BOLD fMRI Signal Interpretation and Calibration

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Introduction

The vast majority of functional magnetic resonance imaging (fMRI) studies of the brain are based upon measures of the blood oxygenation level dependent (BOLD) signal. Differences in the BOLD signal between conditions or populations are typically interpreted as differences in neural activity. However, the BOLD signal reflects the hemodynamic response to neural stimulus and exhibits a complex dependence on functional changes in a number of physiological variables such as cerebral blood flow (CBF), the cerebral rate of oxygen metabolism ($CMRO_2$), and cerebral blood volume (CBV). As a result, the interpretation of changes in the BOLD signal can be complicated by variations in these physiological quantities that are caused by factors such as age, disease, or medication. In this talk we will review the origins of the BOLD signal and discuss the factors that can complicate the interpretation of the signal. We will also review methods that can be used to normalize or calibrate the BOLD signal and discuss how these methods can aid in the interpretation of fMRI experiments.

In this lecture we will cover the following topics:

1) ***Origins of the BOLD Signal*** As noted in the introduction, the BOLD signal is a complex function of a number of physiological variables [1]. We will begin by reviewing existing models of the BOLD response.

2) ***Sources of Variability in the BOLD Signal*** Because the BOLD signal is a reflection of neural, vascular, and metabolic factors, variations in any of these factors can give rise to differences in the BOLD signal [2,3]. We will review the role that vascular and metabolic factors can have on both the amplitude and shape of the BOLD response.

3) ***Normalization Methods*** There are a number of potential methods for addressing the variability introduced by vascular and metabolic factors. These include hypercapnic normalization [4-6], the use of measures of baseline CBF as a covariate [7], and the application of measures of venous oxygenation [8,9]. We will review and compare these methods.

4) ***Calibrated fMRI*** When combined with measures of functional CBF changes, BOLD signal measures can be used to form estimates of functional changes in $CMRO_2$. This approach is often referred to as calibrated fMRI [10-11]. Estimates of functional $CMRO_2$ changes may provide a more accurate reflection of changes in neural activity than either CBF or BOLD. We will review the calibrated fMRI approach and discuss its applications.

Related References

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