Software Tools for the Analysis of Functional Magnetic Resonance Imaging

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A B S T R A C T

Functional magnetic resonance imaging (fMRI) has become the most popular method for imaging of brain functions. Currently, there is a large variety of software packages for the analysis of fMRI data, each providing many features for users. Since there is no single package that can provide all the necessary analyses for the fMRI data, it is helpful to know the features of each software package. In this paper, several software tools have been introduced and they have been evaluated for comparison of their functionality and their features. The description of each program has been discussed and summarized.

1. Introduction

Functional Magnetic resonance imaging (fMRI), a modern technique of imaging, is a powerful non-invasive and safe tool which is used for the study of the function of the brain based on measure of the brain neural activation (Farah, 2002). The fMRI can localize the location of activity in the brain which is caused due to sensory stimulation or cognitive function (Gabral, Silveira, & Figueredo, 2011). In clinical field, fMRI allows the researchers to study how are the healthy brain functions, how different diseases affect the brain functions, how healthy brain function is recovered after damage and how drugs can control the diseases effect on the brain activity (Daliri & Behroozi, 2012). In the research field it allows to address these questions: how cognitive states are encoded in the brain activities and how the human brain represents the conceptual knowledge. The answers to these questions require some softwares for

analysis the fMRI data to extract information about the different stimuli (Matthews, Shehzad, & Kelly, 2006).

Generated data from fMRI have very large amount. The handling, processing, analysis and visualization of fMRI data are not feasible without computer-based methods. Useful neural information from fMRI data is extracted with research, development, and operation of these methods. Reconstruction, fundamental analysis (motion correction) and visualization tools are embedded in softwares controlling modern MRI scanners. Research and development of advanced methods for analysis of accurate activation patterns, physiological modeling based on reality, etc., makes a lively space for development of the large number of fMRI data analysis tools (Poldrack, Mumford, & Nichols, 2011).

To extract the information from fMRI data it is necessary to do global data analysis, and since there are many available options for the data analysis, the fMRI research groups prefer to consider, ''which available

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software package will be useful for their needs?''. In this article, we review the features of different available software packages for fMRI.

The major paradigm for fMRI analysis is the hypothesis-driven and voxel-based approach. In this method activation responses to a brain function between the subjects are determined. Normally the multi-step processing plan is required for the analyses of the fMRI data where the typical steps involve: 1) spatial realignment of the individual fMRI scans for head motion correction; 2) co-registration between functional (T2* weighted) and anatomical (T1 weighted image with high spatial resolution) scans; 3) spatial normalization of the subjects involved in the study into standard brain atlas (multi subject analysis), e.g., based on anatomical MRs of different subjects; 4) spatial smoothing; 5) performing the statistical parametric maps in which they show the effect of a behavioral brain function in each voxel; 6) finally using a statistical test on these effects and reporting the activated voxels. A number of publicly available packages have functions for most of the necessary processing steps: SPM, FSL, AFNI, DPTools, BrainVoyager, VoxBo and etc. (see Table 1).

The features of software package that must be considered for the fMRI data analysis include:

• **Address/availability:** the URL for each software package involves information whether the package is commercially or freely available or shareware.

• **Platform/operating system:** which software and hardware is required for each package installation.

• **Preprocessing:** Before statistical analysis and signal detection, it is necessary to convert the fMRI raw data to a form known by each software package and to improve the signal quality by preprocessing the raw data obtained from the MRI scanner, including artifact detection, baseline correction, realignment, movement correction, co-registration, normalization, and smoothing.

• **Input of data:** the software is able to load the 2D, 3D, and 4D images.

• **Image display:** this feature includes image manipulation tools, output options(e.g. regions, locations, and size), summary statistics, post hoc analyses, and whether the image cloud be viewed in three orthogonal planes.

• **Region of interest (ROI) analysis:** in this method brain activity signal is extracted from specific region of interest and each area of the brain is analyzed separately.

• **Statistical model:** which statistical methods are used for the analysis: parametric models or the non-parametric methods?

In this study we evaluated several software packages that are used for the analysis of the fMRI data.

2. SPM (Statistical Parametric Mapping)

Statistical Parametric Mapping is a statistical technique to determine the difference in recorded brain activity by construction of spatially extended statistical processes used to test hypotheses during the functional neuroimaging experiments using neuroimaging technologies (Penny et al., 2006). These ideas have been included in a software that is called SPM. Brain imaging data sequences are applied to SPM software for the analysis. The sequences can be a series of images from different subjects, or time-series from the same subject. The current package is designed for the analysis of fMRI, PET[1], SPECT[2] , EEG[3] and MEG[4] . SPM was developed by members and collaborators of the Wellcome Trust Centre for Neuroimaging for analyzing functional imaging data. SPM is made freely available to the neuroimaging community across laboratories. The software is a complete analysis package that represents the implementation of the theoretical concepts of Statistical Parametric Mapping. The SPM software is a MATLAB (The MathWorks, Inc) based functions and subroutines with some externally compiled C routines. The current version of SPM is SPM8. It is available for all versions, both 32 and 64 bit version of MATLAB.

2.1. SPM Analysis Steps (Fig 1)

2.1.1. Temporal Processing:

This Step Includes the Following Operation

• **Slice timing:** in this step, sessions are corrected for the differences in image acquisition time between the slices. The parameters that we need to know for doing this session are number of slice, TR [5], TA [6], slice order, and reference slice.

2.1.2. Spatial Processing:

This Step May Include

• **Realign:** in this session all time-series of images are realigned to the first functional image, so that the position of the brain during the time is same. For doing

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1. Positron emission tomography
2. Single-photon emission computed tomography
3. Electroencephalography
4. Magnitoencphalograhy
5.Time Repetition
6. It is usually calculated as TR - (TR/n slices) in second

this step a least squares approach with a 6 parameter (rigid body) spatial transformation is used. A rigid-body transformation (in 3D) can be parameterized by three translation and three rotation parameters about the different axes. The aim is primarily to remove movement artifact in fMRI data (Friston et al., 1995).

• **Co-registration:** in this session time-series of functional images are aligned into the anatomical images within-subjects. Doing this session needs a rigid-body model. You get the options of estimating the transformation, re-slicing images according to some rigid-body transformations, or estimating and applying rigid-body transformations (Collignon et al., 1995).

• **Segmentation:** This function is used for the bias correction, spatially normalizing or segmenting the fMRI data (Ashburner & Friston, 2005).

• **Normalization:** Vvarious subjects have different brain size. In group analysis it is necessary that all brains have the same size and orientation so that brains can be compared in these conditions (Ashburner & Friston 1997).

• **Smoothing:** for doing this session, image volumes are convolved with a Gaussian kernel of a specified width that is caused to increase the overlap of activa-tion between subjects. It is used as a preprocessing step in multi subject analysis.

2.1.3. fMRI Statistics:

This Step Can Consider the Following Issues

• **fMRI model specification:** Statistical analysis of fMRI data uses a mass-univariate approach based on General Linear Models (GLMs). It comprises the following steps (1) specification of the GLM design matrix, fMRI data files and filtering (2) estimation of GLM parameters using classical or Bayesian approaches and (3) interrogation of results using contrast vectors to produce Statistical Parametric Maps (SPMs) or Posterior Probability Maps (PPMs) (Lazar 2008).

• **fMRI model estimate:** Model parameters can be estimated using classical (ReML - Restricted Maximum Likelihood) or Bayesian algorithms (Friston et al., 2002).

3. Brain Voyager

BrainVoyager QX is a powerful neuroimaging software package (Goebel, Esposito, & Formesano, 2006).
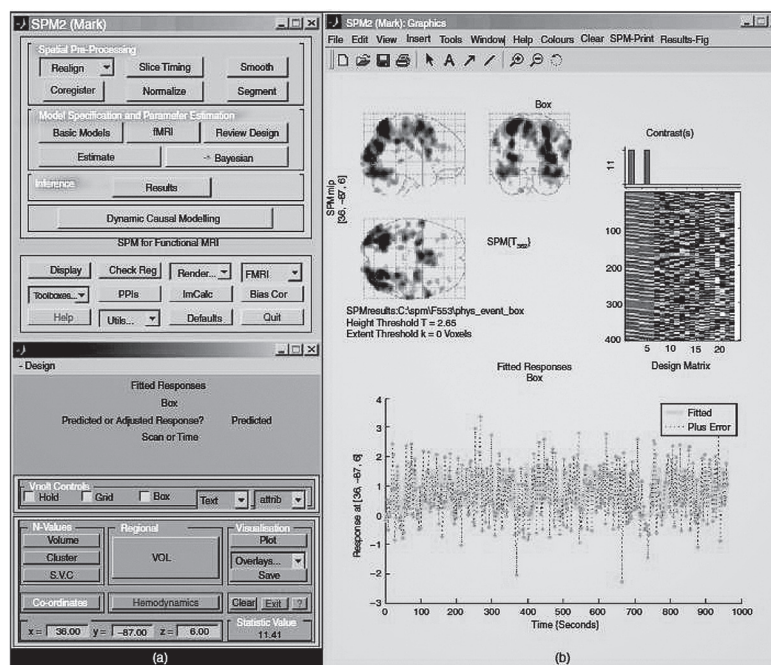
Figure 1. A screen shot of SPM. (a) Two windows used as an interface for design specification and analysis. (b) The activation map (as a maximum intensity projection, corrected for multiple comparisons using FDR correction (P < 0.05), a graphical interpretation of the design matrix, and a time-series plot from a single voxel (400 samples). The time series originates from the voxel with maximal probability of being activated in a visuo-motor experiment (versus the baseline, which is not modeled explicitly in this analysis). The RETROICOR method is used for modeling the confounding signal from respiration and cardiac pulsation (Nielsen et al., 2006).

It started as a tool for the analysis of anatomical and functional MRI data sets but it could develop during the years into a multi-modal analysis tool for fMRI, DTI[7], TMS[8], EEG and MEG data. The software includes univariate (hypothesis driven) and multivariate (data driven) analyses of fMRI time series, several methods to correct for multiple comparisons, and tools to run multi-subject volume and surface-based region of interest (ROI) analyses. The software also contains extremely fast and highly optimized 2D and 3D analysis and visualization routines; a comprehensive set of efficient pre-processing tools, including motion correction, high-pass filtering and slice scan time correction; volume and cortex-based hypothesis-driven statistical data analysis using the General Linear Model (GLM); random-effects ANCOVA analysis for advanced multi-factorial designs and correlation with external (e.g. behavioral) variables; multi-voxel pattern analysis (MVPA) tools, including support vector machines (SVMs) and recursive feature elimination (RFE); analysis of Diffusion-Weighted Imaging (DWI) including combined visualization of tracked fiber bundles with structural and functional MRI; dynamic statistical thresholding using the False Discovery Rate (FDR) approach for correction of multiple comparisons; cluster-size thresholding for correction of multiple comparisons for volume and surface maps; multi-subject Volume-of-Interest (VOI) and surface Patch-of-Interest (POI) analysis; volume and cortex-based data-driven analysis using Independent Component Analysis (ICA) performing single run as well as group analyses; cortical thickness analysis for advanced morphometry; automatic co-registration of functional and diffusion-weighted data with high-resolution 3D anatomical data sets advanced methods for automatic brain segmentation; surface reconstruction, cortex inflation and flattening; cortex-based inter-subject alignment based on gyral / sulcal pattern of individual brains going beyond standard volumetric normalization approaches such as Talairach transformation; advanced visualizations of anatomical and functional data sets with real-time GPU-based volume rendering; a real-time neuronavigation module as part of the TMS Neuronavigator system.

The software is highly optimized and user friendly running on all major computer platforms including Windows (XP/Vista/7), Linux (i.e. Ubuntu, SUSE, Fedora) and Mac OS X (10.6 or higher). It is available for all platforms both a 32 and a 64 bit versions. To obtain maximum speed on each platform, BrainVoyager QX has been completely programmed in C++ with op-

7. Diffusion tensor image
8. Transcranial magnetic simulation

timized and highly efficient statistical, numerical, and image processing routines.

BrainVoyager QX provides a comprehensive cross-platform solution embodied in a single product. Data analyzed on one platform - for example Windows - can be moved to another platform - for example Mac OS X on Intel or PowerPC hardware - and processed further without any problem.

3.1. BrainVoyager Analysis Steps (see fig. 2 for a view of the software)(http://support.brainvoyager.com/)

3.1.1. Analysis in original space –FMR-STC projects

This step explains how to create BrainVoyager project from raw data. This step may include

• Creation of a functional project: FMR project files are simple text files containing the information defining a functional project created from raw MRI data, typically from EPI sequences. The actual time course data is contained in STC ("slice time course") files, which are referenced in the FMR file.

• **Creation of the stimulation protocol:** stimulation protocol defines the events at the lengths of presentation of stimuli.

• **Statistical tests and time courses:** this step explains how to use statistical test for define which areas of brain active on the FMR file (2D image).

• **Preprocessing of FMR projects:** a series of mathematical operations is typically performed prior to statistical data analysis to reduce artifact and noise-related signal components. The most essential steps of these preprocessing operations are: removal of global signal fluctuations, slice scan timing correction, head motion detection and correction, spatial and temporal smoothing of the data, removal of linear and non-linear trends in voxel time courses (Behroozi et al., 2011).

• **Statistical analysis with the General Linear Model (GLM)**: this step explains how to use GLM to analyze the fMRI data. The GLM goes beyond simple correlation or t-tests by allowing for specifying advanced statistical models containing many explanatory variables also called "predictors". In addition, the fit tells us whether one or more individual explanatory variables contribute significantly to explain the voxel time series data. It is also possible to test contrasts, i.e. whether the estimated effect (beta weight) of a pre-

dictor A is significantly larger (or smaller) than the estimated effect of a variable B.

3.1.2. Analysis is standard 3D Space-VMR-VTC projects:

This step may include

• **Creation of 3D anatomical project:** this step explains how to create 3D anatomical projects. The 3D data set will be used in the next step for co-registration with the functional data.

• **Co-registration of functional and anatomical data:** this step explains how to align functional slice-based data of an FMR project with a 3D data set. This allows for relating brain activity more easily to anatomical locations and it prepares the transformation of the functional data into stereotaxic (Talairach) space.

• **Talairach transformation:** this step explains how to transform a recorded 3D data set into Talairach space, which is a commonly used "standard" space for reporting locations of activated brain regions and for averaging data across subjects. This step is needed in multi subject analysis.

• **3D-3D alignment:** Several experimental designs are needed for acquiring data of one subject in multiple scanning sessions. In this case it is necessary to align the data of all sessions to one high-quality anatomical data set. Therefore, this step explains how to automatically align two anatomical 3D data sets with each other. This allows us to find a mapping between the intra-session 3D data set and the extra-session high-quality 3D data set. This mapping is another important piece of information to transform our functional data into Talairach space.

• **Talairach transformation of functional data:** this step explains how to transform our functional data into Talairach space. The result of this process is a VTC[9] file, containing the data from a corresponding FMR project.

• **Statistical analysis of 3D functional data:** this step explains how to run statistical tests with VTC functional data.

3.1.3. Surface Space Analysis –SRF_MTC projects:

This step may include

• **Surface reconstruction of head:** this step explains how to invoke a surface module window. The surface module of BrainVoyager QX can be used to create

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9. volume time course

advanced 3D renderings and to apply various surface-based techniques like cortical flattening. Here we will learn how to create a 3D model of a subject's head from a 3D MRI data set. The resulting visualizations are instructive in it-self but they are also important for advanced applications such as the spatial co-registration of a subject's MRI 3D coordinate system with that obtained from other imaging modalities like EEG or MEG.
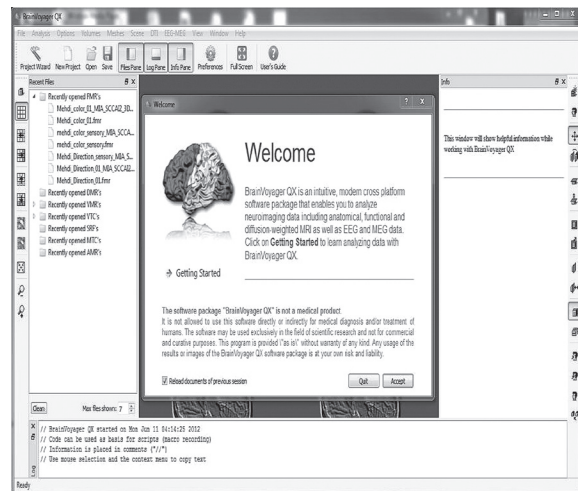
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Figure 2. A screen shot of BrainVoyager.

• **Navigation in the surface module window:** this step explains how to navigate within the surface window.

• **Slicing a polygon:** this step explains how to slice a loaded or created polygon mesh. Sliced views of the head or brain provide useful information about the spatial relation of 3D renderings and the 2D images from which they have been built.

• **Automatic cortex segmentation:** this step explains how to automatically segment and reconstruct the cortex of both hemispheres of the brain.

• **Cortex inflation:** this step explains how to inflate a mesh representing the cortical sheet and how to show curvature information of the folded cortex on the inflated cortex representation.

• **Statistical maps on cortex meshes:** this step explains how to visualize statistical maps on inflated cortex meshes. We will also learn how to define surface patches as regions-of-interest, and to invoke time course plots for these regions.

4. AFNI (Analysis of Functional NeuroImages)

The idea of AFNI software was expressed by Robert Cox for the first time, which was originally developed

and is currently maintained by him at the NIH (see Fig. 3). AFNI is a rich software package for processing and displaying fMRI data (Robert, 1996). AFNI is a powerful package of C programs that is described for processing, analyzing, and visualization of three dimensional human brain functional magnetic resonance imaging (fMRI) results. The software can map the neural activation onto higher resolution anatomical scans with different colors. Slices in each cardinal plane can be viewed simultaneously. Manual placement of markers on anatomical landmarks allows transformation of anatomical and functional scans into stereotaxic (Talairach-Tournoux) coordinate. Several statistical analysis methods for 3D functional datasets are available in this software. This software has an interface for AC-PC alignment and transformation to Talairach coordinates. It can map the fMRI activation pattern onto 2D and 3D structural (anatomical) images. Here, temporal data processing and visualization is utilized. There are different plug-ins for Fourier and wavelet filtering, real-time fMRI analysis, histogram generation, and etc.

The programs are written in ANSI C and Motif 1.2. Software can run on UNIX+X11+Motif systems, including SGI, Solaris, Linux, and Mac OS X. It is available in both source code and binary executable for download. It is freely available software (in C source code format, and some precompiled binaries) for research purposes.

4.1. AFNI Analysis Steps

4.1.1. Preprocessing

The goal of preprocessing is to eliminate different kinds of artifacts such as motion correction. Pre-processing consist of spatial or temporal filtering of fMRI data and improving the image resolution. For applying various processes onto images, initially they must be converted to the format that the software can read them. The raw functional image format from fMRI set is .dcm or .IMA. In AFNI Functional images format are converted to p-files. After converting, the raw data have low resolution (64x64) and for statistical analysis, they need to be reconstructed, renamed, made into 3D bricks, reregistered (to head motion correction), deconstructed, formatted into another type of image file, and normalized with MGH and Matlab routines. Although, all the preprocessing steps are the same for Block and Event-Related designs. It is necessary to have programs that can reconstruct the raw fMRI files and rename them, so the grecons5x is used for this purpose. The afnireg-2bshort script can be used to translate files from AFNI

format to MGH format (http://cnl.web.arizona.edu/afni-preprocess.htm).

4.1.2. Anatomical Preprocessing and Centering

These are high resolution (256x256 output) *.MR files. There are generally 2 series: series 2 with ~ 17 images; series 4 with ~124 images. These *.MR files are used to make the 3D volume (http://cnl.web.arizona.edu/afnianat.htm).
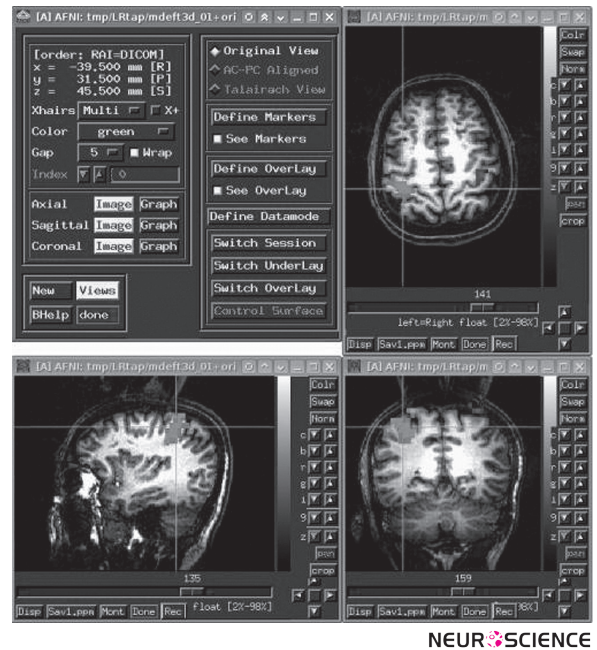
4.1.3.

Figure 3. A screen shot of AFNI.

4.1.4. Standard Analysis

Standard Analysis is available for analysis of two different types of stimulus designs (Block analysis, Event related Analysis) which are used in the studies of fMRI.

4.1.5. Special Analyses

This step may include

• **Talairach Realignment:** Talairach realignment aligns an individual brain to a standard atlas. Ideally, this allows one to identify anatomical structures based on their absolute Talairach coordinates. This step is needed in multi subject analysis.

• **Creating Waver Files:** All voxels in the functional brain image are followed through time, so that there are time-series of images. In the fMRI scan, each vox-

Table 1. The list of software for fMRI and MRI processing and analysis. "ROI" is dedicated region of interest (region-based) functionality.

Name	Usage	URL
DPTools	General Purpose	http://www.fmritools.org
PLS	Multivariate analysis	http://www.rotman-baycrest.on.ca/index.php?section=84
ImageJ	Image analysis	http://rsb.info.nih.gov/ij
Neurolens	General Purpose	http://www.neurolens.org
MIPAV	Image Processing, Analysis, & Visualization	http://mipav.cit.nih.gov
MedINRIA	Image processing	http://www-sop.inria.fr/asclepios
VTK	Image processing and visualization	http://www.vtk.org/
MultiTracer	Visualization	http://bishopw.loni.ucla.edu/MultiTracer/MultiTracer. Html
ITK	Image processing	http://www.itk.org
ITK-SNAP	Image processing	http://www.itksnap.org
Paraview	Image processing	http://www.paraview.org
LOIN	Neuroimaging	http://pipeline.loni.ucla.edu/?software_id=2
AAL	Atlasing	http://www.cyceron.fr/freeware/
AFNI	General Purpose	http://afni.nimh.nih.gov/afni/
AIR	Image registration	http://bishopw.loni.ucla.edu/AIR/
BAMM	General purpose	http://wwwbmu.psychiatry.cam.ac.uk/software/
BrainMap	Databasing	http://www.brainmap.org
BrainSuite	Image processing	http://neuroimage.usc.edu/brainsuite/
BrainVISA	Environment	http://brainvisa.info/
BrainVoyager	General purpose	http://www.brainvoyager.com/
Brede	Databasing	http://hendrix.imm.dtu.dk/services/jerne/
EvIdent	Analysis	http://www.ibd.nrc-cnrc.gc.ca/english/info_e_ evident.htm
FIASCO	General purpose	http://www.stat.cmu.edu/~fiasco/
FisWidgets	Environment	http://grommit.lrdc.pitt.edu/fiswidgets/
fMRIDC	Databasing	http://www.fmridc.org
FMRLAB	Analysis (ICA)	http://www.sccn.ucsd.edu/fmrlab/
FMRISTAT	Analysis	http://www.math.mcgill.ca/keith/fmristat/
FreeSurfer	Visualization	http://surfer.nmr.mgh.harvard.edu/
FSL	General purpose	http://www.fmrib.ox.ac.uk/fsl/
ICBM	Atlas Atlasing	http://www.loni.ucla.edu/ICBM/
INRIAlign	Image registration	http://www-sop.inria.fr/epidaure/software/INRIAlign/
GIFT	Analysis (ICA)	http://icatb.sourceforge.net/
LIPSIA	General purpose	http://granat.cns.mpg.de/Lipsia/
LONI	Pipeline Environment	http://www.loni.ucla.edu/
Lyngby	Analysis	http://hendrix.imm.dtu.dk/software/lyngby/
Marina	ROI	http://www.bion.de/Marina.htm
MarsBaR	ROI	htpp://marsbar.sourceforge.net/
McStrip	Image processing	http://www.neurovia.umn.edu/incweb/
MEDx	General purpose	http://medx.sensor.com/
MM	Analysis	http://www.madic.org/download/MMTBx/
MRI3dx	Visualization	http://www.aston.ac.uk/lhs/sta®/singhkd/mri3dX/
MRIcro	Visualization, ROI	http://www.psychology.nottingham.ac.uk/sta®/cr1/mricro.html
MRIWarp	Image registration	http://hendrix.imm.dtu.dk/software/mriwarp/
MRVision	Analysis	http://www.mrvision.com/

Name	Usage	URL
NIfTI	File format	http://nifti.nimh.nih.gov/
NPAIRS	Diagnostic	http://www.neurovia.umn.edu/incweb/
NeuroGenerator	Databasing	http://www.neurogenerator.org/
SmallTime	Compression	http://www.brainmapping.org
SnPM	Analysis	http://www.sph.umich.edu/ni-stat/SnPM/
SPM	General purpose	http://www.¯l.ion.ucl.ac.uk/spm/
SPMd	Model diagnostic	http://www.sph.umich.edu/~nichols/SPMd/
Stimulate	Analysis	http://www.cmrr.umn.edu/stimulate/
SumsDB	Databasing	http://sumsdb.wustl.edu:8081/sums/index.jsp
SureFit	Visualization	http://brainvis.wustl.edu/resources/surefitnew.html/
SurfRelax	Visualization	http://www.cns.nyu.edu/~jonas/software.html
Talairach Damon	Atlasing	http://ric.uthscsa.edu/projects/talairachdaemon.html
VoxBo	General purpose	http://www.voxbo.org/
WFU Pick Atlas	ROI	http://www.fmri.wfubmc.edu/
Yale	Analysis	http://mri.med.yale.edu/individual/pawel/fMRIpackage.html

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Table 2. Number of references to different softwares of fMRI analysis and visualization. The number of references was obtained from the Google scholar website until 12 August 2012.

Software Name (Reference to the original paper)	Number of References
SPM: Statistical parametric maps in functional imaging: A general linear approach(K.J. Frinston, 1995)	6095
AFNI: Software for analysis and Visualization of Functional Magnetic Resonance Neuroimages.(Robert W. Cox, 1996)	3055
FSL: Advance in functional and structural MR image analysis and implementation as FSL. (Stephen M. Smith, 2004)	1909
AIR: Automated Image Registration: I. General Methods and Instrasubject, Intramodality Validation. (Roger P. Woods, 1998)	1422
FreeSurfer: Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. (B. Fischel, 2002)	1039
MRICRO: Stereotaxi display of brain lesions. (C. Rorden, 2000)	946
fMRLAB: An ICA toolbox for fMRI data analysis(J. R. Duann, 2002)	348
BrainVoyager: Analysis of FIAC data with BrainVoyager QX: From single-subject to cortically aligned group GLM analysis and self-organizing group ICA. (R. Geobel, 2006)	295
VOXBO: Viewing facial expressions of pain engages cortical areas involved in the direct experience of pain. (M Botvinick, 2005)	254
PLS: Partial least squares analysis of neuroimaging data applications and advances.(A. R. McIntosh,2004)	236
BrainVISA: software platform for visualization and analysis of multi-modality brain data(Y. Cointeps, 2001)	71
DPTools: Whole Brain quantitative CBF and CBV measurement using MRI blus tracking: comparison of methodologies.(Anne M. Smith, 2000)	58
Neurolens: NeuroLens: an integrated visualization and analysis platform for functional and structural neuroimaging. (R.D. Hoge, 2004)	6

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Table 3. Summary of the features in four conventional fMRI analysis softwares.

Features	SPM8	AFNI	BrainVoyager	FSL
Platform/operating system	SGI, Sun DEC Alpha/ Unix, 128-Mb 300-Mb swap	SGI, Sun Solaris, Linux, HP/ Unix, 64 Mb	Windows (XP/Vista/7), Linux (i.e. Ubuntu, SUSE, Fedora) and Mac OS X (10.6 or higher)	Windows XP or Vista(32 or 64 bit) need to VMware, Linux(i.e. Ubuntu, Fedora), Mac OS X., 2GB RAM
Base language/software	MATLAB	ANSI C, motif 1.2	C++	C++
Source code availability	Yes	Yes	NO (Some plugins)	Yes (for the Qt non-commercial edition)
Graphical display minimum	No minimum	8-bit	No minimum	No minimum
Documentation/ support	User's manual/ Course/ course notes/on-line help	User's manual/on-line help	User's manual/ on-line help/ Forum	Extensive manual/ tutorial/ on-line help/ technical support
Referencing First release	Journal articles, book chapters, course notes 1994	User's manual; journal Articles 1995	User's manual; journal Articles 1992	User's manual; ; journal Articles 2004
Preprocessing	Raw images converted to ANALYZE format	Raw images must be converted	Data format is dicom	Analyze and NIFTI-1 data format
Data input 2D,3D or 4D	2D, 3D, 4D	2D, 3D, 4D	2D, 3D, 4D	2D, 3D, 4D
Statistical analysis	t-test, F-test, Eigen-image analysis	Correlation, t-test, ANOVA, descriptive	Correlation, t-test, ANCOVA,ICA, POI, FDR, MVPA	t-test, f-test, cor-relation, various tools for Functional MRI(FEAT, MELODIC, FLOBS,FABBER)
Image manipulation tools	Yes, image subtraction and addition	Yes, various maps, modify palette, and threshold	Yes, co-registration of CT and MRI, Various map, image subtrac-tion.	Yes, spatial and tem-poral filtering, statistic conversion (e.g. z to p-values), diffusion tensor decomposition, and TFCE calculation, orientation-related utilities
Output of regions, location, size	Yes	Yes	Yes	Yes
3 orthogonal views	Yes	Yes	Yes	Yes
Statistical output	z-, t-, and F-statistics, maps, P	Correlation coeffi-cients, probabilities, various maps Descrip-tive statistics, t-, F-statistics, P	z-, t-, and F-statistics, Correlation coeffi-cients, various maps, P	Correlation coefficients, probabilities, various maps, F-, T- statistics.
ROI analysis	NO (add toolbox-Marsbar)	NO	Yes	Yes

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el displays a pattern (of intensity variation) through time that indicates the blood oxygen level variation in that particular location at a particular time. These patterns can be compared with the predicted hemo-dynamic response associated with a task. AFNI 1-D files are files that include predicted hemodynamic responses to be correlated to actual hemodynamic patterns displayed by our functional analyses. For identifying the locations/voxels in the brain that ap-pear to be activated during the task, the correlations between the predicted pattern and the pattern in each voxel can be used. Waver is the program that is used to make these 1-D files.

• **Group Analysis (Averaging):** standard group analysis of fMRI data rely on spatial and temporal averaging of individuals.

5. AIR (Automated Image Registration)

AIR was developed by Roger P. Woods at the UCLA School of Medicine and includes routines for registering images of the same and differing imaging modalities (Woods et al., 1998). AIR was designed for automated registration of 3D (and 2D) images within and across subjects and within and sometimes across imaging modalities. AIR was implemented to be compatible across platforms. AIR source code is written in C language and it is available to the research community freely for download. The code can be compiled for UNIX, PC or Macintosh platforms. Only source code is available (no executable) for this package. CLP [10] in the AIR is necessary for linear and nonlinear image registration and image preprocessing utilities for re-slicing, re-orienting, re-sizing, and averaging, and etc.

6. BrainVisa

BrainVisa/Anatomist was developed as a collaborative effort between L'Institut Fédératif de Recherche 49 (IFR49) and the Frederic Joliot Hospital Service (Cointepas, 2010). BrainVisaISA is a software, which was designed for image processing. The BrainVisa control panel is very simple and allows the user to be able to trigger some sequences of handlings on series of images. The sequences of handlings are performed by calls to command lines provided by different laboratories. It is distributed with a toolbox of building blocks devoted to the segmentation of T1-weighted MR images. This software package includes various options such as: grey/white classification for voxel based morphometry, meshes of each hemisphere surface for visualization purpose, spherical meshes of each hemisphere white matter surface, a graph of the cortical folds, a labeling of the cortical folds according to a nomenclature of the main sulci. BrainVisa has tools for fMRI, MEG/EEG, and MR diffusion imaging analysis as well as measuring cortical thickness, gyrification index, sulcal length, and sulcal depth. Superior feature of the BrainVisa is its own Anatomist software to visualize data and analysis results.

7. FMRLab

FMRLab was developed by Duann at the University of California, San Diego for fMRI data analysis using Independent Component Analysis (ICA) (Perlbarg, Bellec, & Anton, 2007). In FMRLab software, users work in single framework and can complete the analysis without switching between softwares. It has an integrated

10. cleft lip and palate

surrounding to accomplish processes and analyses of the fMRI data in a single framework. Since fMRI data analysis is a complex procedure, including digital image processing, statistical analysis and data visualization, an integrated framework with all processing options is desired eagerly by users in the neuroimaging community. Recently, large numbers of software tools for data analysis and visualization have been developed for this purpose which most of these tools use model-based statistical methods. They assume that the users know the hemodynamic response (HR) for their paradigm in advance and can specify a reasonable HR model, but often, accurate or reasonable response HR models are unavailable. To address this problem, an alternative data-driven method, infomax ICA (McKeown & Sejnowski, 1998), was proposed. This method does not require a priori the HR model, instead deriving HRs of spatially independent components of the entire data set from the higher-order statistics of the data themselves. FMRLab is a toolbox running under MATLAB containing necessary components for data-driven fMRI data analysis using the highly reliable infomax ICA algorithm, normalized (Amari, 1999), and extended (Lee, Cirolami, & Sejnowski, 1999). In addition, it provides an interactive MATLAB graphic user interface (GUI) environment to manage, process, and analyze fMRI data in a single framework. All the necessary processes to apply ICA to fMRI data and review its results can be run from the graphic interface. The FMRLab processing steps are straightforward. FMRLab has been developed under MATLAB 6.1 running on Red Hat Linux. The software includes: flexible data importing; computationally efficient; defined FMRI data structure; independent component browser; smooth (transparent component exporting and spatial normalization process); interface with other software for further analysis or visualization; and SPM-style component plots (MIP, 2-D slice overlay and 3-D).

8. DPTools

DPTools was developed at the Laboratoire d'Imagerie Médicale Expérimentale et Clinique for fMRI data analysis. It provides a suite of functional and structural MRI processing utilities (Ducreux et al., 2005). Since the software has not been FDA approved, you cannot use DPTools for clinical purposes. This software contains: a GUI-based environment; analysis for fMRI, diffusion, and perfusion imaging; a visualization tools for all forms of analysis; tools for registration and segmentation; measuring MR flow; performing brain extraction; and calculating statistics from fMRI maps and diffusion tensor maps.

9. FreeSurfer

FreeSurfer is a biomedical image analysis software that was developed as collaboration between CorTechs and the Athinoula A. Martinos Center (Fischl et al., 2002). This software is able to analyze and visualize the structural and functional brain imaging data recorded from neuroimaging technologies, as well as for reconstructing the brain's cortical surface from structural MRI data and overlaying fMRI data onto the reconstructed surface. The main data type that is used in this software is divided to two types: volumetric data (volumes of voxels) and surface data (polygons that tile a surface). In the Freesurfer, for making the best visualization, image is available to be inflated and/or flattened. It contains a fully automatic structural imaging stream for processing cross sectional and longitudinal data. FreeSurfer provides many functional and anatomical analysis tools, including: ROI analysis, group analysis, multi model integration, representation of the cortical surface between white and gray matter, representation of the pial surface, segmentation of white matter from the rest of the brain, skull stripping, B1 bias field correction, nonlinear registration of the cortical surface of an individual with a stereotaxic atlas, labeling of regions of the cortical surface, statistical analysis of group morphometry differences, labeling of subcortical brain structures, measuring cortical thickness, methods for volume-based and surface-based region labeling and surface-based statistical analyses.

FreeSurfer is available for the Linux and Mac OS X operating systems. It can also be used on Windows with VirtualBox (but runs a bit slower). It is freely available for research aims.

10. FSL (FMRIB Software Library)

FSL is functional neuroimaging analysis software that was written by members of the Analysis Group, FMRIB, Oxford, UK (Martino et al., 2009). FSL is an extensive library of GUI- and CLP-based image analysis and statistical tools for fMRI, MRI, and DTI brain imaging data. FSL functions that are available for neuroimaging data are: FET (Model-based fMRI analysis with straightforward but power GUI), MELODIC (Model-free fMRI analysis using probabilistic independent component analysis), FLOBS (Generation of optimal HRF basis function and Bayesian activation estimation), and SMM (Spatialmmixture modeling) for functional MRI; BET (brain extraction tool), SUSAN (nonlinear noise reduction), FAST (FMRIB's automated segmentation tool), FLIRT (FMRIB's linear image registration tool), FUGUE (unwarps geometric in EPI images using B0 field maps), SIENA (structural brain change analysis) for structural MRI; and FDT (FMRIB's diffusion toolbox), TBSS (tract-based spatial statistics) for diffusion MRI. The features that are existing for this software are: fMRI preprocessing (e.g., motion correction, de-noising and analysis, first-level time-series analysis, and Bayesian mixed effects analysis methods); a suite of structural MRI utilities like brain extraction, tissue segmentation, linear and nonlinear inter and intra-modality registration, model-based segmentation, distortion correction, structural brain change analysis, voxel-based morphometry of gray matter, and nonlinear noise reduction; tools for diffusion MRI for diffusion parameter reconstruction, tractography, and voxel wise analysis of multi subject data.

FSL is available for Apple and PCs (Linux and Windows), and is very easy to install. Most of the tools can be run both from the command line and as GUIs.

11. MRIcro

MRIcro was developed by Chris Rorden at the University of South Carolina (Rorden & Brett, 2000). MRIcro allows Windows and Linux computers view medical images. It is a standalone program, but includes tools to complement SPM (software that allows neuroimagers to analyze MRI, fMRI and PET images). MRIcro allows efficient viewing and exporting of brain images. In addition, it allows neuropsychologists to identify regions of interest (ROIs, e.g. lesions). MRIcro can create Analyze format headers for exporting brain images to other platforms. MRIcro allows users to view medical images in a stand-alone program. It includes: tools to complement the analysis tools available with SPM; converts medical images to SPM friendly Analyze format; view Analyze format images (big or little endian); create Analyze format headers (big or little endian); create 3D regions of interest (with computed volume & intensity); overlap multiple regions of interest; rotate images to match SPM template images; export images to BMP, JPEG, PNG or TIFF format; yoked images: linked viewing of multiple images (e.g. view same coordinates of PET and MRI scans). This software is only for the visualization of fMRI data.

12. NeuroLens

NeuroLens was developed at the Unité de neuroimagerie fonctionnelle in Montreal as a Mac application for the analysis and visualization of functional neuroimages (Clohery et al., 2010). NeuroLens has an integrated envi-

ronment for the analysis and visualization of functional neuroimages. It is intended to provide extremely fast and flexible image processing, via an intuitive user interface that encourages experimentation with analysis parameters and detailed inspection of both raw image data and processing results. All processing operations in NeuroLens are built around plug-in architecture, making it easy to extend its functionality. NeuroLens runs on Apple computers based on the G4, G5, or Intel chipsets and running MacOSX 10.4 (Tiger) or later. It is available freely for download for academic and non-profit research use. This software includes: GUI-based environment; tools for region painting; flexible viewing of numerous dataset types; volumetric time-series and cortical surfaces, in multiple windows; Input/output for many commonly used image formats in neuroimaging research.

13. PLS (Partial Least Squares)

PLS was developed by Randy McIntosh at the Rotman Research Institute (Hulland, 1999). PLS is a popular method for soft modeling in the industrial applications. It is a method for constructing predictive models when the factors are many and highly collinear. PLS is a MATLAB toolkit for performing multivariate analysis of neuroimaging data. PLS is a method for extracting distributed signal changes related to changing task demands. It has also been applied to measuring distributed patterns that affect task performance and task-dependent changes in the relation between brain regions. PLS analysis has been used to characterize distributed signals measured by neuroimaging methods such as PET, event-related fMRI, blocked fMRI, structural MRI, event-related potentials, and magnetoencephalography.

14. VoxBo

VoxBo was developed by Poldark at the Center for Functional Neuroimaging at the University of Pennsylvania (Poldrack, Mumford, & Nichols, 2011). VoxBo is one of the MRI data analysis programs which is used in many laboratories. It works a bit differently than most other programs. In most data analysis programs, or for that matter programs in general, you start the program, open up a file, do some stuff with the data, and save some sort of results. VoxBo is distinctly different. In VoxBo, you create a set of instructions (called "jobs"), then sit back and wait for them to be executed. This may sound a bit like programming or scripting (e.g. in MATLAB), but VoxBo doesn't work quite like that either. The actual work is done by a process which is always running in the background on every Linux computer. You set up a list of jobs, and the process gets around to complet-

ing them eventually. VoxBo is a free software package for the processing, analysis, and display of data from functional neuroimaging (chiefly fMRI) experiments. VoxBo includes preprocessing tools for structural and functional images.

15. Discussion

This paper provides a general view about the most available software packages that are used for the analysis of functional magnetic resonance imaging data. There are various software packages for fMRI data analysis (see Table 1). A software package has many options and a tool is selected based on need to a special analysis at the laboratory. Most laboratories are looking to use freel softwares. SPM and FSL are freel softwares that have been used in various studies for GLM analysis. In contrast, BrainVoyager is commercially available software. It is expensive but it is very easy to use. The most striking feature of the Brainvoyager is having various models for analysis like, GLM, VOI, ROI, MVPA and etc.

In table 2, we summarized the number of references for each software, which shows, SPM, AFNI as free softwares and BrainVoyager as commercial software used conventionally. Based on this result, we summarized the number of features of these softwares in table 3 (Gold and et al, 1998).

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