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Real-time functional MRI for patient monitoring during a language task

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Abstract— **Monitoring patients' cooperation for a given cognitive task is required in the clinical fMRI. The current study is aiming to develop a real-time fMRI platform to monitor the patient performance during the language task, which is usually done covertly. Successive estimation of task-related activation, deactivation and inter-regional connectivity was performed to evaluate patient's task involvement. The effect of scan numbers was assessed to determine minimal scan numbers in detecting the brain status. The preliminary results demonstrated the feasibility of real-time patient monitoring in the neurosurgical application of fMRI.**

Keywords - Real-time monitoring; Functional connectivity; functional magnetic resonance imaging

I. INTRODUCTION

Real-time functional magnetic resonance imaging (rt-fMRI) has been an important tool to monitor the brain activity [1-3]. In spite of its technical innovation, the practical application of rt-fMRI has been limited especially in the clinical application.

In the current study, we considered that rt-fMRI could be useful in the monitoring of the language process of the neurosurgical patients. So far, fMRI has been adopted in the conservative clinic to find the language area with an aim of replacing Wada test or awake surgery. Among language tasks for fMRI, verb generation and sentence generation tasks have widely been used to localize the Broca's area. Since the language tasks are generally done covertly, operators do not know whether a patient is conducting the task well or not. Some patients could not perform a given task inside MRI due to the patient's intelligence, fatigue or other reasons. In clinics, MRI technician, who are not familiar to the task, may ignore this situation. What makes the worse is in the misinterpretation of the results, which may lead to wrong clinical decision. Neurosurgeons may attribute the results either to altered lateralization of the language area in the patient or to the functional alteration due to the lesion.

Therefore, real-time monitoring of patients' performance is clinically important. If we can detect the degree of performance of the patient, we can alarm the status of the patients. For this purpose, we proposed an rt-fMRI monitoring system to analyze the patient functional data in real-time and give a feedback to the patient or clinicians.

So far, real-time classification of task-related spatial components and thus identification of the brain state using fMRI has been researched mainly based on the activation maps [4, 5]. In the current study, however, we included the connectivity indices of whole brain network in the patient monitoring in addition to the task-related activation indices.

We demonstrated the feasibility of connectivity mapping in the monitoring of verb generation task. We also tested the potential usage of the connectivity indices driven from a default mode network [6], which is known to be activated during resting state and deactivated during an attention demanding task. Since the early detection of brain state is as important as the detection accuracy in clinical application, we further evaluated the effect of scan numbers to find minimal number of scans to determine the brain status as early as possible without a significant loss of the accuracy.

II. METHODS AND MATERIALS

Real-time monitoring system

On the 3.0 Tesla MRI scanner (Siemens, Tim-Trio), fMRI scanning was performed for five right-handed adult volunteers and five neurological patients using EPI sequences with TR= 3,000 ms, TE=30 ms, voxel=3.0×3.0×4.5 mm, and matrix size=64×64×30. All subjects were scanned during a verb generation task that lasted 5 minutes. The EPI data from the image reconstruction workstation were sent to an external computer via TCP-IP in real-time. All real-time calculation and visualization was done on this external computer using an in-house program working on MATLAB (Mathworks. USA).

Subject's head motion was estimated by the rigid-body transformation providing three translational and three rotational parameters. These motion parameters were displayed in real-time, through which we could observe subjects' head motions. The first EPI data was used to derive a nonlinear spatial transformation to MNI EPI template in SPM2 (Wellcome department, UCL, England). Using this nonlinear transformation, anatomical automatic labeling (AAL) map [7] containing 116 brain regions was transformed to individual brain space to define regions of interest (ROI) within the individual brain.

Real-time statistical analysis and connectivity mapping

After linearly detrending the time activity curves, the real-time system calculated parameters of the general linear model to estimate task-related activation and deactivations. As an index for inter-regional functional connectivity, correlation coefficients between regional time activities from successive input data were calculated. The system included an effective connectivity mapping module between brain regions using Granger causality test [8, 9], which is based on the temporal latency between activities of significantly active regions. The task-related activations and inter-regional connectivity were simultaneously visualized in 3D template model.

Evaluation of the effect of scan numbers

We evaluated the effect of scan numbers to determine minimum number of scans that were required to reliably reflect the brain status of participating patients based on the assumption that the statistical result from full data set (100 scans) is a target reference value. The deviation (error) from the target value was evaluated at different scan numbers.

III. RESULTS

Realtime monitoring system

Figure 1 shows a graphical user interface (GUI) for rt-fMRI monitoring system, where 3D functional connectivity and activations, 2D fMRI data, and 3D translation/rotation motion graphs during a verb generation task in a patient was displayed.

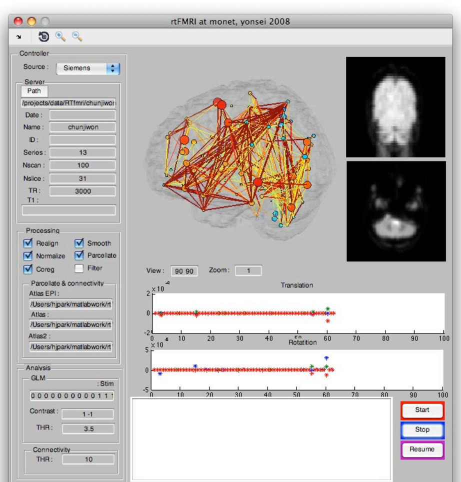

Figure 1. MATLAB-based rt-fMRI for real-time monitoring.

As shown in Figure 1, increased inter-regonal connectivity was found between the Boca's area and other brain regions while regional activations were mainly found in the superior frontal and temporal lobes. The superior frontal lobe and the dorsolateral prefrontal cortex were found to be more involved in the verb generation than the Broca's area of this patient. Connectivity mapping showed left lateralized connectivity increase during a verb generation task in this patient.

Connectivity during the task and resting state

The difference in the functional connectivity was evaluated during the attention-demanding task compared to the resting state. Figure 2 shows significant functional connectivity maps during the verb generation task and the resting state. Verb generation task elicited increased functional connections than the resting state from the Broca's area.

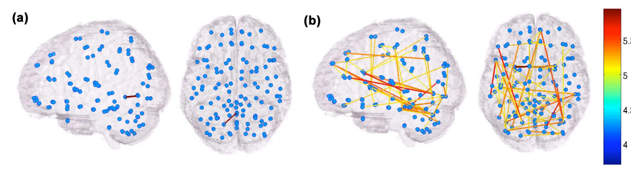

Figure 2. (a) Significant connectivity (correlation) maps (a) during the resting state and (b) during the verb generation task state (FDR-corrected q<0.03) Measures on color bar were –log10 scaled.

Granger causality connectivity

A Granger causal connectivity difference between the task and resting state was also found as shown in Figure 3.

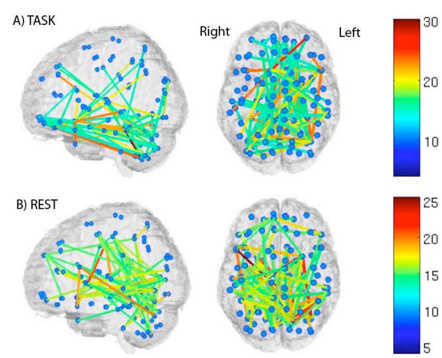

Figure 3. Region-to-region Granger causality map in which connectivity was expressed by F-statistics (p<0.001, uncorrected). Top and bottom figures represent task (A) and resting state (B), respectively.

Effective scan numbers

Effective scan numbers were evaluated in terms of mean deviation from the results driven from a whole data set at each scan numbers. Figure 4 demonstrates group functional connectivity statistical maps from five healthy volunteers according to number of scan samples. Figure 5 shows that the activation map converged as early as 20 scans while the deactivation map and the connectivity maps continued to decrease with accumulation of scans.

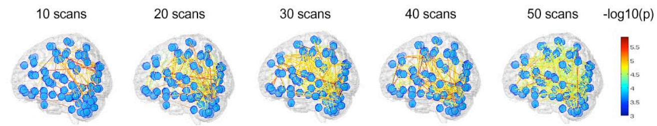

Figure 4. Functional connectivity according to accumulation of scans.

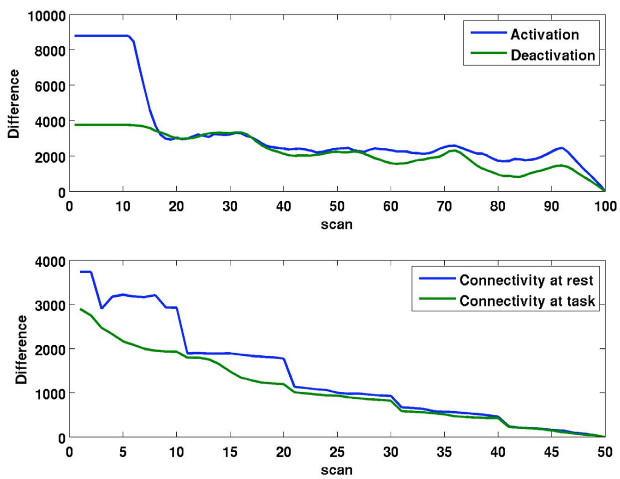

Figure 5. Activation, deactivation and connectivity deviation curves as the number of scans increases. Curves represent the deviation from the result with full data scans (n=100). Activation and deactivation deviation from the full data scans (top). Connectivity deviation from the full data scans during the task and the resting state (bottom)

Connectivity in the default-mode network

The feasibility of the default mode network as an index to monitor functional participation of the patient was tested. Functional connectivity from a seed voxel at the posterior cingulated cortex (PCC) was displayed on the MNI template space as in Figure 6. The functionally connected regions from the PCC decreased during the verb generation task compared to the resting state. This result showed the applicability of the functional connectivity defined in the default mode network as an indicator of the performance level in the patient.

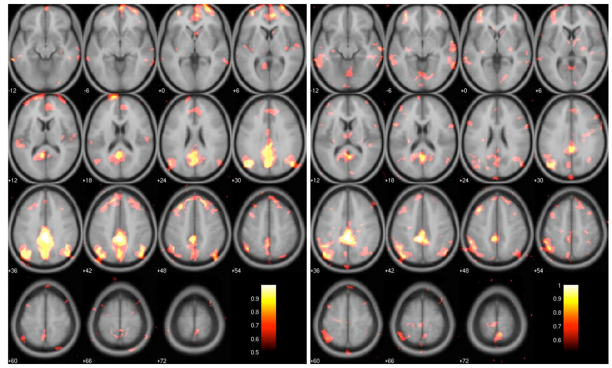

Figure 6. Functionally connected areas from the PCC during resting state (left) and during verb generation task state (right) overlain on the MNI template.

A patient data with right-lateralied language area

A neurological patient with a meningioma at the left frontal lobe was evaluated using rt-fMRI, which was shown in Figure 5. The patient showed right-lateralized language activation. As shown in Figure 7, rt-fMRI activation results were very similar to activation results with off-line analysis. rt-fMRI also provided on-line connectivity mapping of verb generation in this patient.

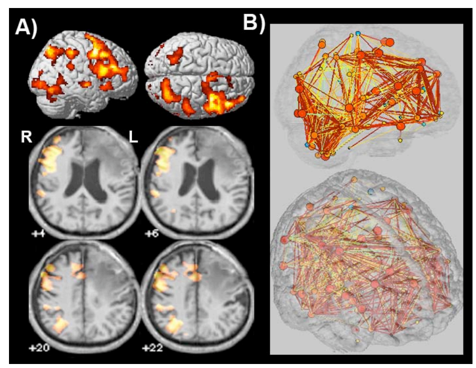

Figure 7. Activation and connectivity map of a neurological patient with a left hemisphere lesion during the verb generation task. Both map showed a right hemisphere dominant activation. A) SPM analysis (offline) and B) online rt-fMRI analysis with a connectivity mapping.

IV. CONCLUSIONS

Our preliminary results demonstrated the feasibility of monitoring patient performance using rt-fMRI with functional connectivity indices as well as activation indices. Though activation maps played a dominant role in detecting task-related activity, the functional connectivity provided additional information in the determination of functional status during a verb generation task. Further evaluation on the reliability of the language localization would be required in comparison to Wada test or intra-op stimulation tests.

In conclusion, rt-fMRI could be an important method in the performance monitoring of the neurological patients in real time, which may lead to successful evaluation of the patient language localization.

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Appendix

Succesive calculation of correlation map

Consider an *r-order* sample moment for *(n+1)-dimensional* data defined as

$$E(X_{n+1}^r) = (n+1)^{-1}\sum_{i=1}^{n+1} x_i^r$$

It is derived as a function of the prior moments

$$\begin{aligned} E(X_{n+1}^r) &= (n+1)^{-1}\sum_{i=1}^{n+1} x_i^r \\ &= (n+1)^{-1}(n\cdot E(X_n^r) + x_{n+1}^r) \\ &= \{1-(n+1)^{-1}\}E(X_n^r) + (n+1)^{-1}x_{n+1}^r \end{aligned}$$

Therefore, we can calculate the correlation between region X and Y accumulatively such as

$$r_{x,y} = \frac{E(XY) - E(X)E(Y)}{\sqrt{E(X^2) - \{E(X)\}^2}\sqrt{E(Y^2) - \{E(Y)\}^2}}$$