



## An image analysis pipeline for the semi-automated analysis of clinical fMRI images based on freely available software

Christof Karmonik<sup>a,\*</sup>, Michele York<sup>b</sup>, Robert Grossman<sup>a</sup>, Ekta Kakkar<sup>a</sup>, Krutina Patel<sup>a</sup>, Hani Haykal<sup>c</sup>, David King<sup>c</sup>

<sup>a</sup> Department of Neurosurgery, The Methodist Hospital, Houston, TX, USA

<sup>b</sup> Michele York, Department of Neurology, Baylor College of Medicine, Houston, TX, USA

<sup>c</sup> Department of Radiology, The Methodist Hospital, Houston, TX, USA

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### ABSTRACT

The technique of functional Magnetic Resonance Imaging (fMRI) has evolved in the last 15 years from a research concept into a clinically relevant medical procedure. In this study, an efficient, semi-automated and cost-effective solution for the analysis of fMRI images acquired in a clinical setting is presented relying heavily on open source software. The core of the pipeline is the software Analysis of Functional NeuroImages (AFNI, National Institute of Mental Health (NIMH)) combined with K-PACS and ImageJ. Its application is illustrated with clinical fMRI exams and with a research study involving comparing subjects diagnosed with Parkinson's disease and age-matched controls.

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### 1. Introduction

Functional Magnetic Resonance Imaging (fMRI) based on blood-oxygenation level-dependent (BOLD) contrast has been established as a non-invasive method to probe brain activation when performing a variety of tasks ranging from simple motor functions to complex cognitive processing [1–4]. fMRI has been accepted as a noninvasive and safe procedure for recording activation maps of the human brain with an excellent spatial resolution (typically, in the order of mm). fMRI is being increasingly used as a preoperative tool for assessing patients undergoing brain surgery, i.e. for the removal of a neoplastic lesion or for treatment of epilepsy seizures [5–14].

In the last 15 years, improvements have occurred in acquisition techniques, including magnetic resonance imaging (MRI) pulse sequence design, in stimulus presentation hardware and in software for analyzing of the acquired MRI images [15–24]. Recent efforts have also focused on combining fMRI with other imaging modalities such as electroencephalography (EEG) [25]. A variety of analysis software exists, either provided by the vendors of the clinical MRI scanners as add-on options, by third parties as commercial implementations (often termed 'turn-key' systems) or by academic institutions placed in the public domain or made available as open source, which often only specialize in one aspect of the image analysis process [26–31]. For integration into the clinical workflow, the fMRI image analysis has to be performed in

a timely manner so that the functional brain activation maps and other types of analyses can be provided to the clinical clinician at the time of the interpretation of the anatomical MRI exam. A seamless and mostly automated implementation of the fMRI image analysis is therefore essential.

We report the implementation of a semi-automated image analysis pipeline (IAP) at our institution that uses only open source software or software freely available. Automation of the analysis steps enabled us to provide the results minutes after the completion of the fMRI exam. While this IAP was designed for the analysis of clinical studies, it has also shown to be effective for a clinical research study of subjects with Parkinson's disease [32]. Many steps of the analysis process are automated, therefore the radiologist or other imaging professionals do not need to be involved in executing the IAP. The procedure was designed to work with a commercial clinical MRI scanner, to minimize user interaction time and to be easily transferable.

### 2. Methods

The work has been approved by the appropriate ethical committees related to the institution in which it was performed.

#### 2.1. Image analysis software

The software package called Analysis of Functional NeuroImages (AFNI) [27] was chosen as the core of the IAP. This decision was motivated by the free distribution of AFNI (as open-source

\* Corresponding author. Tel.: +1 713 441 1583.

E-mail address: [ckarmonik@tmhs.org](mailto:ckarmonik@tmhs.org) (C. Karmonik).

software) by the NIMH as part of the NIH and its application by a variety of groups and individuals since its first publication from the Medical College of Wisconsin in 1994. AFNI is available for several operating systems and for our implementation, we chose the Linux gcc32 compilation as offered at the AFNI website (<http://afni.nimh.nih.gov/afni/download/afni/releases/latest>). AFNI was installed on dual processor 32-bit Centos 5 (<http://www.centos.org/>) workstation.

## 2.2. Image transfer software

Clinical MRI images are readily available for transfer from the MRI scanner via the Digital Imaging and Communications in Medicine (DICOM) standard transfer protocol [33]. DICOM is managed by the Medical Imaging and Technology Alliance a division of The Association of Electrical and Medical Imaging Equipment Manufacturers (NEMA, (<http://medical.nema.org/>)). To enable image data transfer to a dedicated imaging workstation, the freely available software K-PACS ([www.k-pacs.de](http://www.k-pacs.de)) was chosen and installed at Windows XP x64 (Microsoft Inc.)-based PC (PC workstation) as the DICOM client. MRI scanner and the PC workstation were connected via the institutional 1 GBit/s intranet. Communication between the Centos 5 workstation and the PC workstation was established using Xming X Windows server (<http://sourceforge.net/projects/xming>). Data was stored on a shared network drive mapped at the PC workstation and the Centos 5 workstation via Samba (for a schematic overview of this configuration, see Fig. 1a).

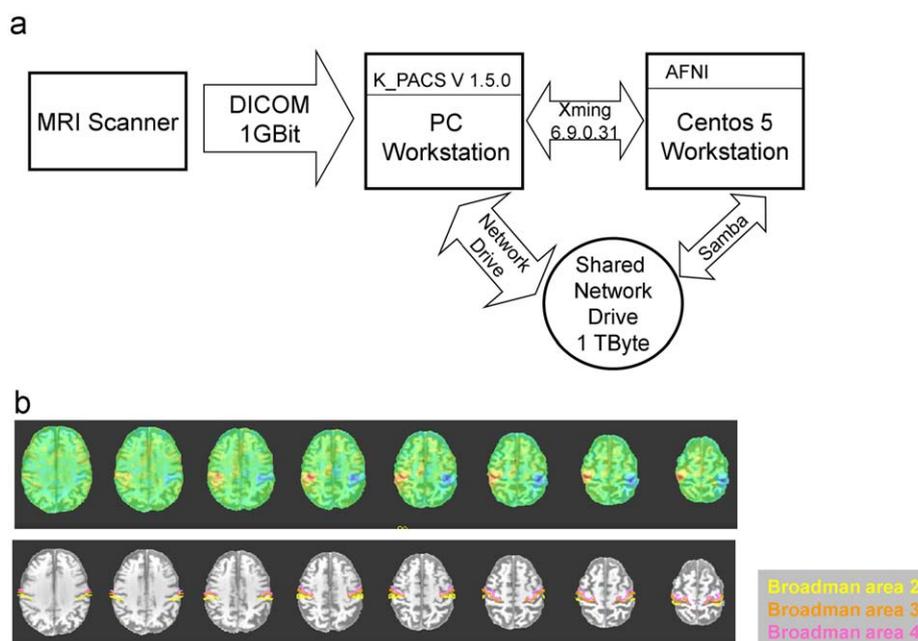
## 2.3. Clinical fMRI imaging protocol

The clinical fMRI imaging protocol was used as implemented by Thulborn Associates, Inc on a 3T GE Excite HD human scanner. The rationale for the use of high field 3T MR scanners is based on

the BOLD mechanism, and the use of fMRI on 3T for clinical purposes has been demonstrated [34]. The clinical fMRI protocol consisted of four tasks or paradigms in block-design alternating between stimuli every 45 s where slices covering the whole brain were acquired every 3 s. Since its implementation, eight patients have been scanned with this protocol. In task 1, the subjects performed alternate fist clenching of the left and right hands guided by visual written instructions visible on a projection screen located in front of the subjects eyes. In task 2, the subjects were instructed to follow the horizontal saccadic motion of a dot on the projection screen. In task 3, written statements and questions were presented to the subjects and in task 4, the subjects had to recall pictures presented during the first part of this paradigm. Stimuli in tasks 2–4 were interspaced by periods of rest (fixation on a cross hair). All paradigms followed the block design and varied in length from 4½ min to 8½ min (gradient EPI, matrix 64 × 64, isotropic spatial resolution about 3 mm). Typically during such a clinical fMRI exam, about 14,500 images were acquired. For anatomical reference, a high resolution MRI scan (3D FSPGR, isotropic spatial resolution 1 mm) was acquired.

## 2.4. Research fMRI imaging protocol

The event-related paradigm consisted of 256 visual global-local stimuli presented in 12 min and 48 s with switches randomly distributed. The number of images acquired for this fMRI task was in the order of 12,000. The visual paradigm for the research study was created with Adobe Audition 3 and Adobe Premiere CS 3 (Adobe Systems Inc.) as an AVI video file to achieve the necessary temporal accuracy. We report here preliminary data of an interim analysis including 6 subjects with Parkinson's disease (PD) and 6 age-matched healthy controls (HC). Average age in the PD group was  $68 \pm 4$  and in the HC group  $63 \pm 7$  [32].



**Fig. 1.** (a) Schematics of the interconnection of the computer network created for the analysis of the fMRI image data. The MRI scanner is connected via a 1 GBit/s network with the PC workstation. The images are transferred using the K-PACS DICOM client. The Centos 5 workstation (with AFNI) and the PC workstation share a network drive on which all data is stored. The output of the data analysis is stored on that network drive and can be accessed with Matlab and PowerPoint to create the final report. (b) Illustration of functional brain activation maps overlaid on the images from the high-resolution anatomical dataset (upper row). Representative for all 118 areas analyzed, the Brodmann areas 2–3 are marked on high-resolution anatomical images (lower row). The high correlation coefficient in these areas (as expected from a motor task) can be appreciated in these areas in the functional brain activation maps.

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