

Comparative Analysis of Methods for Calculating the Interactions Between the Human Brain Regions Based on Resting-State fMRI Data to Build Long-term Cognitive Architectures.

A.Poyda¹, M. Sharaev², V. Orlov¹, S. Kozlov¹, I. Enyagina¹, V. Ushakov^{1,3,4} (Poyda_AA@nrcki.ru).

¹NRC "Kurchatov Institute", Moscow, Russia, ²Skolkovo Institute of Science and Technology, Moscow, Russia, ³NRNU MEPhI, Moscow, Russia, ⁴Institute for Advanced Brain Studies, Lomonosov Moscow State University, Moscow, Russia

MOTIVATION

In this work, we compared many different methods proposed for calculating the functional interaction of brain regions based on resting-state fMRI data. We compared them according to the criterion of the stability of the results to small changes in the parameters of both the methods themselves and the input data including different levels of noise. By stability, here we mean that small changes in the parameters and level of noise will lead to small changes in the obtained estimates of the interaction. Since fMRI has a temporal resolution of about 2 seconds, here we focused on long-term architectures (400 seconds or more).

DATA ACQUISITION

The data was obtained using a SIEMENS Magnetom Verio 3 Tesla scanner. To obtain fMRI data, the following parameters were used: TR = 2000 ms, TE = 20 ms, number of slices - 42, voxel size-2x2x2 mm³. Additionally, field mapping data were obtained to reduce spatial distortions of echo-planar images.

To select the regions of interest, we used the method for selecting functionally homogeneous regions, which we developed earlier and described in detail in the article [2]. After applying our method to fMRI data, 280 regions ranging in size from 10 to 33 voxels were identified.

Next, the dynamics of all voxels in each region were averaged, resulting in 280 initial time courses - one per region. To speed up calculations the number of regions was reduced to 20 representative regions.

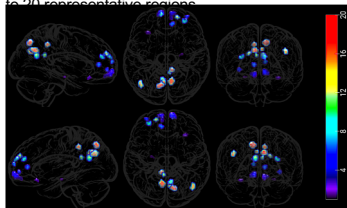


Fig.1. Selected 20 regions encoded with colors: 1 - Parahippocampal Gyrus L, 2 - Hippocampus R, 3 - VLPFC L, 4 - MPFC R, 5 - MPFC L, 6 - MPFC L, 7 - FP (BA10 R), 8 - FP (BA10 R), 9 - FP (BA10 L), 10 - PCC L, 11 - FP (BA10 R), 12 - FP (BA10 L), 13 - PCC L, 14 - PCC R, 15 - FP (BA10 R), 16 - LIPS, 17 - PCC L, 18 - PCC R, 19 - PCC R, 20 - PCC L.

METHODS

To select and evaluate the functional connectivity measures, we used the results obtained in [1], where various functional connectivity measures were evaluated using synthetic fMRI and EEG data. We chose methods that showed good results on synthetic fMRI data. We chose 14 methods from 4 families (here and next we use the same notation as in [1]):

- Transfer entropy family includes measures based on Transfer entropy: BTED, PTED, BTEU and PTEU. The prefix B- corresponds to the binary measure between each pair of regions without taking into account other connections while the prefix P- corresponds to a partial connection, in which the influence of other connections is removed. The suffixes U and D correspond to directional and undirectional cases.
- The Correlation family includes measures based on Pearson's correlation: BCorrD, BCorrU, where prefix B- and suffixes D, U have the same meanings as for the transfer entropy.
- The Granger causality family includes measures based on Granger causality: GC (classic Granger causality), CondGC (conditional Granger causality) and PGC (partial Granger causality).
- Coherence family includes measures calculated in the frequency domain: BCohF, PCohF, BCohW, and PCohW, where suffix W corresponds to wavelet transforms, while the suffix F corresponds to the Fourier transform. We also included the Instantaneous coherence measure which previously showed good performance.

For our experiments, we used a modified open-source MULAN framework developed by the authors of [1] in the MATLAB programming language.

Our study consists of two parts. First, we aimed at assessing the stability of the measures in relation to the initial choice of the time interval. This stability suggests that a small shift of a time window (by a few percent in relation to its total length) should not lead to a significant change in the values of the estimated connection strength, even if we assume dynamic connectivity.

Second, we assessed the stability in relation to the level of noise. This stability assumes that smooth changes of the noise level in the signal lead to smooth changes of estimated connections strength. This is important for real data since the real fMRI signal contains both physiological and hardware noise the level of which is difficult to estimate.

TIME INTERVAL SHIFT STABILITY

Table 1. The results of the time interval shift stability analysis

Method	STD of Values	STD of derivatives
BCorrD	0.27	0.12
BCohW	0.33	0.17
Instcoherence	0.33	0.19
BCorrU	0.35	0.23
PCohW	0.49	0.29
BTEU	0.63	0.35
BTED	0.67	0.35
BCohF	0.44	0.36
PTED	0.74	0.40
PTEU	0.74	0.42
GC	0.81	0.53
PGC	0.85	0.54
CondGC	0.87	0.57
PCohF	0.64	0.59

We can see that according to the STD of derivatives the measures could be divided into three groups: measures which showed the best result about 0.2 (BCorrD, B CohW, instcoherence, BCorrU); measures which showed a result in the range of 0.3-0.4, and measures which showed a result about 0.5 and worse. Considering that we normalized the data in such a way that standard deviation of data was equal to 1, the average of STD of derivatives equal to 0.5 indicates fluctuations with an amplitude of 50% or more of the normalization interval. The lowest measures of the STD of values correspond to the group of measures that showed the smallest values of the STD of derivatives. The large values indicate that connections strength changes over time while small values indicate that the connection strength remains stable over time.

NOISE STABILITY

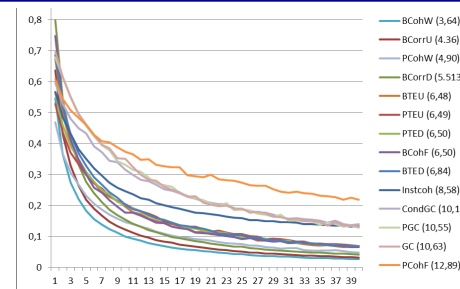


Fig.2. Noise stability of measures at various SNR levels. Along the X-axis are SNR values, along the Y-axis are normalized difference between noisy and "true" values of measures. The value of the integral under the curves is in parentheses.

Analyzing the graph we can note that:

- For SNR of 1, all measures have deviations from true value 0.45 to 0.8.
- Starting from SNR=3 measures can be divided into two groups: the PCohF, GC, PGC, CondGC measures converge more slowly than others, and the instcoherence measure joins them from SNR=10.
- Other measures behave similarly and converge to the "true value" with increasing SNR.

DISCUSSION

Among the measures that showed the best results in both studies, we should highlight BCohW, BCorrD, BCorrU, PCohW. Measure instcoh showed robustness to choosing a time interval, but was not the best (compared to other methods) in noise stability test.

Comparing the results for measure families, it can be noted that the best result was shown by Correlation and Coherence families. Transfer entropy measures are in the middle of the performance table for both studies. Granger causality measures showed the worst results. Comparing our results with the previous study on synthetic data [1], we note that Correlation and Coherence families also showed a slightly better result compared to other measure families on synthetic data in the case of identifying medium-strength connections, that might be specific for resting-state fMRI data in comparison to task-based paradigms.

Comparing bivariate and partial measures (prefixes B- and P-), in most cases measures B- showed a better result.

CONCLUSIONS

Our studies showed that measures of Correlation and Coherence families demonstrate slightly better values of the stability of the results for the initial choice of the time interval and noise level when estimating functional connectivity between the human brain regions based on resting-state fMRI data to build long-term cognitive architectures. This result is in good agreement with the previous result obtained in [1] on synthetic fMRI data evaluating medium-strength connections, which might be the case of resting-state brain activity.

We imply that the best-performing methods should be considered as potential methods for assessing short-term connectivity, which should be the subject of further research.

ACKNOWLEDGMENTS & REFERENCES

This work was supported by the Russian Foundation of Basic Research: grant RFBR 18-29-23020 mk "Investigation of functional architecture of the human brain's resting state networks as the basic model of energy-efficient information processes of consciousness". Data acquisition was performed within the grant RFBR 17-29-02518 of-m supported by the Russian Foundation of Basic Research.

[1]. Wang, H.E., Bénar, C.G., Quilichini, P.P., Friston, K.J., Jirsa, V.K., and Bernard, C. (2014). A systematic framework for functional connectivity measures. *Front. Neurosci.* 8:405. doi: 10.3389/fnins.2014.00405

[2]. Kozlov, S., Poyda, A., Orlov, V., Malakhov, Vadim Ushakov, V., and Sharaev, M. (2020). Selection of functionally homogeneous brain regions based on correlation-clustering analysis. *Procedia Computer Science* 169, 519-526. doi: 10.1016/j.procs.2020.02.215