COURSE

"Functional Connectivity: MRI Measures of Spontaneous Fluctuations in Intrinsic Networks"

TALK TITLE

"Studying Brain Function with Task-Free fMRI"

SPEAKER

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PREFACE

If you regularly attend meetings on functional brain mapping you cannot escape the impression that task-based fMRI is 'out' and task-free fMRI (usually termed resting state fMRI: rsfMRI) is 'in'. Many researchers seem to have switched from task-based to task-free approaches. But do these different fMRI approaches 'measure the same thing'? Can resting state fMRI simply replace task based fMRI? The best answer to these questions is "No". A more elaborate answer will be given in this lecture. Or to put the main topic of this talk in other words: If resting state fMRI is the (methodological) answer…. what was the right question?

INTRODUCTION

For a long time it has been known that neural activity – even in the absence of any obvious task – fluctuates spontaneously. While this has sometimes been regarded as 'noise' which – in experimental studies – can be 'overcome' by averaging, in the last two decades it has become obvious that significant components of this 'noise' has non-random signal characteristics and has relevant functional implications. For example, in a landmark paper Arieli and colleagues have shown that “background neural activity” as measured with invasive electrophysiological recordings explains large parts of the variance of evoked activity (Arieli et al. 1996).

fMRI, the most widely used functional neuroimaging methods measures neuronal activity only indirectly via associated changes in hemoglobin oxygenation (BOLD based fMRI). The pronounced spontaneous fluctuations of hemoglobin oxygenation (Obrig et al. 2000) and (accordingly) the BOLD signal have long been thought to be dominated by ‘purely’ vascular components such as ‘heart-beat/pulse’, respiration-related modulations and vasomotion (a low-frequency oscillation of vessel size and blood flow known to be present even in isolated vessels outside a tissue environment). These “vascular” background signals have sometimes been termed ‘physiological noise’ without any relevance for the ‘signal of interest’. However, more and more information has been accumulated demonstrating that neural noise and vascular noise are related, and it seems so especially in the low-frequency range. The seminal contribution by Bharat Biswal has demonstrated that based on a cross-correlation of the fMRI-BOLD signal of different voxels in the low-frequency range, ‘neural connectivities’ can be identified as well as networks consisting of brain areas with highly correlated activity (Biswal et al. 1995). This has been the birth of resting state fMRI.

In this talk, the physiological basis of rsfMRI will be discussed as far as it is relevant for applications in which brain function is investigated.

APPLICATIONS IN COGNITIVE NEUROSCIENCE

At first sight rsfMRI seems like a miracle approach: Based on just one brief (e.g. 5 min) MRI scan, one can investigate almost any functional system of the brain, such as language, attention, executive function, motor function, vision etc.. And you do not even have to think about a stimulation paradigm. Is there any drawback? What is left for task-based fMRI?

A typical question to be addressed by task-based fMRI is: “Is region x active during task A” or – as usually two (or more) conditions are compared, the question may be “Is region x more/less active during task A than during task B?” RsfMRI cannot answer such a question as it is based on an assessment of connectivity between different brain areas rather than on the (isolated) activity of one area and it is (usually) not performed DURING task performance. Furthermore, in order to have enough statistical power to establish connectivity the time period for acquiring resting state data is usually on the order of 5 min or more. During that period, the system is implicitly assumed to be stable, at least with respect to the measure of connectivity. Currently, new methods are being developed which take into account potential changes in the brain states during the observation time.

The relationship of rsfMRI derived measures of connectivity to cognitive features is typically established by correlating them with results of cognitive and/or behavioral tests which were performed before or after the fMRI measurement. With newly developed tools such as Eigenvector centrality measures it is also possible to compare two states, e.g., hungry versus sated. Analogously, rsfMRI seems a highly appropriate tool to identify plasticity effects, for example changes in brain connectivity after learning a certain task (e.g., Taubert et al. 2011).

In this talk an overview on applications of rsfMRI for cognitive studies (including studies on brain plasticity) will be given. Common features of ‘possible studies’ will be identified and ‘rules of thumbs’ for future applications will be given. Advantages and disadvantages will be discussed.

DATA ANALYSIS OF RESTING STATE FMRI

A large number of different methods to analyze rsfMRI data has been proposed (Margulies et al. 2010). Which method is useful for which application? What is the 'meaning' of a result obtained with a certain way to analyze rsfMRI data as opposed to other methods?

Furthermore, based on rsfMRI studies, researchers refer to "brain connectivity", (task-positive, task negative) resting state networks, default mode network etc. What do these terms mean?

In this talk, different analysis methods will be categorized with respect to their usefulness for cognitive studies; Definitions will be given for important concepts in rsfMRI and its interpretation.

TARGET AUDIENCE

Everybody interested in assessing brain function non-invasively with fMRI.

OBJECTIVES OF THIS LECTURE

1) A clarification of terminology with respect to the use of resting state fMRI such as:

    Resting state
    Resting state network: RSN
    Task-positive RSN, Task-negative RSN
    Default mode network (DMN)
    Functional Connectivity
    Structural connectivity
    Brain networks
    Resting state networks

2) 'Positioning' of rsfMRI in the "orchestra" of structural and functional brain imaging methods by
    - giving examples of research questions
        a. for which rsfMRI is an appropriate method
        b. for which rsfMRI is NOT an appropriate method
    - showing strength and weaknesses
    - showing relationship of findings to other MRI methods (task based fMRI, diffusion MRI, anatomical MRI)
    - comparing the type of information gained with rs fMRI findings to the information obtained with other (resting state) neuroimaging approaches, e.g., EEG, MEG, NIRS

3) Demonstration what different ways of analyzing rs fMRI data (seed-based-, ICA-based, Eigenvector centrality etc.) can tell us about brain function

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