AN UPDATED SOFTWARE TOOL FOR GROUP FMRI DATA PROCESSING

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Abstract: This paper describes an updated version of MATLAB program proposed to help neuroscientists processing fMRI data, especially to optimize parameters of connectivity analysis in fMRI datasets, such as subjects and regions selection. Presented exploratory tool allows user to view both group and single-subject activation map at the same time, so he can evaluate similarity of brain activation patterns between subjects to ensure dataset consistency for subsequent group data processing. Alternatively, user can view variability of group data or minimal statistics map. The advanced user interface is designed to maximize productivity by offering all necessary functions by one click; special attention was devoted to work with ROI coordinates. Users can export list of suitable subjects and/or regions to complete the connectivity analysis.

Keywords: fMRI, connectivity, DCM, group analysis, general linear model, MATLAB

1. INTRODUCTION

Brain mapping using functional magnetic resonance imaging (fMRI) started in the early nineties of the last century. Along with the broad availability of MRI scanners and increase of computational power of modern computers, fMRI method spread rapidly and now it is used by dozens of scientific teams. In contrast to other methods, fMRI provides excellent spatial and acceptable temporal resolution. The great advantage is zero radiation dose to the examined persons. The basic principle of the fMRI is recording of the blood oxygen level dependent (BOLD) signal which indirectly reflects neuronal activity [1]. Alteration of stimuli conditions during experimental stimulation (i.e. visual, auditory, etc.) during MRI data acquisition enables to distinguish activated brain areas.

Monitoring the spatial distribution of active brain regions during various experiments enables identification of the neural networks, which are the basic principle of brain function. Method for analysis of the relationships between different parts of the brain is called the connectivity analysis [2]. It can be performed on individuals, but generalized conclusions can be drawn only from group results. Currently available software packages designed to work with fMRI datasets offer only limited support to work with group data, such as widely used Wellcome Thrust's software tool SPM8 for MATLAB environment.

2. FMRI DATA PROCESSING

The input data are time series of 3D brain volumes represented by T2*-weighted scans, which represent BOLD signal changes during the experiment, more in [1]. Statistical evaluation of brain activation is very sensitive to the quality of input data, therefore the first step performed prior to analysis is multilevel preprocessing which involves realign (registration of scans over time), coregistration (functional to high-resolution anatomical scans), normalization (according to common template) and spatial smoothing (increase of signal to noise ratio - SNR). Complete fMRI

data workflow is depicted in Figure 1. The evaluation itself utilizes general linear model (GLM) for analysis of the tracked stimulation effects followed by calculation of the corresponding statistical tests. The result of this analysis is the statistical parametric map (or activation map after thresholding) that shows places where there was a change in neuronal activity due to stimulation during the experiment. Subsequent group level analysis for higher level inferences consists of statistical testing of tracked effects over multiple subjects.

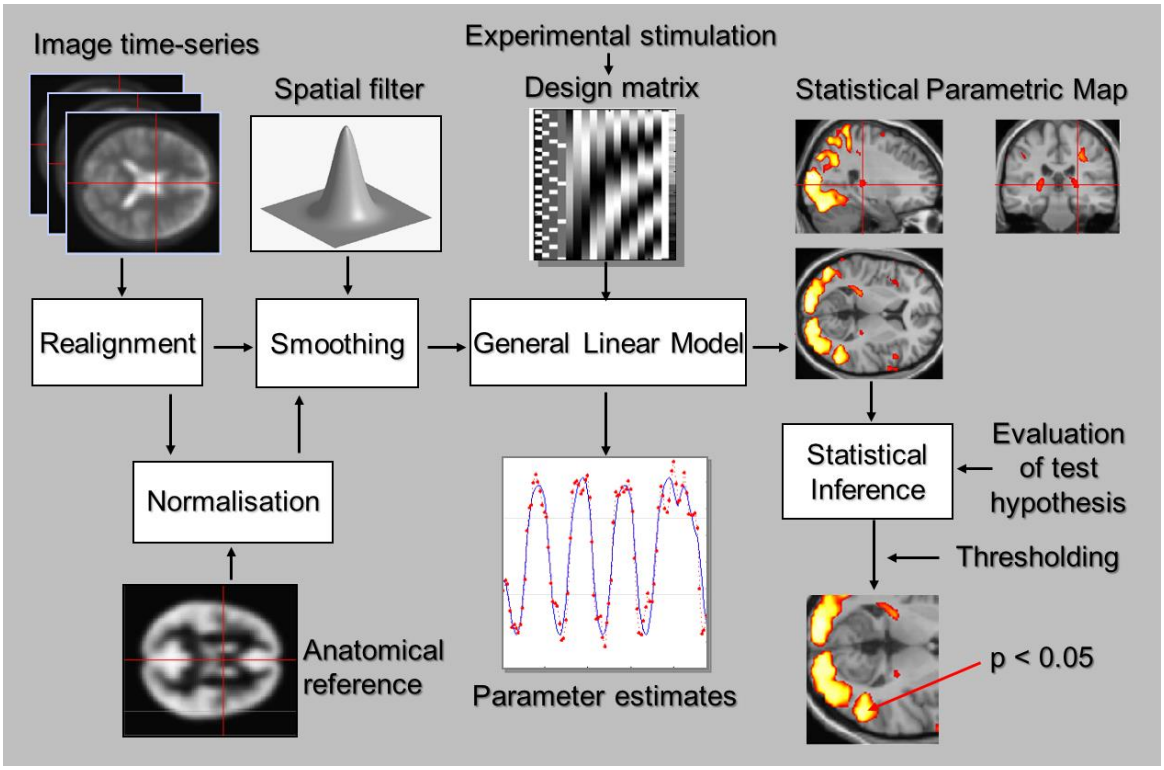

Figure 1 – FMRI data workflow

2.1. GROUP INFERENCE PROBLEMS

People can apply different strategies for solving specified tasks during experimental stimulation, which results in diverse patterns of brain areas activation. There could be even more disturbing situations such as if the examined person doesn't pay attention to experimental stimulation or don't understand the assigned task at all. Although this behavior is completely natural, it can be unsuitable in some cases. When there is no other feedback from examined person, neuroscientists can do only a little for identification and possible exclusion of mentioned cases from processed dataset. If such datasets enter the processing pipeline, they lower the group statistics making the inferences more difficult. From statistical point of view, this problem can be seen as outliers identification.

2.2. CONNECTIVITY ANALYSIS USING DYNAMIC CAUSAL MODELING

The effective connectivity analysis is special case of fMRI data analysis. It serves for identification of the connections strength and direction between distinct brain areas, which allows neuroscientists to explore brain functions and its organization. The standard method for analyzing effective connectivity is dynamic causal modeling (DCM) [3]. The method input consists of specific parameters describing the generative model (involved regions, connections, modulatory effects, inputs, etc.). By inversion of the forward model, DCM infers (hidden) neuronal processes by fitting the generated signal to the experimentally measured signal [4]. Correct localization and extraction of the brain signals from regions of interest (ROIs) directly influences the result.

The signals for DCM analysis are often extracted based on the positions of local maxima in group activation map (common coordinates for all data). Normalization step during data preprocessing ensures correct alignment of individual data, however the registration error and individual brain proportions creates room for imperfections. This can be avoided by manually inspecting activation maps of all subjects and refining the ROI position individually with respect to brain anatomy. Since this requires advanced knowledge of neuroanatomy, it is usually performed by doctors.

2.3. ENSURING DATASET CONSISTENCY

Visual inspection of all individual datasets is a basic step for correct and meaningful group analysis; no matter what kind of data processing it involves (ICA, DCM, Granger causality, Psychophysiological interaction, etc.). Spatial patterns of brain activity should be comparable. If there are various groups of patterns, i.e. due the different strategies for solving specified tasks during experimental stimulation, the data can be divided into groups and processed individually. Specific procedure depends on the aim of the study.

When performing signal extraction, the exact rate of activation can vary among subjects. Without thresholding the data, there is no guarantee that output signal is related to experimental stimulation. On the other side, setting a threshold to maintain specified SNR (signal related to experiment) could lead to disqualification of excessive number of subjects. There exist multiple solutions in this situation, such as using individually refined coordinates or modifying the threshold value to balance the SNR and number of subjects. In order to do this, user must be able to view activation value among all datasets and ROIs. Unfortunately, this is not possible either in current version of SPM8 toolbox or any other freely available software packages for fMRI data processing.

Based on the above mentioned problems, there came idea for creating software tool for exploring activation maps. The simultaneous view of both group and individual data seems the most user-friendly way of data inspection. Easy ROI definition and handling is necessary condition to facilitate the work with group data.

3. SOFTWARE TOOL DESCRIPTION

Presented program was designed as an exploratory tool for optimizing the selection of persons and brain areas suitable for the connectivity analysis. The inputs to the program are both group and individual statistical parametric maps in NIfTI-1 format (i.e. from the SPM8 toolbox). User can enter the coordinates of ROIs, where certain value of activation is required. By examining the summary statistics table, it can be easily verified that all the subjects in the study meet the specified requirements. Eventually, change of the threshold value, shift the coordinates or make selection of appropriate subjects is also possible.

Viewing of 3D data takes the form of three mutually orthogonal slices that dynamically respond to clicking the cursor and providing the user with spatial orientation. The graphical interface (see Figure 2) is divided into two parts. The left panel is used to work with a group activation map, while the right panel has multiple purposes, as it can show:

- Activation maps of individuals (selecting from a list on the rightmost side)
- Map characterizing the variability within a group
- Minimal statistics map (minimal value of statistics for all subjects)

Figure 2 – Main graphical user interface

First version came up in 2012 by the author T. Slavíček. Program now requires for its proper operation the MATLAB R2009b (or later) environment with latest version of SPM8 toolbox. It can adapt to different screen sizes without compromising clarity of displayed data. Both Windows and Linux platforms are supported in the newest version, as well as automatic selection of Czech or English captions according to system settings. Placement of all control elements has been revised since the original version. Numerous ROI coordinates can be easily entered or removed, updated version automatically switches display to appropriate coordinates when defined ROI is highlighted. For user convenience, program displays actual coordinates in millimeters of MNI space, as well as voxels of both template and data. The default program output is a text file containing list of selected subjects and coordinates matching user-defined conditions. Working scheme of the program captures the diagram in Figure 3.

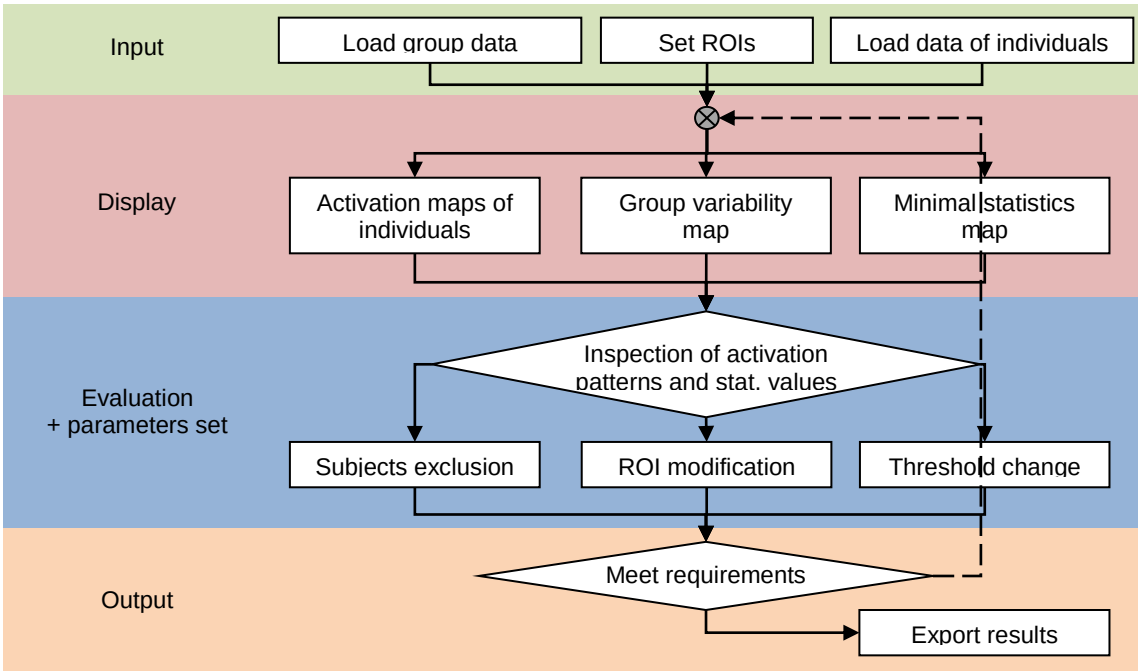

Figure 3 – Working scheme of the program

4. PRACTICAL EXAMPLE

The tool has been successfully used in our recent study [5] devoted to sensitivity analysis of the DCM method against random ROI shifts. Dataset consisting of 32 subjects has been manually inspected. Two subjects have been rejected because of registration errors, their identification took just few seconds when using presented tool. Figure 4 shows functional data (up) registered to anatomical data (bottom) for both excluded subjects (left, middle) and one correctly registered subject. Three brain areas were determined for DCM analysis; exact coordinates for signal extraction have been modified according to both group and individual statistics. The threshold value was identified as minimal value of activation in all ROIs among selected persons, which have been easily found thanks to the advanced group data processing of the presented software tool. The time saving was significant benefit as well as overall facilitation of work with the large dataset.

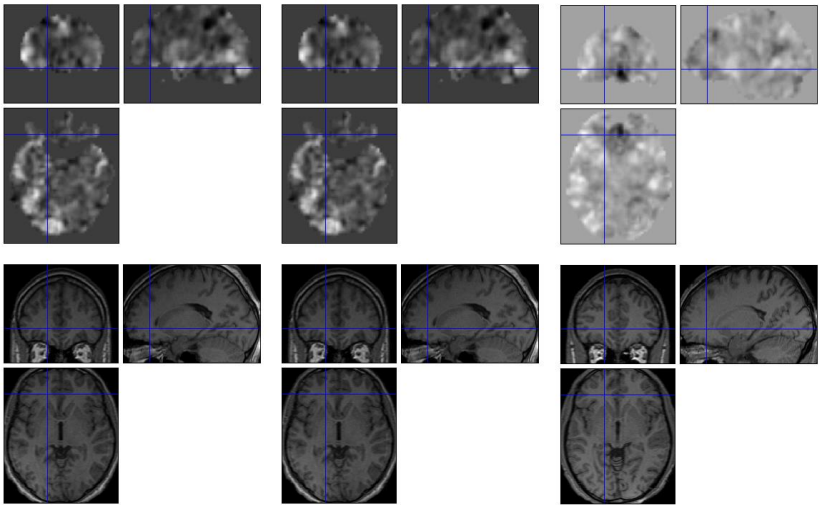

Figure 4 – Functional data misregistered for two subjects (left, middle), correct case (right)

5. CONCLUSION

Novelty software tool for work with the fMRI data has been presented in this work. It can be used to easily and efficiently perform the selection of parameters for the analysis of connectivity, as well as just quick inspection of statistical parametric maps. The tool can be downloaded for free at Brno University of Technology website and it complements missing functionality of the SPM8 toolbox in the field of neuroscience research.

ACKNOWLEDGEMENT

The research was supported by the grant GAČR P103/12/0552.

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