The dynamic pattern of functional connectivity during a working memory task was investigated by means of the short-time directed transfer function. A clear-cut picture of transmissions was observed with the main centres of propagation located in the frontal and parietal regions, in agreement with imaging studies and neurophysiological hypotheses concerning the mechanisms of working memory. The study of the time evolution revealed that most of the time short-range interactions prevailed, whereas the communication between the main centres of activity occurred more sparsely and changed dynamically in time. The patterns of connectivity were quantified by means of a network formalism based on assortative mixing—an approach novel in the field of brain networks study. By means of application of the above method, we have demonstrated the existence of a modular structure of brain networks. The strength of interaction inside the modules was higher than between modules. The obtained results are compatible with theories concerning metabolic energy saving and efficient wiring in the brain, which showed that preferred organization includes modular structure with dense connectivity inside the modules and more sparse connections between the modules.
The presented detailed temporal and spatial patterns of propagation are in line with the neurophysiological hypotheses concerning the role of gamma and theta activity in information processing during a working memory task.

1. Introduction

The idea that the brain can be considered as a complex network of interacting dynamic systems has already gained broad recognition in the scientific community. This kind of approach has a potential to offer an insight into information processing in the brain, and may elucidate the origins of brain pathology. Understanding functional organization of the brain is a problem approached from different directions by means of experimental techniques, such as: electro- and magnetoencephalography, functional magnetic resonance imaging (fMRI), diffusion tensor imaging, and also scaling considerations concerning grey and white matter. The repertoire of theoretical approaches includes graph theoretical analysis, models of unweighted [1] and weighted [2] networks, and measures estimating community structure in networks [3]. The concept of small-world networks has gained a lot of attention [4,5]. The architecture of the networks has to be built upon measures of connectivity. In this context, the choice of proper measures of connectivity is of great importance.

A wide range of measures has been developed for the determination of connectivity, among which we can distinguish: bivariate and multivariate approaches, linear and nonlinear estimators, undirected and directed measures. When comparing different methods, one of the crucial factors is sensitivity to noise, since noise is always present in biological time series. It was reported in several works that nonlinear methods are more sensitive to noise [6–8]. They are limited practically only to bivariate measures. It was demonstrated that for systems consisting of more than two interacting channels it is crucial to consider all signals as parts of one system, and not to treat them by a pair-wise approach. When pair-wise connectivity is computed, it is not possible to know if two given channels are really connected, or whether they are driven by a third channel; therefore, as a result of bivariate measures application, many spurious connections are generated and patterns of connections become very complicated [9,10].

The methods taking into account multivariate structure of data and accounting for directedness of interactions are based on the extension of the concept of Granger causality [11,12]: they involve partial directed coherence (PDC) [13], squared partial directed coherence (SPDC) [14], directed transfer function (DTF) [15] and its modifications: nDTF (non-normalized DTF) [16] and dDTF [17]. The measure directly derived from the Granger causality principle is the Granger Causality Index (GCI) [18], which operates in the time domain, whereas PDC and DTF are defined in the frequency domain. In information processing in the brain different rhythms may play a specific role [19,20]; thus, frequency-dependent estimators, PDC and DTF, seem to be more suitable for exploring the way in which the brain works, also the extension of GCI to the multivariate case is cumbersome [21,22].

A review of the properties of different multivariate estimators is beyond the scope of this work. The performance of different multivariate measures of connectivity was investigated in Winterhalder et al. [23] by testing their ability to detect direction of interrelation, differentiating direct from indirect connections, coping with nonlinearities. In the study of Florin et al. [22] the ability of identification of connections for two simulation schemes of several measures, PDC, SPDC, DTF, nDTF, dDTF, was tested against noise level, data length and model order by means of two methods of significance estimation. The results varied depending on the simulation scheme and the method of establishing the significance.

Herein, we shall use DTF, since it is robust in respect to noise [15] and we have longstanding experience with this function, which in a multitude of applications revealed excellent agreement with the known anatomical and physiological evidence and with imaging studies [19,20,24–28].
In the investigation of information processing in the brain, the time evolution of connectivity is of interest. It is possible to introduce time dependence in PDC and DTF by means of recursive algorithms or ensemble averaging combined with the sliding window technique. In the study of Astolfi et al. [29] adaptive multivariate autoregressive (MVAR) modelling based on recursive least-squares algorithm with forgetting factor was applied for estimation of time-varying PDC and DTF estimators. This approach was also used in a study of time-varying connectivity for foot movement [30]. An alternative approach proposed in [31] involves calculation of covariance matrix of MVAR model for short data windows and ensemble averaging over trials. Short-time directed transfer function (SDTF) [16,19,20,26] based on this concept applies a sliding window for estimating the time-dependence of directed connectivity.

In this study, SDTF will be used for estimation of time–frequency and spatial patterns of electroencephalogram (EEG) propagation during a working memory task. In order to quantify patterns of connectivity, network formalism is frequently used and quantities such as cluster coefficient and path length are estimated. However, these measures rely on the assumption that there exists at least one path connecting any couple of nodes. This assumption does not hold in the general case and particularly in our case, since obtained patterns of connectivity are very sparse. Therefore, we propose to use the approach introduced on the field of social sciences [3] and novel in the field of brain networks.

The method allows one to take into account directedness of interactions and their strength, the values of which are usually neglected in the conventional network applications. The approach described in [3] estimates a property known as assortative mixing, which makes it possible to break the network into separate communities. By means of application of the above method, we have demonstrated the existence of a modular structure of brain networks, of different density of connections inside and between the modules.

2. Experimental material

Twelve right-handed young adults (five men and seven women) without history of neurological disorders or chronic diseases participated in the study. All participants gave informed consent in accordance with the Ethical Review Board at the Medical University of Warsaw.

In all tasks, capital letters were used as stimuli, and a symbol indicating relation between elements (‘>’) was presented. There were two conditions in this study—reasoning and memory tasks. The design of the experiment is shown in figure 1.

There were two phases of each task: learning and testing. In the learning phase of reasoning condition, participants had to integrate the presented information from three premises, where the first two were not related until the third premise appeared (e.g. A > B was followed by C > D and in the end by B > C). In the test phase, subjects had to answer questions about relations between the presented elements as well as about relations between the elements which were not directly presented (e.g. A > C or A > D).

Every premise was presented for 5 s; the fixation point (inter-stimulus interval) between them was shown randomly for 3.5, 4 or 4.5 s (figure 1). Electrical brain activity was analysed during
learning phases of each trial, in which subjects were required to create a mental representation of stimuli by integrating incoming information. A more detailed description of the experiment may be found in [28].

The EEG was recorded from 64 Ag/AgCl electrodes arranged according to the 10–20 system in the WaveGuard EEG Cap (Advanced Neuro Technology). Additionally, the EOG-channel was recorded. A linked mastoid reference was used. Impedance was kept below 10 kΩ. Bioelectrical signals were recorded with a sampling rate of 512 Hz, and then were offline down-sampled to 128 Hz. The EEG recordings were visually inspected for any artefacts, and the epochs with artefacts were rejected from further processing. For the purposes of the DTF analysis, 20 electrodes were chosen. The selected 20 electrodes were Fp1, Fpz, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, Cp5, Cp6, P7, P8, P3, P4, Pz, O1 and O2. The epochs of 6 s duration were examined (1 s before premise presentation and 5 s after the presentation). The data are stored at http://eeg.pl/data.

3. Methods

The DTF is based on the transfer function \( H(f) \) of the MVAR model. The DTF describes causal influence of channel \( j \) on channel \( i \) at frequency \( f \) in the following form [15]:

\[
\text{DTF}_{j \rightarrow i}(f) = \frac{|H_{ij}(f)|^2}{\sum_{m=1}^{k} |H_{im}(f)|^2}. \tag{3.1}
\]

The canonical structure chosen for our MVAR model explicitly does not contain instantaneous causality terms (which conversely may be included for some applications with a triangular matrix structure [32]), hence DTF has non-zero value only when there is a delay between channels \( i \) and \( j \).

The robustness of DTF to noise was demonstrated in [15], where it was shown that even in the case when noise has an amplitude three times as big as the signal (variance nine times as big), the direction of propagation is correctly estimated.

Estimation of the SDTF—the time-varying version of the DTF—is based on application of a short sliding data window and ensemble averaging over realizations, which are obtained by repetition of an experiment [33]. We divide a non-stationary recording into short time windows (of \( N_S \) data points), short enough to treat the data within a window as quasi-stationary. The estimation of MVAR coefficients is based on calculation of the correlation matrix \( R_{ij} \) of \( k \) signals \( X_i \) from multivariate set. First, we calculate the correlation matrix between channels for each trial separately. Then we average over \( N_T \) trials. The resulting correlation matrix has the following form:

\[
\tilde{R}_{ij}(s) = \frac{1}{N_T} \sum_{r=1}^{N_T} R_{ij}^{(r)}(s) = \frac{1}{N_T} \sum_{r=1}^{N_T} \frac{1}{N_S} \sum_{l=1}^{N_S} X_{i}^{(r)}(t)X_{j}^{(r)}(t + s). \tag{3.2}
\]

The averaging concerns correlation matrices (the model is fitted independently for each short data window); the data are not averaged in the process. The errors of the SDTF may be evaluated by means of the bootstrap method [34]. This procedure corresponds to simulations of other realizations of the experiment. Statistical distribution of the function value is obtained by repeated calculation of the results for a randomly selected (with repetitions) pool of the original data trials.

In order to quantify network properties of the observed transmissions, we applied the approach proposed by Newman [3]. The conventional formalism based on the measures such as the clustering coefficient or the shortest path is hardly applicable in our case since the assumption that there exists at least one path connecting any couple of vertices of the network, which can be achieved by a finite number of steps, is violated. There are vertices that are not connected to any other. Furthermore, the conventional measures do not take into account directedness of the connections and their weights. Both of these factors are crucial for the determination of community structure in networks.

Therefore, we have applied a method based on assortative mixing [3]. This approach makes it possible not only to take into account direction, but also the intensity of flow. The method
estimates assortative mixing according to enumerative vertex characteristics. The connectivity matrix $E_{kl}$ is defined to be a fraction of edges in a network that connects a vertex of group $k$ to one of group $l$. Indexes $k$ and $l$ do not refer to the channels present in the definition of $DTF_{ij}$, but to the groups defined in the framework of assortative mixing. (In our case, these groups encompass integrated DTFs as will be explained below.) In an undirected network matrix $E_{kl}$ is symmetric in its indices $E_{lk} = E_{kl}$, while in directed networks it may be asymmetric. Mixing is highly assortative when the diagonal elements of matrix $E_{kl}$ are significantly higher than the off-diagonal ones. It corresponds to the situation of strongly connected modules, with weaker bonds between these modules.

In our case, the elements of matrix $E_{kl}$ are represented by the propagations (DTFs) either inside the module ($E_{kk}$), or between the modules ($E_{kl}$). The $E_{kl}$ matrix is calculated according to the formula

$$E_{kl} = \sum_{n \in \text{channels in module } k} \sum_{m \in \text{channels in module } l} DTF(n \rightarrow m),$$

where $DTF(n \rightarrow m)$ denotes average value of $DTF_{n \rightarrow m}(f)$ in the given frequency range. The $E_{kl}$ matrix is then averaged over subjects. When all elements of that matrix are calculated, the resulting matrix is normalized in such a way that the sum of all its elements is equal to 1.

Considering the elements of matrix $E_{kl}$, we may deduce if our case corresponds to the situation of highly assortative mixing $E_{kk} > E_{kl}$. If indeed it is so, we can say that the connectivity is stronger inside the modules than between the modules.

4. Results

In order to evaluate the overall pattern of transmissions during working memory task, we calculated DTF estimators for the period 0–3 s (0 corresponding to the stimulus presentation), and we averaged them over subjects. The applied autoregressive model order was (after checking by the Akaike information and Schwarz criteria) typically in the range 4–7; in the SDTF calculations a sliding window of 128 samples was used, shifted each time by 10 samples. The results are shown in figure 2. One can observe that the activity is propagating from well-defined locations, namely electrodes P4, P3, Fpz, Fz, to a lesser degree from Pz and C3. The corridors of errors, estimated by means of the bootstrap method, show 90% confidence range.

In figure 3, the pattern of propagation is illustrated in the form of arrows. It can be seen that the sources of propagating activity are localized in the frontal and parietal regions, which is in accordance with the fMRI study for the task [35].

We shall now consider the propagation in time and space in more detail. The time-varying propagation was evaluated by means of the SDTF. We constructed movies representing changes of propagation with time. An example of such an animation is presented at http://brain.fuw.edu.pl/~kjbl/Cognitive_MOV.html. Inspecting this movie, one can see that most of the time the transmission involves neighbouring electrodes at well-defined centres, and only from time to time are the long-range connections between the active centres activated. This tendency is illustrated in figure 4, where snapshots from the movie are shown.

In order to characterize these patterns of propagation quantitatively, we applied the simplified formalism of graph theory taking into consideration local and distant connections separately. We have defined as local: connections between the neighbouring electrodes in the (10–20) system along the grid lines and the ones along the diagonals of squares formed by the neighbouring electrodes. We considered all longer connections as distant (figure 5). Then in four frequency bands, we integrated all distant and all local connections (expressed by the corresponding SDTF values) separately. The time courses of transmissions for four subjects are shown in figure 6. The broad coloured curves account for errors found by means of the bootstrap method (they show 90% confidence range). The time courses for particular subjects differ since different strategies of solving the task are reflected in different time evolution of propagation. However, for all subjects,
Figure 2. DTFs during memory task averaged over subjects. In each box, DTF is shown as a function of frequency (0–60 Hz). The corridors of errors (90% confidence range) are shown. The values in the same column correspond to outflows from the electrodes marked below to the electrodes marked on the left-hand side of the picture. (Online version in colour.)

Figure 3. Pattern of propagation during memory task averaged over subjects. The colour of arrows depicts the intensity of flow (red the strongest).
Figure 4. Snapshots from the movie showing the time-varying pattern of propagations for the representative subject. The colour of the arrows depicts the intensity of flow (red the strongest). The numbers in the upper left corners correspond to the time (s) after the stimulus presentation.

Figure 5. Scheme showing the definition of short-range and long-range connections. The distances between neighbouring electrodes in the (10–20) system are 1, between electrodes from the denser grid (e.g. Fpz, Cp5, Cp6) and other electrodes are 0.5.
Figure 6. The time courses of propagation for close (dark grey/blue) and distant (light grey/red) connections. The thin lines correspond to the corridors of errors (90% confidence range) obtained by means of the bootstrap method. (Online version in colour.)

Table 1. The relative strength of short- and long-range connections.

<table>
<thead>
<tr>
<th>frequency band</th>
<th>4–8 Hz</th>
<th>8–12 Hz</th>
<th>15–30 Hz</th>
<th>35–60 Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>local</td>
<td>0.184 ± 0.01</td>
<td>0.181 ± 0.012</td>
<td>0.165 ± 0.013</td>
<td>0.137 ± 0.018</td>
</tr>
<tr>
<td>distant</td>
<td>0.131 ± 0.010</td>
<td>0.126 ± 0.012</td>
<td>0.111 ± 0.013</td>
<td>0.095 ± 0.018</td>
</tr>
<tr>
<td>ratio local/distant</td>
<td>1.4</td>
<td>1.43</td>
<td>1.49</td>
<td>1.44</td>
</tr>
</tbody>
</table>

Local connections are stronger than distant ones. Average values of local and distant connections are shown in table 1, together with their errors.

A more detailed analysis of time courses of propagation for local and distant connections showed that before the stimulus local and distant connections often go together (in phase). Around 1 s, both distant and local connections have in most cases a minimum. Later distant and local connections go in anti-phase (sometimes not exactly in anti-phase, but slightly shifted). Usually when distant connections increase, the local ones reduce their values.

Next, we considered the decrease of connectivity with distance for the flows outgoing from particular electrodes, integrating SDTF$_{ij}$ in the time epoch 0–3 s over j (outgoing flows) and over all subjects. First, we made calculations for the four different frequency bands separately. The obtained values were the highest for the theta band and the smallest for gamma; however, the evolution with distance was very similar. Therefore, we integrated the SDTF values corresponding to the outflows from electrodes over frequency band 4–60 Hz. The results averaged over subjects are shown in figure 7 together with the corridors of errors. For some electrodes, there is a sharp decrease of connectivity values at the distance corresponding to the neighbouring electrode distance. It is interesting that the electrodes for which the drop with the distance was very sharp are the sources of propagating activity (cf. figures 1–3). It is quite understandable that the sites which are ‘silent’—i.e. are not engaged in the process of sending the information (low DTF values)—do not reveal any particular distance dependence.

The above results led us to the conclusion that there exist particular modules in the brain, within which there is a strong coupling, and these modules are bound by weaker links. Considering the patterns of transmissions, we were able to tentatively divide network nodes
into groups within which network connections are dense, but between them they are sparse. We distinguished four main modules: frontal (F) involving electrodes Fp1, Fp2, Fpz, F3, F4, Fz, F7, F8, central (C): C3, Cz, C4, Cp5, Cp6, and two parietal: PI (P7, P3, Pz, O1) and PII (P8, P4, Pz, O2).

The arguments for the choice of the above-defined modules were based on:

— empirical observation concerning the decay of DTFs with a distance and the dynamical pattern of transmissions,
— imaging studies; namely in fMRI and positron emission tomography (PET) experiments concerning working memory tasks the involvement of frontal and posterior parietal regions was reported [35,36], and
— physiological evidence and hypothesis; e.g. in [37] involvement in visuospatial working memory tasks of frontal and parietal areas of the brain was postulated. As our task was spatial in nature, it was interesting to see whether it would involve both or only one (right) parietal site.

Although the adopted division into modules is partly based on observed connectivity strength and its spacial decay, the application of assortative mixing formalism gives the opportunity to quantitatively estimate inter-module and between-module connectivity strengths.

In order to construct the matrix $E_{kl}$, we integrated DTFs in four frequency bands and in the time epoch 0–3 s, and we calculated the matrix according to equation (3.3). The elements $E_{kk}$ corresponded to the connection strength inside the module, that is, DTF values between close electrodes, belonging to the same group, e.g. for PI—between electrodes P7, P3, Pz, O1. Elements $E_{kl}$ corresponded to the DTFs between electrodes belonging to different modules.
Table 2. The assortative mixing matrix $E_i$ for four modules in five frequency bands (figure 9).

<table>
<thead>
<tr>
<th>Module</th>
<th>$F$ (%)</th>
<th>$C$ (%)</th>
<th>$PI$ (%)</th>
<th>$PII$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Theta</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F$</td>
<td>$13 \pm 4$</td>
<td>$7 \pm 3$</td>
<td>$4 \pm 1$</td>
<td>$4 \pm 1$</td>
</tr>
<tr>
<td>$C$</td>
<td>$5 \pm 1$</td>
<td>$9 \pm 3$</td>
<td>$7 \pm 2$</td>
<td>$7 \pm 2$</td>
</tr>
<tr>
<td>$PI$</td>
<td>$2 \pm 1$</td>
<td>$8 \pm 2$</td>
<td>$7 \pm 2$</td>
<td>$5 \pm 2$</td>
</tr>
<tr>
<td>$PII$</td>
<td>$2 \pm 1$</td>
<td>$6 \pm 2$</td>
<td>$6 \pm 2$</td>
<td>$7 \pm 2$</td>
</tr>
<tr>
<td><strong>Alpha</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F$</td>
<td>$11 \pm 3$</td>
<td>$9 \pm 3$</td>
<td>$4 \pm 1$</td>
<td>$5 \pm 1$</td>
</tr>
<tr>
<td>$C$</td>
<td>$3 \pm 1$</td>
<td>$8 \pm 3$</td>
<td>$7 \pm 2$</td>
<td>$8 \pm 2$</td>
</tr>
<tr>
<td>$PI$</td>
<td>$1 \pm 0$</td>
<td>$8 \pm 3$</td>
<td>$8 \pm 2$</td>
<td>$6 \pm 2$</td>
</tr>
<tr>
<td>$PII$</td>
<td>$1 \pm 0$</td>
<td>$6 \pm 2$</td>
<td>$6 \pm 2$</td>
<td>$8 \pm 3$</td>
</tr>
<tr>
<td><strong>Beta</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F$</td>
<td>$10 \pm 3$</td>
<td>$8 \pm 2$</td>
<td>$5 \pm 2$</td>
<td>$5 \pm 1$</td>
</tr>
<tr>
<td>$C$</td>
<td>$3 \pm 1$</td>
<td>$8 \pm 2$</td>
<td>$8 \pm 2$</td>
<td>$9 \pm 3$</td>
</tr>
<tr>
<td>$PI$</td>
<td>$2 \pm 0$</td>
<td>$7 \pm 2$</td>
<td>$8 \pm 2$</td>
<td>$7 \pm 2$</td>
</tr>
<tr>
<td>$PII$</td>
<td>$1 \pm 0$</td>
<td>$4 \pm 1$</td>
<td>$6 \pm 2$</td>
<td>$10 \pm 3$</td>
</tr>
<tr>
<td><strong>Gamma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F$</td>
<td>$8 \pm 3$</td>
<td>$7 \pm 3$</td>
<td>$5 \pm 1$</td>
<td>$5 \pm 1$</td>
</tr>
<tr>
<td>$C$</td>
<td>$4 \pm 1$</td>
<td>$8 \pm 3$</td>
<td>$7 \pm 2$</td>
<td>$9 \pm 3$</td>
</tr>
<tr>
<td>$PI$</td>
<td>$2 \pm 1$</td>
<td>$8 \pm 3$</td>
<td>$8 \pm 2$</td>
<td>$6 \pm 2$</td>
</tr>
<tr>
<td>$PII$</td>
<td>$3 \pm 1$</td>
<td>$6 \pm 2$</td>
<td>$5 \pm 1$</td>
<td>$10 \pm 3$</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F$</td>
<td>$10 \pm 3$</td>
<td>$8 \pm 2$</td>
<td>$5 \pm 1$</td>
<td>$4 \pm 1$</td>
</tr>
<tr>
<td>$C$</td>
<td>$4 \pm 1$</td>
<td>$8 \pm 3$</td>
<td>$7 \pm 2$</td>
<td>$9 \pm 3$</td>
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<tr>
<td>$PI$</td>
<td>$2 \pm 1$</td>
<td>$7 \pm 2$</td>
<td>$8 \pm 2$</td>
<td>$6 \pm 2$</td>
</tr>
<tr>
<td>$PII$</td>
<td>$2 \pm 1$</td>
<td>$6 \pm 2$</td>
<td>$6 \pm 2$</td>
<td>$9 \pm 3$</td>
</tr>
</tbody>
</table>

The results are presented in table 2 for four frequency bands (and additionally integrated in the whole frequency band) showing the percentage of coupling strength (errors are included), and in figure 8 as a matrix of colour boxes. On the diagonal of the matrices the strength of coupling inside the module and off-diagonal strength of coupling between the modules are illustrated; purple and red the strongest, blue the weakest. It is easy to see that the coupling inside the modules is stronger than between them.

We have also made the calculation for the five modules distinguishing two frontal regions: FI: Fp1, Fpz, F7, Fz; and FII: Fp2, Fpz, F8, F4, Fz. The results (figure 9 and table 3) show that in this case the tendency of strong intra-module coupling in comparison to between-module coupling is less prominent, especially for FI and FII.

5. Discussion

The pattern of propagation obtained herein is compatible with imaging studies (see review by Cabeza & Nyberg [36]) which reported the involvement of the frontal and posterior parietal regions in working memory tasks in PET and fMRI experiments. In the fMRI study, based on
Figure 8. The assortative mixing in the network for four modules in four frequency bands: (a) theta (4–8 Hz), (b) alpha (8–13 Hz), (c) beta (13–30 Hz), (d) gamma (30–60 Hz) and (e) in the whole (4–60 Hz) frequency band. The causal coupling from the module marked below the column of boxes to the module marked at the left. On the diagonal coupling inside the modules. In each box, the strength of coupling is illustrated with colour (dark red the strongest, dark blue the weakest).

Figure 9. The assortative mixing in the network for five modules, connection strength integrated in the whole (4–60 Hz) frequency band. The causal coupling from the module marked below the column of boxes to the module marked at the left. On the diagonal coupling inside the modules. In each box, the strength of coupling is illustrated with colour (dark red the strongest, dark blue the weakest).

the same paradigm as the one considered here [35], also the involvement of the right frontal and bilateral parietal regions was observed.

The vital role of alternate anterior and posterior interactions could be better understood in the light of the results of recent imaging experiments concerning functional neuroanatomy of
Table 3. The assortative mixing matrix $E_{ij}$ values for five modules in 4–60 Hz frequency range.

<table>
<thead>
<tr>
<th></th>
<th>FI (%)</th>
<th>FII (%)</th>
<th>C (%)</th>
<th>PI (%)</th>
<th>PII (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FI</td>
<td>4.56</td>
<td>4.09</td>
<td>4.87</td>
<td>2.81</td>
<td>2.57</td>
</tr>
<tr>
<td>FII</td>
<td>4.30</td>
<td>4.95</td>
<td>4.56</td>
<td>2.94</td>
<td>3.05</td>
</tr>
<tr>
<td>C</td>
<td>2.50</td>
<td>2.33</td>
<td>6.29</td>
<td>5.79</td>
<td>6.65</td>
</tr>
<tr>
<td>PI</td>
<td>1.44</td>
<td>1.33</td>
<td>5.80</td>
<td>5.90</td>
<td>4.77</td>
</tr>
<tr>
<td>PII</td>
<td>1.46</td>
<td>1.40</td>
<td>4.36</td>
<td>4.29</td>
<td>6.99</td>
</tr>
</tbody>
</table>

complex working memory task. Areas mediating this kind of cognitive activity were found to be distributed across the brain, but they are especially visible within the bilateral frontal and parietal regions [38]. Some authors, e.g. Fangmeier et al. [37], claimed that this particular activity within the fronto-parietal network is mainly due to maintaining and processing of visuospatial information. Other studies showed frontal theta band involvement in working memory and also in other cognitively demanding tasks [39]. The results obtained in our study provide a new insight into the nature of information exchange between these previously established anatomical and functional connections. Especially interesting are the observations concerning dynamic changes of theta and gamma oscillations. As is known from previous studies, theta and gamma coding is the most probable neuronal mechanism in the short-term and working memory systems [40,41]. What our study showed are detailed temporal and spatial patterns of those two oscillation evolutions during information maintaining, with gamma being mostly involved in binding nearby neuronal ensembles and theta involved in both—information exchange within close as well as between more distant neuronal networks. It seems, generally, that lower frequencies (theta and alpha) are more prevalent in linking distant centres of information processing, whereas higher frequencies (beta and gamma) are mostly involved in processing information within these centres. Such results are in agreement with the postulated role for lower and higher frequency oscillations in neuronal networks [42].

In recent years, the trend has emerged to investigate collective properties of neural assemblies by means of complex networks formalism. The studies considering optimal organization of the networks from the point of view of metabolic energy and efficient wiring showed that preferred organization includes modular structure with dense connectivity inside the modules and more sparse connections between the modules [43,44]. It is generally acknowledged that modular organization increases stability, robustness and flexibility of biological systems [45,46]. We can conjecture that the brain is partitioned into a collection of modules, representing functional units, separable from each other, but related to other modules. The study of the anatomical database [2] of cortico-cortical connections in the brains of macaque (69 cortical areas and 413 connections) and cat (55 areas and 564 connections) revealed the small-world characteristics of the modules. The results indicated also that in the cortex each region is intermingled with other regions and it has grown following the balance between cost, local necessities and wide scope interactions. The efficiency of the local connections for both animals was higher than the global ones, the ratios being, respectively, 1.2 and 1.34. Incidentally, the ratio of local to distant connections found by us was not far from these numbers; namely, it took values from 1.40 for theta to 1.49 for beta rhythm (table 1). Functional connections as determined by the DTF do not reproduce anatomical connections, since in the given experimental condition only some connections are activated; nevertheless, anatomical and functional connectivities are to some extent related.

The modularity of brain networks is often described with the so-called ‘small-world’ features. Small-world networks are characterized by small average distance between any two nodes as random graphs, and a high clustering coefficient as regular lattices [1]. The small-world topology stays between regular and random organization. The small-world properties in the framework of unweighted networks are usually defined by means of cluster coefficient and path length, one of the assumptions being that there exists at least one path connecting any couple of nodes [1,4].
In specialist literature, several papers may be found where the small-world architecture was detected \cite{47–49}, as well as in other papers quoted in \cite{5}. However, in some cases, small-world features were barely distinguishable from randomness \cite{49,50}.

Our findings not only point out the modular architecture of the brain networks, but also allow one to identify modules with strong internal bonds. In our case, these strongly connected regions are: frontal, central and two parietal regions. Whole frontal region seems to be strongly interconnected, since breaking it into two modules, right and left, decreases the bonds inside the modules. Even more important, this pattern of results is in agreement with previous work on EEG correlates of working memory. Onton et al. \cite{39} showed that working memory-related theta increase is visible mainly over central-frontal electrodes. They also identified the source of frontal theta enhancement in anterior cingulate cortex, which lies in the middle of prefrontal cortex, exactly between the two hemispheres. This evidence explains the strong coupling of the whole frontal module observed by us.

In the study of Micheloyannis et al. \cite{50}, EEG was recorded during a working memory task for better- and less-educated people. It was reported that for better-educated people small-world properties were not prominent and the connectivity pattern was close to random. This finding for a task very similar to the one considered in our paper is quite opposite to the evidence reported herein, where a clear-cut pattern of connectivity was established.

In our opinion, close to random connectivity structures found in this paper and many other come from methodological errors in estimating connectivity. They are due to: (i) unrobust methods of connectivity estimation, and, even more important, (ii) application of bivariate methods. The mechanism of generation of false connections in the case of bivariate networks was elucidated in \cite{9,10}.

The existence of well-defined sources of brain activity, connected with particular experimental conditions, is well established in fMRI experiments, by means of inverse solution methods and intracortical measurements. This kind of deterministic structure of brain activity should have an impact on functional connectivity, so a random or barely distinguishable from random connectivity structure reported in some works may be considered as a surprising phenomenon. When multivariate robust measures of connectivity are used a clear picture of functional connectivity emerges \cite{19,20,24,25,27,28,51}.

Summarizing our findings, we may state that we have demonstrated the existence of a modular, well-defined structure of brain networks during the performance of a working memory task. Inside the modules, there is a strong coupling of the networks, whereas the connections between the modules are more sparse. This observation is in line with the works considering the structure of brain networks from the point of view of efficiency of information transfer and saving metabolic energy. Our work, besides the confirmation of the hypothesis of modularity, additionally supplies information on the mechanisms of operation of the networks. Namely, the communication between the modules takes place in certain moments only, whereas the computations inside the modules take place almost constantly, sometimes decreasing to some extent during long-distance information transfer. The long-distance frequency-specific information transfer occurring transiently is in line with the postulated mechanisms of brain function integration involving the transient synchronization between distant and specific neural populations \cite{52}.

The above results were obtained for a memory task; nevertheless, we may speculate that it is a general mechanism operating in the brain. Inspecting a time-varying, frequency-specific propagation in experiments conducted by us concerning hand movement or constant attention test we can observe similar tendencies—short-range communication prevails; however, in certain moments long-range transmissions occur. They serve the performance of a particular task, e.g. in the case of CAT experiments this would be suppression of the movement. It is our belief that our work elucidates functional organization of the neural networks and sheds new light on their dynamic performance.

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References


