OMICS Journal of Radiology
ISSN: 2167-7964

Daliri and Behroozi, OMICS J Radiology 2013, 3:1
DOI: 10.4172/2167-7964.1000e123

Editorial Open Access

Advantages and Disadvantages of Resting State Functional Connectivity Magnetic Resonance Imaging for Clinical Applications

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Functional Magnetic Resonance Imaging (fMRI) is a powerful non-invasive technique for imaging BOLD (Blood Oxygenation Level Dependent) signal changes that is due to changes in brain hemodynamics responses associated to local neuronal activity to identify activated brain regions [1,2]. This technique allows researchers in laboratory environment to investigate the BOLD signals to determine the activated brain reigns for different stimuli or the processing of various cognitive tasks [3,4]. Furthermore, fMRI can be used in clinical applications to determine the brain abnormalities in population of subjects with neurological disease.

Our knowledge about brain functions comes from task-state studies in the presence of external stimuli that the neural activity and subject responses are measured for analysis. However, the brain is very active in resting-state without any stimuli. Recent findings that have been proven very valuable in the clinical area of fMRI applications, involves investigation of brain fluctuations at resting condition and their results demonstrate that spontaneous modulation of the BOLD does not produce randomly. Spontaneous modulations in BOLD signal are structured in spatial patterns that make correlated networks between various brain regions. The analysis of brain fluctuations in BOLD signal usually involves spatial patterns of correlated activity across regions of interests that are known as resting state connectivity networks. After data acquisition and preprocessing [5], there are two important data analysis techniques for studying the resting state functional connectivity: seed-based correlations approaches that are based on calculating the correlation between extracted regions of interests to identify spatial pattern of spontaneous activity and ICA (Independent Component Analyses)-based approaches that use all brain voxels activity to separate brain functional networks that are correlated with spontaneous component of BOLD signal (to account for non-neural noise with considering maximally independent spontaneous BOLD fluctuations) [4,6-8]. Functional connectivity approaches are divided into resting state and task state studies [4,9,10].

There are several motivations to use functional connectivity in resting state with respect to task- state. Some of them are discussed here:

• In resting state functional connectivity MRI same data can be used for studying the various systems in human (example: language and motor studies), but in task state functional connectivity MRI for each one of the systems, a different experiment must be designed.

• Energy consumption in resting state is one-fifth of the body's energy that most of it, is used to support of ongoing neuronal signals [11-15]. In contrast, the increasing neuronal metabolism (consumption energy) in task-state is usually small (<5%) in compared to large resting energy consumption [14]. Therefore, most of our knowledge about the difference between normal and pathological populations comes from minor component of brain functional activity.

• One of the most common motivations for using resting state functional connectivity MRI is that it makes a scientist to use broader samples of patients in different diseases. Because in task state functional connectivity MRI, most of the patients could not do the experiment correctly in fMRI scanner.

• The results in different studies demonstrate that the signal to noise ratio in resting state studies is better than task based approaches. In task state approaches when subjects focus to do behavioral task, the task related fluctuations account only for 20% of the total BOLD activity. This means that may be less than 20% of the fluctuations of BOLD signals are discarded as desired signal (more than 80% of the signals are noise) [4,16-18]. In contrast, the ongoing spontaneous BOLD modulations are focused on resting state functional connectivity MRI, so the most of the signals are used as desired signals.

• In resting state functional connectivity MRI, the important advantage is that it may ignore the parameters that may make problems to interpretation of the task. In task state functional connectivity MRI, controlling the different parameter of the experiment for example, the state of the subject, controlling conditions, and the level of disease across the subjects, are very hard.

In contrast, there are some disadvantages for functional connectivity MRI that are discussed in the following:

• It is not yet clear that there are individual differences in brain activity across sleep state and wake state. So, resting state fMRI sometimes may be dull for most of the subjects so the subjects sleep in the fMRI tunnel. Control of this, is difficult.

• If we want to study the special brain network, like auditory network, we have to study the task state fMRI.

• There are poor acknowledge about the neural interactions and their relation to individual skill. So we have to study the task related fMRI to characterize the nature of functional networks in distributed brain regions to define the structural network.

• For multi subject analyses, brain default energy is directly related to the subject mental state, like tired or excited, and etc. So, the control of this parameter is impossible in functional connectivity analysis but in task related experiments we can study the difference between two different states. For example, in schizophrenia disease, working memory task is used. So we can study the difference between baseline period and stimuli presentation period (block design paradigm, [19].

• The last problem is that there is no control on the patient's

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Received November 27, 2013; **Accepted** November 28, 2013; **Published** December 05, 2013

Citation: Daliri MR, Behroozi M (2013) Advantages and Disadvantages of Resting State Functional Connectivity Magnetic Resonance Imaging for Clinical Applications. OMICS J Radiology 3: e123. doi:10.4172/2167-7964.1000e123

memory while they don't think about a special thing in resting state functional connectivity MRI.

Conclusions

fMRI is a noninvasive modality with high spatial resolution with respect to other imaging modalities for studying the brain functions which can be used in clinical environment. Fluctuation in BOLD signals in resting state functional connectivity MRI can provide good signal to noise ratio to detect the functional networks in the brain, can be observed under anesthesia, and broader sampling of patients. Spontaneous modulation of BOLD signals are generated in different condition of subjects on fMRI tunnel, awake, sleep, excited, or sedated [20-22]. Most of previous studies focused on the investigation of brain functional connectivity during resting state when subjects are awake. If there are individual differences during the awake state, it can be a reason to observe the individual difference during the various state of the subjects, sleep or sedation state. This is an important area of research that there is no clear response for it. If there is the individual difference during the various state of the subjects, how we can control subjects to stay in same state across resting state data collection.

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