardless of whether one uses the 'pessimistic' $(c(N) = \sum 1/i)$ or 'optimistic' (c(N) = 1) variant of FDR, the lowest *P*-value is always compared to the Bonferroni level α/N .

Setting, e.g. $\alpha = 0.05$ means that on average, 95% of all detections are true detections. The ratio true detections/all detections is defined as always being one if the denominator (and hence also the numerator) is zero. This means that if there is no true effect in (at least) 95% of hypothetical repetitions of the experiment, one does not detect anything significant.

2298

3. Interhemispheric connectivity in voluntary finger movement

3.1. Paradigm and preprocessing

In this experiment, nine right-handed subjects were asked to perform brisk voluntary movement with either left or right-hand fingers lasting approximately 1 s with an interval of about 10 s between movements. The subjects were supposed to switch randomly between left and righthand finger movements which, in practice, turned out to be dominated by alternating movements.

The EEG was measured continuously in 122 channels at a sampling rate of 1 kHz with reference set to the right earlobe. Impedances were kept below 5 k Ω . Four occipital channels were taken out either because they were corrupted by artefacts or because different analogue filter settings were chosen, which significantly affects the analysis of the imaginary part of coherency. EMG and EOG were measured simultaneously. The remaining EEG channels were divided into 20 s epochs with movement onset set to 10 s. Each epoch was divided into 80 non-overlapping segments of 250 ms duration. Since the epochs are very long, there were eye-blinks in almost all of them. Therefore, we corrected for eye-blinks (and other artefacts) segment-wise by taking out an artefact if the maximum of the detrended signal is above 100 µV in any of the EEG or EOG channels. Coherency was calculated for each segment and for all electrode pairs by applying a Fourier-transform to Hanning windowed data.

3.2. Coherence and power

In this motor experiment, we expect to find coherence/ coherency especially between electrodes over central areas close to motor regions such as C3 and C4 which is the usual approach in the literature. Let us first look at the coherence between C3 and C4 as a function of time and frequency which is presented in Fig. 5 for left and right-hand finger movement and with and without subtraction of a baseline. Here (and for all the following plots), we averaged over all 9 subjects. If we subtract a baseline, calculated from a timeaverage between -7.5 and -5 s, we observe a strong increase of coherence during movement and a decrease of coherence after movement (left column) which is well known in the literature. It is instructive to also look at the same coherence without subtracting a baseline (right column). Apparently, coherence is very low in the betarange almost during the whole cycle but returns to 'normal' during movement. This figure suggests that an observed increase of coherence with respect to baseline during movement is due to the absence of beta-activity during activity which itself is just less coherent than background noise. In view of the later analysis of the imaginary part of coherency, we also plotted the difference of coherences between left and right-hand movement. Although the main

effects (of course) cancel out, slight and temporarily blurred differences remain.

That the absence or presence of activity in the beta range is a factor contributing to the observed increased or decreased coherences is supported by Fig. 6. We observe synchronization and desynchronization at the same times as we observe changes in coherence. Interestingly, the power also changes in the alpha range with less pronounced change in coherence. This discrepancy between alpha and beta indicates that a mere change in the strength of the rhythm is probably too simple an explanation for the observed changes in coherence. For a more detailed discussion of phenomena and possible explanations for coherence in the alpha range, we refer to the work of Florian et al. (1998). We emphasize that we do not claim that coherence is only a consequence of volume conduction. It is just difficult to interpret: we do not know what part reflects real interaction and what part is due to volume conduction.

For completeness, we present the spatial pattern of power in the beta range during and after movement in Fig. 7. These findings are well known. Desynchronization during movement is essentially bilateral while synchronization after movement is clearly contralateral.

Finally, we show the full coherence during (at t = 125 ms) and after (averaged from 2 to 4 s) movement for left hand finger movement in Figs. 8 and 9, respectively. During movement we observe three rather than two foci of activity: left and right motor area and a slightly frontal area. While left and right motor areas are common candidates for coherence analysis for this type of paradigm, the frontal area is somewhat a surprise. Again, whether the observed coherence reflects a true interaction is difficult to deduce from coherence itself. Even more difficult is interpreting the spatial pattern of coherence after movement which also shows somewhat central, but at least spatially asymmetric structures. It is conceivable that the relevant activities stem from SMA but a detailed source analysis is beyond the scope of this paper.

3.3. The imaginary part of coherency

The imaginary part of coherency between C3 and C4 as a function of time and frequency is displayed in Fig. 10. The most prominent feature is a burst approximately 2-4 s after movement. For left hand finger movement, this imaginary part is positive and for right-hand movement, it is negative. This is most clearly seen in the left column where a baseline is subtracted but it is even visible in the coherency without baseline subtraction, although a relatively strong background activity is present mainly in the alpha but also in the beta range.

In general, if the imaginary part of C(x, y) is positive, then x and y are interacting and x is earlier than y, indicating that information is flowing from x to y. At specific frequencies, however, 'earlier' and 'later' are ambigious; e.g. at 10 Hz 10 ms earlier is the same as 90 ms later. For the present interpretation we assumed that the smaller delay in



Fig. 5. Coherence as a function of time and frequency for right and left hand finger movement. In the left column, a baseline was subtracted consisting of the coherence time-averaged in the interval $[-7.5 \ s, -5 \ s]$.



Fig. 6. Relative power as a function of time and frequency in C3 and C4. Displayed is $\log(P/P_{rest})$ where P_{rest} is calculated from a time average between -7.5 and -5 s.



Fig. 7. Spatial pattern of relative power in the beta-range during movement (at t = 125 ms) and after movement (averaged from 2 to 4 s) for left and right-hand finger movement. Displayed is $\log(P/P_{rest})$ where P_{rest} is calculated from a time average between -7.5 and -5 s.

absolute value is the more probable explanation; e.g. in the above example we would favor '10 ms earlier' over '90 ms later'. Note, that we can make this interpretation just from the sign of the imaginary part of coherency without actually calculating a delay for which we would need a reliable real part of coherency. The signs for the post-movement activity indicate that the interaction is directed from the ipsilateral to the contralateral side. This might be considered as surprising since, generally, the contralateral hemisphere is expected to control movements. However, over a relatively long period of approximately 5 s prior to movement, we also observe the opposite



Fig. 8. Coherence in the beta range between all channel pairs during left hand finger movement.



Fig. 9. Coherence in the beta range between all channel pairs after left hand finger movement.



Fig. 10. Imaginary part of coherency as a function of time and frequency for right and left hand finger movement. In the left column a baseline was subtracted consisting of the coherency time-averaged in the interval [-7.5 s, -5 s].

behaviour: the imaginary part of coherency between C3 and C4 is largely negative. This can only be seen if we do not subtract a baseline and most clearly if we look at the difference between left and right-hand finger movement.

In contrast to coherence, subtracting left and right finger movement for the imaginary part of coherency enhances the signal we are interested in. This is indeed a consequence of the antisymmetry of the imaginary part ($Im(C_{ij}) = -Im(C_{ji})$). If we have a paradigm where the left and right hemispheres switch their roles, then the difference is potentially a very useful quantity. Let us denote by C_{ij}^R and C_{ij}^L coherencies of right and left hand finger movement, respectively. If we assume that

$$C_{\text{C4,C3}}^{\text{L}} \approx C_{\text{C3,C4}}^{\text{R}} \tag{19}$$

we get for the difference

$$Im(C_{C3,C4}^{L}) - Im(C_{C3,C4}^{R}) \approx Im(C_{C3,C4}^{L}) - Im(C_{C4,C3}^{L})$$
$$= Im(C_{C3,C4}^{L}) + Im(C_{C3,C4}^{L})$$
(20)

and we double the signal. Note, that in this difference, anything which is not task-related cancels out and hence the task itself serves as an almost perfect baseline. Similar to the study of lateralized readiness potentials (Vidal et al., 2003), we also miss interactions which are identical in left and right-hand finger movement. However, since for the imaginary part of coherency, this difference gives the clearest signal, from now on we will focus on this difference. We want to emphasize that for this construction to be meaningful it is unnecessary that the hemispheres exactly switch their roles between the left and right-hand paradigm; rather, we enhance that part which does have this property. In other words, we look for this property rather than assume it; Eq. (20) is the reasoning behind taking the difference rather than an assumed accurate property of brain interaction.

In Fig. 11, we show the statistically significant imaginary part of coherency between C3 and C4 in a time-frequency plot under various notions of 'significance'. The postmovement interaction is very strong and survives any type of correction for multiple comparisons including a Bonferroni correction. The pre-movement interaction is somewhat weaker. In the optimistic (see Section 2.4.2) FDR method, we see remnants of it as a few blue spots. For these data, the pessimistic FDR method gives the same result as the Bonferroni correction: nothing is significant apart from the post-movement interaction.

The spatial patterns of the imaginary part of coherency before movement (averaged in the interval [-5 s, 0 s]) and after movement (averaged in the interval [2 s, 4 s]) are shown in Figs. 12 and 13, respectively. The activity before movement is very clear: the electrodes over the left motor area are coherent with the electrodes over the right motor area and vice versa. The stronger post-movement activity appears to be more

complex. Apart from an involvement of the left and right motor area, frontal areas also seem to be involved. We emphasize that an area specification such as 'left motor area' cannot be accurate without making an inverse calculation. Here, the assignments arising from the nature of the paradigm are meant to be descriptive rather than quantitative.

Finally, we show in Fig. 14 the significant part of the imaginary part of coherency for the pre-movement activity using the pessimistic FDR method. Compared to the time-frequency plot, the statistics are much better because we also averaged 20 non-overlapping time segments. The effective cut-off in coherency makes the pattern appear less blurred but essentially we obtain the same figure as when we look at the whole coherency.

4. Discussion

In this paper we explored the imaginary part of coherency as a reflection of true brain interaction in contrast to artefacts from volume conduction which mainly dominate coherence, the absolute value of coherency. The fact that a significant imaginary part of coherency is inconsistent with non-interacting sources is, in our opinion, simple and obvious. Rather, the interesting question is whether we can find such a non-vanishing imaginary part in (literally) real data. Indeed, we found too much of it in the sense that the task-dependent imaginary part of coherency was masked by on-going rhythmic interactions. In order to suppress these ongoing interactions, we subtracted coherency from left and right-hand finger movements which revealed information transfer from contra- to ipsilateral hemisphere before movement and from ipsi- to contralateral hemisphere after movement. It must be noted that this interpretation of coherency in terms of information flow is based on the relative timing of two signals which is necessarily ambiguous if one looks at a specific frequency.

However, what is not ambiguous is that the imaginary part of coherency does reflect true interaction. Therefore, we strongly suggest looking for that in any type of coherence analysis. Since the calculation of an imaginary part is typically an intermediate step to obtain amplitude and phase of coherency, which are standard measures of coherence analysis, we can hardly call our procedure a new method. Rather, it is a new look at an old method. The rationale behind it is that first we rigorously eliminated 'selfinteraction' caused by volume conduction. This largely facilitates interpreting our measures in terms of an interacting brain. What we have to show is: (a) that a non-vanishing imaginary part is significant, and (b) that an observed structure in the imaginary part comes from the brain. Although, in practice, significance may turn out to be difficult to prove, the concepts are straightforward. In case of doubt, one can always run more subjects to clarify



Fig. 11. Lower right panel of Fig. 10 with non-significant values set to zero for various notions of 'significant'.



Fig. 12. Imaginary part of coherency in the beta range between all channel pairs time-averaged between -5 and 0 s. Right-hand finger movement was regarded as a baseline for left hand finger movement.



Fig. 13. Imaginary part of coherency in the beta range between all channel pairs time-averaged over the post-movement interval from 2 to 4 s.



Fig. 14. Imaginary part of coherency in the beta range between all channel pairs time-averaged between -5 and 0 s with non-significant values set to zero. Right-hand finger movement was regarded as a baseline for left hand finger movement. Significance was estimated by the pessimistic FDR method.

an issue. That an observed structure originates from the brain is usually quite obvious from the qualitative spatial pattern of the interaction. One can obtain a more detailed picture of the origin of the coherency from inverse calculations which, however, is beyond the scope of this paper.

The important question in the context of this paper is whether the imaginary part of coherency is superior to other measures of brain connectivity. In our opinion, this is clearly the case if the citerion is how robust the method is to artefacts from volume conductions. Recently, more complicated methods have become popular. In the directed transfer function (DTF) approach, a linear autoregressive model is fitted to the data and interaction is deduced and characterized from mixing coefficients (Baccala and Sameshima, 2001; Cassidy and Brown, 2003; Hesse et al., 2003; Kaminski et al., 2001; Korzeniewska et al., 2003; Mima et al., 2001). DTF can be regarded as a special version of the more general concept of Granger causality (Chavez et al., 2003; Hesse et al., 2003; Kaminski et al., 2001). A signal A is said to Granger cause signal B if the present and past of signal A contains information about the future of signal B not contained in the present or past of signal Bitself. Ideally, this solves the problem of volume conduction because a copy of a signal does not contain additional information. The problem, however, is additive noise. If A contains a simple and predictable signal plus white noise, then all we can expect in the prediction of the future is a good estimate of the predictable part. This estimate will be improved if we average the channels A and B, the latter, say, containing the same signal plus white noise independent of the noise in A.

A similar argument applies to estimating the direction of information flux. This direction is usually estimated from the asymmetry in the Granger causality: the information flux goes from A to B if A provides more useful information to predict B than vice versa. Asymmetries, however, can also be due to asymmetric noise levels. Let us discuss an extreme case: if A is noise-free and contains only a simple and predictable signal and Bcontains the same signal plus white noise then B cannot contribute additional information to predict the future of A but knowing A is optimal to predict the future of B. In practice, channels are not noise-free but noise levels or signal-to-noise-ratios vary substantially between channels, and it is conceivable that an estimated direction of information flux using Granger causality merely indicates the direction from 'good' to 'bad' channels.

Coherency is a linear measure: for a linear (and stationary) system the cross-spectrum, on which coherency is based, completely determines the dynamics. There is nothing more to know. For non-linear systems, however, coherency might yield only an incomplete picture and more general non-linear measures might be preferable. However, 'sensitive to more' also means 'potentially less robust'. With regard to the difficulty to even detect non-linear dynamics in human EEG (Stam et al., 1999; Theiler and Rapp, 1996), it is questionable whether non-linear methods are superior to linear ones, unless, of course, the non-linearity of the dynamics is the objective of a study itself.

We believe that the imaginary part of coherency is a very useful measure to study brain connectivity. Being inconsistent with non-interacting sources its presence necessarily reflects a dynamical interaction in contrast to volume conducted 'self-interaction'. Since volume conduction is, in our opinion, the main obstacle in interpreting EEG/MEG data in terms of brain connectivity, the value of such a property cannot be overemphasized. It is possible that in many studies the imaginary parts of coherencies essentially vanish. This could mean that there is no interaction (measured by EEG/MEG) or that the interaction between two sources is not delayed or rather symmetrically delayed such that none of the sources leads the other one.

This was found by Roelfsema et al. (1997), where the authors report 'zero time-lag synchronization among cortical areas' in visuomotor integration studied in cats. However, the title of that paper is rather sketchy, e.g. the authors found a small ($\approx 2 \text{ ms}$) but non-zero time-lag between area 18 and 21. A time-lag of 2 ms at 20 Hz can induce an imaginary part of the coherency up to $\sin(2 \times$ $ms \times 2\pi/50 ms) \approx 0.25$ which is much larger than what we have observed. Indeed, the authors argue that the observed synchronization is not mediated by volume conduction because the time-lag is non-vanishing and because the cross-correlation is asymmetric. Since a symmetric crosscorrelation is equivalent to a vanishing imaginary part of coherency, which follows from the fact that the imaginary part of the cross-spectrum is the Fourier-transform of the antisymmetric part of the cross-covariance, our argument is also equivalent.

Larger time-lags in the beta-range were found by Tallon-Baudry et al. (2001) in visual areas during rehearsal of an object in visual short-term memory studied with intracranial EEG in epilepsy patients. The authors report for two subjects stable time-lags of 5.4 and 12.4 ms in waves with period 50 and 62.5 ms, respectively. Note, that the time-lag in the second subject is almost a quarter period giving rise to an almost vanishing real part of the coherency.

There is always a trade-off between how much we want to say about a system and how sure we are that what we say is correct. By looking at the imaginary part of coherency, we take an extreme position. We see, at best, only half of the picture. But that half is safe. In conclusion, we do not think that our approach can replace 'classical' analysis, but we recommend analyzing the imaginary part of coherency separately in all coherence studies.

References

Amjad AM, Halliday DM, Rosenberg JR, Conway BA. An extended difference of coherence test for comparing and combining several

independent coherence estimates: theory and application to the study of motor units and physiological tremor. J Neurosci Methods 1997;73: 69–79.

- Andrew C, Pfurtscheller G. Lack of bilateral coherence of post-movement central beta oscillations in the human electroencephalogram. Neurosci Lett 1999;273:89–92.
- Baccala LA, Sameshima K. Partial directed coherence: a new concept in neural structure determination. Biol Cybern 2001;84:463–74.
- Baillet S, Mosher JC, Leahy RM. Electromagnetic brain mapping. IEEE Signal Process Mag 2001;18:14–30.
- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practicaland powerful approach to multiple testing. J R Stat Soc B 1995;57:289–300.
- Benjamini Y, Yekutieli D. The control of the false discovery ratein multiple testing under dependency. Ann Stat 2001;29:1165–88.
- Cassidy M, Brown P. Spectral phase estimates in the setting of multidirectional coupling. J Neurosci Methods 2003;127:95–103.
- Chavez M, Martinerie J, Le Van Quyen M. Statistical assessment of nonlinear causality: application to epileptic EEG signals. J Neurosci Methods 2003;124:113–28.
- Fein G, Raz J, Brown FF, Merrin EL. Common reference coherence data are confounded by power and phase effects. Electroencephalogr Clin Neurophysiol 1988;69:581–4.
- Florian G, Andrew C, Pfurtscheller G. Do changes in coherence always reflect changes in functional coupling? Electroencephalogr Clin Neurophysiol 1998;106:87–91.
- Genovese CR, Lazar NA, Nichols T. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. Neuroimage 2002;15:870–8.
- Gerloff C, Andres FG. Bimanual coordination and interhemispheric interaction. Acta Psychol (Amst) 2002;110:161-86.
- Ginter Jr J, Blinowska KJ, Kaminski M, Durka PJ. Phase and amplitude analysis in time-frequency space: application to voluntary finger movement. J Neurosci Methods 2001;110:113–24.
- Gross J, Kujala J, Hamalainen M, Timmermann L, Schnitzler A, Salmelin R. Dynamic imaging of coherent sources: studying neural interactions in the human brain. Proc Natl Acad Sci USA 2001;98:694–9.
- Hesse W, Moller E, Arnold M, Schack B. The use of time-variant EEG Granger causality for inspecting directed interdependencies of neural assemblies. J Neurosci Methods 2003;124:27–44.
- Lachaux JP, Rodriguez E, Martinerie J, Varela FJ. Measuring phase synchrony in brain signals. Hum Brain Mapp 1999;8:194–208.
- Leocani L, Toro C, Manganotti P, Zhuang P, Hallett M. Event-related coherence and event-related desynchronization/synchronizationin the 10 Hz and 20 Hz EEG during self-paced movements. Electro-encephalogr Clin Neurophysiol 1997;104:199–206.
- Kaminski M, Ding M, Truccolo WA, Bressler SL. Evaluating causal relations in neural systems:granger causality, directed transfer function and statistical assessment of significance. Biol Cybern 2001;85: 145–57.

- Korzeniewska A, Manczak M, Kaminski M, Blinowska KJ, Kasicki S. Determination of information flow direction among brain structures by amodified directed transfer function (dDTF) method. J Neurosci Methods 2003;125:195–207.
- Manganotti P, Gerloff C, Toro C, Katsuta H, Sadato N, Zhuang P, Leocani L, Hallett M. Task-related coherence and task-related spectral power changes during sequential finger movements. Electroencephalogr Clin Neurophysiol 1998;109:50–62.
- Mima T, Matsuoka T, Hallett M. Functional coupling of human right and left cortical motor areas demonstrated with partial coherence analysis. Neurosci Lett 2000;287:93–6.
- Mima T, Matsuoka T, Hallett M. Information flow from the sensorimotor cortex to muscle in humans. Clin Neurophysiol 2001;112:122–6.
- Nunez PL, Srinivasan R, Westdorp AF, Wijesinghe RS, Tucker DM, Silberstein RB, Cadusch PJ. EEG coherency. I. Statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales. Electroencephalogr Clin Neurophysiol 1997;103:499–515.
- Nunez PL, Silberstein RB, Shi Z, Carpenter MR, Srinivasan R, Tucker DM, Doran SM, Cadusch PJ, Wijesinghe RS. EEG coherency. II. Experimental comparisons of multiple measures. Clin Neurophysiol 1999;110:469–86.
- Pfurtscheller G, Andrew C. Event-related changes of band power and coherence: methodology and interpretation. J Clin Neurophysiol 1999; 16:512–9.
- Roelfsema PR, Engel AK, Konig P, Singer W. Visuomotor integration is associated with zero time-lag synchronization among cortical areas. Nature 1997;385:157–61.
- Rosenberg JR, Amjad AM, Breeze P, Brillinger DR, Halliday DM. The Fourier approach to the identification of functional coupling between neuronal spike trains. Prog Biophys Mol Biol 1989;53:1–31.
- Plonsey R, Heppner D. Considerations on quasi-stationarity in electrophysiological systems. Bull Math Biophys 1967;29:657–64.
- Sarvas J. Basic mathematical and electromagnetic concepts of the biomagnetic inverse problem. Phys Med Biol 1987;32:11–22.
- Stam CJ, Pijn JPM, Suffczynski P, Lopes da Silva FH. Dynamics of the human alpha rhythm: evidence for non-linearity? J. Clin. Neurophysiol. 1999;110:1801–13.
- Stinstra JG, Peters MJ. The volume conductor may act as a temporal filter on the ECG and EEG. Med Biol Eng Comput 1998;36:711–6.
- Tallon-Baudry C, Bertrand O, Fischer C. Oscillatory synchrony between human extrastriate areas during visual short-term memory maintenance. J Neurosci 2001;21:RC177.
- Theiler J, Rapp PE. Re-examination of the evidence for low-dimensional, non-linear structure in the human electroencephalogram. Electromyogr Clin Neurophysiol 1996;98:213–22.
- Vidal F, Grapperon J, Bonnet M, Hasbroucq T. The nature of unilateral motor commands in between-hand choice tasksas revealed by surface Laplacian estimation. Psychophysiology 2003;40:796–805.