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Evaluation of a pre-surgical functional MRI workflow: From data acquisition to reporting

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ABSTRACT

Purpose: Present and assess clinical protocols and associated automated workflow for pre-surgical functional magnetic resonance imaging in brain tumor patients.
Methods: Protocols were validated using a single-subject reliability approach based on 10 healthy control subjects. Results from the automated workflow were evaluated in 9 patients with brain tumors, comparing fMRI results to direct electrical stimulation (DES) of the cortex.
Results: Using a new approach to compute single-subject fMRI reliability in controls, we show that not all tasks are suitable in the clinical context, even if they show meaningful results at the group level. Comparison of the fMRI results from patients to DES showed good correspondence between techniques (odds ratio 36).
Conclusion: Providing that validated and reliable fMRI protocols are used, fMRI can accurately delineate eloquent areas, thus providing an aid to medical decision regarding brain tumor surgery.

1. Introduction

In medicine, Magnetic Resonance Imaging (MRI) is typically used to image the structure of organs. MRI is however also used to obtain information about perfusion, diffusion, vascularization and physico-chemical state of tissues. Functional MRI (fMRI) is a technique that measures hemodynamic changes after enhanced neural activity [1], allowing to image non-invasively and with relatively high spatiotemporal resolution, the entire network of brain areas engaged when subjects undertake particular tasks [2]. Soon after its inception, fMRI has been used for clinical cases [3]. Nowadays, clinical research using fMRI encompasses many areas of neurology, from developmental, psychiatric, and dementia related disorders to strokes and brain tumors [4]. Despite the popularity of fMRI in cognitive and clinical research and its proven utility for surgical planning [5], it is not used extensively in day to day clinical practice. There are four main reasons for this: (i) fMRI requires special equipment, (ii) dedicated protocols must be in place, (iii) collected data have to be post-processed to obtain a final image, and (iv) results from analyses must be made available to the clinicians in a usable format.

fMRI delineates areas of the brain involved in motor or cognitive functions (so called eloquent areas) by asking patients to perform different tasks whilst image time-series are acquired. For motor related areas, a simple finger tapping (mapping the primary motor cortex) or more complex finger sequences (mapping the premotor cortex) may, for instance, be performed. For language areas, visual or auditory stimuli are presented whilst scanning, and patients perform different tasks such as reading, listening, repeating, etc. All patients must perform several trials, and crucially these trials must be synchronized with image acquisition. The tight coupling between stimulus presentation, task and image acquisition is mandatory for the statistical analysis, contrasting task periods vs. rest periods, or contrasting different tasks periods against each other (Fig. 1). This implies that MRI compatible equipment is available to interface between the scanner and the software used to design the tasks. The fMRI hardware, is also used to deliver instructions to the patient via MRI compatible head-

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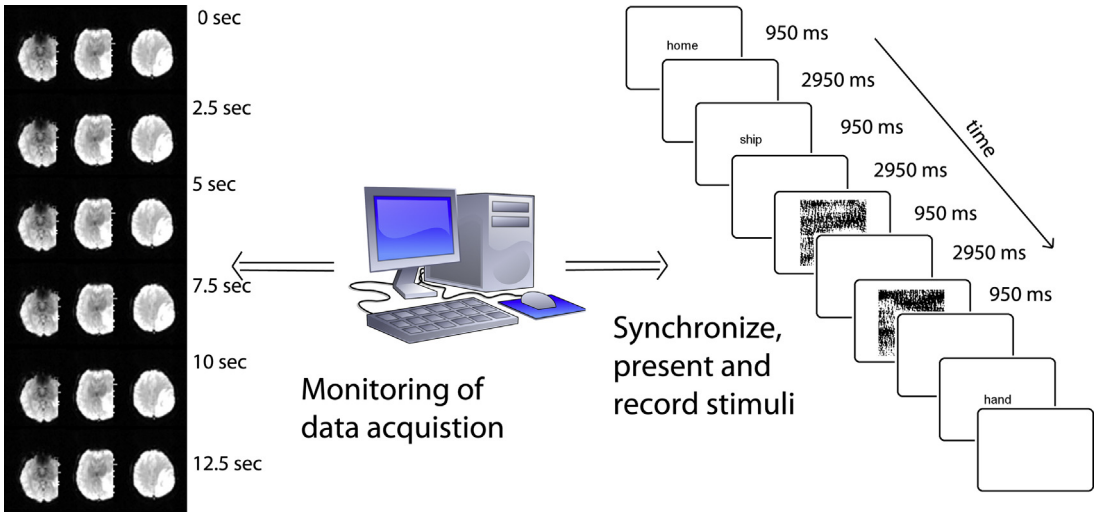

Fig. 1. Illustration of hardware setting for fMRI: (1) on the left side is shown EPI data acquired by an MRI scanner with a repetition time of 2.5 s; (2) in the middle a dedicated computer with specific hardware monitors the scanner data acquisition while presenting stimuli at specified times (3) on the right is a series of stimuli showed inside the scanner using MR compatible goggles, corresponding to our verb generation task. The synchronization between the MR images acquired (left) and the stimuli presented (right) is mandatory to contrast brain images acquired while the patient was seeing words vs. seeing noise stimuli.

phones, screen, goggles, etc. and possibly also to record behavioral responses (via e.g. microphone, response pads), all of this in phase with the image acquisition. Typically, such equipment is available in research centers but not hospitals, constituting an obstacle to day-to-day application of fMRI.

In many university hospitals, research centers with fMRI equipment are present on site (and even sometimes in or next to the clinical department), and therefore patients can be scanned without the need for transportation to a different location. To ensure good clinical practice, established fMRI protocols must however be in place. These protocols must allow the mapping of given brain areas with high specificity. Because, there are many possible tasks to map the same brain area [6,7] and these have also been developed for group studies, there are no 'off-the-shelf' protocols that can be used to elicit reliable activations at the single subject level. It is therefore mandatory to establish standards to define 'good clinical fMRI protocols' and create such protocols to establish fMRI as a clinical tool.

Assuming that such protocols are in place, and can be run by trained radiographers, the data must be processed before reporting because, in contrast to standard structural imaging (e.g. T1 or T2 weighted images), there is no direct output from the scanner. Although scanner manufacturers offer fMRI acquisition mode, which in theory allow obtaining results after a scanning session, the schemas are extremely rigid and do not fit modern complex protocols. Off-line analyses must therefore take place, and this can take from half an hour to several hours depending on the length of the processing pipeline, number of tasks performed, the complexity of the analyses, and the hardware used. Such analysis also requires expert knowledge. Together, these constitute another strong deterrent to clinical fMRI. We believe that this complexity in data analysis can be overcome by creating automated analysis workflows that (i) allow checking data quality and analysis and, (ii) output 'ready-to-use' reports and images.

The images produced by fMRI software and the images used in the clinical environment have different format. This might seem trivial but it is still a major problem. Data coming out of the MRI scanner are in the DICOM format (http://dicom.nema.org/) but researchers using fMRI typically convert them to NIfTI format (Neuroimaging Informatics Technology Initiative http://nifti.nimh.nih.gov/) because it has many advantages for research use, and in particular it facilitates interoperability among software. In addition to changing format, data are often de-identified, making the conversion back to DICOM and its use on clinical PACS and other tools like neuro-navigation difficult.

Having previously developed a set of tasks suitable for patients [8], we present here (i) a validation of those protocols, showing higher within than between-subjects reliability and (ii) an automated analysis pipeline from data transfer to reporting, fitting with the busy day-to-day clinical practice. Pipeline analysis and optimization can take many different forms, but this is out of the scope of this article. We focus here on the implementation of such pipeline using open source software and the clinical validity of the results obtained.

2. Materials and methods

2.1. Participants

All participants (healthy controls and patients) signed a written informed consent for this study that was approved by the NHS Lothian ethics committee.

2.2. Protocol validation in healthy controls

We investigated the within-subject reliability of the 5 tasks described in Gorgolewski et al. [9]: one motor task to map the hand, foot and lips regions of the motor cortex, three language related tasks to map the auditory cortex, Wernicke and Broca areas, one attentional task to map the intra-parietal cortex (IPC). For each task, ten healthy participants (four males and six females, of which three were left-handed and seven right-handed according to their own declaration, with a median age at the time of first scan of 52.5 years; min = 50, max = 58 years) underwent two separate sessions and the reliability of activation maps was assessed. We consider a protocol as clinically valid when areas of activations are more reliable within-subjects than across subjects. Concretely that means that despite the same region of the brain being activated across subjects (for instance the hand area), the obtained maps must be more similar when repeated over two sessions in a given subjects than across subjects.

For every subject, T1 volumes from both sessions were coregistered, resliced and averaged using SPM8 [10]. A Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DAR-