Technologies for studying functional neural networks of the human brain based on data of nuclear functional magnetic tomography

I M Enyagina¹, A A Poyda¹, V A Orlov¹, S O Kozlov¹, A N Polyakov¹, V L Ushakov ² and M G Sharaev ³

¹National Research Center “Kurchatov Institute”, Moscow, 123182, Russia.

² Institute for Advanced Brain Studies Lomonosov Moscow State University, Russia.

³ Skolkovo Institute of Science and Technology, Moscow, Russia.

e-mail: enyagina_im@nrcki.ru

Abstract. Nuclear functional magnetic resonance imaging (fMRI) is one of the most popular methods for studying the functional activity of the human brain. In particular, this method is used in medicine to obtain information about the state of the functional networks of the patient's brain. However, the process of processing and analysis of experimental fMRI data is complex and requires the selection of the correct technique, depending on the specific task. Practice has shown that different processing methods can give slightly different results for the same set of fMRI data. There are a number of alternative specialized software packages for processing and analysis, but the methodology still needs improvement and development. We are working in this direction: we analyze the effectiveness of existing methods; we develop our own methods; we create software services for processing and analysis of fMRI data on the basis of the distributed modular platform “Digital Laboratory”, with the involvement of the supercomputer NRC “Kurchatov Institute”. For research we use experimental fMRI data obtained on the scanner Siemens Verio Magnetom 3T at the Kurchatov Institute. One of our tasks within the framework of this project is to improve the technology for studying large-scale functional areas of the cerebral cortex at rest. To build a hierarchical model of interaction of large-scale neural networks, a verified binding of functional areas to anatomy is required. Today, there are a number of generally accepted atlases of the functional areas of the human cerebral cortex, which, nevertheless, are constantly being finalized and refined. This article presents the results of our study of the Glasser atlas for the consistency of voxels within one region and the connectivity metrics of voxel dynamics.

1. Introduction

Today there are a number of works devoted to the division of the human cerebral cortex into functional zones [1], [2], [3], [4]. It is assumed that all voxels included in one zone perform a similar function and have similar dynamics. This assumption is used in many studies, in which, to reduce the dimensionality of the data, all dynamics of voxels included in one functional zone are replaced by one, obtained, for example, by their averaging. However, as practice has shown, the developed atlases do not fully comply with this assumption.
In favor of the fact that the existing division into zones can be improved is the fact that the work on the refinement of the atlas of functional zones is actively continuing. One of the latest works in this direction is the atlas constructed by M. Glasser and colleagues [5]. The work showed that previous atlases were not entirely accurate, since they did not take into account all neurobiological properties. Glasser and colleagues have proposed a new atlas that breaks down the human cortex into 180 zones.

It was this Glasser atlas that we chose as the object of our research. As a result of our experiments, not only the atlas itself was investigated, but also the corresponding connectivity metrics. However, analyzing the dynamics of the brain according to Glasser's atlas using Pearson's correlation, we could not confirm here that voxels included in the same zone have a high correlation coefficient. In the course of the study, a test was carried out on experimental fMRI data - how well Glasser's atlas divides the brain into functional zones, both in terms of interaction within one region, and in the case of interaction between regions.

2. Experimental fMRI data
In our studies, we used experimental fMRI data at rest for 25 healthy subjects (right-handed people aged 18 to 35 years), obtained on a Magnetom Verio 3T MR t scanner (Siemens) using a 32-channel head MR coil. Anatomical data were obtained with high resolution based on T1-weighted sequence (TR 1900 ms, TE 2.21 ms, 176 slices, voxel size 1x1x1 mm). Functional data recording based on the EPI sequence (TR 2000 ms, TE 20 ms, 30 slices, voxel size 3x3x3 mm) with a duration of about 33.5 minutes. Each subject was instructed to lie still (try not to move) with their eyes closed and purposefully not think about anything.

3. Analysis of methods for brain regions connectivity estimation using Glasser Atlas
3.1. Correlation as a measure of voxels dynamics similarity
We have compared spatially connected sections of voxels located in one atlas region but in different parts of this region. We selected two DMN atlas regions for the study: one lies in the PCC zone, other in the MPFC zone. Pearson correlation was used to assess the connectivity between the selected regions. Figure 1 shows the comparison results in the form of correlation matrices, in color representation: high correlation values correspond to shades of red, low values correspond to shades of blue. The values on row i and column j correspond to the correlation between the dynamics numbered i and j. Correlation matrices contain information about the relationship between 19 dynamics. In Figure 1.a dynamics correspond to areas located in the PCC region, while in Figure 1.b dynamics correspond to areas located in the MPFC region.

Figure 1. Results of measure the consistency of voxels in one region using Pearson correlation as the connectivity metric of voxel dynamics.

Consider Figure 1.a, corresponding to an atlas region that lies within the PCC area of the DMN. Correlation matrix values from 1 to 19 correspond to 19 selected areas. Plot number 1 is the entire satin
region, plots numbered 2-10 correspond to spheres with a large overall overlap. Plots 11-19 also correspond to spheres with a large overall overlap, but spheres 2-10 and 11-19 lie in different regions of the satin region. We can see that the correlation between the overlapping spheres is high, but between any sphere in the 2-10 range and any sphere in the 11-19 range, it is low. The minimum correlation is 0.15.

Similar results can be observed for the atlas region in the MPFC zone (1.b): the correlation between spatially separated spheres is low (the minimum value is 0.42).

Thus, the conducted studies indicate that either the atlas regions selected for the study do not correspond to one functionally homogeneous region (areas located in different parts of the atlas region have low connectivity), or the correlation is not a suitable metric for the similarity of voxel dynamics. Since closely spaced areas have a high level of correlation, it is most probably that the first of these two assumptions is true.

3.2. Coherence as a measure of voxels dynamics similarity

In addition to Pearson's correlation, coherence was used as a metric for the similarity of voxel dynamics. In the course of data analysis, it was revealed that a necessary stage in preparing data for analysis is the use of the band-pass frequency filtering procedure (in the range of 0.1Hz-0.01Hz) and the removal of polynomial trends. As shown by additional studies, the largest contribution is made by the removal of polynomial trends of 0-3 orders. Removing trends of 4-5 orders of magnitude gives insignificant changes from the point of view of the analysis results. Removal of trends of the 6th and higher order did not reveal significant changes in the analysis results.

In the course of the analysis, it was shown that in terms of assessing the connectivity of voxel dynamics obtained from fMRI data, coherence gives results that are similar in relative values to the results of correlation. Figure 2 illustrates this statement.

![Figure 2. Comparison of metrics. 2.a - coherence, 2.b - correlation.](image)

Figure 2.a shows the results of the consistency of voxel areas taken in different atlas regions (atlas regions from the DMN network: PCC, MPFC, LIPC, RIPC; a region not from the DMN network is taken separately - Brodman zone 10), with using coherence as connectivity metrics. Figure 2.b shows similar results for the same areas, but using Pearson's correlation as the connectivity metric. We see that the results differ in absolute values, but in relative values, they are very similar. In particular, the interrelation between different dynamics obtained from the same region is very high in terms of both correlation and coherence, and between different regions the relationship is lower for both metrics.
Thus, we can conclude that correlation and coherence can be interchangeable and complementary metrics when analyzing the connectivity of voxel dynamics.

3.3. Mutual information as a measure of voxels dynamics similarity

Mutual information was also used as a metric for the similarity of voxel dynamics. During the analysis of the data, it was revealed that to compare the results, it is necessary to use normalized mutual information:

$$\text{NMI}(X, Y) = \frac{I(X, Y)}{\sqrt{H(X)H(Y)}}$$

From the point of view of assessing the connectivity of voxel dynamics obtained from fMRI data, mutual information gives results that differ significantly in relative values from the results of the correlation. Figure 3 illustrates this statement.

Figure 3.a shows the results of the consistency of voxel dynamics taken in different atlas regions using normalized mutual information as a connectivity metric. Figure 3.b shows similar results for the same regions, but using Pearson's correlation as the connectivity metric. It can be seen that the mutual information between the dynamics of one region practically does not differ from the mutual information between the dynamics of different regions. This result is not similar to the results of using correlation and coherence as a metric, and also contradicts the assumption that connectivity within a region should be significantly higher than connectivity between regions.

4. Verification stability of the functional connectivity

The goal of this task was the selection of small areas within PCC and MPFC regions and verification that with a small change in the configuration of the selected areas (for example, a shift with large overlap), the functional connection changes smoothly (i.e., the functional homogeneity of the region is checked).

As the analyzed small areas, we chose spheres with a radius 9 mm centered at peak voxel (peak voxels are voxels with maximum Fisher statistics when compared with a discrete set of cosines). And as changes in the configuration of these spheres, transformations are used: a shift by 1 voxel in each of the 6 directions, a change in the radius of the sphere (6 mm and 12 mm). Thus, 9 spheres are obtained. We obtained two datasets: one for the PCC region (the center of the initial sphere is at coordinates [31, 23, 39]) and one for the MPFC region (the center of the initial sphere is at [31, 59, 22]).
Next, we calculated the functional connectivity between the dynamics averaged over all voxels of the compared sphere regions. Figure 4 shows a matrix of functional relationships between all spheres-regions of the MPFC zone (horizontal axis) and spheres-regions of the PCC zone (vertical axis).

![Figure 4. Interconnection between the PCC and MPFC regions by Pearson correlation.](image)

So it can be seen that, in general, a high level of stability of the results, depending on a smooth and small change in the initial conditions of the experiment, is not observed (the correlation varies from 0.35 to 0.5), although these results show greater stability in comparison with similar results obtained for the case of using transfer entropy and DCM as functional connectivity metrics.

5. Results

Based on the conducted studies of the Glasser atlas and the connectivity metrics of voxels dynamics, the following conclusions can be drawn:

- Verification of the consistency of the voxels of the atlas regions using the example of the default network DMN led us to the conclusion that the current partition of the Glasser atlas does not always correspond to the partition into functionally homogeneous regions. Plots of voxels taken from different regions of the same atlas region are weakly related to each other.
- Calculation of functional connectivity based on Pearson correlation showed unstable results. This suggests that even in regions with high activity at rest (MPFC and PCC regions of the default network DMN), homogeneity of functional connections is not observed, which confirms the need to develop original methods for isolating brain regions for ROI analysis.
- Correlation and coherence metrics show similar results. When using coherence, more research should be done to find the frequencies, the best reflect the connectivity of the brain voxel dynamics at the functional level.

6. Conclusion

In this article, we presented the results of our research in the field of analysis of methods for human brain regions connectivity estimation using Glasser Atlas. These works were carried out as part of the project, the main goal of which is to improve the technologies for studying functional neural networks of the human brain based on the data of nuclear functional magnetic resonance imaging (fMRI). For our study, we used experimental fMRI data obtained on a scanner Siemens Verio Magnetom 3T of the Kurchatov Institute. The conclusions obtained in this study were used by us in the future when creating...
original methods for isolating functionally homogeneous neuronal regions of the human brain [7]. Then the software implementation of the developed methodology was carried out in the form of a software module of the Digital Laboratory platform of the NRC Kurchatov Institute [8],[9]. Thus, at present, researchers at the NRC KI have access to the system for applying our original technique for analysis of the experimental fMRI data.

7. Acknowledgement
This work was supported by the RFBR research project No 18-29-23020 mk and by the Kurchatov Institute research activities on the project «Creation of a distributed modular research and development platform “Digital Laboratory”» approved by order of the Kurchatov Institute on July 02, 2020, No. 1055.

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